Information Processing in Chronic Fatigue Syndrome

The Role of Cognitive Bias and Negative Illness Cognitions in the Perpetuation of Symptoms of Chronic Fatigue

Iana Alexeeva
Wolfson College

DPhil Experimental Psychology

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Department of Experimental Psychology

University of Oxford

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Abstract

This thesis investigated cognitive biases in attention, interpretation, and memory and their role in symptom perpetuation of Chronic Fatigue Syndrome (CFS). The first empirical study presented in the thesis used a quasi-experimental design to explore the interaction of attention and a cognitive state of rumination in 33 people with CFS and 33 healthy controls, who were randomly assigned to undergo either rumination or distraction induction. In these altered cognitive states participants have completed an exogenous cueing task measuring allocation of attention towards threatening or neutral linguistic stimuli. The CFS group did not show attentional bias towards threatening illness-related information following the rumination induction, compared to the CFS group in the distraction state or healthy controls. However, being in a state of either rumination or distraction led to greater mood volatility in CFS group than in healthy controls.

The second empirical study similarly used a quasi-experimental design to investigate the interaction of attention and mood in a sample of 16 people with CFS, 25 people with asthma, and 28 healthy controls. The study explored later-stage conscious allocation of attention when in neutral or depressive mood, under either low or high cognitive load. CFS, asthma and healthy control participants were randomly allocated to a depressive or a neutral mood induction. Then the participants completed two cognitive tasks, a visual probe (high load) and an exogenous cueing (low load), to measure allocation of attention towards health-threat words and pictures. Attentional bias towards health-threat emerged under the condition of high cognitive load and neutral mood in CFS and healthy controls, but not in the asthma group. Depressive mood did not exert an influence on attentional bias towards health-threat in CFS.

The third empirical study, using a quasi-experimental design, investigated later-stage conscious allocation of attention towards activity and exertion-related stimuli in the conditions of neutral and depressive mood, and low and high cognitive load, utilising the same method as the second empirical study, described above. The same sample of participants consisting of 16 people with CFS, 25 asthma and 28 healthy controls completed a visual probe and an exogenous cueing task to measure allocation of attention towards activity words and pictures. Under high cognitive load CFS group showed increased attentional avoidance of activity-related stimuli, compared to healthy controls.

Empirical Study 4 investigated the process of interpretation of ambiguous information collecting and analysing the data from the sample of 33 people with CFS and 33 healthy control volunteers who also participated in Study 1 on attention and rumination. The study

used a quasi-experimental design. The participants completed a lexical decision task, which measured their reaction times to the presentation of ambiguous information that could be interpreted either in a threatening or in a neutral manner. The CFS group did not show a tendency to interpret ambiguous information in a negative illness-related fashion, compared to the healthy control group.

The fifth study, a survey conducted via the Internet, utilised a mixed methods design to investigate features of autobiographical memory, specificity and perspective, in 87 people with CFS, 56 people with asthma, and 60 healthy controls. Participants completed a memory task, where they were asked to recall four types of events (happy, pain, fatigue, physical activity), and questionnaires assessing symptoms, functioning, activity, mood, and coping. The CFS and asthma groups recalled more specific memories of activity, compared to healthy controls. For CFS and asthma groups general activity memories were associated with more personal, field memory perspective. The activity memories recalled by CFS group were rich and diverse in content, reflecting a complex multidimensional view of activity. Healthy controls viewed activity specifically as sport and exercise-related. Fatigue memories recalled by the CFS group reflected a stable, global, profound view of fatigue.

The overall findings partially supported the hypothesis that people with CFS may cognitively over-process the information related to potential health-threat. Enhanced cognitive processing of health-threatening information may underpin increased monitoring and overperception of CFS symptoms. Methods that can address cognitive processing, for example reduce over-processing of potential health-threat or modify perception of activity, may be of benefit in treatments that aim to increase activity levels in people with CFS, such as Graded Exercise Therapy.

Detailed Abstract

Background: Cognitive theories of Chronic Fatigue Syndrome (CFS) implicate biased information processing, such as heightened attentional focus on health-threat and interpretation of ambiguous information in a health-threatening fashion, in the perpetuation of the symptoms of CFS. The aim of this thesis was to test empirically the hypothesised bias in attention, interpretation, and memory in CFS. The second aim was to contribute to the refinement of the cognitive accounts of CFS that implicate vicious cycles of influence in symptom onset and perpetuation. The findings may have clinical implications for the cognitive-behavioural treatments of CFS.

Study 1: Attention and Rumination Experiment investigated the presence and magnitude of attentional bias in two cognitive states, rumination and distraction, in a sample of 66 people, 33 in the CFS group and 33 in a group of healthy controls. The study used a quasi-experimental design to compare the two groups of participants testing pre-specified hypotheses. The method included an exogenous cueing task to examine attentional processing at the preconscious stage, using a short stimulus duration (100ms). Participants underwent a cognitive state induction, either rumination (17 in the CFS group and 17 healthy controls) or distraction (16 in the CFS group and 16 healthy controls), prior to completing the cognitive task measuring attention. The hypothesis, that the CFS group would demonstrate enhanced attention towards illness-related words in the condition of self-focused rumination, was not supported. The main effects and interactions of induced cognitive state, group, and word type (Illness, Social Threat, Neutral) did not reach statistical significance**,** all $F < 1$, $p > .05$. In contrast, the hypothesis that CFS group would experience a greater degree of mood fluctuation following the rumination/distraction induction than the control group was supported. In the CFS group, but not in healthy controls, the negative mood increased after the rumination and decreased after the distraction. CFS participants in the rumination induction had significantly higher negative mood compared to CFS participants in the distraction induction, $t(31) = 2.43$, $p = .021$.

Study 2: Attention and Mood Experiment used a quasi-experimental design to examine the interaction of the attentional bias, mood, and cognitive load in a sample of 16 participants with CFS, 25 people with asthma, and 28 healthy controls. The study employed mood induction and two cognitive tasks, exogenous cueing and visual probe, to measure the attentional process at a later conscious elaborative stage of processing under neutral or

depressive mood, and high (visual probe tasks) and low (exogenous cueing task) cognitive load. Three groups of participants (CFS, asthma, and healthy controls) underwent depressive (CFS *n* = 8, asthma *n* = 13, healthy control *n* = 15) or neutral mood induction (CFS *n* = 8, asthma *n* = 12, healthy control *n* = 13) before completing the two tasks that measured allocation of attention towards health-threat words and pictures.

The results provided mixed evidence for the hypothesised attentional bias in CFS, demonstrating a significant interaction of Group with Mood Induction $F(2,61) = 4.06$, $p = .022$, $\eta_p^2 = .118$ in the visual probe task, the high cognitive load condition. In the neutral mood the CFS group showed significantly greater attentional bias towards health-threat compared to asthma group $t(18) = 2.99$, $p = .008$. However, the difference between CFS and healthy control groups was not significant, $p > .80$. Depressive mood did not have a significant effect on attentional bias in CFS group, $p > .50$ in the test of group differences.

Study 3: Attention and Activity Experiment investigated potential attentional bias towards exertion and activity-related information, also using a quasi-experimental design. Study 3 analysed the data collected from the same sample of participants as Study 2: Attention and Mood Experiment namely, 16 people with CFS, 25 with asthma, and 28 healthy controls. In Study 3 two cognitive tasks, visual probe and exogenous cueing, incorporated words and images of activity and exertion in order to explore potential attentional bias in depressive or neutral mood and in the high or low cognitive load. Three groups of participants (CFS, asthma, and healthy controls) underwent depressive (CFS *n* = 8, asthma *n* = 13, healthy control *n* = 15) or neutral mood induction (CFS *n* = 8, asthma *n* = 12, healthy control *n* = 13) before completing the two tasks. It was hypothesised that the CFS group would selectively attend towards activity-related stimuli, perceiving activity as health-threatening. In support of the hypothesis the CFS group showed greater attentional engagement when presented with the images of Activity, compared to the healthy control group, $t(21) = 2.17$, $p = .041$, and the Asthma group, $t(19) = 2.63$, $p = .016$. However, that enhanced attentional engagement for the CFS group was present only when under low cognitive load and in depressive mood. Under a high cognitive load, in contrast to the hypothesised direction, CFS group demonstrated greater attentional avoidance in response to activity stimuli $F(2,63) = 3.82$, $p = .027$, $\eta_p^2 = .108$ than healthy controls ($p = .021$), but not when compared to the asthma group ($p > .40$).

Pilot Study 3B: Activity Survey - this preliminary study aimed to test a new measure of activity and investigated the patterns and types of activity in 79 people with CFS, 44 with asthma, and 132 healthy controls. The study was designed as a web-based survey administered via the Internet, and included a battery of questionnaires on activity, mood, functioning, fear cognitions, and coping.

The newly developed scale contained items measuring different dimensions of activity: leisure and sport, activity at home, outside, and online, social activity, work and education, and mental activity. The scale also aimed to measure the construct of inactivity, as represented by sedentary behaviours, such as staying in bed during the day. The results showed a pattern of significant correlations between the scores on the activity scale and other measures of functioning and activity in the CFS and asthma groups. The lack of significant relations between the new activity scale and other measures of activity and functioning within the healthy control group indicated the measure may be more suitable for assessing activity patterns in groups with chronic illness than in healthy people.

For the CFS group higher symptomatology, fear of movement, and depressed mood were associated with an increase in sedentary behaviours. Elevated fatigue was associated with a decrease in work/daily activity and in mental activity. More online activity in the CFS group was related to more frequent symptoms, stronger beliefs in the seriousness of their illness, and higher negative affect. Involvement in community activities or education was associated with stronger beliefs in the seriousness of their illness, anxiety and behavioural disengagement, but also with greater physical functioning.

Study 4: Interpretation Experiment employed a lexical decision task in order to measure preferences in the interpretation of ambiguity in a sample of 66 people, 33 participants with CFS and 33 healthy controls. The study had a quasi-experimental design and collected the data from the same participants who took part in Study 1: Attention and Rumination Experiment. The aim of study 4 was to measure an online interpretation bias, the interpretations made at the moment when the ambiguous information is encountered for the first time, as opposed to the later stages of the elaborative, retrospective reinterpretation, and selective production of response towards ambiguity. The hypothesis that CFS participants would show quicker responses on the lexical decision task to the illness-related disambiguation of the ambiguous auditory primes (homophones that could be interpreted in a neutral or threatening manner), compared to healthy controls, was not supported**.** The analysis did not reveal a significant group difference or any interactions with

the group factor, all $p > .05$. The results showed that the CFS group was not susceptible to the priming effect of ambiguous words, one-sample comparisons were non-significant all $p > .30$. In contrast, a strong priming effect occurred for the healthy controls, particularly for the ambiguous primes that could be interpreted either in a health-threatening or in a neutral fashion $p > .001$, compared to social threat primes (words that could be interpreted in a socially-relevant or a neutral manner) or ambiguous neutral primes (words that could be interpreted in various non-threatening manner). However, the healthy control group did not show a preference for either health-threatening or neutral disambiguation of the illness-related ambiguous prime, indicating the absence of interpretation bias.

Study 5: Memory Survey was a mixed-methods quasi-experimental investigation of the features of autobiographical memory for four different types of life events in CFS and asthma. Study 5 was conducted via the Internet aiming to access a larger group of people with CFS, in order to address the challenges of recruiting volunteers with CFS for laboratory-based experimental studies. The sample of participants whose data were analysed for study 5 consisted of 87 people with CFS, 56 people with asthma, and 60 healthy control participants matched on age, gender and education level. A proportion of these participants have also been used in the pilot study assessing the utility of the newly devised activity scale (Pilot Study 3B: Activity Survey).

The participants were asked to recall memories about fatigue, pain, physical activity, and happiness. The study tested two contrasting hypotheses with regard to overgeneral memory phenomenon frequently observed in depression. The hypothesis that CFS group would demonstrate overgeneral memories was not supported. On the contrary, the hypothesis that CFS group would demonstrate overly specific memories of physical activity was supported. CFS and asthma participants recalled more specific memories of activity, while healthy control group recalled more general activity memories. The CFS and asthma groups also demonstrated that their general memories of activity were more likely to be recalled from a field memory perspective (an emotionally involved, psychologically and physically focused, first person point of view). This was counter to the prediction that overgeneral memories would be associated with an observer perspective (an impersonal, detached, third person point of view).

The thematic analysis of memories revealed that for the CFS group the memories of activity were much more varied in content, ranging from primarily physical activity, including walking, to general pleasant events, such as parties or family outings, to activities that were

work-, chores- and, particularly, health-related. Only the CFS and asthma groups recalled activity memories that mentioned health, illness, symptoms, hospital, or some sort of physical rehabilitation. In contrast, for the healthy controls activity memories involved mainly sport and physical exercise. Fatigue memories showed a similar pattern, with a greater variation of memory themes in the CFS group, and to a lesser degree in the asthma group, than among the healthy controls. Fatigue memories in CFS group reflected a stable, global, and profound view of fatigue.

Conclusion: The empirical evidence provided mixed support for the hypothesis that there is enhanced processing of health-threat or illness-related information in people with CFS, which may maintain symptom overperception and consequently exacerbate the symptoms of CFS. The evidence showed that self-focused rumination may lead to increased emotional distress. The early attentional and interpretation processes appear to be unbiased. There is tentative evidence pointing towards cognitive avoidance of activity-related information at a later processing stage under a high cognitive load. Methods that can redirect cognitive processing from avoidant or catastrophic to positive meaningful engagement, particularly with respect to activity-related information, may be of benefit in treatments that aim to increase activity in people with CFS, such as Graded Exercise Therapy. High specificity of activity memories in people with CFS may be one of the facets of enhanced processing of illness-related information. Exploration of the content of memories suggested that people with CFS might have a perception of fatigue and activity as more complex, pervasive, and multidimensional phenomena, than healthy people. For the CFS group the construct of fatigue seemed to have achieved the status of a global, stable and profound characteristic that defined all their activities. This may also be relevant to cognitive-behavioural treatments of CFS, that aim to modify that kind of global, negative, and stable view into a less pervasive and catastrophic concept in order to reduce avoidance and fear of activity, increase functioning, and promote health.

Chapter 1: Introduction

Thesis Aims

Illness cognitions and their maintaining mechanisms, such as the cognitive processing of illness-related information, are integral features of the biopsychosocial approach to diagnosis and treatment of Chronic Fatigue Syndrome (CFS). The biopsychosocial model appears most suitable for solving a riddle such as CFS, because it reflects the complex multidimensional nature of the illness and the interaction of the multiple causal factors. However, the biological, psychological and social factors within the biopsychosocial approach, as applied to CFS, are not easily separated, and their interactions are difficult to trace. Due to the heterogeneity and complexity of CFS there is no consensus on its definition, diagnosis or treatment strategy. Consequently, the empirical findings can be inconsistent and contradictory. However, the evidence is accumulating in support of the effectiveness of interventions based on a cognitive-behavioural framework. Thus, it would be informative to explore the psychological arm of the biopsychosocial approach. It would help to elucidate the cognitive processes that may underpin specific cognitions and behaviours, which then can be targeted by cognitive-behavioural treatments (CBT) of CFS.

In the light of the above, the purpose of this thesis was twofold. The first aim was to experimentally test the hypothesis that there is an enhanced cognitive processing of illness-related information in CFS guided by a negative illness schema. This biased cognitive processing, an over-processing of illness-related information, may lead to overperception of symptoms, which may play a role in perpetuation of CFS. The second aim was to contribute to the refinement of the cognitive accounts of CFS that implicate vicious cycles of influence in symptom onset and perpetuation.

Cognitive models of CFS converge on the concept of a vicious cycle of maladaptive cognitions and behaviours that maintain the severity of CFS symptoms (Deary, Chalder, & Sharpe, 2007; Moss-Morris, 2005; Surawy, Hackmann, Hawton, & Sharpe, 1995). The proposed mechanisms of perpetuation suggest that negative illness cognitions may bias information processing towards overperception of somatic symptoms, or alternatively, these cognitions may themselves arise through selective information processing that over-focuses on health-threat (Moss-Morris, 2005). Such negative illness cognitions may influence the choice of coping strategies and lead to harmful patterns of behavior. These harmful behaviours manifest as disrupted activity patterns and/or abrupt reduction of activity, which contribute to physiological deconditioning and muscle deterioration. This may lead to the experience of increased symptom severity and frequency. The enduring perception of illness

and increased disability feed back into the negative illness view and biased information processing.

Thereby, the empirical studies described in the thesis focused on three key cognitive processes: attention, interpretation, and memory. The cognitive processing was measured via objective experimental tasks, such as visual probe, exogenous cueing, lexical decision, and cued recall. These are extensively used validated measures of cognitive processing that have been utilized in previous studies of mood disorders, chronic pain, functional disorders such as Irritable Bowel Syndrome (IBS), asthma, eating disorders, as well as other medical and psychological conditions. The tasks measured preconscious automatic and conscious voluntary processing of information related to illness, health-threat and activity. The self-report measures were used to investigate the presence and nature of illness cognitions; thoughts related to mood; thinking patterns related to body, movement, exertion, exercise and activity; and coping methods with illness and stress.

The associations and directions of influence between the information processing, and cognitive, emotional, and behavioural factors, and illness status and health outcomes were investigated with two goals in mind. One aim was to clarify the role of the enhanced cognitive processing in CFS and of the interactive nature of the cognitive, emotional and behavioural factors in the hypothesised vicious cycles of influence. The second aim was to contribute to the methods of cognitive-behavioural interventions that focus on reevaluating and restructuring the key cognitions and cognitive processes. These interventions aim to turn the vicious into virtuous cycle and lift the burden of illness, aid in recovery, and promote health.

This chapter presents a brief review of the current state of research on CFS. Firstly, the debate about CFS definition and diagnosis is reviewed. The lack of consensus is a problem that lies at the heart of the methodological and empirical struggles within the field. The current causal accounts and the treatments developed on their basis are discussed within the context of the debate over the CFS definition. The specific area of interest, the information processing in CFS, is presented as one of the core features of the cognitive models of CFS. The arguments for the importance of this research area are outlined, including how this thesis may contribute to the knowledge about CFS. The final section reviews another illness, asthma, and presents that reasons for comparing it to CFS, arguing that such comparison would elucidate the role of biased cognitive processing in CFS.

Chronic Profound Exhaustion: The Case of a Missing Definition

The phenomenon of extreme, disabling, and unexplained fatigue has had a number of names, including neuromyasthenial idiopathic chronic fatigue and myalgia syndrome, benign myalgic encephalomyelitis, chronic infectious mononucleosis, Royal Free disease, postviral fatigue syndrome, fibrositis-fibromyalgia, and chronic fatigue syndrome (Wessely, 1994). Nevertheless, individuals diagnosed with CFS are presumed to belong to a phenotypically similar group. After several decades of research the terms have been narrowed down to Chronic Fatigue Syndrome (CFS), Myalgic Encephalomyelitis (ME), or a combination, either ME/CFS or CFS/ME. The choice to use CFS or ME or a combination term depends on whether the emphasis is on the speculated neuroimmunological pathogenesis (ME) or on the complex interaction of multiple factors including physiological and psychological (CFS, CFS/ME) (Brurberg, Fonhus, Larun, Flottorp, & Malterud, 2014). While a full review of case definitions is beyond the scope of this thesis, it is a vital issue that needs to be addressed before any discussion of the nature of the condition can commence. The following review is not exhaustive. Its primary aim is to discuss the most impactful case definitions and the conflicting views about the biological and psychological nature of CFS.

Under the CFS umbrella

The term Chronic Fatigue Syndrome refers to a multifaceted and prolonged illness defined primarily by severe, debilitating, persistent and/or relapsing mental and physical fatigue, disproportionate to exertion, exacerbated by even a smallest amount of activity, not relieved by rest, and resulting in profound negative impact on daily functioning (Fukuda et al., 1994). The fatigue in CFS cannot be explained by a significant increase in activity, by any current medical condition, or an existing organic dysfunction. Therefore, the diagnosis of CFS is confirmed after an array of laboratory tests rules out any other explanation for the condition. That course of action adds to the complexity because there is no certainty that all possible tests have been conducted to rule out all potential explanations.

Evidence suggests that a substantial number of cases (reported to be 40%) can be ruled out as CFS following closer investigation at CFS specialist clinics (Newton, Mabillard, Scott, Hoad, & Spickett, 2010). Newton and colleagues (2010) cautioned that people not meeting particular criteria for CFS may not get referred to specialist clinics, and therefore do not have access to care in spite of suffering from extreme fatigue. The authors suggested that it would be vital to address the issue of treating and managing fatigue as a major symptom of CFS and a more general symptom of other comorbid or overlapping conditions,

rather than fully focusing on the refinement of a diagnostic criteria or fruitlessly searching for the underlying cause. The same line of argument is followed in this review, that the symptom of fatigue may be of a similar nature whether the underlying cause of CFS is biomedical or psychosocial. Therefore, the cognitive-behavioural interventions can be effective in reducing fatigue in CFS, whatever may be the proposed cause(s) or the used diagnostic criteria.

Fatigue is one of the most commonly reported symptoms in primary health care and not specific to any particular illness (Nicholson, Stewart, & Thind, 2015; Skapinakis, Lewis, & Mavreas, 2003). In the case of CFS, however, the fatigue is so profound and the energy decline is so severe that it may completely interrupt regular activity, employment, and social relationships for an extended period of time (Afari & Buchwald, 2003; Evengard, Schacterle, & Komaroff, 1999). In the United States the value of lost productivity due to CFS was calculated at 9.1 billion, or 20,000 dollars per person, following the reduction in productivity and loss of employment, based on the prevalence rate of 0.2% (Reynolds, Vernon, Bouchery, & Reeves, 2004), not including the health care costs. The individual cost of CFS in the UK, including the use of health care services and loss of employment, was estimated to be on average £1406 per three month period (McCrone, Darbishire, Ridsdale, & Seed, 2003).

For healthy people fatigue is attributed to increased exertion and diminishes following recovery. In the context of other illnesses the symptom of fatigue can be a secondary symptom that arises either due to treatment or disease burden, for example cancer-related fatigue (Berger, Gerber, & Mayer, 2012). However, in the case of CFS, fatigue is not attributable to any physiological abnormality or to an excessive increase in activity. The absence of physiological markers or symptoms unique to CFS is one of the main problems fuelling the debate over its diagnosis. Additionally, measurement complications arise because the sensation of fatigue has no direct biological markers or tests that can directly assess its severity, frequency or duration. The majority of fatigue measures are indirect via self-assessment and self-report (Neuberger, 2003; Tyson & Brown, 2014), or tests of cognitive function (Williamson, Feyer, Mattick, Friswell, & Finlay-Brown, 2001), or narrowly focused tests of physiological function such as muscle contraction, measuring specifically muscle fatigue (Vøllestad, 1997). In the absence of direct measures and physiological markers for CFS, clinicians and researchers rely on case definitions as diagnostic tools to identify populations for empirical research and for clinical purposes. There is, however, no current consensus among researchers and clinicians on the CFS definition, diagnostic

criteria, causes, pathophysiology, and treatment (Brurberg et al., 2014; Prins, van der Meer, & Bleijenberg, 2006).

CFS includes a wide range of symptoms in addition to the primary fatigue, including physical symptoms (flu-like symptoms, sore throat, headache, muscle ache and weakness, joints pain); cognitive impairments affecting concentration and memory; disrupted sleep patterns (insomnia or hypersomnia); and affective symptoms, such as depressed mood or emotional distress. The proposed causes of CFS also include a wide range of processes, implicating a complex interaction of genetic, physiological, neurological, cognitive, behavioural, affective, personality, and social factors (Hooper, 2007; Prins et al., 2006). Thus, we are dealing with a multifaceted and much disputed condition. This greatly complicates assessment, diagnosis and treatment and presents a challenge for the empirical research.

Centre for Disease Control: Evolving Definition

Initially the phenomenon of unexplained severe fatigue has been linked to a viral infection and aptly named Epstein-Barr virus syndrome (Holmes et al., 1988). However, the Centre for Disease Control and Prevention (CDC) in the United States released a working definition of newly renamed Chronic Fatigue Syndrome, reasoning that the causal link with the virus was tenuous and contentious due to a lack of empirical support (Holmes et al., 1988). The new name was meant to reflect the core symptom of the condition, a profound fatigue, but without making any claims concerning its viral origins.

CDC definition specified a new onset of persistent fatigue with no previous history of a similar condition, which does not resolve by rest, and highly impacts daily activity. The new definition has also established a time frame of 6 months for the presence of such fatigue. Other potentially fatiguing conditions were to be excluded after thorough laboratory testing and clinical measurements. Holmes and colleagues listed eleven accompanying symptoms, most of which were of a physical nature (for example, fever, headache, muscle pain), but the definition also included cognitive impairments (forgetfulness, concentration difficulties), and affective symptoms (depression). It was the affective component, specifically depressed mood, that became a source of further contention in the clinical and research communities. The issue of distinguishing CFS from psychological disorders like depression was raised with every new definition proposed.

The CDC definition has undergone revision in 1994 aiming to improve identification of true cases of CFS, for a more consistent application in practice, and clarification of terms (Fukuda et al., 1994). The main definition of fatigue has been refined as clinically evaluated,

unexplained, persistent or relapsing chronic fatigue that is of new or definite onset (has not been lifelong); is not the result of on-going exertion; is not substantially alleviated by rest; and results in substantial reduction of activity. Time requirement for prolonged fatigue was set as 1 month, and 6 months for chronic fatigue. This would partially fulfil the goals of distinguishing more severe cases of CFS, and providing access to care for people who do not meet the full criteria.

Additional symptoms were clarified and reduced to eight with the requirement that at least four needed to be present for a minimum of 6 months and accompany the onset of fatigue. The physical symptoms that were retained included post-exertional malaise, unrefreshing sleep, muscle and multi-joint pain, new headaches, tender lymph nodes, and sore throat. Cognitive symptoms of short-term memory and concentration impairments remained but the depression symptom was removed.

The main argument for removal of depression from CFS diagnosis was based on the potential danger of misclassifying CFS as depression. That is reasonable given that inclusion of depression as a diagnostic symptom would imply that the majority of individuals with potential CFS have depressed mood. Recent data showed that the majority of people with CFS did not have a mood or anxiety disorder, although the prevalence of depression and anxiety was indeed higher in the CFS population compared to the general population (Janssens, Zijlema, Joustra, & Rosmalen, 2015). The exclusion of depression from the list of accompanying CFS symptoms added precision to the definition. However, it is important to note that negative affect is a common and natural occurrence accompanying a major illness, and depression is comorbid with physical illness in general (Qin, Hawton, Mortensen, & Webb, 2014; Shahar, Lassri, & Luyten, 2014) and CFS specifically (Arpin-Cribbie & Cribbie, 2007; Faulkner & Smith, 2008; Sohl & Friedberg, 2008). While it may be prudent to exclude depression from the list of diagnostic criteria for CFS, it should not be excluded from the treatment strategy.

It is important to note that the definition of the core symptom itself, the fatigue, would not change through all the revisions of case definitions. The debate over the diagnostic criteria would circle around those secondary identifiers of the disease, raising questions about which symptoms, and of what kind of frequency, duration, and severity, would help most in distinguishing CFS from other conditions. Specifically, the symptom of post-exertional malaise would become the source of contention and the CDC/Fukuda criteria would be criticized for not making that symptom essential. It would be argued that post-

exertional malaise should be required for the diagnosis, rather than just be one of the concurrent symptoms.

The importance of identifying the clusters of accompanying symptoms would be underlined with every revised definition. It would be argued that a proper classification and measurements of those symptom clusters would make for a case definition that can fully encompass the complex illness. It would be stressed that the case definition should be broad enough to reflect the full range of cases, but not too broad as to misclassify cases as CFS when they in actuality belong in another organic and/or psychological disease category. Alternatively, it would be argued the case definition should be sensitive enough to discriminate between a CFS case and a non-case, but not so narrow as to exclude true cases.

Myalgic Encephalomyelitis (ME)

In the UK, the definition of chronic fatigue has been undergoing a slightly different evolution than in the USA. The term Myalgic Encephalomyelitis (ME), proposed by Acheson (1959) and Ramsay (1988) was meant to emphasize strongly the neurological nature of the condition and reflect better its possible organic cause, argued to be a viral infection (Dowsett, Ramsay, McCartney, & Bell, 1990). Dowsett and colleagues (1990) described ME as a "multisystem syndrome including nervous, cardiovascular, endocrine and other involvement, distinguished by severe fatigue following trivial exertion". The symptom of fatigue itself was defined as general or local muscular fatigue following minimal exertion with prolonged recovery time, described as chronic and volatile in its intensity, and attributed to a prolonged respiratory or gastrointestinal infection. The Dowsett and colleagues' definition stood out in that it explicitly specified a muscular fatigue. However, later ME definitions, such as the Canadian Consensus Criteria, expanded it from a purely physical to also include a mental domain (Carruthers et al., 2003). Accompanying symptoms included a wide, rather unspecific, range of neurological, cognitive, sensory, cardiac, endocrine, and gastrointestinal impairments.

The ME definition, put forward in opposition to the CDC/Fukuda criteria, strongly emphasised the severity of fatigue following the infection that led to ME, and especially highlighted the experience of the disproportionately high level of fatigue compared to the low level of activity performed. However, the CDC/Fukuda (1994) criteria similarly described fatigue that was disproportionate to exertion, led to significant reduction in activity, and was not relieved by rest. The fundamental difference between the terms ME and CFS is that the former argued for the existence of, and attempted to reflect, the viral origin and

physiological deficits, while the latter emphasised the profound and multi-systemic nature of fatigue. Dowsett and colleagues (1990) did not deny the term CFS but regarded it as a less severe condition and more likely to be of psychological origin. These hypothesised differences between the causes of ME and CFS, biological and psychological, continue to fuel the conflict within research and clinical communities.

The definition of ME has also undergone several revisions. These have resulted in the London criteria produced by the The National Task Force on Chronic Fatigue Syndrome (1994). This definition is notable because the fatigue was defined as "exercise-induced", although with a clarification that mental or physical activity prior to fatigue should be trivial, as compared to the individual's previous exercise tolerance level (London, 2010).

The London criteria have been used recently in a treatment trial (PACE) in a modified form (Version 2) (White et al., 2011), which required the presence of post-exertional fatigue. Both versions recognized fluctuations of symptoms, had a 6-month requirement, included cognitive symptoms of poor memory and concentration, and emotional distress, and used primary depression or anxiety as reasons for exclusion. The main issue in discussing the London-criteria is that the original document has not been published and there have been very few studies that have utilized it, the PACE trial being one of the recent ones.

Canadian Consensus Criteria (CCC) further promoted the neurological and neurocognitive nature of the disease and proposed clinical criteria for primarily diagnostic purposes. The term ME/CFS recognised both names, but emphasised the ME and hence, the biomedical nature and the viral origin of the condition (Carruthers et al., 2003). In accordance with the ME concept, the authors argued that individuals falling under the CCC demonstrate more severe symptoms and substantially reduced functioning than those meeting the criteria for CFS. However, the core fatigue symptom definition remained unchanged in its description and similar to the CDC/Fukuda criteria: new onset, unexplained, persistent, or recurrent physical and mental fatigue that substantially reduces activity.

The Canadian criteria included additional symptoms that reflected neurocognitive deficits and autonomic dysregulation, endocrine and immune systems impairments, with a view that additional symptomatology is essential in distinguishing ME/CFS from other fatiguing illnesses and from psychiatric conditions. The problem with Canadian criteria common to other ME revisions is that while it overlaps less with depression, symptom-wise it greatly overlaps with other neurological conditions, for example, multiple sclerosis. The inclusion of many comorbid entities (among them fibromyalgia, depression, irritable bowel syndrome) also undermines the exclusivity of the diagnosis. The distinguishing features are

primarily based on the severity of fatigue in ME/CFS as opposed to CFS. The first problem is that increased severity does not suggest that ME is qualitatively different from CFS, or even from other fatiguing conditions. The second problem is the lack of clear guidelines on the measurement of such severity. In spite of being favourably received, the Canadian criteria did not gain in popularity with either clinicians or researchers (Brurberg et al., 2014).

The International Consensus Criteria (ICC) further promoted the case for separating CFS and ME (Carruthers et al., 2011). The CFS term was viewed as reflecting a more psychosocial construct, and the CDC/Fukuda criteria set was deemed too inclusive and identified a too heterogeneous population. ICC argued that the term ME reflects the underlying organic pathophysiology of the illness and placed a widespread inflammation and multi-systemic neuropathology at the core of it. The proposed inflammation involved the Central Nervous System (CNS), immune system, cellular metabolism and cardiovascular system.

While ME may aim for a narrower diagnostic criteria, it still suffers from the lack of agreed-upon objective assessment tools that would aid in a more accurate classification of cases. Carruthers and colleagues (2003, 2011) contended that the CDC/Fukuda criteria could not differentiate CFS from depression, and suggested that focusing on physical disability would help discriminate between depression and ME. The problem though, as with the Canadian criteria, is that ICC criteria do not appear to differentiate well from other neurological conditions due to the overlapping symptom clusters. These include neurological problems, like concentration and memory impairments, sleep disturbance, and pain; immune, or gastrointestinal, or genitourinary impairments; energy metabolism disruption, like cardiovascular or respiratory problems. In their attempt to emphasise the physiological nature of ME, ICC allowed for a great overlap between ME and unidentified viral and bacterial infections, as well as IBS or even respiratory conditions, opening more doors for a misdiagnosis.

In their drive to promote the biomedical direction, ICC emphasized two constructs: a post-exertional neuroimmune exhaustion in place of fatigue, which was deemed to be too broad and confusing, and a post-exertional malaise, the latter is similarly included in the CDC/Fukuda (1994) definition. ICC particularly stressed that even the most minimal activity can lead to severe exhaustion, highlighting the imbalance between activity and fatigue. ICC criteria aimed to identify people with a pathologically low threshold of fatigability. Stressing the importance of measuring the severity of fatigue, ICC removed the duration requirement of 6 months or more and included the severity ranking: mild (50% reduction in activity),

moderate, severe, very severe (bedridden). However, this was with little indication of how to standardize that measurement of severity.

Importantly, ICC gave cognitive dysfunction an equal place with the physical dysfunction, recognising the importance of cognitive processes in the onset and maintenance of the condition, albeit not in the way that cognitive theories of CFS do. In ME, as defined by ICC, the cognitive dysfunction is meant to be one of the symptoms reflecting the impairment in the Central Nervous System, rather than a higher-level voluntary process of distorted self-monitoring of the body and somatic symptoms that may lead to symptom overperception and trigger the onset of severe fatigue and perpetuation of CFS. Although, Carruthers and colleagues (2011) did state that processing of pain and sensory information was distorted and patient did perceive simple tasks as requiring a substantial effort. Carruthers and colleagues attributed this to physiologically based dysregulation of CNS, rather than to higher level cognitive processing, such as attention to somatic symptoms, negative interpretation of ambiguous body sensations, or catastrophic and avoidant cognitions.

Currently, the question, whether ME is a qualitatively different condition from CFS or alternatively a more severe case of CFS with additional contributing factors (infection), remains unanswered by any researcher arguing for the separation of the diagnostic criteria. Overall, nobody appears to contest the possibility that people with ME may also fall under the umbrella of CFS; thus potential ME cases might be a subset of CFS cases. The ME subpopulation might have experienced an infection, which triggered an onset of the illness, and led to lasting damage being expressed on physiological, neurological and cognitive levels, resulting in symptoms of greater severity. That argument is somewhat supported by the review conducted by Brurberg and colleagues (2014), who analysed a model of applying sequentially different case definitions with increasing sensitivity (which include CDC/Fukuda and a number of ME-based definitions) to the same population. Their analysis showed that those who meet the narrower definitions also meet the CDC/Fukuda criteria. Jason et al. (2012) similarly compared CDC/Fukuda, ME and Canadian criteria and found that case definitions that emphasise ME identify a more profoundly impaired and more severely affected sub group of individuals. Although, it appears that there was not a qualitative difference between primarily CFS and primarily ME populations, but rather a quantitative one. All individuals in the study by Jason and colleagues fell on the same symptom continuum of profound fatigue, which was not relieved by rest, disproportionate to exertion, and accompanied by a significant reduction in activity. Similar results were obtained in

another study suggesting ME diagnosis may identify a more severely affected group than CFS; however that study made no claim that the two would be mutually exclusive (Jason, Sunnquist, Brown, Evans, & Newton, 2014).

The Oxford criteria (1991), in parallel to the continuously revised ME definitions, took into account a subset of CFS cases that may be due to an infectious agent (Sharpe et al., 1991). However, the Oxford team utilised the term CFS to describe a severe disabling fatigue of uncertain cause that affects physical and mental functioning. CFS was adopted as an umbrella term that would specifically encompass any cases that present with primary fatigue that is unexplained by any physiological deficits, and that is also severe, persistent, and highly disabling. The Oxford criteria required fatigue as the core symptom, plus concurrent symptoms including myalgia, sleep disturbance, and mood symptoms, lasting minimum for 6 months.

Currently, CFS remains primarily a diagnosis of exclusion, requiring that all other explanations for the fatigue be ruled out after a battery of laboratory tests. However, there is no agreed-upon list of exclusionary medical tests to run. GPs would refer their patients to various specialists who would run a number of assessments of their patients' physical and psychological condition until all alternative explanations are ruled out. CFS diagnosis in the end is presented as a mixture of clusters of unexplained symptoms. Thus, we can demonstrate what CFS is not, but have great difficulty in demonstrating what it is.

The important point is that the unexplained, persistent and pervasive mental and physical fatigue, which is severely disproportionate to effort, remains the core feature of all the definitions. So, while the populations under investigation may differ in details, they are more likely to represent different clusters within one population of people experiencing that unexplained phenomenon of extreme lasting fatigue (Jason, Brown, Evans, Sunnquist, & Newton, 2013). The systems, physiological and neurocognitive, involved in the experience of fatigue itself may not differ between CFS or ME populations. Moreover, these systems may not necessarily differ between unexplained fatigue and fatigue due to known medical conditions (Harvey & Wessely, 2009).

Additional difficulty for the diagnostic process is that the course of CFS is long, intermittent and diverse; the severity of symptoms is subject to a great degree of fluctuation; and the prognosis is uncertain (Cox & Findley, 1999; Hill, Tiersky, Scavalla, Lavietes, & Natelson, 1999; Nisenbaum, Jones, Unger, Reyes, & Reeves, 2003; Taylor, Jason, & Curie, 2002). At times CFS or ME can be asymptomatic, and the course of the illness can vary from seeming recovery to a sudden flare up in symptom severity (Jason, King, et al.,

1999; Jason, Timpo, et al., 2009). Such changes may happen even during the diagnostic process, because some of the proposed tests, particularly MRI, may involve a long wait, and the symptomatology may change while the patient is on the waiting list. Furthermore, these symptoms may appear at different stages of the disease, which means that, if an individual is diagnosed only when all the symptoms are present together, then the disease might have progressed very far ahead. This makes treatment more difficult, and undermines the development of any potential preventive strategies (Reeves et al., 2005). It would be productive to investigate potential risk factors (including cognitive biases in information processing) in order to identify populations vulnerable to developing CFS or ME. Furthermore, these cognitive processes may be unique to CFS population, therefore could be added to the diagnostic tools for CFS.

The lack of objective assessment tools that could directly measure and identify a unique set of deficits and dysfunctions that determine a case of CFS, or ME, or CFS/ME, is spurring on the debate about operational definition and diagnostic criteria. To address the problem of reliable and valid measurements, Reeves et al. (2005) called to standardize the assessment tests through the uniformity of measures across studies and clinical settings. The authors argued that clarity and transparency of the process of assessment and diagnosis and rigorous protocol when following exclusionary guidelines are essential for empirical research. Otherwise, the differences in recruitment locations and strategies and in the application of different case definitions across different studies would mean that studied populations would be too heterogeneous to generalize across. Many inconsistent or conflicting empirical findings can be explained by difference in samples resulting not only from the application of different definitions but also from inconsistent measurements (Aslakson, Vollmer-Conna, Reeves, & White, 2009; Wilson et al., 2001).

A review by Reeves et al. (2003) attempted to address ambiguities in the CDC/Fukuda criteria. Fully recognizing CFS as diagnosis of exclusion (when all other explanations for fatigue and disability are ruled out) the authors stressed the importance of verifying the list of conditions recommended for exclusion, outlining the guidelines for dealing with comorbidity, and dividing the CFS population into subgroups depending on the presence/absence of comorbidities. For example, in the case of mental health conditions such as depression and anxiety, Reeves and colleagues took a softer approach and suggested that mental health conditions such as depression and anxiety should not fall into the list of exclusionary criteria if they have been absent for longer than five years. Similarly, while CDC/Fukuda specified that the fatigue should be of new onset, Reeves and colleagues

suggested that patients could be stratified on the basis of comorbid or pre-existing conditions, in which fatigue is life-long and chronic (foe example, somatization disorder), rather than being altogether excluded from research or treatment. On the clinical side, the focus should be on providing treatment. Criteria that are too stringent may exclude people whose suffering is real and quality of life is compromised, and may ignore important comorbid conditions that need to be addressed to help treat the illness itself and improve the quality of life.

Reeves and colleagues (2003, 2005) proposed specific measures of fatigue and other symptoms making an emphasis on the validity of the assessment tools and their consistent and proper application, such as Short-Form – 36 for functional impairment (Ware & Sherbourne, 1992), Multidimensional Fatigue Inventory (Smets, Garssen, Bonke, & De Haes, 1995), and the Symptom Inventory (Wagner et al., 2005). They attempted to refine the measure of fatigue severity under CDC/Fukuda criteria, pointing out the ambiguity of the statement that fatigue is not due to current activity. Instead, they suggested criteria that current fatigue should be out of proportion with the current activity level, not due to some high stress extreme activity and be combined with post-exertional malaise lasting more than 24 hours; this is similar to the Canadian and ICC definitions. Moreover, they proposed specific cut-off scores to assess fatigue and symptoms severity; establishing < 70 as a cut-off score on the physical functioning subscale of SF-36. Agreement on the cut-off scores to differentiate degrees of symptom severity would help replication and comparison between studies. Following the suggestions of Reeves et al. in the studies described in this thesis, CDC/Fukuda criteria were used with measures of the duration, frequency and severity of CFS symptoms, fatigue and physical functioning.

While the International CFS Study group revisions (Reeves et al., 2003; Reeves et al., 2005) were a step forward in improving the assessment strategy, they have been criticized by Jason et al. (2010) for being too inclusive and relying too much on quantitative rather than qualitative evaluation. Jason and colleagues argued that the goal is to define the type of impairment in CFS rather than the degree of impairment based on cut-off scores. They claimed that a person with a psychiatric disorder would meet the empirical criteria for CFS and thus would be misclassified as a case of CFS. The authors criticised the Multidimensional Fatigue Inventory (Smets et al., 1995) as too inclusive and the suggested cut-off scores as too low, which would have the effect of broadening the range of symptom severity. They further pointed out that the Symptom Checklist deviates from CDC/Fukuda criteria (at least four symptoms being present for 6 months), modifying it to time period of just one month.

Overall, Jason et al criticised Reeves and colleagues' empirical criteria for a lack of specificity and sensitivity, which may lead to over diagnosis of CFS while missing, according to their own research, 35% of true CFS cases.

It is important to point out that Jason and colleagues prioritised a search for biological markers, and therefore would focus on the need to have criteria that identify a very homogenous population. However, if CFS is a multisystem illness we should not expect to find homogeneity, and the search for it may be counterproductive. The issue appears unresolvable if we rely fully on the diagnostic criteria and case definitions to identify people with the "true" condition. The big problem is not necessarily the heterogeneity of the population itself, but the heterogeneity of the studies, which might or might not have assessed similar populations. Therefore, the proposal of Reeves and colleagues (2005) to use similar methods of assessment, rather than proposing newer and more refined case definitions, was a good step towards validation of the existing criteria and their more consistent application.

In summary, there exist a number of overlapping case definitions of CFS/ME, including an empirical, an epidemiological, and a clinical definition. They range from the bio-medically oriented to those more inclusive of psychosocial factors. CFS presents as a broad umbrella term which also subsumes CFS/ME emphasis on CFS, ME/CFS emphasis on ME, or pure ME. CFS is a serious illness, highly disabling, primarily characterized by unexplained extreme mental and physical fatigue, highly disproportionate to the current activity level, and no amount or particular patterns of rest allow recovery to occur. Dysfunctions observed include immune, neurocognitive, muscle, cardio, endocrine, and gastrointestinal systems. No single causal factor can be identified. Multiple potential causes have been suggested, however the causal pathways are not confirmed, and the interaction between multiple causes is not understood. Proposed causal factors range from genetic to psychosocial. Infectious agents are implicated in the onset and maintenance, but are not consistently confirmed, because the disease also occurs in the absence of infection, though there remains a possibility that the infection was not identified. Most of the research and theories seem to suggest that the mechanism at the heart of CFS is one of dysregulation, whether immune, affective or cognitive, or related to the central nervous system, or to the adaptive pattern of activity-recovery. Nonetheless, the causes and the mechanism of that dysregulation also remain elusive. The symptoms of such dysregulation overlap with other illnesses, physiological or psychological in nature, and therefore prevent a clear-cut diagnosis. The lack of diagnostic tests means that clinicians and researchers continue to rely on case definitions. Persisting

problems with case definition include: the lack of agreement between and within clinical and research communities; heterogeneity of the diagnosed and studied populations where different case definitions were applied; the lack of distinct clinical boundaries between CFS and other disorders; unreliability of diagnostic procedures or diagnostic case definitions utilized, which prevents the drawing of consistent and clear conclusions from empirical research concerning causes of CFS and the effectiveness of treatments.

Having said that, a recently conducted clinical trial of the effectiveness of several treatments for CFS/ME (PACE) utilised different case definitions: Oxford 1991, International CFS Study group 2003 (Reeves et al., 2003), London ME 1994/National Task Force (White et al., 2011). The trial demonstrated that the effectiveness of a type of treatment was independent of the case definition used. The results suggest that Cognitive-Behavioural (CBT) and Graded Exercise (GET) therapies were more effective than adaptive pacing or specialist medical care, in reducing CFS fatigue. Proponents of ME criticized the PACE trial (Stouten, Goudsmit, & Riley, 2011), mainly coming from the premise that GET and CBT are inappropriate treatments for severe CFS or ME, meaning a neuroimmunological condition that requires biomedical research and treatment (Maes & Twisk, 2010b; Twisk & Maes, 2008). Conversely, Brurberg and colleagues (2014) point out there have not been a lot of treatment studies employing the ME-based definitions. Therefore, there is not enough evidence to back up the claim that specifically ME sufferers as opposed to CFS would benefit from alternative biological treatments.

The results of the PACE trial support the argument that the main distinction between diagnostic criteria may not be qualitative but quantitative, representing the range of severity and level of disability presented by the patients. Therefore, it may be premature to argue that different diagnostic criteria identify qualitatively different populations rather than populations who are on the continuum of severity and disability. A recent analysis by Brurberg and colleagues (2014) showed that the severity of CFS increases with the application of more narrow and exclusive criteria, which means that individuals diagnosed under both the CDC/Fukuda (broad) and Canadian (increasingly narrow) criteria show a greater degree of severity than those diagnosed according to the CDC/Fukuda criteria only. Brurberg and colleagues proposed that different case definitions allow classification on the basis of severity, which may be useful for prognosis and treatment, however without diagnostic tests the qualitative differences between case definitions would remain elusive. The authors reported little evidence to support the hypothesis that some case definitions can identify a more specific neuroimmunological condition.

The big issue has been whether individuals with primary psychopathology (anxiety or depression) have been excluded from CFS diagnosis. However, there does not appear to be any strategy for identifying true comorbidities, seeing as mood disorders can be comorbid with physical illness in general (Qin et al., 2014). Moreover, an argument can be made that it is unethical to exclude people with comorbid psychopathology because it denies them treatment, particularly as CBT is an effective treatment not just for CFS but for depression and anxiety (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015). Indeed, even addressing the depressive symptoms alone may increase functioning and quality of life in CFS (Hadlandsmyth & Vowles, 2009). Even definitions that claim to narrow the focus of the diagnostic processes need to take into account the presence of psychopathology. At the moment no case definition provides clear specific guidelines on how to distinguish comorbid depression secondary to CFS from primary depression that might have preceded it.

The case for CDC/Fukuda criteria

The current state of affairs suggests that the CDC/Fukuda and the Oxford definitions are the most used and validated criteria within the context of potential treatments (Smith et al., 2015; White et al., 2011). Similarly, Brurberg et al (2014) reported the CDC/Fukuda as the most extensively validated case definition (Hickie et al., 2009), often used as the evaluation standard in validation studies. Research requires standardized procedure, and criteria applied in clinical practice should be initially validated in research practice, and only CDC/Fukuda and the Oxford criteria meet that requirement (Brurberg et al., 2014).

The profound, disproportionate, and debilitating fatigue in all case definitions is of the same nature, and the cognitive processes, explored in this thesis, that accompany the sensation and perception of fatigue, may be shared by all the subpopulations under the umbrella of CFS. Therefore, the findings obtained from the population diagnosed on the basis of the CDC/Fukuda criteria should not differ from those obtained following the application of other CFS/ME criteria. White and colleagues (2011) suggested that as long as fatigue is the main symptom of the studied subpopulation the results would be generalizable across subgroups under the broadest CFS definition. Consequently, the decision was made to use the CDC/Fukuda (1994) criteria in the empirical studies in this thesis. It is a more inclusive and broader set of diagnostic criteria, which encompasses the subgroups that may meet other more narrow diagnostic criteria, as reviewed above. The core symptom of fatigue is present in the CFS population and its subpopulations regardless of the diagnostic process. This thesis argues that the nature of the fatigue in CFS (which cannot be explained

by an organic abnormality, is disproportionate to exertion, and does not recede following rest) can be explained by dysregulation in cognitive information processing by that individual. Such cognitive processes could be characteristic of the CFS population in the broadest sense.

The CDC/Fukuda criteria set has been reported as the most widely used, most cited, and best validated case definition (Brurberg et al., 2014), and is adopted internationally (Johnston, Brenu, Staines, & Marshall-Gradisnik, 2013b). No definition emerged as superior to others based on validation studies alone (Brurberg et al., 2014). Thus, a good alternative would be to go with the most widely and consistently used definition in research and clinical settings, such as CDC/Fukuda criteria. Importantly, the vast majority of the empirical studies reviewed in this thesis have also used CDC/Fukuda criteria, therefore the use of the same criteria in the studies described in this thesis would make the results more comparable.

Since CDC/Fukuda are the most common criteria in the literature, they would be most applicable to individuals coming from a wider community, as opposed to clinical databases, because narrower case definitions might have been used in specific clinical settings. Furthermore, if CDC/Fukuda is the broadest case definition, applying a narrower one may exclude a large number of people diagnosed with CFS using CDC/Fukuda criteria, and therefore using it may improve ecological validity and produce more generalizable findings. Moreover, considering the potential practical difficulties of recruiting people from a population experiencing high levels of fatigue and disability, it may be counterproductive to narrow the selection criteria to the point of making such a population inaccessible.

It could be argued that it would be more appropriate to use the ME-based criteria for the studies conducted in the UK. However, the National Institute for Health and Care Excellence (NICE) uses the guidelines for CFS/ME that majorly overlap with CDC/Fukuda criteria, focusing on the unexplained and persistent fatigue, post-exertional malaise, sleep disturbance, pain symptoms, and cognitive impairment (NICE, 2007). The differences between NICE guidelines and the CDC/Fukuda criteria consist of a requirement for a more detailed and greater number of symptoms to be noted, and a reduction in the duration requirement to 4 months. The added symptoms include worsening of symptoms due to mental and physical exertion, flu-like symptoms and general malaise (in other words post-exertional malaise), dizziness and nausea, and heart palpitations. However, the NICE guidelines suggest that only one of the concurrent symptoms would be sufficient to consider CFS/ME diagnosis, unlike Fukuda's 4 out of 8. That shows that the CDC/Fukuda definition

may be sensitive enough to identify individuals with CFS/ME who were diagnosed following NICE 2007 guidelines, without being so broad as to make the sample overly heterogeneous.

In this thesis, the term Chronic Fatigue Syndrome (CFS) was used for the following reasons. The cluster of symptoms exhibited by the individuals who participated in the studies presented in the thesis fit the criteria for CFS as proposed by CDC/Fukuda (1994). The individuals making up the current sample have not undergone the battery of physiological tests of the functioning of their immune system for the purposes of these studies specifically, and consequently cannot be referred to as ME patients. Similarly, the names CFS/ME or ME/CFS are not utilized, because in line with the review above, CFS is a suitable name to reflect the broadest but sufficiently sensitive diagnostic criteria.

A major issue is that CFS is not a name preferred by individuals diagnosed with CFS/ME, who prefer a term that recognizes and emphasises the physical origin and nature of their symptoms and disability (Picariello, Ali, Moss-Morris, & Chalder, 2015). However, seeing as the CDC/Fukuda definition describes "a clinically evaluated, unexplained, persistent or relapsing chronic fatigue that is of new or definite onset (has not been lifelong); is not the result of on-going exertion; is not substantially alleviated by rest; and results in substantial reduction of activity", it does in fact recognize the physical disability of the condition, but stops short of making any judgments about its origin. The list of symptoms also places greater emphasis on the physical suffering: postexertional malaise, unrefreshing sleep, muscle and multi- joint pain, new headaches, tender lymph nodes, and a sore throat. Only memory and concentration impairments reflect a more cognitive nature of the illness.

The studies in this thesis set out to test the CFS population. The question as to whether the ME population is a subset of the CFS population, or whether ME and CFS populations are completely different and separate entities, cannot be answered fully at the moment. The reviewed literature points to the likelihood of ME being subsumed within the CFS population (Brurberg et al., 2014).

Furthermore, the goal of this thesis was to test a wider community-based population, which, on the one hand, risks producing a heterogeneity that would compromise comparisons, and, on the other hand, may contribute to constructing a fuller profile of the disease that reflects its variability in the population at large. For example, recruiting from a CFS specialist clinic may reflect referral bias, particular practices, and more severe disease. Selecting a homogenous group of individuals from a specialist clinic would increase validity,

but may reduce generalizability and applicability, which are important when one takes into account that CFS is a multi-systemic, complex condition.

In summary, CFS is an umbrella term for an illness that has a wide range of symptoms and does subsume several subgroups. However, these subgroups are mostly distinguished by the severity of their disability rather than by any qualitatively different organic nature of their conditions. Therefore, CFS refers to a complex, multifaceted condition, hypothesized to have specific information-processing styles, which were the focus of the empirical investigations described in this thesis.

The Mind Body Dilemma

The research so far has not pinpointed clear cause(s) of CFS (NICE, 2007). Comprehensive reviews of the current evidence consider multiple biological, psychological and behavioural factors: genetic predisposition, viral triggers, immune system dysregulation, impairment in endocrine function, central nervous system sensitization, brain structural abnormalities; cognitive deficits; muscle impairments, physiological deconditioning, cognitive biases and negative illness representations, fear and avoidance cognitions and behaviours, personality factors, – and their interactive effects that may lead to the onset and perpetuation of CFS (Evengard et al., 1999; Maquet, Demoulin, & Crielaard, 2006; Prins et al., 2006). Due to conflicting and inconsistent findings, current evidence is inconclusive and CFS remains classified as a medically unexplained syndrome. This inconclusiveness is only compounded by the difficulty of comparing across studies, owing to the heterogeneity of the sampled populations, diagnostic measures, methodologies, and treatments (Deary et al., 2007). CFS is recognised as a multi-systemic disorder affecting the organism on multiple levels (Green, Cowan, Elk, O'Neil, & Rasmussen, 2015; NICE, 2007). However, in discussing potential causes of CFS, multiple parties emphasise different systems: biological, psychological, or behavioural. Such debate could inspire and drive research to disentangle the multi-causality of this complex condition. However, in the field of CFS, that debate has resulted in a considerable amount of controversy, which has hindered, and continues to hinder the research. Some of the controversy is rooted amongst the misconceptions, misunderstandings, a number of worrying assumptions, and misuse of research methods and findings.

One troubling assumption is the simplistic dualist conception of the human organism: there is the biological and there is the psychological, and never the twain shall meet. This conception does not fit the complex multidimensional nature of CFS. This Cartesian split

defines the debate on CFS aetiology. One side (mainly consisting of researchers and clinicians) is perceived as believing that it is a psychological or a psychiatric disorder. The other side, consisting of some researchers, clinicians, patient advocacy groups and patients, is perceived as believing it is an organic illness brought on by a biological causal agent, for example, a virus. The word "perceived" is used, because, firstly, both sides are not uniform in their beliefs, and secondly, theories and hypotheses proposed by both sides are more complex than such simplistic descriptions as psychological versus biological.

The problem is that this perceived dualism appears to erase the mind in order to preserve the body. There is a widespread misconception that, if the illness is proposed to be of psychological origin, it is akin to the proposition that it does not exist, because "it is all in your mind". A recent study on patients' perspective shows the frustration experienced by people with CFS when psychological terms are used to describe their experience (Picariello et al., 2015). It is not unfounded – as there probably are a number of researchers, clinicians, and people in general who may not believe in the actual existence of the condition, as discussed by Van der Meer and Lloyd (2012).

However, the problem is that the debate questioning whether CFS is a real illness or not, and the related misconception that "psychological = not real", suggests that the only way to make it a "real" illness is to find an underlying organic, concrete and tangible abnormality (Komaroff, 2015). Any intangible mental health related issues are thus dismissed as not "real", which should be deeply worrying. While the continuing insistence to differentiate CFS from comorbid depression and/or anxiety, may help to diagnose "purer" CFS cases, this appears to disregard the very real suffering of people who do have comorbid CFS and depression and/or anxiety.

This prevailing misconception that psychological equals not real has once again pushed clinicians, researchers, and patients to reassert the legitimacy of the suffering by adapting yet another name: a Systemic Exertion Intolerance Disease (SEID) proposed by the Institute of Medicine in the United States (Clayton, 2015; Ganiats, 2015). The new definition makes a strong emphasis on abnormal reaction to exertion and activity, contending that adverse reaction to exertion is the essential characteristic of the condition. It only requires the presence of three main symptoms, fatigue, postexertional malaise and sleep disturbance, and a reduction in occupational, educational, social, and personal activities persisting for 6 months.

The description of fatigue in SEID is word for word the CDC/Fukuda description: new onset, not the result of on-going effort, and not alleviated by rest. The other two primary

symptoms are also from the CDC/Fukuda list: post-exertional malaise and sleep disturbance. However, while in CDC/Fukuda they are only two of the eight symptoms, and in whose absence CFS can still be diagnosed, the SEID criteria require the presence of those two symptoms for the diagnosis. The report on the new SEID criteria also summarises the tools and assessment tests that can be used for the diagnosis, although without strict guidelines on cut-off scores, expected results, or the basis on which an inclusionary or exclusionary diagnosis can be made. Thus, in spite of yet another name and diagnostic criteria, the problem of dealing with psychiatric comorbidities remains unsolved.

The disturbing trend of denying the psychological and erasing the mind is evident in the theories and research into organic causes of CFS. Biological causal theories of CFS include persistent viral infection, dysregulations in immune and nervous systems, and deficits in muscle cells metabolism, specifically in mitochondrial dysfunction.

Going viral

The controversy erupted after the publication of the findings of infectious retrovirus XMRV, Xenotropic Murine Leukemia Virus (Lo et al., 2010; Lombardi et al., 2009; Mikovits, Lombardi, Pfost, Hagen, & Ruscetti, 2010). However, these original papers were retracted following the ensuing lack of replication (Satterfield et al., 2011; Switzer et al., 2010; Van Kuppeveld et al., 2010), reports of mouse DNA contamination of human tissue tested for XMRV (Hue et al., 2010; Robinson et al., 2010), and public debates (Kakisi, Robinson, Tettmar, & Tedder, 2013; Van Kuppeveld & Van der Meer, 2012; Weiss, 2010). The search for viral infections, immune dysfunction and any resulting impairments like mitochondrial dysfunction, however, continued on (Morris, Berk, Galecki, & Maes, 2014; Morris & Maes, 2013a, 2013b, 2014).

The Epstein-Barr virus has been detected based on the presence of antibodies in a subset of CFS patients (Lerner, Beqaj, Deeter, & Fitzgerald, 2004). The problem with the presence of the traces of viral infections is that these features are not specific to CFS, although they may be present in CFS subgroups and related to greater severity of CFS (Ganiats, 2015). Immune biomarkers are not specific to CFS, and are often absent in the CFS population, and there is insufficient evidence to conclude that ALL cases of CFS are preceded by infection, whether by the Epstein Barr virus, or other bacteria, fungi, viruses or parasites (Clayton, 2015; IOM, 2015).

The evidence for either the viral infection, in terms of detection of antibodies, or compromised immune system function, in terms of low number of T-cells and/or natural

killer cells and/or their decreased function, remains at the moment inconclusive due to conflicting and inconsistent findings (Bassi, Amital, Amital, Doria, & Shoenfeld, 2008; Lyall, Peakman, & Wessely, 2003). This is due, on the one hand, to the lack of evidence of the differences in markers of viral infections between healthy controls and individuals with CFS (Oakes, Hoagland-Henefield, Komaroff, Erickson, & Huber, 2013; Reeves et al., 2000) including a study of monozygotic twins (Koelle et al., 2002), and on the other hand, to the lack of findings concerning the benefits of drug-based treatments (Smith et al., 2015).

New reports implicated cytokine-related dysregulation, for example, people in the early stages of CFS showed greater activation of anti- and pro-inflammatory cytokines, compared to the healthy case-matched controls (Hornig et al., 2015). In contrast, those who had CFS for a long time showed lower amounts of cytokines, compared to healthy samples. When the short- and long-duration CFS individuals were combined into one group and compared to healthy controls no significant differences were seen, leading Hornig and colleagues to suggest that previous findings had been inconsistent because they had not taken into account duration of illness. These newer findings point to the possibility of viral origin and consequent immune system dysregulation as a casual pathway of CFS. Currently, however, the findings have not yet been replicated. There is also a problem of establishing causality: was it the virus affecting the immune system or an initially impaired immune system that was vulnerable to the virus? This is representative of the general state of confusion between causes and symptoms in CFS. Based on the current state of research in CFS and the prevalence of cross-sectional studies it is difficult to establish whether an observed dysfunction is the cause or the consequence of the condition.

Exercise: perception of harm and the evidence of benefit

Biomedical models, theories, and evidence are often used to argue that exercise is not the proper treatment for people with CFS, that exercise is harmful in CFS, particularly so for ME, due to existing mitochondrial dysfunction, acidosis, inflammation and compromised immune system (Maes & Twisk, 2010a, 2010b; Twisk & Maes, 2008). There are three problems with the above argument. First, the evidence for mitochondrial dysfunction is lacking. Second, exercise can be beneficial for mitochondrial dysfunction. Third, the argument that the exercise is harmful for people with CFS may be based on flawed understanding of research methodologies.

Mitochondrial dysfunction has been proposed as one of the organic abnormalities in CFS (Morris & Maes, 2014). However, the empirical findings on mitochondrial oxidative

function do not show significant differences between CFS groups and matched controls (Barnes, Taylor, Kemp, & Radda, 1993; Jones, Hollingsworth, Taylor, Blamire, & Newton, 2010; McCully, Smith, Rajaei, Leigh, & Natelson, 2004). Mitochondria are highly sensitive to the signals that initiate muscle contraction, and thus, their function can be improved by either stimulating those signals naturally through exercise or mimicking them pharmacologically (Russell, Foletta, Snow, & Wadley, 2014). Furthermore, there is accumulating evidence of the benefit of exercise treatments that prevent mitochondrial dysfunction and enhance oxidative processes in skeletal muscles in people with chronic heart failure (Chien & Wang, 2011). Exercise can improve the capacity of mitochondria to utilize oxygen in lymphocytes, enhancing the function of immune system in healthy sedentary individuals (Chang & Wang, 2015). Exercise can slow down the decline in muscle metabolism, including mitochondrial function associated with ageing (Zampieri et al., 2015). Exercise can be beneficial for mitochondrial function in chronic diseases like diabetes (Lumini, Magalhaes, Oliveira, & Ascensao, 2008), amyotrophic lateral sclerosis or conditions that demonstrate exercise intolerance due to mitochondrial dysfunction (Russell et al., 2014). Finally, exercise can contribute to the biogenesis, that is formation of new mitochondria in skeletal muscles (Little, Safdar, Bishop, Tarnopolsky, & Gibala, 2011; Serpiello et al., 2012), and improve mitochondrial structure and function (Bishop, Granata, & Eynon, 2014; Holloszy, 2008; Menshikova et al., 2006).

There is evidence of delayed recovery from exercise among CFS individuals due to abnormalities in intramuscular acidity and prolonged restoration of the intramuscular pH (acid/base balance), and due to the lacking connections between the autonomic nervous system and muscle recovery processes (Jones et al., 2010). However, Jones and colleagues pointed out that causality is currently impossible to establish due to the cross-sectional design of most studies.

Acidosis, the build up and dysregulation of lactic acid in the muscles, appears to be present in CFS individuals, which compromises recovery post-exercise and may account for the symptom of post-exertional malaise (Jones et al., 2012; Lengert & Drossel, 2015). The data may provide an explanation for why the recovery is delayed but the authors do not attempt to make claims concerning treatment. Delayed recovery does not suggest that exercise is harmful, but rather that a proper plan of exercise and rest needs to be established and followed. The increase in exercise should also be gradual, preventing the boom and bust cycle, precisely as advocated by Graded Exercise Treatment (White, Sharpe, Chalder, DeCesare, & Walwyn, 2007).

Furthermore, Jones and colleagues (2012) explored whether repeated bouts of exercise can result in higher levels of acidosis in CFS individuals, which may lead them to perceive fatigue that is out of proportion to exertion. They found the evidence for increased acidosis in CFS group compared to healthy controls. However, the findings were not uniform within the CFS group, leading the researchers to identify two CFS subgroups. The study first measured maximal voluntary contraction (MVC) in CFS group and healthy controls. Then the participants were asked to exercise at the capacity of 35% of their maximal voluntary contraction. Healthy controls and one subgroup of CFS showed comparable MVC values and comparable values of depletion of phosphocreatine, a substance crucial for production of energy in muscle function. Its depletion is a natural process during exercise. However, the second CFS subgroup showed abnormally low levels of phosphocreatine depletion. These were in turn explained by abnormally low initial MVC. That initial MVC was not low because of an impaired ability to exercise. If it were the case, that CFS subgroup would have shown high levels of phosphocreatine depletion. Researchers discovered that the initial MVC was low because a particular CFS subgroup did not exercise initially to their capacity, however their perception of effort did not differ from the other CFS subgroup with the normal range of MVC. The study suffered from small sample size (10 and 8 CFS individuals per subgroups) and has not yet been replicated, and is therefore not generalizable. However, the authors proposed that the subgroup of CFS individuals, who showed low MVC, represent the CFS population, who demonstrate conscious or unconscious avoidance of exercise. This could be related to a fear of exercise or a desire to preserve energy. Jones and colleagues suggested that exercise would be a logical treatment for acidosis, but highlighted the following issue. A subpopulation of people with CFS may report exercising, because they perceive that they are putting the effort in, when in actuality they are not exercising to the required capacity. Therefore an exercise-based treatment may not show to be effective for this subpopulation or show mixed results (Jones et al., 2012).

Concerning the relationship between exercise and immune system, consistent moderate exercise was found to be beneficial for immune system (Pedersen & Toft, 2000) and exerted positive influence on the regulation of anti- and pro-inflammatory cytokines (Gleeson et al., 2011; Nieman, 2011). Aerobic exercise reduced pro-inflammatory cytokines and increased anti-inflammatory cytokines in individuals with heart disease (Goldhammer et al., 2005). Regular walking exercise was found to be safe and beneficial in terms of reducing pro-inflammatory cytokines exerting protective effect post-exercise in people with kidney disease (Viana et al., 2014).

A systematic review of immune system response to exercise in CFS demonstrated their cytokines levels and regulation post-exercise were comparable to the values found in a healthy population (Nijs et al., 2014). Crucially, Nijs and colleagues pointed out that studying the effect of exercise as a therapy, such as GET, is not at all the same process as studying the effect of an acute bout of exercise on physiology for the purposes of assessing and understanding symptoms of CFS. In these two instances, responses to exercise would be different. Therefore, it is inappropriate to infer from these studies investigating the effect of exercise on physiology that exercise within the context of GET trials necessarily causes harm to a person with CFS, as for example demonstrated by Twisk and Maes (2008).

A controversy concerning the application of CBT and GET treatments arose amidst the reports of nation-wide support groups such as Action for M. E. (2001) and ME Association (2010) that symptoms may worsen following GET and CBT, and also subsequent to the publication of the results of the PACE trial (Lancet, 2011). These reports were not echoed by the empirical research, which instead showed that symptoms rarely worsen after GET or CBT due to the treatment itself (Clark & White, 2005; Edmonds, McGuire, & Price, 2004; Smith et al., 2015). Even though the gathered data were not detailed enough to be firmly conclusive, the reports showed rarity of adverse reactions to treatment (Smith et al., 2015). However, to prevent harm, which may occur if the treatment is mismanaged and badly administered, it is important that GET and CBT are delivered by a qualified professional adapting the program to the needs of the patient, with the cooperation of the patient (Clark & White, 2005).

A recent report from Action for M.E. (2008) has also shown more positive outcomes following treatment, with 50% of patients benefitting from CBT, compared to only 7% in their 2001 report, and 45% benefitting from GET, up from 34% in 2001. Symptom deterioration has also decreased, with 34% getting worse after GET and 7% after CBT in the 2008 report, compared to 50% and 26% respectively in 2001. However, the report reinforced that pacing is the most effective method of managing ME. It is the approach that NHS specialists and therapists chose most frequently to discuss with patients, and according to the report, pacing resulted in 82% of patients feeling better, with only 3% experiencing the worsening of symptoms. A middle position between biomedical and psychological views was taken by the theoretical approach behind adaptive pacing, amidst the concern about the potential harms of exercise-based treatments.

At the core of adaptive pacing theory is the concept of limited energy resources, called the energy envelope, which contains the available energy for expenditure (Jason, 2008; Jason, Benton, Torres-Harding, & Muldowney, 2009). The activities need to be

planned and executed, that is paced, in accordance with that available limited energy. Pacing, as a strategy, helps stay within the energy envelope. According to the adaptive pacing theory people with CFS are meant to avoid over- and under- exertion in order to maintain the optimal level of activity over time, staying within the range of their energy expenditure. Therefore, some people should be encouraged to increase their activity if they perceive they have the energy for it, while others need to be encouraged to reduce their activity, which would decrease the discrepancy between their perceived and expended energy (Jason, Benton, et al., 2009). If individuals do not stray outside their energy envelope, their fatigue would be reduced and they would perceive that they have more energy (Jason, Benton, et al., 2009; Jason, Brown, Brown, et al., 2013). The approach was proposed primarily with the view to manage CFS symptoms (Jason, 2008; Jason, Benton, et al., 2009; Pesek, Jason, & Taylor, 2000; Shepherd, 2001) and is prominently endorsed by patient support groups and associations (Action for M. E. 2008; ME Association, 2010).

The problem is that the energy envelope theory relies heavily on individual "perception" of fatigue and energy. Such perception can be faulty when experiencing fatigue in general (Strober & Deluca, 2013), but specifically within CFS, people may underestimate their activity, physical or mental (Fry & Martin, 1996a, 1996b; Gibson, Carroll, Clague, & Edwards, 1993; Metzger & Denney, 2002) and demonstrate a discrepancy between subjective ratings of sleep and the objective measures (Majer et al., 2007).

The assumption that the energy envelope is *limited* also appears unsubstantiated by evidence other than by another assumption that there is a physiological deficit, which would be the cause of the limited envelope of energy. It is not specified whether the cause is a prolonged infection or immune dysfunction or muscular-skeletal deficits, or perhaps metabolism, or an autonomic abnormality.

In terms of empirical support, the data did not compare pacing with non-pacing interventions. Jason et al. (2007) demonstrated that individuals who stayed within their energy envelope had significantly decreased fatigue compared to those who strayed outside of the envelope. However, that conclusion was reached following a randomized controlled trial that compared CBT with exercise therapy alone, cognitive therapy alone, and relaxation. There was no trial that compared pacing with non-pacing interventions. The analysed data included self-rating of perceived and expended energy over the past week. However, there was evidence that people with CFS recalled significantly higher levels of fatigue at the end of the week when compared to their momentary ratings of fatigue throughout the week, suggesting inaccuracies in perception and overestimation of fatigue levels during

retrospective recall (Friedberg & Sohl, 2008, 2009b; Sohl & Friedberg, 2008). Most importantly, due to small sample sizes, Jason and colleagues (2009) haven't analysed a subgroup of those who have exceeded the envelope and improved, compared to those who have exceeded the envelope and experienced no change, versus those who have gotten worse. Additional limitations of the theory include reliance on case studies, small samples, and very few studies that directly compare pacing to other interventions (Jason, Brown, Brown, et al., 2013). Besides, according to the authors, their energy envelope and pacing treatment approach includes many components: in addition to explaining the energy envelope theory it incorporates cognitive coping skills, social support, personal relationships, nutrition, relaxation. That makes it unclear which particular components may contribute to reduced fatigue and improved functioning.

Finally, the PACE trial showed that pacing was less beneficial to people with CFS than GET and CBT (White, Goldsmith, Johnson, Chalder, & Sharpe, 2013; White et al., 2011). The main difference between pacing and therapies like GET is that, based on the envelope energy theory, the goal is not to increase activity, but to moderate its levels in order to conserve energy. This would reduce perceived fatigue severity and sustain functioning by preventing relapses. In particular, it would break the cycle of over-activity followed by crash, the Boom and Bust cycle. Notably, the pacing protocols discussed by Jason and colleagues (2013) are not crucially different from planned and well-managed graded exercise programs (like the one in the PACE trial), which start with pacing before introducing increases in exercise. However, Jason et al (2013) criticised the PACE trial for its pacing protocol, specifically for the suggestion not to go beyond 70 percent of the envelope. Jason and colleagues argued that the arbitrary cut-off point was not in accordance with their energy envelope approach and explained that longer periods of inactivity might have given the participants time to focus on symptoms, therefore preventing recovery. It should be noted that the idea that increased focus on symptoms may compromise recovery is fully in line with cognitive models of CFS (Knoop, Prins, Moss-Morris, & Bleijenberg, 2010; Moss-Morris, 2005). The main difference between energy envelope theory and the cognitive-behavioural approach would be the surmised causal roots, presumed to be physiological by the energy envelope theory, which is at odds with the cognitive-behavioural theoretical framework.

Cognitive, emotional, neural sensitization

Nijs, Meeus, Van Oosterwijck, et al. (2012) attempted to combine the immune-based and cognitive-behavioural theories in understanding CFS, bridging the mind body gap.

Having reviewed the evidence for increased responsiveness of individuals with CFS to external and internal stimuli (e.g. light, sound, temperature, pain), the authors attributed it to the Central Nervous System (CNS) sensitization, which can be maintained by cognitive and emotional processes, such as attention, vigilance, and reaction to stress.

Nijs and colleagues (2012) proposed that CNS sensitization in CFS involves an overactive representation of pain in the cortex, which may account for the symptom of widespread muscle and joint pain in CFS. Furthermore, the cortex does not exert strong enough influence on the processing of pain because of weakened inhibitory pathways that descend from the cortex through the brain stem to the spinal cord. When healthy people exercise their pain thresholds rise increasing their tolerance for exercise, because the brain can inhibit sensory processing of pain and release endogenous opioid such as endorphins. This mechanism of inhibition, because of the weakened inhibitory pathways, may be malfunctioning in CFS based on the evidence that when people with CFS exercise their pain thresholds remain low, as compared to healthy people (Heinricher, Tavares, Leith, & Lumb, 2009). Cognitive processes like hyper-vigilance and heightened attentional focus may play a role in weakening the inhibitory pathways therefore sensitizing the spinal cord neurons to stimuli like pain or temperature changes, which may account for low exertion tolerance in CFS.

Nijs and colleagues (2012) proposed that from the other direction, the bottom-up mechanisms involve the activation of the spinal cord neurons by pro-inflammatory cytokines released in response to infection or injury, which may account for the flu-like symptoms and for the wide spread pain. Additionally, a malfunctioning hypothalamic-pituitary-adrenal system leads to reduced levels of cortisol that are not enough to inhibit pain, as compared to a healthy system. Increased amount of pro-inflammatory cytokines and reduced cortisol further promote CNS hypersensitivity.

Therefore, the CNS sensitization theory proposes that the interaction of the physiological and cognitive processes which together increase sensitivity to painful stimuli underpins the fear of activity and consequent avoidance of activity (Nijs, Meeus, Heins, et al., 2012; Nijs et al., 2013). CNS sensitization theory is also consistent with the Moss-Morris (2005) and Knoop et al. (2010) cognitive theories that attentional vigilance for somatic sensations plays a role in the onset and perpetuation of CFS symptoms.

Nijs et al (2012) advocated combination therapies of CBT, GET and pharmacological treatments addressing the CNS sensitization, for example, serotonin and norepinephrine reuptake inhibitors that can exert a regulating influence on the CNS. Decreased CNS

sensitization would allow a person to initiate and engage in graded activity treatment and maximize its effect, while CBT would reduce somatic symptom focus and fear-provoking cognitions concerning exercise and activity.

Nijs and colleagues referred to Brosschot's (2002) concept of cognitive-emotional sensitisation. Brosschot mapped cognitive sensitization, which he equated to the concept of cognitive bias in cognitive psychology, onto the physiological sensitization. Cognitive bias is preferential processing of information deemed important, for example any information made salient by current fears and worries. The physiological neuronal sensitization happens because neural networks are strengthened each time fear-related stimuli are processed. These neural networks are therefore being sensitized to certain types of information, which leads to increased focus on somatic sensations and interpretation of ambiguous sensations as physical symptoms of serious illness (Brosschot, 2002; Brosschot, Pieper, & Thayer, 2005).

Brosschot (2002) emphasised fear and worry as the core features in the effect of cognitive bias on coping behaviour in medically unexplained symptoms, such as CFS. Fear about one's health and about illness sensitizes cognitive systems (attention, interpretation, and memory processes), gearing them towards constant vigilance for illness-related information. Emotional arousal (for example the distress due to symptoms or the anxiety over the seriousness of the illness) would alert the system even more towards monitoring for health-threat (Brosschot, 2002).

This state of vigilance manifests itself as a permanent state of worry about health and of rumination about the illness condition. This state increases sensitivity to potential health-threat and enhances attentional focus, the tendency to make threatening interpretations of ambiguity, and memory for illness-related information (Brosschot et al., 2005). The resulting behavioural choice for people with CFS, then, would be avoidance of exertion and activity, due to increased fear of pain, symptom exacerbation, escalating fatigue and ill-health (Brosschot, 2002). Also, avoidant coping was found to be associated with a higher perception of fatigue and reduced physical and mental functioning, therefore making it all the more likely to contribute to symptom perpetuation (Afari & Buchwald, 2003). The research focus, then, moves towards investigating the potential mechanisms of CFS perpetuation where the cognitive processing of fatigue and pain may play a central role in maintaining fear cognitions that lead to reduction in activity and increase in fatigue.

Cognitive Approach: the Mind leading the Body

Early incarnations of cognitive-behavioural theories of CFS took into account the potential interaction between the organic cause (for example, a viral infection), an individual's negative psychological reaction to illness, and their behavioural coping strategies, which would together result in perpetuation of the fatigue (Wessely, Butler, Chalder, & David, 1991). Cognitive theories of CFS emphasise the role of cognitive-behavioural factors, firstly in the onset and perpetuation of CFS symptoms; secondly, in the observed discrepancy between the subjective reports and the objective measures of functioning; and thirdly, in influencing the outcomes of CBT and GET treatments of CFS.

Symptom Focus and Somatic Interpretation

Somatic amplification is one of the core concepts of the cognitive approach to explaining CFS, and is described as a 'tendency to experience somatic sensation as intense, noxious, and disturbing' (Barsky, Goodson, Lane, & Cleary, 1988). Its essential features include hypervigilance towards, and attentional focus on, somatic symptoms, preferential cognitive processing of potential health-threat, interpretation of ambiguous sensations as illness symptoms, and attribution of somatic sensations to underlying physical illness. Negative mood and catastrophising illness cognitions further add to the amplification of symptom sensations. Thereby, somatic amplification is thought to explain the persistence of functional somatic syndromes (CFS, Irritable Bowel Syndrome (IBS), fibromyalgia) in the absence of organic abnormalities (Barsky & Borus, 1999). Therefore, monitoring of the internal state and the environment and perception of body and behaviour are the central processes that need empirical investigation to test the model of somatic amplification. The link between heightened self-focus, catastrophising, avoidant coping strategies and increase in symptom severity has received support through empirical testing (Dendy, Cooper, & Sharpe, 2001; Moss-Morris & Petrie, 2001; Petrie, Moss-Morris, & Weinman, 1995).

Moss-Morris (2005) discussed how illness perceptions can guide the information processing in CFS. Illness perceptions consist of beliefs about causes of illness, perceived control over it, its curability, duration, severity and impact, in accordance with the Common-Sense model (Leventhal, Brissette, & Leventhal, 2003; Leventhal, Meyer, & Nerenz, 1980). After reviewing empirical research, two specific illness perceptions were identified as contributing to greater impairment in CFS: 1) illness identity, specifically labelling it as physical illness, and 2) beliefs that the illness has serious consequences (Moss-Morris, 2005). Negative illness schema consisting of beliefs that the illness is serious, severe, long-term and

is caused by a biological agent (a virus) directs the information processing. In this way, attention is focused on the body and cognitive resources are spent on processing the information pertaining to somatic sensations. These sensations are interpreted as illness symptoms and attributed to the perceived cause of the illness, for example an on-going viral infection. That negative illness schema can maintain and perpetuate CFS symptoms by guiding the attention and maintaining the state of somatic hypervigilance (Moss-Morris, 2005). Somatic hypervigilance may be described as an increased attentional focus on body sensations and physical symptoms. The important role of heightened attention in CFS is supported by the evidence that decreased focus on the symptoms was found to be the mechanism that led to decrease in fatigue, rather than enhanced physical fitness or increase in activity, as reported in a randomized controlled trial of GET in CFS and mediation analyses (Moss-Morris, Sharon, Tobin, & Baldi, 2005; Wiborg, Knoop, Prins, & Bleijenberg, 2011; Wiborg, Knoop, Stulemeijer, Prins, & Bleijenberg, 2010).

On the assumption that human attentional capacity is limited, Moss-Morris (2005) proposed that hypervigilance towards symptoms can overwhelm attentional capacity, leaving fewer cognitive resources, which would compromise cognitive functioning and make an individual hyper aware of their symptoms. Therefore, the information processing characteristics of people with CFS in terms of attention to, and interpretation of, body signs, somatic sensations, and emotions are central to the CFS symptom perpetuation and disability. Empirical evidence also supports the presence of distortions and biases in cognitive processing in CFS, such as interpretation of ambiguous information as somatic (DiClementi, Schmaling, & Jones, 2001; Moss-Morris & Petrie, 2003) and attentional biases towards health-threat (Hou, Moss-Morris, Bradley, Peveler, & Mogg, 2008; Hou et al., 2014).

The negative illness schema can also influence the choice of general coping strategies for dealing with illness, such as avoidance, denial and disengagement, as well as the specific coping strategies for managing CFS. These specific strategies include avoidance of activity due to a heightened fear of negative consequences of activity, for example fatigue exacerbation or experience of post-exertional malaise (Petrie et al., 1995; Silver et al., 2002). Change in negative beliefs about activity and its consequences lead to the reduction in fatigue severity and functional impairment (Deale, Chalder, Marks, & Wessely, 1997; Deale, Chalder, & Wessely, 1998).

Noting that people with CFS are not uniform in their response, Moss-Morris (2005) identified two groups of differing patterns of behaviour. In one group the behaviour is predominantly passive and they are avoidant of activity. The second group exhibits active

and all-or-nothing behaviour (the Boom and Bust cycle), where periods of extreme activity alternate with periods of physical disability post-activity. The passive behaviour pattern, due to negative illness beliefs and avoidance of activity, leads to greater overall disability. The all-or-nothing pattern, due to more erratic activity patterns and attributions of symptoms to physical illness, leads to greater fatigue. Both groups, passive and all-or-nothing, are characterized by heightened attention to symptoms and symptom concerns, and avoidance of activity, and resulting deconditioning leading to higher disability. The two patterns were targeted in treatment trials, which included initiation of a graded activity for the passive group, and orientation towards more balanced activity for the active group. Both treatment types resulted in similar outcomes, namely reduced fatigue and increased functioning (Bazelmans, Prins, & Bleijenberg, 2006; Stulemeijer, de Jong, Fiselier, Hoogveld, & Bleijenberg, 2005).

Somatic amplification may help explain the persistence and maintenance of symptoms, but not necessarily their origin and onset (Surawy et al., 1995). Surawy and colleagues (1995) proposed a detailed cognitive-behavioural model of CFS based on the studies of cognitive styles exhibited by people with CFS. The theory tracks the development of CFS from predisposing factors (personality type, an achievement oriented view of self and others, overactive and stressful lifestyle) to precipitating factors (illness, trauma, psychosocial stress), which interact with each other and maladaptive coping responses leading to CFS onset. Individuals perceive that fatigue is brought on by activity, and their the chosen behavioural response is avoidance of exertion and increased inactivity. Resulting deconditioning leads to physiological changes in muscle functioning and metabolism, which are followed by further reduction in activity and escalating fatigue and pain. On the cognitive level, beliefs in the seriousness of illness, the focus on disease, somatic attributions, catastrophising cognitions, and fear of symptom exacerbation lead to abrupt reduction in activity. However, in adopting an avoidant coping style, people may experience conflicts motivated by personality, self-view, and concepts of self-efficacy, and therefore attempt to return to premorbid levels of functioning before recovery is complete. They would, then, push past their current physiological limit in a sudden burst of activity, which amplifies symptoms, illness experience, emotional distress, and frustration (Surawy et al., 1995).

Developing the concept of deconditioning further, Clark and White (2005) proposed that the reversible process of deconditioning perpetuates the symptoms of fatigue, and this is the theoretical model which is the basis for GET intervention for CFS. It postulates that individuals with CFS feel fatigued after a minimal amount of activity (why they feel fatigue in

such disproportion to exertion can be explained by the above model by Moss-Morris (2005) in conjunction with other cognitive theories of CFS, that is the heightened attention to somatic sensations leading to somatic amplification). Due to elevated feelings of fatigue, individuals avoid further physical activity, because of the fear of symptom exacerbation. The consequence of such avoidance is continuing loss of fitness, which means that when they engage in physical activity again, the fatigue occurs sooner, confirming their beliefs that they are suffering from a serious physical illness. This vicious cycle perpetuates symptoms of CFS. The effects of that deconditioning can be reversed via GET, which serves as a graded exposure therapy. It starts by habituating the individual to a minimal amount of tolerable activity, and then the amount, duration and intensity of activity are increased gradually until goal fitness is achieved.

It should be noted that the model by Clark and White does not make suggestions concerning the initial causes of fatigue, but is built entirely on preventing the perpetuation of symptoms by breaking down the maintaining mechanism of avoidance and deconditioning. GET includes an explanation of the process of the treatment as part of the therapeutic process, addressing the fears of symptom exacerbations and emphasizing strategies for adherence. It was found to be more efficacious when physiological explanations of symptoms were provided alongside the exercise (Powell, Bentall, Nye, & Edwards, 2001; Powell, Bentall, Nye, & Edwards, 2004) or when people engaged in monitoring of activity by redirecting their focus from the symptoms towards objective physiological signs like heart monitoring (Moss-Morris et al., 2005).

Surawy and colleagues (1995) produced a model that gave a more detailed account of symptom onset and perpetuation, but did not explain the discrepancies observed between the subjective reports of cognitive deficits in attention, concentration and short-term memory and the absence of objectively measured cognitive deficits (Metzger & Denney, 2002) Likewise, their model did not explain the discrepancies between the self-reported physical disability and fatigue and the absence of physiological impairment or muscle abnormalities; or between the subjective reports and objective ratings of activity levels (Fry & Martin, 1996a).

Fry and Martin (1996b) expanded the cognitive model by focusing more on symptom perception, functioning, and disability. First, they suggested that cognitive processes heighten the perception of the body sensations, somatic symptoms, and severity of illness. Enhanced processing and overperception of exertion and body sensations sustain the beliefs in the seriousness of the illness and influence the choice of coping behaviours, for example

avoidance of activity, followed by further deconditioning and greater sensation of fatigue, confirming the perception of severe illness. Second, Fry and Martin speculated that people with CFS might have unrealistically high expectations of the regular levels of functioning in healthy people and of their own. Therefore, the model emphasized the possible distortions in cognitive processes that give rise to unrealistic expectations and illness cognitions. The account relied on the key empirical finding that activity levels of children with CFS as reported by the children themselves and by their parents were significantly lower than those observed via objective measurement by using electronic activity monitor (Fry & Martin, 1996a). In the area of cognitive functioning, Metzger and Denney (2002) observed a similar pattern, where the group with CFS showed unrealistically high expectations of the performance of healthy people and a consistent underestimation of their own performance. Greater discrepancy in those expectations was related to higher ratings of mental effort and fatigue (Metzger & Denney, 2002).

Given the link between the distorted perception of functioning levels and illness beliefs, Vercoulen et al. (1998) presented a statistically tested model of fatigue persistence in CFS. One of the arms of the model incorporated the increased focus on symptoms, which directly led to impaired functioning and elevated fatigue. The other two arms included 1) the low sense of control over symptoms directly leading to increased fatigue, and 2) the causal attributions of somatic sensations to the on-going illness (as opposed to normalizing attribution to deconditioning, or psychological attributions to current stress) indirectly leading to increased fatigue via a reduction in activity. Therefore, increased attentional focus on somatic sensations and interpreting them as symptoms of illness are hypothesized to be at the heart of maladaptive illness beliefs that result in maladaptive behavioural responses, like activity reduction, that lead to symptom perpetuation (Vercoulen et al., 1998).

The complexity of theoretical models grows in order to incorporate new information from the empirical studies and to account for the interactive processes implicated in the illness onset and maintenance. According to the Self-Regulation theory by Leventhal, Weinman, Leventhal, and Phillips (2008) the cognitive-emotional representations of the illness and symptoms, and consequently the cognitive processes that underpin them, determine the choice of responses to stress and illness, which in turn lead to health outcomes. These outcomes are interpreted through the system of existing illness representations. Therefore, the organism is constantly monitoring the internal and external environment for information, and modifying and adjusting behaviour on the basis of the

cognitive emotional representations of that information in order to deal with threat in the most effective way and either maintain or restore health (Leventhal et al., 2003).

Within the framework of Self-Regulation theory, a recent multifactorial model tried to integrate and organize multiple processes perpetuating CFS (Deary et al., 2007). To summarize, a combination of genetic, developmental, personality, cognitive and behavioural factors place individuals at risk of developing CFS. An acute illness, trauma and psycho-social stress lead to the onset of illness. Then an interaction of physiological changes, illness cognitions, worry and rumination, biased cognitive processes, maladaptive behaviours, chronic emotional distress, and social factors create a vicious cycle that traps the individual in prolonged physical and psychological distress.

The problem with conceptually integrative models is that they become too broad and unwieldy, and due to the logistical constraints of research (small sample sizes, access to populations, statistical power considerations), they become difficult to test, especially in CFS, where it is the interactions of processes that are of particular interest. Within the broad structure of Self-Regulation Theory, the research can focus on specific factors and mechanisms that regulate relationship between cognitive processes and illness representations that give rise to them. Knoop et al. (2010) identified three specific cognitive processes hypothesized to be responsible for CFS symptom perpetuation. One involves negative cognitive representations of fatigue as the central feature of CFS. A second concerns the attentional focus on fatigue that may lead to the amplification of symptom sensations. The third includes negative cognitions about the role of activity in the increase of fatigue severity that result in avoidance and reduction of activity. Models proposing that symptom focus and fear cognitions leading to activity avoidance may perpetuate CFS symptoms received support from the empirical literature. Mediation analysis of treatment trials suggested that reduced symptom focus (Moss-Morris et al., 2005; Wiborg et al., 2011) and change in fear avoidance beliefs (Chalder, Goldsmith, White, Sharpe, & Pickles, 2015; Stahl, Rimes, & Chalder, 2013) were the mechanisms behind decreased fatigue and improved functioning.

Treatment

Central to the debates surrounding CFS is the question of the effectiveness and the suitability of currently offered treatments, and particularly the role of exercise. Graded Exercise Therapy (GET) is one of the choice treatments for CFS (NICE, 2007; Smith et al., 2015; White et al., 2011). However, a number of researchers, clinicians and patients argue

that GET may be harmful to those individuals whose fatigue is extremely severe and who experience an exertion (cognitive or physical) intolerance (Action for M.E., 2008; Lancet, 2011; Morris & Maes, 2013a, 2013b). Meanwhile an analysis of the results of treatment trials showed little evidence of GET being harmful (Smith et al., 2015). Morris and Maes (2013a, 2013b) claimed that the way to recovery is through reduction in activity. GET, in contrast, involves a gradual increase in activity with the aim to reverse the effects of deconditioning.

There is accumulating evidence of the efficacy and effectiveness of the psychological and behavioural interventions, generally represented by Cognitive-Behavioural Therapy (CBT) and GET, as compared to pharmacological and immunological treatments, adaptive pacing, specialist medical care, education and counselling (Afari & Buchwald, 2003; Friedberg, 2010; Malouff, Thorsteinsson, Rooke, Bhullar, & Schutte, 2008; Smith et al., 2015; White et al., 2011). CBT and GET appear to be comparable treatments reporting no significant differences in their effects; both produce substantial reduction in fatigue. Long-term follow up also suggests that CBT continues to exert positive effect – albeit the evidence is scarce (Deale, Husain, Chalder, & Wessely, 2001). In spite of that, there is a continuing Mind/Body, psychological/biomedical standoff in the debate over the results of trials, often stemming from the same misconceptions, misunderstandings, and misuse of methods and evidence.

The PACE trial provided recent evidence of the effectiveness of CBT and GET, compared to adaptive pacing or specialist medical care (White et al., 2013; White et al., 2011; White et al., 2007). The three treatments, CBT, GET, and Pacing, map onto a range of the theories of causal and perpetuating mechanisms of CFS, as discussed above. CBT targets cognitive factors, such as negative illness beliefs, symptom focus, fear of activity and activity avoidance (Knoop et al., 2010; Moss-Morris, 2005; Nijs, Meeus, Heins, et al., 2012; Surawy et al., 1995) and behavioural processes allowing participants to plan gradual increases in mental/physical activity. GET focuses on exercise intolerance and reversible physiological deconditioning due to activity avoidance (Clark & White, 2005). It involves planning and executing a gradual increase in physical activity, using established heart rate ranges to monitor exertion to prevent over-exercising. Adaptive pacing aims to moderate the activity amount within a limited energy envelope that results from presupposed organic cause of CFS (Jason, 2008; Jason, Brown, Brown, et al., 2013). Pacing tries to establish an adaptive cycle of activity and rest in order to prevent depletion of energy.

In spite of reports of harmful effects or non-effects of CBT and GET (Action for ME 2001; 2008), the PACE trial participants expressed similar levels of satisfaction with CBT, GET, and pacing. 84% regarded GET treatment as logical, which was the same as for pacing, and 70% were confident about it, again similar to pacing (72%). Drop out rates were also similar for all treatment groups, in the range of 6% for GET to the highest of 11% for CBT. Informatively, a comparable trial of physical activity intervention for healthy sedentary adults aged 45-74 recorded only 25 percent of participants completing the trial (Stevens, Hillsdon, Thorogood, & McArdle, 1998). A systematic review of physical activity interventions among cancer survivors showed the average drop-out rates at follow-up to be 11.2% (Speck, Courneya, Masse, Duval, & Schmitz, 2010). These data showed that compared to healthy and other illness populations, CFS groups perform similarly when it comes to adhering to physical activity intervention, which supports the notion that it is unlikely that exercise-based treatments are more harmful or less beneficial for CFS individuals than they are for either healthy ageing people or those with other fatiguing illnesses, such as cancer.

In terms of two main outcomes of the PACE trial, fatigue and physical function, participants benefited from GET and CBT significantly more than from adaptive pacing and specialist care. Participants were assessed as far into the future as 52 weeks, and their functioning and fatigue levels retained the effects of CBT and GET, which demonstrated it continued to be effective after the completion (White et al., 2013). Importantly, the results did not show worsening of symptoms, thus again undermining the criticism of behavioural treatments by the supporters of the organic ME model (Maes & Twisk, 2010a, 2010b; Twisk & Maes, 2008). Notably, the researchers measured adverse events and reactions, and found little evidence of serious adverse effects or deterioration in health in response to treatments. As for non-serious adverse events (with a very broad definition that encompassed any clinical change, disease, or disorder reported, whether or not related to treatment), there were fewer in the CBT group than in the adaptive pacing or specialist care groups. The trial also compared the results of participants who met the Oxford 1991 criteria, London 1994, and the International CFS Study group (Reeves et al., 2003), finding that these outcomes did not differ between groups meeting different criteria. This suggests that regardless of specific differences, these various case definitions identify a population of people who can benefit from treatments such as CBT and GET.

The most recent systematic review similarly confirmed the effectiveness of cognitive-behavioural and exercise based treatments, having analysed 35 treatment trials of medication, alternative therapies, exercise, CBT, or combination of these (Smith et al.,

2015). Exercise-based trials using GET significantly improved physical function, fatigue, and work impairment. The analysis did not reveal significant differences in outcomes when trials compared GET and CBT, suggesting equivalent effects. Importantly, no significant harms were reported. Reports of adverse reactions attributed to the intervention did not differ between GET and comparison groups (usual care, pacing, or CBT), providing evidence against the argument that exercise-based treatments are harmful to individuals with more severe case of CFS (Maes & Twisk, 2010a, 2010b; Twisk & Maes, 2008).

The evidence of the effectiveness of CBT and GET has been accumulating steadily. A very broad review by Whiting et al. (2001) included any treatment of CFS, any diagnostic criteria (CFS, ME or combination terms), and randomized controlled trials (RCT) or just controlled trials. CBT (3 out of 4 RCTs) and GET (3 RCTs) more consistently showed positive effect on reducing fatigue and improving physical functioning. In comparison, the results of immunological (antibiotics and antiviral) and pharmacological (antidepressants or hormone treatments) trials were less consistent. Also, more severe adverse effects were reported for immunological trials and greater rates of withdrawal from studies due to side effects. Problematically, CBT and GET trials suffered higher drop-out rates, 19% and 18% respectively, than pharmacological and other types, 11% and 8% respectively. Importantly, none of the CBT or GET trials reported negative outcomes, such as the ones where the treatment group would get worse compared to the control group.

The review by Chambers, Bagnall, Hempel, and Forbes (2006) included randomized and non-randomised trials looking for evidence of the effectiveness of not only single types of treatment but also combination treatments. Conclusive evidence was gathered for the positive effect of GET and CBT on reducing fatigue and improving physical function. However, GET trials did not include severely affected individuals. This is a widespread criticism of GET and CBT trials: that they exclude severely affected populations, and this suggests that results would not be generalizable to those populations. However, this limitation is not unique to GET and CBT trials. All treatment trials, and the research on CFS in general, suffer from that limitation. While a number of GET and CBT RCTs showed high withdrawal rates, those rates were similar for all groups within trials and were not higher than in alternative treatments (Chambers et al., 2006). Reasons for withdrawals were not reported, and therefore we cannot judge if and how they were related to adverse events or effects.

An updated review continued to report on the significant positive effect of CBT and GET on the symptoms of fatigue and physical functioning, while immunological treatments

had positive outcomes but more adverse effects (Bagnall, Hempel, Chambers, Orton, & Forbes, 2007). Dropout rates for GET/CBT were higher, but adverse effects reported in immunological and pharmacological treatments were more severe. However, adverse reactions to drugs can be more evident and therefore more measurable than adverse effects of psycho-behavioural treatments, where it is harder to judge whether such adverse effects are due to treatment. That may explain a more consistent reporting of adverse effects in immuno- and pharmacological trials. The review again noted lack of involvement in trials of severely affected CFS individuals. However, the questions that remain unanswered concern the exact proportion of the severely affected individuals in relation to the whole CFS population, and the proportions of that population who do not participate due to the severity of their condition or due to a lack of belief in the treatment.

Price, Mitchell, Tidy, and Hunot (2008) Cochrane database review found significant positive effect of CBT leading to reduced fatigue and improved physical functioning, with secondary effects of decreased depression, anxiety, and psychological distress; this review included 15 randomised controlled trials with 1,043 participants and the follow-up data for up to 8 months. Notably, CBT that incorporated increase in activity as part of the intervention had a greater positive effect, compared to usual care and CBT without the activity component.

Meta-analysis of 13 RCTs recorded drop-out rates in the range of 0-42% with a mean of 12%, among a total of 1371 participants involved in treatments that had a cognitive and/or behavioural emphasis, as compared to control participants on waiting lists, taking treatment as usual, or stretching/relaxation (Malouff et al., 2008); these drop-out rates were in line with other reviews. Effect sizes for the 13 trials ranged from 0.23 (small) to 1.67 (high). Two trials had negative effect sizes, -0.04 and -0.06; however their samples were of chronic fatigue groups rather than CFS. The overall effect size was d = 0.48 showing a significant difference between CBT and control groups, indicating considerably reduced fatigue levels following CBT.

Cochrane systematic review (Edmonds et al., 2004) and its recent update (Larun, Brurberg, Odgaard-Jensen, & Price, 2015) of RCTs of exercise-based treatments only included 336 participants. Trials compared exercise to relaxation, to antidepressant medication (fluoxetine), and to combination therapies (exercise alone vs exercise and pharmacological or education). Exercise-based trials significantly reduced fatigue and improved physical function and sleep. Serious adverse effects were rare, however conclusions on adverse effects were tentative due to a lack of detailed data. Exercise trials

suffered from high withdrawal rates, although comparison interventions suffered from similar withdrawal rates. More importantly, no evidence was found of exercise producing harmful effects.

Summary of Causes/Treatment

Though the evidence for the positive effects of CBT and GET (as based on cognitive-behavioural theories) is substantial and growing, it is accompanied by controversies (Lancet, 2011). Theoretical approaches emphasizing the role of psychological factors, cognitions and behaviours, have led to prolonged and heated debates within research, clinical and patient communities on the aetiology of CFS and the best treatments for it (Van der Meer & Lloyd, 2012). It may appear that the goal of understanding the nature of fatigue in CFS would be regarded by some researchers, clinicians and patient groups as a fruitless search for managing the symptom rather than the cause. The argument presented by patients is that while fatigue is the main symptom it is not all there is to the condition. Therefore, the name CFS is perceived as inappropriate because it emphasizes the fatigue rather than the physically debilitating nature of the condition (Picariello et al., 2015). However, having considered that, fatigue is the core symptom of all case definitions, be they CFS, ME, ME/CFS or CFS/ME, and no person can be diagnosed without presenting with prolonged profound severe fatigue. Therefore, it would be crucial to understand the nature of the phenomenon of the extreme fatigue, which is the defining feature of the condition.

The final problem is the lack of agreement on what would constitute a cure for CFS, on how best to measure the health outcomes, and on what magnitude of improvement is to be expected post treatment. These outcomes are measured through the improvement in physical and mental function, the reduction in fatigue, the increase in activity, the return to premorbid level of functioning (Prins et al., 2006). The PACE trial has used reliable and well-validated tools to measure the change in fatigue and physical function score; these are the Chalder Fatigue questionnaire (Chalder et al., 1993) and Short-Form-36 subscale (McHorney, Ware, & Raczek, 1993; Ware & Sherbourne, 1992) respectively. These two outcomes map directly onto the primary symptoms of CFS, extreme fatigue and reduction in activity, and therefore would be the essential outcomes to assess when investigating treatment effects. However, the PACE trial was being criticized by patient groups and ME-based researchers precisely on the basis of their definition of the outcomes (Stouten et al., 2011). The problem is that they don't provide feasible alternative solutions, and therefore the debate appears to be at a standstill.

The success of CBT as an intervention does not necessarily imply a psychological cause of CFS, or even a psychiatric nature of the illness. Yet, the presence and impact of psychiatric comorbidity in CFS is high, and the evidence-based cognitive-behavioural interventions were found to be effective in improving the outcomes of medical disorders in general (McCombie, Gearry, Andrews, Mikocka-Walus, & Mulder, 2015). Given these factors, it is important to consider the role that cognition, mood, and behaviour may play in the perpetuation of CFS symptoms, aiding recovery, lifting the burden of disease and improving quality of life.

Behavioural processes, such as the nature of activity and rest cycles, exercise habits, daily planning, and recovery patterns, may determine the success of psychological interventions and improvement in health outcomes (Bazelmans et al., 2006). Furthermore, there are recent reports of positive outcomes in CFS after Mindfulness training, such as reduction in fatigue, depression, catastrophic thinking and all-or-nothing behaviours (Rimes & Wingrove, 2013; Surawy, Roberts, & Silver, 2005). Mindfulness is a treatment that involves attending to current sensations, thoughts, and emotions but in a more observational fashion, without judgment and without attempts at change or avoidance (Rimes & Wingrove, 2013; Surawy et al., 2005). The outcomes of Mindfulness trials further indicated that the cognitive processes of attention and interpretation might play a vital role in symptom reduction and recovering from CFS.

In light of the above review, the purpose of the empirical studies described in this thesis was to investigate the cognitive processes implicated in the onset and perpetuation of CFS. These studies aimed to contribute evidence for the cognitive-behavioural theories of CFS, and specifically they aimed to provide more detailed understanding of the enhanced processing of information related to illness and symptoms. The first process under investigation was attentional processing of stimuli that contained information about symptoms, body, and activity. The second process investigated was interpretation of ambiguous information and somatic sensations, to explore whether individuals with CFS have a dominant cognitive style of somatic and illness-related interpretation of ambiguous information. The final study examined the properties of memory for illness-related information.

The overall aim was to provide empirical evidence for the presence of enhanced cognitive processing, a cognitive bias for illness-related information, and amplified perception of health-, illness-, and body-related information in people with CFS. The theoretical aim was to argue that the processes of voluntary over-monitoring and conscious and preconscious over-perception, exemplified by the biased attention, health-threatening

interpretation, and enhanced memory processing, were the processes perpetuating the symptoms of CFS, fitting with the cognitive models of this enigmatic illness. The thesis aimed to contribute to further refinement of CBT and GET interventions for CFS, by elucidating the role of the cognitive processes that may help form and maintain maladaptive cognitions and underpin avoidant behaviours and coping strategies.

Cognitive nature of CFS

The multifaceted nature of CFS presents the challenge of disentangling the unique contribution of physiological, cognitive, emotional, and behavioural factors, but also understanding the nature of their interactions in determining the course of the illness and its outcomes. This thesis aimed to investigate the nature of the interaction of cognitive and emotional processes in CFS, in order to understand their roles in symptom perpetuation.

Cognitive and emotional mechanisms are two of the key dimensions impaired in people with CFS (Hickie et al., 2009; Nisenbaum, Reyes, Unger, & Reeves, 2004). The evidence suggests that impaired attention is one of the core cognitive deficits and the observed impairment of other psychological processes stem from the initial disordered attentional process (Dickson, Toft, & O'Carroll, 2009), particularly sustained attention (Capuron et al., 2006). Meta-analysis of studies of cognitive deficits in CFS identified consistent impairments in the speed of information processing and aspects of attention, but no deficits in verbal, spatial-visual, and cognitive reasoning abilities (Cockshell & Mathias, 2010). Most components of memory (recognition, long-term storage) also appear unaffected (Tiersky, Johnson, Lange, Natelson, & DeLuca, 1997).

Self-reported cognitive deficits are associated with negative mood, emotional distress, and fatigue, but in comparison with objective neurocognitive tests, self-reports seem to overestimate the degree of cognitive impairment (Moss-Morris, Petrie, Large, & Kydd, 1996). However, cognitive deficits in the speed of processing were shown to be independent of psychological comorbidities, such as depression (DeLuca et al., 2004; DeLuca, Johnson, Ellis, & Natelson, 1997; Michiels & Cluydts, 2001; Short, McCabe, & Tooley, 2002). Additionally, the discrepancy between the subjective reports and objective measures of cognitive function may be in part due to the greater degree of variation in performance of people with CFS if measured over time (Fuentes, Hunter, Strauss, & Hultsch, 2001).

Brain imaging studies provide additional evidence for the slowed down and inconsistent cognitive response in CFS. The observed pattern of activation of the cerebral regions suggested that impaired movement planning and motor responses of people with

CFS may be compensated for by utilizing other non-impaired regions, such as visual processing areas (de Lange et al., 2004). A similar pattern was present in a brain imaging study of complex auditory processing, in which people with CFS utilized more extensive brain areas and recruited working memory regions to aid in the processing of auditory stimuli (Lange et al., 2005). This use of additional resources may underpin escalation of mental fatigue, which consequently affects performance, and also may explain the discrepancy between the self-reported cognitive deficits and their objective measurements (Lange et al., 2005). When fatigue was induced in healthy and in CFS groups by a complex visual search task, both of them showed a reduction in responses in the regions involved in the task but only the CFS group demonstrated additional weakened activity in regions unrelated to the task (Tanaka et al., 2006). Likewise, Barnden et al. (2011) demonstrated evidence of midbrain dysfunction and impairments in feedback loops and regulatory mechanisms, which may underlie the cognitive deficits in CFS. The above review of brain imaging evidence suggests that impairments in brain control mechanisms in CFS may underpin the increase in mental fatigue. Under the demands of increasing task difficulty, more non-task specific resources are utilized in order to continue performance, but the reduced functioning of those task irrelevant resources and impaired regulatory processes result in slowed and inconsistent performance.

People with CFS demonstrated cognitive volatility over time, slowed information processing speed, and difficulties on attentional tasks that involved fast and complex visual search and sustained focus, which were independent of other psychological variables but might have been influenced by increasing levels of mental fatigue (Michiels & Cluydts, 2001). This is important to consider when implementing objective measures of attention, interpretation, or memory with a goal of finding evidence for a cognitive bias – that is to say, a marked preference for processing one type of information over others. Therefore, the current studies of attention, interpretation and memory took into account task difficulty and increased cognitive burden, and the results were considered in the context of potential cognitive deficits in CFS.

Attention

The role of attention is to monitor the environment in order to detect novel events, which is a first step in the overall process of evaluation, judgement, decision-making, and determining the final action in response to the environmental stimuli. The environment can be external: the surrounding world, events, and people. It can also be internal, in the form of

physiological, affective, and cognitive states. The monitoring of physiological, cognitive, and emotional states is part of a self-directed attentional process. External and internal monitoring for health-threat with the aims of detecting symptoms of illness, disturbances in regular functioning, or injuries can be advantageous. This monitoring process may aid in the early detection of a health problem and help make coping decisions and determine actions necessary to deal with the problem before it escalates. In this case, under-monitoring may result in a failure to detect early signs of illness, of exhaustion, or distress, leading to the failure to engage in either preventive action or early stage coping to prevent escalation. On the other, hand over-monitoring, or an oversensitivity and heightened focus on negative information at the expense of alternative stimuli, may turn the adaptive monitoring into a process wrought with anxiety, fear, panic, depression, denial, catastrophising, and hopelessness.

Hadjistavropoulos, Craig, and Hadjistavropoulos (1998) explored how individuals with low and high health-related anxiety responded to the same external stimuli. The group high in health anxiety reported a focus on the negative information, catastrophic cognitions, and amplification of unpleasant sensations – negative somatic monitoring. On the contrary, the low anxiety group reported a monitoring strategy that involved detection and attention to concrete physical sensations in a neutral, elaborative and meaningful manner – positive somatic monitoring. In a similar vein, men with HIV and women with cervical dysplasia demonstrated greater catastrophic and negative beliefs and consequent avoidant coping if they showed high monitoring tendencies (Miller, Rodoletz, Mangan, Schroeder, & Sedlacek, 1996). Conversely, self-monitoring was found to be a protective and adaptive strategy in diabetes (O'Kane, Bunting, Copeland, Coates, & group, 2008) and weight control (Baker & Kirschenbaum, 1993).

Thus, monitoring, internally and externally, would be a particularly important process in CFS, a long-term intermittent illness, with unclear causes and undetermined prognosis. Attention is the initial step in that monitoring process, and involves numerous elements: detection and engagement with potential health-threat; the maintenance of attentional focus; and the ability to shift and switch attention between various internal and external stimuli to gather as much of the information as possible in order to make the most informed and appropriate choice of coping strategy.

Logically, the experimental paradigms and theoretical models of the attentional process have been most developed in anxiety research, particularly in identifying two aspects of selective attention: hypervigilance and difficulty in disengagement (Koster,

Crombez, Verschuere, & De Houwer, 2004; Koster, Crombez, Verschuere, Van Damme, & Wiersema, 2006). Hypervigilance refers to over-monitoring, a state of constant alertness, and selective focus on threat or negative information over neutral or positive. Difficulty in disengagement defines an impairment in the shifting of attention from one event to another, meaning a prolonged attentional dwelling on threat (Koster et al., 2006; Mathews & MacLeod, 2005). The two concepts of interest reflect separate stages of attentional processing defined as attentional orienting, capture or engagement, and secondly, disengagement or shift towards a different information source (Posner & Petersen, 1990).

Experimental paradigms that assess the course of attention include the modified Stroop, the visual probe, and spatial cueing tasks. The advantage of those tasks is the objective assessment of selective attentional processing of threat by measuring the degree of interference that task irrelevant threat-related stimuli has on task performance, therefore preventing the influence of response bias (MacLeod, Mathews, & Tata, 1986). The modified emotional Stroop task involves naming the colour of words that vary in emotional meaning. It is hypothesised that if the words were threatening (pain, illness, death) then it would slow down the colour naming. Thus, the magnitude of response latencies demonstrates presence or absence of selective attention to threat. If participants are slower to colour-name threat words as opposed to neutral or positive words, then the biased attention towards threat is inferred (Mathews & MacLeod, 2005).

In health research, studies that used the Stroop task demonstrated that individuals who experienced recent minor illness were slower to colour-name words related to illness and health than general threat or neutral stimuli (Karademas, Sideridis, & Kafetsios, 2008). People with asthma showed interference with asthma-related words, but not general negative words (Jessop, Rutter, Sharma, & Albery, 2004; Martinez-Moragon, Perpina, Belloch, de Diego, & Martinez-Frances, 2003). Individuals experiencing chronic pain also showed interference on a Stroop task with affective and physical pain words (Pincus & Morley, 2001; Roelofs, Peters, Zeegers, & Vlaeyen, 2002). Although, later studies failed to demonstrate Stroop interference for pain words therefore the findings from Stroop are inconclusive (Andersson & Haldrup, 2003).

Attentional bias to somatic content in CFS was investigated by Moss-Morris and Petrie (2003), using an unmasked Stroop task, but provided no supporting evidence for the selective attention in people with CFS. The researchers measured colour-naming latencies of somatic words compared with neutral or depressed words, hypothesising that somatic stimuli would be more distracting for participants with CFS and hence resulting in longer

colour naming times, because the illness-related somatic information was expected to command their attentional resources. The long presentation of the words in an unmasked Stroop is thought to measure higher order strategic or conscious attentional processing (Mogg, Bradley, de Bono, & Painter, 1997).

Experiments using masked modified Stroop tasks (whose brief stimuli presentation times allow the measurement of preconscious automatic processing) demonstrated attentional bias in conditions such as anxiety (Mogg, Bradley, Millar, & White, 1995), phobia (van den Hout, Tenney, Huygens, & de Jong, 1997), IBS (Afzal, Potokar, Probert, & Munafo, 2006), and asthma (Martinez-Moragon et al., 2003). Therefore, according to the hypervigilance hypothesis in CFS the attentional bias may manifest at the preconscious automatic attentional stage, reflecting early orientation of attention towards threat, and may not necessarily be evident at the later elaborative stage that was measured by Moss-Morris and Petrie (2003).

One of the problems identified with the Stroop task is that it involves both early and late stages of processing, which makes it difficult to separate the interference with the colour-naming because of attentional bias towards threat from the cognitive avoidance of unpleasant stimuli (de Ruiter & Brosschot, 1994). Masked and unmasked Stroop can assess the automatic preconscious and strategic voluntary stages, respectively (Mogg et al., 1995). However, the problem of identifying the specifics of attentional bias at different stages remains, because the difference in colour-naming latencies could result from either participants orienting faster to threat stimuli, or having difficulty, once drawn to threat, in disengaging from it (Fox, Russo, Bowles, & Dutton, 2001). Therefore, Stroop tasks would not be appropriate for testing the model of attentional vigilance to threat in CFS, which would need to be distinguished from the disengagement effect.

Another criticism of the Stroop task is that it measures emotional processing rather than visuo-spatial attention process, hence the problem of the separation of the bias effect at each attentional stage (Hou et al., 2008; Mathews & MacLeod, 2005). Asmundson, Wright and Hadjistavropoulos (2005), having compared the results of unmasked and masked modified Stroop and visual probe tasks in a study on attentional bias in chronic pain, suggested that the two paradigms may together measure different attentional phenomena, because of the lack of correlation obtained between measures on the three tasks. Consequently, employing an alternative method such as visual probe may tap into the subtleties of the attentional process among people with CFS that are not discovered by using the Stroop task (Asmundson, Wright, & Hadjistavropoulos, 2005). In line with this account, a

number of visual probe studies have demonstrated attentional bias at shorter presentation times of 100ms in anxiety (Koster et al., 2006; Mogg et al., 1997). Children with abdominal pain showed attentional bias towards pain words at the preconscious level, but avoided pain at the conscious elaborative level (Boyer et al., 2006). Recent meta-analysis of chronic pain studies using visual probe methods showed quite consistent bias towards pain stimuli (Schoth, Nunes, & Liossi, 2012). The advantage of the visual probe task is that the processes of engagement and disengagement can be distinguished, owing to the ability to measure participants' reaction times on the neutral trials and using them as a baseline for comparison (Koster et al., 2004).

In contrast to the first study of attentional bias in CFS, Hou et al. (2008) successfully obtained evidence of attentional bias towards health-threat in people with CFS, using the visual probe task. Participants were presented with pairs of health-threat and neutral words/pictures for 500ms. One half of the pair was presented in the upper half of the screen above the fixation point, and another in the lower half of the screen below the fixation point. The disappearance of the words/pictures was followed by a probe appearing in the position of one of the words/pictures, either at the top or bottom. The CFS group responded faster to a probe in the same location as the health-threat stimulus, indicating attentional preference for processing health-threat over neutral information. Similarly, in this thesis a study on attentional bias in CFS employed the visual probe task, with a detailed exploration of the processes of approach or avoidance of threat, and engagement and disengagement stages. The use of the same cognitive task would make it easier to compare the results across the studies.

However, the simultaneous presentation of the two competing stimuli and the long exposure (500ms) are thought to measure higher order, strategic information processing, and are more likely to point to difficulty in disengaging from threat (Fox et al., 2001). So the attentional bias evidence from the visual probe task does not necessarily signify that selective attention is at work at an earlier preconscious automatic stage, which would be stronger evidence for the hypervigilance hypothesis and over-monitoring tendencies. This said, eye movement studies do show evidence of quicker initial and more frequent eye movement towards the threat by the people with generalized anxiety, as compared to people with depression and health controls, thus supporting the hypervigilance hypothesis in anxiety (Mogg, Millar, & Bradley, 2000).

Fox et al. (2001) proposed that because in the visual probe task the stimuli are presented within the field of the central vision, all the stimuli in the surrounding space are

attended to at the same time. The attentional process in regards to other events in the surrounding environment, for example to the peripheral cues that are beyond the central field, is not being measured by the visual probe task. Responses on the visual probe may be subject to the influence of higher order cognitions, but an alternative exogenous cueing task would not be. In the exogenous cueing task stimuli are presented peripherally, on the left or the right side of space. Fox and colleagues considered this a more suitable method for assessing automatic orientation of attention, because the novel stimuli in the peripheral field of vision would act upon the reflexive and automatic attention. Therefore, the visual probe may successfully measure more elaborative processing of competing stimuli, but it would not be a sensitive enough measure of the early orientation and capture of attention, particularly preconscious automatic processing.

Additionally, the measurement of the engagement and disengagement of attention in the visual probe task may be obscured by the possibility of participants attending to both competing stimuli through rapid shifts of attention between them, whereas the exogenous cueing would be better at separating the components of attention and therefore measuring the attentional movement of the participants (Fox et al., 2001). The distinguishing feature of the exogenous cueing task is the presentation of a single linguistic or pictorial stimulus in one of two locations, which is then replaced by a probe either in the same location (coded as "valid") or in the other ("invalid"). The difference in reaction times, depending on the validity of trials, forms the basis for the measurement of attentional movement from orienting, to engagement, to disengagement. The facilitated response time on valid trials indicates vigilance to threat, and slowed response time on invalid trials measures disengagement from threat.

The exogenous cueing has not been used previously in the investigation of attentional bias in CFS. In studying anxiety, the task has been successfully used to provide supporting evidence for the role played by the difficulty in disengaging from threatening pictures (Fox et al., 2001). Meanwhile in IBS, the evidence from the exogenous cueing pointed towards the attentional engagement with social threat when in a state of rumination (Martin & Chapman, 2010) and the orientation of attention towards pain words (Chapman & Martin, 2011a). A study of attentional bias towards low and high-fat foods showed an attentional engagement with low-fat food among the restrictive eaters (Veenstra & de Jong, 2012). This thesis presents the first application of the exogenous cueing paradigm in the study of attentional bias in CFS. The experiment in this thesis investigated preconscious automatic

orientation of attention and the initial engagement of attention with threat, testing the hypervigilance hypothesis in CFS.

Mogg and Bradley (1999) discussed the conceptual and practical differences between a task that requires locating a probe and the task that requires identification of a type of probe. In the two attentional studies described in the thesis, the visual probe task was the probe classification task, where participants were asked to identify the type of probe (for example, right arrow or left arrow). Such a task is considered more difficult, and therefore may put higher cognitive load on a participant's limited attentional system. On the other hand, the exogenous cueing task is a direct probe position task, where participants have to locate the probe on the right or on the left by clicking on the corresponding key; therefore the task is considered easier (Mogg & Bradley, 1999). Consequently, the two tasks can measure attentional bias in CFS under two different conditions, high and low cognitive load. Increased burden on limited cognitive resources may be one of the factors that underpins selective attention to threat, overperception of symptoms and over-monitoring for threat.

In this thesis, the results of exogenous cueing and visual probe tasks were compared and discussed in the framework of high and low cognitive load. The task stimuli reflected internal and external information, such as symptom-, fatigue-, illness-, and activity-related words and pictures. The cognitive processes of attentional approach and avoidance, attentional engagement and disengagement were explored in detail, and the relationship between attentional processing, cognitive states and mood and symptoms was investigated.

Interpretation

The experience of somatic sensations, pain, fatigue, and a variety of physical symptoms (all in the context of a poorly understood illness with an unknown origin) can cause distress, unease, increased concern and worry. Fatigue itself can be interpreted in a variety of ways: as a benign symptom of tiredness and a signal for rest and need to recover, or as a symptom of an underlying serious illness, or perhaps a side effect of a treatment, medication, or substance use.

Fatigue in CFS can be interpreted as any of the above, and other physical symptoms can be regarded as the consequence of fatigue and deconditioning, or as symptoms of a serious medical condition. For example, anti-viral and anti-depressant drugs often used in the treatment of CFS have increased fatigue and drowsiness as some of the main accompanying side-effects (Chambers et al., 2006; Maquet et al., 2006; Prins et al., 2006). Patients taking medication would experience fatigue as both the main symptom of their

illness and a side-effect of the treatment. Similarly, the initial increase in activity during GET may lead to elevated sensations of fatigue before the deconditioning process is reversed and physical fitness is restored. Unplanned and unmonitored sudden increases in activity can also lead to the escalation of symptom intensity and frequency (Newton et al., 2011).

It follows that, firstly, general somatic sensations in CFS are inherently ambiguous. Secondly, over-monitoring and over perception may lead to the amplification of symptom experience and catastrophic cognitions, as well as inaccurate perception and understanding of body signs (De Peuter, Lemaigre, et al., 2007; Moss-Morris, 2005; Moss-Morris & Chalder, 2003). Such lack of a clear distinction between the physical symptoms, their origins, and their meanings may strengthen the tendency, as a precaution, to interpret somatic sensations in a catastrophic way. Sensations are perceived to be a sign of serious underlying illness, which may lead to reduced activity, deconditioning, increased fatigue and pain, decreased physical, cognitive and social functioning, and greater illness severity. Consequently, this thesis presents an empirical investigation of an interpretive bias in people with CFS.

Studies that have investigated attributional styles in CFS, mostly through self-report measures, observed a tendency to attribute a wide range of body sensations and symptoms to physical illness, accompanied by strong beliefs in the biological origin of CFS (Moss-Morris & Petrie, 2001). Similar effect has been observed in people with IBS (Crane & Martin, 2003; Martin & Crane, 2003). The above studies demonstrated that such cognitive style and illness beliefs are associated with negative health outcomes in CFS and IBS, such as perpetuation and higher severity of symptoms. The above data suggests common cognitive mechanisms underpinning symptom perception in conditions where the organic origin of symptoms is unexplained. Compared to multiple sclerosis, patients with CFS were also most likely to interpret their symptoms as indicators of physical illness, and less likely as signs of a possible psychological condition (Dendy et al., 2001). Evidence also suggests that people with CFS hold catastrophic beliefs about pain and fatigue, as associated with reduced physical functioning (Nijs, Meeus, Heins, et al., 2012; Nijs, Van de Putte, Louckx, Truijen, & De Meirleir, 2008). The findings indicate that people with CFS show preference for interpreting a variety of physical sensations, including fatigue and pain, as symptoms of a serious physical illness with which it is beyond their ability to cope.

Interpretive bias in CFS, a tendency to resolve ambiguity in an illness-related way, has been observed previously (Moss-Morris & Petrie, 2003), using the experimental method of ambiguous cueing, which also consistently demonstrated interpretive bias in chronic pain

(Edwards & Pearce, 1994; Pincus, Pearce, McClelland, Farley, & Vogel, 1994; Pincus, Pearce, & Perrott, 1996). Moss-Morris and Petrie (2003) presented healthy controls and participants with CFS with ambiguous words that have either illness-related or neutral meaning (growth - cancer, growth – tall), and asked the participants to write down the word associations that first came to mind. The CFS group generated more somatic interpretations of the ambiguous cues, compared to healthy control group. This finding provided support for the existence of enhanced cognitive processing of illness-related information and a negative illness schema in CFS (Moss-Morris, 2005). Ambiguous information about a wide range of physical sensations when filtered through such schema may be given interpretations that are illness-related and health-threatening, rather than non-illness-related and neutral. That may lead to a prolonged state of malaise, a greater degree of suffering due to symptoms, and worse health outcomes.

Evidence for interpretive bias in CFS would have important implications for CBT/GET interventions. The breakdown of cognitive processes behind the interpretation of ambiguity would enable the individual to develop in-depth understanding of the explanations they generate for their symptoms. Meanwhile, learning to distinguish between the sensations as warning signs, symptoms, or side effects of treatment would help in the planning of activity increase and the modification of maladaptive behavioural patterns.

However, to date Moss-Morris and Petrie's (2003) study appears to be the only published experimental objective investigation of the interpretive bias in CFS. So, even while the implications of the bias for CFS are potentially significant, the lack of empirical investigations holds back further development and refinement of methods of enquiry and limits understanding of the interpretation process in CFS. As we have seen this process is complex and multi-staged, beginning with the initial preferential orientation (as part of the attention process) through the preconscious and then voluntary response stages, and finally to the linking with higher order cognitions, emotional and behavioural responses, coping strategies and health outcomes.

In light of the above, the first study described in this thesis aimed to explore the early stages of attentional and interpretive bias in CFS, testing the hypothesis that there is a hypervigilance for somatic information in CFS. An interpretive bias in CFS may be a manifestation of the hypothesised negative illness schema (Moss-Morris, 2005). Within that schema over-monitoring and increased attention towards illness information may be accompanied by the tendency to interpret physical bodily sensations in a catastrophic

health-threatening fashion, which may further amplify the physiological, cognitive, and affective symptoms in CFS.

Memory

Impairment in short-term memory and concentration is one of the eight concurrent symptoms of CFS (Fukuda et al., 1994) and memory dysfunction is one of the most disabling symptoms reported by the majority of the patients (Jason, King, et al., 1999; Jason, Richman, et al., 1999). However, the Fukuda criteria specify that a minimum of four symptoms need to have been present for 6 months or more for an individual to be diagnosed with CFS. Therefore, whilst memory dysfunction is one of the accompanying symptoms, it does not need to be present for the CFS diagnosis. That may account for the conflicting and inconsistent findings surrounding memory dysfunction in CFS (Cockshell & Mathias, 2010). Methodological and statistical limitations also contribute to the problems in investigating memory processing in individuals with CFS. Additionally, the deficits are hypothesised to be subtle and pertaining to specific sub-conditions within the umbrella of CFS (Moss-Morris, Petrie, Large, et al., 1996; Tiersky et al., 1997). Cockshell and Mathias' (2010) meta-analysis of 32 studies all assessing visual, verbal, and working memory reported small effect sizes for the majority of studies, with only seven reporting medium and large sizes. The deficits seemed to affect verbal memory, immediate and delayed recall, recognition memory, and sustained effort in working memory. These deficits were independent of negative mood (Cockshell & Mathias, 2010; Dickson et al., 2009). However, long-term autobiographical memory processes in relation to health and illness have not been explored for either impairment or bias.

CFS is a long-term condition, which is also characterised by wide variability and fluctuations in functioning, fatigue levels, symptoms and mood (Fuentes et al., 2001; Sohl & Friedberg, 2008; Stone et al., 1994; Wood, Magnello, & Sharpe, 1992). As we have seen, there is strong theoretical and empirical support for the peculiarities of attentional and interpretive processes in CFS, and the arising symptomatic complications associated with those are well-documented. Putting these information processing irregularities in CFS in the context of a maladaptive illness schema, it would be expected that memory process would also be implicated in contributing to that schema (Beck & Clark, 1997). If perception and information about self, symptoms, sensations, and behaviours are filtered through a structure of negative illness representations, then the information encoded and stored would reflect the bias inherent in the illness schema.

Alternatively, biased memory processing may be the primary mechanism. In this way, it would influence the attentional focus on symptoms and fatigue, and the avoidance of activity (due to memory for previously experienced adverse effects). Biased memory processing would also distort the perception of current exertion and tiredness (by comparison with past experiences) and contribute to the formation of fear and catastrophising cognitions. Adding the effect of mood states on thoughts and behaviours, and the comorbidity of depression in CFS (Hadlandsmyth & Vowles, 2009), we would see the retrieval of memories for previous experiences of illness, activity and fatigue being further distorted by the kinds of cognitive processing observed in depression, which include preferential recall of negative information, impaired recall of positive memories, and overgeneralization of past memories (Gotlib & Joormann, 2010).

With regard to other health conditions, an investigation into the memory bias in IBS and asthma patients reported that an IBS group showed enhanced recall for gastro-intestinal sensation words, while people with asthma were more likely to recall respiratory words (Gibbs-Gallagher et al., 2001). IBS patients also showed preference in recollection of gastro-intestinal words when compared to positive and negative affect words; albeit, they did not differ in that recollection preference from patients with organic gastro-intestinal disease (Posserud, Svedlund, Wallin, & Simren, 2009). IBS patients also showed a significantly greater number of false positives (that is "recalling" gastro-intestinal words which were not originally presented) (Posserud et al., 2009).

Concerning the processing of health-threat among non-clinical populations, a study of healthy people demonstrated that they prioritised the processing and recall of the symptom and pain information that was relevant to a particular activated illness schema (Moss & DiCaccavo, 2005). Participants listened to four types of vignettes (cardiovascular, childhood illness, rheumatic, infectious diseases) that included symptom and pain information consistent and inconsistent with that particular condition, and then were tested for recall. The study showed that under high mental load people recalled pain information significantly better when it was relevant to the condition, while under low mental load no preferential recall for consistent or inconsistent information was shown. This suggests that the bias may manifest when cognitive resources are limited.

The implications for CFS are multiple. For example, the elevated mental fatigue in people with CFS already puts them in a situation of high mental load, which means that the processing of the information they encounter about their condition may be guided through such a schema that would make unhelpful shortcuts in order to conserve resources.

Furthermore, when it comes to the processing of fatigue, pain or exertion, the information consistent with active schema would be given priority. Therefore, if that schema includes fear and catastrophic beliefs, it may lead to heightened sensitivity and amplification of symptoms in accordance with cognitive models (Deary, 2008; Deary et al., 2007; Knoop et al., 2010).

The final study described in this thesis aimed to explore the illness representations in CFS by investigating the properties of autobiographical memory for illness-related information in CFS as a manifestation of enhanced processing of illness, symptom, and health-related information. Evidence for disrupted memory processing in CFS would provide support for cognitive models of illness perception in CFS, and also for theories of the operational illness schema – we recall that this schema serves to filter the processing of information by directing the attentional focus, interpretive predisposition, and the processes of memory formation and expression (Knoop et al., 2010; Moss-Morris, 2005; Surawy et al., 1995).

Comparison group: Asthma

Asthma is a respiratory disease characterized by chronic inflammation and obstruction of the airways. Its worldwide prevalence is estimated to vary between 1 and 18 percent (GINA, 2015) and UK prevalence rates fall on the higher end varying between 14 and 18 percent (Masoli, Fabian, Holt, Beasley, & Global Initiative for Asthma, 2004). Asthma is a chronic, typically life-long, condition with a widely fluctuating severity of symptoms that interfere with functioning and may be fatal, in case of a serious asthma attack, or lead to emergency medical treatment and hospitalization as well as impacting healthcare costs (Avallone & McLeish, 2013; Yii & Koh, 2013).

Asthma symptoms include shortness of breath, wheezing, lung dysfunction, chest discomfort, and coughing (GINA 2015). Asthma exacerbation and asthma attacks can be triggered by an infection, exposure to irritants, various allergens (including those in food and drink), exercise, weather, or stress (Chung et al., 1999). The illness can be asymptomatic showing good lung functioning; however the lungs of a person with asthma remain physiologically vulnerable because of continual hyper-responsiveness and inflammation of the airways. If people do not receive continuous treatment, even when they are not experiencing symptoms, the lung function can deteriorate further and increase the risk of asthma attacks (Peters, Ferguson, Deniz, & Reisner, 2006; Yii & Koh, 2013).

Asthma is diagnosed on the basis of a consistent historical pattern of symptoms featuring airflow obstruction and airway oversensitivity and inflammation (GINA, 2015). There exist a number of objective tests of lung function, in addition to validated and reliable measures of subjective symptom reporting. For example, the spirometer is a reliable tool used by health care professionals and researchers (Burton et al., 2015; Sokol, Sharma, Lin, & Goldblum, 2015), which measures the amount of exhaled air in the first second of a forced expiration (the Forced Expiratory Volume per 1 second – FEV_1) and the total amount of exhaled air (Forced Vital Capacity – FVC). The proportion of FEV_1/FVC represents lung function. Poor lung function is characterised by a disproportionately low amount of air exhaled per the first second of expiration out of the total amount of exhaled air. People with asthma can monitor their daily peak expiratory flow at home, measuring the rate at which the air is leaving the lungs (Ignacio-Garcia & Gonzalez-Santos, 1995).

There is no cure for asthma. Treatments aim to control and manage the symptoms as to allow the lungs to function at full capacity and to prevent deterioration in lung function and asthma attacks (GINA 2015). There are two main ways of treating asthma symptoms: long-term management to maintain every-day healthy lung function and short-term rapid-acting (when symptoms worsen). Inhaled corticosteroids (ICS), and less frequently oral corticosteroids, are used primarily as a long-term maintenance controller medication to reduce airway inflammation and to prevent decline in lung function and symptom exacerbations. Reliever medications, for example inhaled short-acting beta2-agonist (SABA), are rescue medication, used to provide relief from exacerbated symptoms or before exercise to prevent bronchoconstriction. They are not recommended for regular use and are as-needed medications. Therefore, excessive use of relievers is considered one of the signs of uncontrolled asthma (GINA, 2015). In spite of the effective medication that allows individuals to function close to full capacity, there are high rates of uncontrolled or partly controlled asthma (Peters et al., 2006; Thomas et al., 2009), resulting in symptom exacerbation and elevated morbidity (Humbert, Holgate, Boulet, & Bousquet, 2007).

Well-controlled asthma is defined in terms of symptom control and estimation of the future risk of exacerbations (GINA, 2015). Poorly controlled asthma would show greater than normal variations in lung function, excessive use of reliever medication for symptom relief, higher frequency of day- and night-time symptoms, or wide variation in peak expiratory flow readings.

Asthma is generally a condition that is managed by people themselves rather than by healthcare professionals (McWilliam, 2009; Newman, Steed, & Mulligan, 2008). It is

particularly important, in order to ensure well-controlled and well-managed asthma, that individuals can implement the routine use of effective and relatively non-invasive medication, and this is a process influenced by the individual's thoughts and actions (Kaptein, Klok, Moss-Morris, & Brand, 2010). Thus, one of the current research aims in asthma is to understand what cognitive and behavioural factors may influence the decisions that people make concerning management and treatment of their illness.

Asthma: The role of symptom perception

Rietveld (2003) defined symptom perception as conscious awareness of a particular symptom. According to him, two aspects make up the process of symptom perception: symptom intensity and accuracy of perception. The errors in perception of symptoms may result in under-perception, failing to detect and report symptoms in the presence of physiological dysfunction, and over-perception, reporting of symptoms when the physiological deficit is neither present nor detected (Rietveld, 2003).

Janssens and colleagues (2009) proposed that the answer to poorly controlled asthma may lie in better understanding of symptom perception and the cognitive processes behind the condition. Biases in cognition may result in the discrepancy between subjective feeling of asthma and the objective measures of lung function. Janssens and colleagues challenged the concept of over-perception or under-perception as stable characteristics, instead arguing that perceptual accuracy is determined by emotional factors, such as a high negative affect disposition or transient negative mood; and also by cognitive factors, like currently salient expectations of having symptoms; or the use of a repressive coping style. The authors described symptom perception in asthma in terms of the cognitive processes of attention to, and interpretation of, somatic sensations.

These cognitive processes may be shaped by beliefs about illness, health and body – that is to say, the illness representations that make up the illness schema, which directs and filters the information processing (Moss-Morris, 2005; Moss-Morris et al., 2002). What is to be attended to in terms of somatic sensations and how the current body state is to be interpreted depend on an individual's already formed illness beliefs. These beliefs consist of cognitive representations of illness including beliefs about illness causes, its consequences, duration and controllability and/or curability (Moss-Morris, 2005; Moss-Morris et al., 2002). Kaptein and colleagues (2010) suggested that such illness representations, directly and through the mediation of the coping strategies employed in managing asthma, may influence the outcomes. The illness outcomes in question include asthma control where

symptoms are mostly absent, activity at a regular level, fully functioning lungs, no asthma attacks, and the reliever medication not being needed (GINA, 2015; Kaptein et al., 2010).

Janssens and colleagues (2009) emphasised attentional vigilance towards somatic sensations as a key component of asthma symptom perception. They specified that the evaluation of the threat-level of a perceived sensation may determine how that sensation is interpreted, whether as an illness symptom or as a benign sensation. The direction of such evaluation in turn depends on the sources of the gathered information, which may include physiological sensations, current mood state, context and situation. How that information is processed depends on the activated illness schema, the salient mental representations of the illness and of health (Moss-Morris et al., 2002). Furthermore, the illness representations are preserved in memory, and the current situation may further reinforce the strength of such learned associations between sensory, affective and contextual cues (De Peuter, Put, et al., 2007). Symptom perception, according to Janssens and colleagues (2009), occurs if the current information fits the mental representation of asthma, and does not occur if the information does not fit; thus, they attempt to account for both the over- and under-perception of symptoms.

Asthma symptom perception is relevant to the overlapping processes of symptom control and medication adherence. In order to control symptoms, a person has to firstly detect their presence or absence, and secondly has to understand potential causes of their presence or absence, and thirdly has to make a decision to use or not use medication. For example, symptoms can be absent because lungs are functioning well, or symptoms can be absent in spite of lung dysfunction because they have not reached the personal threshold level for detection (Rietveld, 2003).

Erroneous symptom perception is one of the barriers to adherence (Bender & Bender, 2005; Blaiss et al., 2009). Should an individual fail to detect a symptom, it may lead to the belief that the condition is not severe enough to require treatment, and thus the treatment can be discontinued. In such a condition as asthma, the controller treatment needs to be maintained in order to aid functioning of the lungs and to prevent their deterioration. Therefore, such a belief would be maladaptive. On the other hand, over-perception may prevent adherence if catastrophic cognitions lead a person to believe that the treatment is not working or causing severe side-effects, leading them to purposefully discontinue the treatment.

One of the ways to achieve effective control and management of symptoms is by monitoring lung function and somatic symptoms, using objective and subjective measures.

Thus, symptom monitoring is a highly adaptive strategy when it comes to management of chronic illness. Specifically in the case of asthma, being sensitive to symptoms, and thus detecting them when they are still weak, would help an individual to comply with their medication regime, and early detection of symptom deterioration will lead to timely intervention. Such monitoring involves multi-stage processing of information regarding somatic sensations: directing attention to sensations, interpreting the wide range of such sensations, and comparison of current sensations with previously experienced sensations stored in memory, which would help categorise current ones as benign or malignant. In other words, certain patterns of attending to health-relevant information, interpreting it, and remembering it may determine how the symptoms are perceived and subsequently managed and controlled.

Under-perception would clearly be a disadvantage in an illness like asthma, since it places an individual at risk of failing to prevent symptom exacerbations or an asthma attack, or failing to adhere to medication (Davis et al., 2009; Magadle, Berar-Yanay, & Weiner, 2002). While there is a documented link between erroneous symptom perception and poor control, it is possible that most of the poor control is driven by under-perception. Over-perception, other than simple perceptual inaccuracy, is harder to envisage as a maladaptive strategy in asthma. It is much harder to draw the line between adaptive extra-monitoring and the kind of over-perception that may lead to negative outcomes. Maladaptive overperception is more likely to have an indirect effect on symptom exacerbation, when interacting with increased anxiety, panic and fear, negative affect and avoidance (Janssens, Verleden, & Van den Bergh, 2012).

Comparing Asthma and CFS populations

This thesis presents two studies in which the cognitive and affective processes were compared between CFS and asthma groups. The aim of the comparison was to check whether a pattern of over-monitoring and attentional vigilance is typical of the CFS population alone, or if it may be generally characteristic of populations experiencing chronic conditions, and therefore also be evident in the asthma group.

Comparing people with an illness to healthy people is not enough to make any specific conclusions regarding the illness of interest. The differences between how ill and healthy people perceive their bodies would not be surprising. When a person has a chronic illness that demands long-term daily management, such as the daily intake of medication required by asthma or the maintenance of a regular activity level in CFS to prevent deconditioning,

the illness may be accompanied by a heightened degree of monitoring. Sharpe and colleagues (1991) suggested that it would be useful to have a condition leading to inactivity as a comparison group for CFS. Asthma, as one such condition, is suitable for comparing the cognitive processing of information pertaining to health-threat and physical activity.

Both illnesses are long-term, chronic conditions that demand an elevated degree of symptom monitoring. The cognitive processes under investigation may be common to any chronic condition, and thus in CFS they would not necessarily be a contributing causal or perpetuating factor, but a learned response to illness and the need for symptom monitoring. In all chronic illnesses, there may be evidence of biased cognitive processing of somatic sensations, as well as more attention to, and interpretation of, these sensations as pertaining to illness, especially if triggered by contextual environmental cues (Rietveld, 2003). Thus, we could expect both asthma and CFS groups to show similar patterns of attentional vigilance, illness interpretation, and enhanced memory for health-threat and activity information.

However, there are two fundamental differences between CFS and asthma: 1) the presence of detectable physiological abnormality, such that there is none for fatigue in CFS, but there is lung dysfunction in asthma, and 2) the assessment methods, which are subjective in CFS, but both subjective and objective in asthma. There are accurate objective measures of airway obstruction in asthma. The perceptual accuracy and, consequently, the degree and direction of bias in relevant cognitive processes underpinning symptom perception can be measured against objective standards. In CFS, there are no such equivalents. The objective assessment of cognitive processes can only be measured against self-reports of fatigue and other symptoms, unless one employs indirect assessments of physiological fitness, but those tests measure fitness rather than fatigue itself. Thus, asthma is a condition with a present physiological abnormality, where symptoms can be measured objectively, mechanisms of dysfunction are well-understood, and there is an effective treatment. In contrast, CFS has highly heterogeneous symptoms, its causes are unknown, prognosis is unclear, it cannot be objectively assessed, and treatments are still under investigation, although the evidence points towards CBT and GET (White et al., 2011).

In asthma increased symptom monitoring may be an adaptive process. It only turns maladaptive if triggered by negative affect, including depression or anxiety, catastrophic cognitions or repressive coping. In contrast, over-monitoring and over-perception (in the form of enhanced processing of health-threat via amplified attention, negative interpretation of somatic sensations and selective memory) would be maladaptive in CFS

and contributing to symptom perpetuation. Over-monitoring and overperception in CFS would be independent of mood or behavioural factors, but would be of greater magnitude if in interaction with them.

In summary, during illness, heightened perception of the functioning of the organism is expected and adaptive. Comparing cognitive processing in CFS and asthma would elucidate whether the over-monitoring process may be less adaptive in CFS, and whether it is more likely to be a cause of the onset and perpetuation of the condition.

Summary

Taking into consideration the multifaceted and highly interactive causal network underpinning symptom onset and perpetuation in CFS, the thesis focused on the specific characteristics of information processing. The experimental studies described in the thesis investigated the cognitive processes of attention, interpretation, and memory. The studies explored the association between the specific idiosyncrasies of information processing and cognitions, such as attention and rumination. Furthermore, the investigations looked into the effect of mood states on cognitions and cognitive processes. Finally, the behavioural patterns of activity were assessed in connection to cognitions about activity and cognitive processes.

This thesis argues that the adaptive monitoring process is disrupted in CFS, and that an enhanced processing of illness-related information results in over-monitoring, which contributes to the perpetuation of CFS symptoms. Such monitoring disruption underpins fear and catastrophic cognitions as well as harmful behavioural responses, leading to increased fatigue and decreased functioning. Repairing the monitoring process through cognitive-behavioural interventions would reduce the impact of fear cognitions, decrease avoidance of activity, and result in positive health outcomes.

Chapter 2: Study 1: Attention and Rumination Experiment

Introduction

Monitoring for health-relevant information can be an adaptive strategy to aid in the evaluation and management of potential health-threats. The direction and focus of attention towards the internal and external environments are the fundamental aspects of the monitoring process in illness. However, a dysregulation in the monitoring process such as over-monitoring for threat, as guided by fearful, catastrophic or negative illness cognitions, may result in over-perception of somatic sensations and the experience of physical symptoms in the absence of detectable physiological abnormalities (Brosschot, 2002; Hadjistavropoulos, Craig, & Hadjistavropoulos, 1998; Verkuil, Brosschot, & Thayer, 2007).

Cognitive theories propose that in CFS attention may be directed towards illness-related information because it is guided by negative illness cognitions that make up a maladaptive illness schema (Moss-Morris, 2005). This selective and amplified focus on the illness-related information leads to heightened awareness of physical symptoms, therefore maintaining the feeling of ill health (Knoop et al., 2010; Moss-Morris, 2005). This hypothesised state of hypervigilance towards somatic information may point towards over-perception of somatic symptoms and somatic over-monitoring as symptom-perpetuating cognitive and behavioural mechanisms in CFS. Evidence from treatment trials suggests that reducing attentional focus on somatic symptoms improves health outcomes, such as decreasing fatigue and increasing functioning (Moss-Morris et al., 2005; Wiborg et al., 2011).

Experimental evidence supports the presence of attentional bias for health-threat in individuals with CFS, compared to healthy controls, signifying that people with CFS preferentially process health-threat information at the expense of other more neutral information (Hou et al., 2008). However, further questions arise concerning attentional bias in CFS. At what stages of attentional process does the bias occur? What type of information effects the changes in attentional processes? How, in such a multi-systemic and complex condition as CFS, does attentional bias interact with other cognitive processes in perpetuating the symptoms?

Exploring the first question concerning the specific attentional stage at which the bias occurs may determine what the best intervention strategy would be in order to help regulate the attentional process in CFS. If the bias occurs at the automatic preconscious level, then strategies such as Cognitive Bias Modification can be utilized to redirect and decrease attentional focus (Hertel & Mathews, 2011). Similarly, a cognitive-behavioural

intervention can be refined to address the early automatic bias by bringing it to awareness. In addition to understanding whether the bias occurs earlier or later in the attentional process, it is vital to investigate whether the bias is in the orientation of attention towards somatic information (attentional hypervigilance) or in the inability to shift the attention away from somatic information (difficulty in disengagement from threat).

Hou and colleagues (2008) used a visual probe task, where pairs of words and pictures depicting health-threat were presented on a screen for a duration of 500 milliseconds (ms). Presentation of competing stimuli and long exposure (500ms) are thought to measure higher order, strategic information processing, and are as likely to indicate a difficulty in disengaging from threat as the initial direction of attention towards health-threat (Fox et al., 2001). To separate attentional stages and trace the time course of attention, the duration of the stimuli presentation can be varied. Shorter presentation is thought to measure preconscious information processing and thus can provide evidence for initial orientation of attention before the higher cognitive processing come into effect (Fox et al., 2001; Mogg et al., 1997). On the other hand longer presentation duration allows the participants to engage a higher level of information processing (conscious and voluntary), therefore measuring the maintenance of attention and providing evidence for disengagement (Koster et al., 2004; Koster et al., 2006). The features of the visual probe task, such as competing stimuli presentation, are advantageous in the measurement of elaborative processing, but may not be sensitive enough to distinguish the details of earlier attentional engagement.

Therefore, the current study adapted a modified version of the exogenous cueing task (Fox et al., 2001; Posner, Walker, Friedrich, & Rafal, 1984) to investigate whether people with CFS would show hypervigilance towards illness-related information. The task can tap into the initial orientation of attention (or hypervigilance) and separate it from the process of the disengagement from threat. Attentional indices of engagement and disengagement can be calculated by measuring responses on valid trials (where the target is in the same location as the cueing word) and invalid trials (where the target is in the opposite location from the cueing word). Facilitated response time on valid threat trials indicates hypervigilance, whereas slowed response time on the invalid threat trials measures difficulty in disengagement. Additionally, the task would be able to measure approach and avoidance tendencies in relation to threat stimulus. Attentional approach is expressed in faster responses on valid trials, where the target appears in the same spatial location as the threat. In contrast, faster responses on the invalid trials, where the target appears in a different spatial location following the threat, may indicate avoidance.

In the current study the stimuli were presented for 100ms. Shorter presentation time overcomes the possibility that attention is consciously allocated, and this technique has been used to provide evidence for the potential bias in the initial preconscious orientation of attention or hypervigilance (Fox et al., 2001). This use of a shorter stimulus presentation duration (in a visual probe task) has been utilised to demonstrate attentional bias towards threat in anxiety (Mogg et al., 1997) In relation to IBS, there is evidence of attentional bias towards pain (Chapman & Martin, 2011a) and towards social threat from the exogenous cueing task (Martin & Chapman, 2010).

The second question concerns the type of information that may elicit attentional bias. The stimuli type used by Hou et al. (2008) involved high levels of general health-threat (e.g. images of disease, a coffin, disability), rather than specific CFS-, fatigue-, or symptom-related threats. The internal monitoring involves bodily awareness, attention to bodily sensations of fatigue or pain, or to freedom or restriction of movement. For example, words such as virus, death, disease, hospital may be more of an expression of external threat, and consequently would tap into the biased processing in external monitoring, as shown by Hou and colleagues. The current experiment utilised words that reflected the sensation of fatigue specifically and also the additional symptoms of CFS as described in the CDC/Fukuda criteria (cognitive impairment, sore throat, fever, headache, muscle and joint pain, sleep disturbances, and post-exertional malaise). Additionally, words expressing specific personalised social threat were used as control stimuli to check if the attention is not directed towards threat in general (social or symptom-related) but is focused primarily on illness-related, somatic information.

The third question concerns how attentional bias may interact with other cognitive processes in perpetuation of CFS symptoms. Deary, Chalder and Sharpe (2007) in their cognitive-behavioural model of medically unexplained symptoms group attentional processes and rumination as cognitive processes that perpetuate CFS symptoms, proposing that selective attention to illness-related information is a consequence of worry about and preoccupation with current physical state and symptoms. Rumination is defined as a cognitive style consisting of repetitive, passive, negative thoughts and images about a current psychological and physical condition (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Therefore, under such conditions of rumination, a negative illness schema may be accessed and activated and particular kinds of cognitive representations would emerge and amplify selective attention.

The idea is echoed by Brosschot (2002) who points at perseverative negative cognition, rumination or worry as factors that may activate a cognitive illness network (or illness schema) that would guide the information processing (Brosschot et al., 2005). Excessive rumination can direct and focus attention on internal and external illness-related cues. Moreover, rumination can increase emotional arousal, causing distress related to symptoms or anxiety over the potential seriousness of the illness. This would increase the alertness of the cognitive system even more in its monitoring for health-threat (Brosschot, 2002). Therefore, it would be expected that, when in a state of excessive rumination, people with CFS would experience greater negative emotional arousal, and as a result of hypervigilance, would focus their attention on symptom information.

Empirical evidence from other disorders like IBS showed that rumination amplified sensitivity to somatic sensations and symptoms, as demonstrated in increased reporting of severity and frequency of the symptoms (Crane & Martin, 2003). The researchers manipulated the degree of illness perception by either activating an illness schema or a neutral schema by providing IBS participants with illness cues or neutral control cues at the beginning of each day of the study. On the days following an illness cue, participants reported greater focus on the symptoms and greater symptom frequency and severity than on neutral cue days or days without a cue. The illness schema was triggered by directing the focus towards illness, and led not only to heightened attentional focus on bodily sensations and to more sensations being detected, but also to the interpretation of those sensations as symptomatic of the illness (Crane & Martin, 2003). Ruminating on the symptoms may be the triggering mechanism that directs and focuses attention on bodily sensations, illness symptoms, and health threat. This being the case, heightened attention would amplify the experience of fatigue and symptoms, which would keep an individual in that ruminative state, close the vicious cycle of influence, and thus perpetuate the symptoms.

There is a documented relationship between negative mood, emotional distress and rumination (Nolen-Hoeksema, 2000; Nolen-Hoeksema, Morrow, & Fredrickson, 1993; Nolen-Hoeksema et al., 2008) and between negative automatic thoughts and fatigue and emotional distress, cognitive difficulties, and somatic symptomatology in a non-clinical population (Arpin-Cribbie & Cribbie, 2007). Furthermore, Morrison and O'Connor (2008) found that not only negative mood followed high levels of rumination during increased stress, but when negative mood interacted with rumination, positive attentional bias was significantly decreased, and negative attentional bias showed a tendency to increase (Morrison & O'Connor, 2008).

Often people with CFS develop depressive symptoms and negative affect as a secondary condition (Hadlandsmyth & Vowles, 2009; Sohl & Friedberg, 2008). Depressive symptoms in CFS contribute to the increase in illness worry (Taillefer, Kirmayer, Robbins, & Lasry, 2003), which leads to poorer psychosocial functioning (Taillefer, Kirmayer, Robbins, & Lasry, 2002) and fluctuating psychological stress, negative mood, and greater severity of fatigue (Faulkner & Smith, 2008). Therefore, it would be expected that increased ruminative tendencies would be observed in people with CFS, compared to healthy individuals.

One would also expect to see a reciprocal relationship between mood and rumination in CFS, when one takes into account the elevated levels of negative mood characteristic of CFS, as well as the tendency to worry about illness and dwell on the meaning and consequence of the illness. The interaction between mood and rumination would amplify attentional bias towards illness by putting people in a state of hypervigilance.

To test the interaction between rumination, mood and attentional bias, in the current study participants underwent a rumination or distraction induction developed by Nolen-Hoeksema and colleagues (Nolen-Hoeksema et al., 1993; Watkins & Teasdale, 2001). The rumination condition does not specifically activate an illness schema, but induces the participants to ruminate on their physical sensations, thoughts and personality. Therefore, rumination could activate the kind of schema under which the attentional bias would emerge.

The distraction condition primes thoughts about neutral unrelated things. Considering the evidence that reduction in symptom focus produces positive outcomes, for example decreased fatigue and improved functioning (Moss-Morris et al., 2005; Wiborg et al., 2011), it would be expected that a distracted cognitive state may reduce the focus on somatic information and redirect attention towards more neutral stimuli. Therefore, it would be expected that, under the effect of distraction, people with CFS would not differ from healthy people in their attentional patterns, and would not attend to illness-related information more than a control group.

The study tested the following predictions:

Hypothesis 1. The CFS group under the effect of rumination will demonstrate an attentional bias towards illness-related words, compared to the CFS group under the effect of Distraction and the healthy control group in either cognitive state. Social threat words will not elicit attentional bias in the CFS group in either cognitive state, compared to healthy controls.

Hypothesis 2. In accordance with the hypervigilance hypothesis, the CFS subgroup in the Rumination condition will show an attentional bias, which will manifest as attentional engagement with illness-related words, compared to the CFS subgroup in the Distraction condition and the healthy controls. The CFS subgroup in the Distraction condition will not show an attentional bias towards illness-related information and their attention in relation to illness-related information should be comparable to the control group.

Hypothesis 3. The CFS subgroup in the Rumination condition will experience an increase in emotional arousal reflected by an increase in negative mood scores, compared to the CFS subgroup in the Distraction condition and healthy controls. The CFS subgroup in the Distraction condition will demonstrate a decrease in negative mood.

Hypothesis 4. The CFS group, regardless of the induction condition, will score higher on the self-report measure of Ruminative Responses than healthy controls.

Additionally to the main hypotheses, measures of social desirability and anxiety and depression were included in the investigation. In the study by Surawy et al (1996), people with CFS gave descriptions of their personalities as characterized by high achievement, perfectionism, and high standards extending across personal, work and social settings. People with CFS have also been shown to highly value opinions of others. These personality features initially put these people at risk for developing CFS when they kept on pushing through stress or an acute illness driven by high standards. Therefore, the measure of social desirability was included in the study. Particularly, as social desirability may influence responses, it can serve as a check for the response bias (Barger, 2002; Derakshan, Eysenck, & Myers, 2007).

A measure of anxiety and depression was included, because attentional biases have a strong association with depression (Gotlib & Joormann, 2010) and anxiety (Van Bockstaele et al., 2014). Therefore, it is important to determine whether the selective attentional processing in CFS may be due to elevated anxiety or depression.

Method

Full Study Design

The study had a quasi-experimental design with two between-subjects independent variables. The first between-subjects factor was group: people with a CFS diagnosis were compared to age-, gender- and education-matched healthy controls. The second between-subjects factor was cognitive state induction: within each group (CFS, Healthy Control)

participants were randomly allocated to undergo either Rumination or Distraction state induction (Nolen-Hoeksema et al., 1993; Watkins & Teasdale, 2001). Random allocation was achieved manually by coin tossing by the investigator, who therefore was not blind to the condition to which a participant was assigned. The same investigator conducted the induction procedure and the rest of the study procedure, which included two computer tasks and questionnaire measures.

Word stimuli type (Illness, Social Threat, Neutral) was the within-subjects factor. The main dependent variable was Reaction Times (RTs) on the cognitive tasks. RTs from the exogenous cueing task measuring were used to calculate three indices: attentional bias, engagement, disengagement scores, which were the main variables of interest. The second dependent variable was mood scores on visual analogue scales. Additional dependent variables included self-report measures of depression and anxiety, and social desirability.

This study has been reviewed by and received ethics clearance through the University of Oxford Central University Research Ethics Committee (CUREC), assigned reference number: MSD/IDREC/C1/2007/4 (Appendix A.2).

Participants

Participants with CFS were included in the study if they:

1. Reported a primary CFS diagnosis by a qualified medical practitioner (a GP or referred specialist). Any person, who had received a diagnosis of CFS by their GP or at a specialist clinic in the past, during an unspecified period of time, was considered for inclusion into the study.

AND

2. Met the CDC/Fukuda criteria for fatigue – the presence of current primary unexplained, persistent or relapsing fatigue, which is not relieved by rest and results in significant reduction of activities for the last 6 months (Fukuda et al., 1994).

AND

3. Reported additional symptoms from the eight outlined by the CDC/Fukuda criteria: impairment in short-term memory and concentration, sore throat, tender lymph nodes, muscle pain, multi-joint pain, new headache, unrefreshing sleep, and post-exertional malaise longer than 24 hours. For the diagnosis of CFS based on CDC/Fukuda criteria, the minimum number of additional symptoms required is four symptoms experienced in the past 6 months.

Seven participants with CFS reported fewer than four symptoms in the last 6 months, ranging from one to three symptoms. All CFS participants experienced post-exertional malaise. It was decided that those participants would be retained in the study, because of the presence of two crucial characteristics: extreme unexplained fatigue and post-exertional malaise, in addition to the self-reported diagnosis of CFS. The participants had been diagnosed for longer than the last 6 months, and therefore it was possible that they might have been asymptomatic in the past 6 months, but had experienced the symptoms beyond that time period.

Participants were excluded if they reported:

1. A current acute or chronic primary medical or psychiatric diagnosis that may be the cause of extreme fatigue and would preclude the diagnosis of CFS, for example any diagnosis of the conditions outlined by CDC/Fukuda (1994), Reeves et al (2003; 2005), or NICE (2007) guidelines.

2. Current diagnosis and treatment of primary depression, for example depression that was diagnosed prior to receiving a CFS diagnosis in the past 5 years, in accordance with the recommendation by Reeves and colleagues (2003; 2005).

Due to reported comorbidity of CFS and depression (Mccue, Buchanan, & Martin, 2006), the history of depression and anxiety was checked. Seven participants with CFS reported history of depression: five reported comorbid depression due to CFS with the onset occurring following CFS diagnosis; two participants reported being diagnosed with depression longer than 5 years ago (11 and 6 years), but were not experiencing depression currently. Reeves and colleagues (2003, 2005) suggested that such participants, rather than being excluded from studies, might be stratified and included in the analysis. Two other participants with CFS reported comorbid anxiety diagnosis received after the CFS diagnosis (20 and 10 years ago). These participants were included in the study because their depression/anxiety did not preclude their diagnosis of CFS.

Potential depression and anxiety have also been assessed using Hospital Anxiety and Depression Scale (HADS) (Mccue et al., 2006). The recommended cut-off scores for elevated depression for the CFS population are 9-10 points (Morriss & Wearden, 1998). Five CFS participants scored above 9 on HADS. Crosschecking revealed that one person with a high score was the one who reported comorbid anxiety (diagnosed 20 years ago), and two were the participants who reported comorbid depression diagnosed after receiving CFS diagnosis. These participants were included in the study, because their depression/anxiety did not preclude their diagnosis of CFS. The other two participants with high scores were included

because they have only reported CFS diagnosis and no psychiatric comorbidity or history of psychiatric disorder.

Additional inclusion criteria for all participants specified 18 years of age, normal or corrected-to-normal vision, good hearing, good manual dexterity, and English at the standard of a native speaker. None of the control participants reported a current acute or chronic medical or psychiatric condition. Two control participants reported episodes of depression in the past (8 and 10 years ago). They were included in the study, because their depression had been absent during the past five years.

The final sample consisted of 33 participants with CFS and 33 healthy age-, gender- and education-matched controls. CFS participants were recruited primarily from Oxford and Oxfordshire CFS support groups, from among the staff and students of the University of Oxford, through local advertisement, via the Internet (Facebook, local health forums), and through Oxford-based printed and online information sheets (DailyInfo) and newspapers. Healthy controls were recruited via similar advertisement from the staff and students of the University of Oxford, the local communities of Oxford and its surroundings. Volunteers were compensated £5 for their time.

Materials

Cognitive State Induction

The induction took place before computer tasks as the first step in the experimental procedure. Participants were randomly allocated either to rumination or distraction induction. In each condition participants were instructed to read through a list of statements for eight minutes. They were asked to read slowly to themselves, use their imagination and concentration to focus on each of the ideas presented in the sentences, and to visualize each item. For the full induction procedure see Appendix A.5.

The statements in the rumination condition described present physical sensations and appearance, emotions, thoughts, motivations, personal characteristics. In the distraction conditions the statements described neutral external matters and concrete images of buildings, transport, nature. The topics in both induction types were not directly relevant to CFS. The rationale for the rumination induction was the production of passive, repetitive self-focused thoughts, hypothesised to be characteristic of a chronic condition. The induction lasted eight minutes.

Exogenous Cueing Task

The attentional task was completed immediately after the induction. Exogenous cueing methodology was adopted from a study on anxiety (Fox et al., 2001) and another on attentional bias in IBS (Martin & Chapman, 2010). It is a valid measure of attentional processing, assessing early automatic stages of spatial allocation of attention. Eye-tracking research suggests a high degree of correspondence between gaze and attention (Armstrong & Olatunji, 2012; Fox et al., 2001) supporting the validity of the task.

A single cue (a neutral or threat word) was presented either on the left or the right side of a computer screen for 100ms. The cue disappeared and a target (the dot) appeared in one of the two locations, either in the same location as the preceding cue (a valid trial) or on the opposite side of the screen (an invalid trial).

An experimental trial started with a presentation of a central fixation cross (size 14 mm x 14 mm) on a computer screen for 500ms. It was followed by a word presented for 100ms either on the left or on the right of the fixation cross. The words varied in size depending on their length – the length range was 30 – 70 mm and the height 6 – 10 mm. The distance of the word from the fixation point was 46mm. Word presentation was followed by a 50ms blank mask. Then the dot (1mm in diameter) appeared either on the left or on the right side of the screen, 46mm from the fixation point and stayed on the screen until participant responded or for 2500ms. Inter-trial interval was 1000ms. *Figure 1* presents a graphic representation of two alternative types of experimental trial, the valid and the invalid trial.

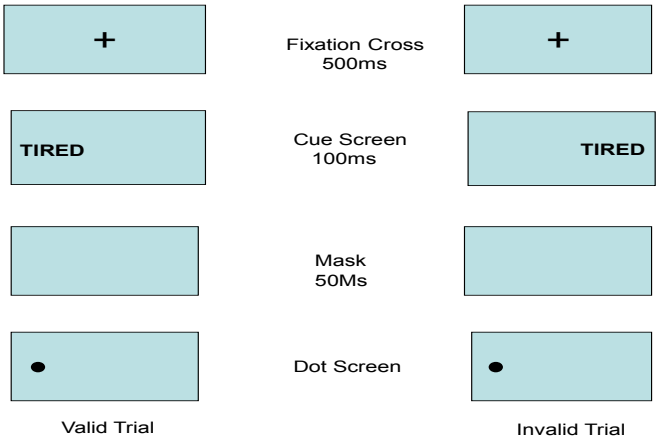


Figure 1. The sequence of stimuli presentation in the exogenous cueing task.

Instructions

Participants were instructed to look at the fixation cross on the monitor and when they saw a dot appear on the left or on the right side of the screen, they were instructed to press a key on a computer keyboard to indicate whether it appeared on the left (**z** key) or on the right (**m** key) side of the screen. Participants were instructed to concentrate on locating the dots and not the words, which might have preceded the dots. They were instructed to be as fast and as accurate as possible and maintain the fixation at the centre of the screen. Participants were instructed to respond as quickly as possible to the appearance of the dot and press the button indicating whether it appeared on the left or on the right. The measured dependent variable was the reaction time of the participant.

After receiving instructions, participants completed a practice block (16 trials), after which they had the opportunity to ask any questions or rerun the practice. Participants completed four blocks of experimental trials, 36 trials in each block. Each word was presented four times, in both positions (left and right), and both trial types (valid and invalid), producing 120 experimental trials overall. Additional 24 catch trials, where just the dots appeared without being preceded by a word, were used to ensure participants focused on the dots and not the words. The presentation of trials in each block was randomized across participants. The task took about 5 minutes to complete.

Stimuli

There were three types of words: Illness (e.g. fever), Social Threat (e.g. timid) and Neutral (e.g. brick) used in the attention task. Ten words of each type were used, 30 overall and ten additional Neutral words for the practice block. Words varied in length (4 – 9 letters) and lexical frequency. The three types of stimuli were matched on length and frequency, both $p > .99$ (see Table 1). The word frequencies were taken from the MRC Psycholinguistic Database (Wilson, 1988) using the Kucera-Francis written frequency (Francis & Kucera, 1967).

Table 1.

Word Stimuli Lengths and Kucera-Francis Written Frequencies for Exogenous Cueing Task

	Length	K-F		Length	K-F		Length	K-F
1 sleepy	6	6	unkind	6	3	heater	6	14
2 fatigue	7	11	idiotic	7	3	roofing	7	4
3 collapse	8	8	rejected	8		banister	8	5
4 lethargic	9		embarrass	9	7	sideboard	9	1
5 sore	4	10	fool	4	37	pane	4	3
6 fever	5	19	laugh	5	28	clock	5	20
7 tired	5	48	timid	5	5	brick	5	18
8 inactive	8	7	detested	8		basement	8	31
9 weary	5	17	stare	5	14	knock	5	15
10 listless	8	1	ridicule	8	5	doorbell	8	
		14.11			**12.75**			**12.33**

Illness words were selected from the previous study on attentional bias in CFS (Moss-Morris & Petrie, 2003). Selection of additional words was based on the descriptions of CFS symptoms and fatigue by people with CFS in literature (Libman et al., 2008), on the description of CFS symptoms in diagnostic criteria (Fukuda et al., 1994), and on discussions of the definition of 'fatigue' in literature (Barofsky & Legro, 1991). The aim was for the Illness type words to be descriptive of the concept of fatigue and CFS symptoms. "Sleepy" reflected the symptom of unrefreshing sleep and fatigue. "Fatigue", "lethargic", "tired", "weary" and "listless" were used to reflect the construct of fatigue. "Collapse" corresponded to post-exertional malaise. "Sore" reflected the symptom of a sore throat, and muscles soreness as element of post-exertional malaise. "Fever" reflected the fever-like symptoms of CFS, e.g. sore throat, tender lymph nodes. "Inactive" reflected the reduction of activity due to fatigue, following the description in CDC/Fukuda criteria. Social Threat words were picked from a stimuli set used in previous studies on chronic pain (Keogh, Ellery, Hunt, & Hannent, 2001).

To evaluate the health threat relevance of the words, independent judges (5 people with CFS and 13 healthy controls) were asked to rate the words using an 11-point scale (0 – not at all, 10 – extremely relevant) on health threat and emotional threat. Participants were drawn from those who volunteered but could not participate in the laboratory-based experiment due to their low mobility or long distance. The aim was to obtain the ratings for the words not influenced by the altered cognitive state and cognitive tasks. Due to the low number of participants, complex statistical analysis for comparing group means was not appropriate.

CFS and healthy control groups did not differ significantly on health-threat and emotional threat ratings, all $p > .55$ (see Table 2). The raters also did not differentiate significantly between their ratings of health threat and emotional threat $p > .70$ (see Table 3)**.** All means were approximately in the range between 2 and 7, middle of the scale, suggesting that participants found the words low to mildly health- and emotionally - threatening.

Table 2.

Ratings of Illness Words on Health and Emotional Threat by CFS and Healthy Control Participants

	CFS *n* = 5		Control *n* = 11		
Illness Words	M	*SD*	M	*SD*	
Health Threat	5.07	1.47	4.50	2.08	$t(14) = 0.54$, $p = .596$
	CFS *n* = 5		Control *n* = 13		
	M	*SD*	M	*SD*	
Emotional Threat	3.91	1.86	4.03	1.69	$t(16) = 0.12$, $p = .905$

Note. The words were rated on a scale 0 - Not at all to 10 - Extremely

Table 3.

Mean Ratings of Illness Words by Independent Raters (5 CFS and 13 Control)

	Health threat		Emotional Threat	
Words	M	SD	M	SD
sleepy	2.20	1.94	3.57	2.85
fatigue	5.25	2.42	5.33	2.54
collapse	7.05	2.52	5.11	3.14
lethargic	3.80	2.59	4.33	2.66
sore	4.35	2.63	1.89	2.00
fever	5.50	2.53	1.94	2.21
tired	4.35	2.68	4.61	3.36
inactive	2.91	1.70	4.21	3.45
weary	3.53	2.40	3.17	3.17
listless	2.94	3.22	5.65	3.30
TOTAL	**4.19**	**1.45**	**3.98**	**1.33**
		$t(18) = 0.33$, $p = .742$		

Note. The words were rated on an 11 point scale (0 Not at all - 10 Extremely)
The words in bold are replicated from Moss-Morris and Petrie (2003).

Data Preparation

CFS and control groups did not differ significantly in accuracy rates CFS $M = 97.8\%$, $SD = 5.3$, Control $M = 98.2\%$, $SD = 2.3$, $p > .70$. The Reaction Time data (RT in milliseconds) were filtered by removing RTs for incorrect answers, scores below 100ms and above 1500ms, and

those more than 2 SDs away from a participant's mean (Asmundson & Hadjistavropoulos, 2007; Fox et al., 2001). Univariate ANOVAs showed that two groups (CFS, Controls) did not differ on accuracy rates, number of outliers, and amount of data included into the analysis (all $p > .50$).

Attentional Bias scores were calculated for each word type by subtracting valid trials RTs from invalid trials RTs (Asmundson & Hadjistavropoulos, 2007). Positive values indicated attentional bias towards particular stimuli type, since RTs on invalid trials were longer than RTs on the valid trials. Negative values indicated avoidance, if the RTs on invalid trials were faster than on valid trials.

Attentional indices of Engagement and Disengagement were calculated for each word type: Illness, Social Threat and Neutral following the procedure outlined in previous studies (Koster et al., 2006). The Attentional Engagement index is computed by subtracting RTs on valid Illness or Social Threat trials from valid Neutral trials ($RT_{\text{valid neutral}} - RT_{\text{valid threat}}$). Positive values on the engagement index suggested faster reaction towards threat on a valid trial, indicating that threat words captured participants' attention.

The Disengagement index was calculated by subtracting RTs on invalid Neutral trials from invalid Illness or Social Threat trials ($RT_{\text{invalid threat}} - RT_{\text{invalid neutral}}$). Positive scores on the disengagement index suggested that participants responded slower to the dot appearing in a different location following threat word, indicating difficulty in shifting attention from the threat to the dot.

Questionnaires

All self-report measures of demographic and illness characteristics, as well as the following questionnaires, were completed at the end of the study after the computer tasks (all measures are presented in Appendix A.4).

Social Desirability Scale (SDS) is a 33 item questionnaire with true/false answers (Crowne & Marlowe, 1960). A higher score indicates a greater degree of social desirability, which suggests that people want to be viewed by others in a positive way and are more likely to give socially acceptable responses. The scale has shown adequate internal consistency, with Cronbach's α in the range of .72 - .96, although it has been primarily tested on healthy student populations (Barger, 2002; Loo & Loewen, 2004). The current study showed Cronbach's α of .74. The social desirability measure has been included, because previous research showed that social desirability differences may affect cognitive biases and the scale can be used to check for potential response bias (Eysenck & Derakshan, 1997).

The Hospital Anxiety and Depression Scale (HADS) consists of 14 items measuring anxiety and depression in populations with non-psychiatric medical conditions, such that the scores are not affected by the physical symptoms of a particular patient's medical condition (Zigmond & Snaith, 1983). Scores range from 0 to 21 for each subscale with a higher score indicating greater severity. The developers suggest the following classification of cases based on the scores: normal range (0 – 7), mild (8-10), moderate (11-15), severe (16 or higher). For people with CFS, a cut-off score of 9-10 is recommended to distinguish people with elevated anxiety or depression (Morriss & Wearden, 1998). The scale has good internal consistency: Anxiety subscale – Cronbach's α was 0.87; Depression subscale - Cronbach's α was 0.79 (Mccue et al., 2006) and has been validated in different medical settings (Bjelland, Dahl, Haug, & Neckelmann, 2002; Mondolo et al., 2006). In the current sample, Cronbach's α for Depression was 0.76 and for Anxiety 0.79. The scale was used to assess psychiatric comorbidity in CFS group. Depression and anxiety may exert an influence on attentional processes (Gotlib & Joormann, 2010; Mogg, McNamara, et al., 2000) therefore HADS scores can be used as covariates in the statistical analysis of attentional bias scores.

Ruminative Responses Scale (RRS) is a 22-item self-report, with items measuring a disposition to focus on self (e.g. "I think about all my shortcomings, failings, faults, and mistakes"), on symptoms ("I think about my feelings of fatigue and achiness"), and consequences ("I think "I won't be able to do my job if I don't snap out of this"") (Nolen-Hoeksema et al., 1993). Responses are rated on a 4-point scale ranging from 1 – Never to 4 – Always. The scores range from 22 to 88, where a higher score reflects a greater tendency to dwell on the negative. The scale demonstrated good construct validity and reliability, with Cronbach's α was 0.90 (Nolen-Hoeksema, 2000). RRS can be divided into three subscales: Depressive – identifies current depression (12 items); Reflecting or problem solving – measures neutral passive contemplative thoughts (5 items); and Brooding – identifies negative passing thoughts or "moody pondering" (5 items) (Treynor, Gonzalez, & Nolen-Hoeksema, 2003). For the Reflecting subscale, Cronbach's α was 0.72 and test-retest correlation was r = .60, and for Brooding, Cronbach's α was 0.77 and test-retest correlation was r = .62. These are adequate for five-item subscales (Treynor et al., 2003). The current analysis focused on the subscales rather than on the total score to separate the measures of ruminative thought (Reflecting and Brooding) from the items measuring depressive state (Depressive subscale) in order to assess the degree of self-focus and symptom focus in participants. In the current study Cronbach's α for Depressive was 0.83, Reflecting 0.77, and Brooding 0.70.

Visual Analogue Scales (VAS) is a continuous graphic measure of current mood ranging from 0 (not at all) to 100 (extremely) on a horizontal scale. It consisted of five unipolar scales measuring Happy, Sad, Anxious, Calm, and Angry moods, presented in that order. Participants were asked to directly mark a position on the scale by placing a cross on the line in a location that reflected how much of that emotion they were feeling at the moment, thus making VAS a continuous measure. VAS is a widely used method across psychiatric and medical settings and has been found to be a valid measure of mood state in healthy and depressed populations (Monk, 1989; Stern, Arruda, Hooper, Wolfner, & Morey, 1997).

One of the advantages of the VAS method is its high sensitivity, a quality that is not always reflected in more discrete measures, and therefore it is useful in assessing mood changes in short periods of time (Couper, Tourangeau, Conrad, & Singer, 2006). It is primarily intended as a measure of change within individuals. Participants were asked to rate their mood five times during the study: 1) prior to the cognitive state induction, 2) after the induction, 3) after the first computer task, 4) after the second computer task, 5) at the end of the study after the questionnaires. Its visual nature makes it an easy, quick and efficient measure to administer without increasing the burden on participants. VAS was used to check the effect of the cognitive state induction in accordance with other research literature (Rood, Roelofs, Bogels, & Arntz, 2012).

VAS has been criticized for having lower test-retest reliability than multi-point Likert scales (Couper et al., 2006). The test-retest reliability between five time points in the current study for each mood were: Happy *r* in the range of .73 - .81, Sad *r* in the range of .78 - .82, Anxious *r* in the range of .64 - .71, Calm *r* in the range of .61 - .65, and Angry *r* in the range of .69 - .79, all $p > .001$.

Participants' scores on the positive VAS subscales Happy and Calm were reverse scored to obtain a consistent direction representing the current negative mood. Higher scores reflected a more negative mood state. Additionally, separate mood scores (Sad, Anxious, Angry, Happy, Calm) were added together to obtain a total negative mood score.

Power Analysis

Attention Bias – Effect Sizes

Hou and colleagues (2008) detected significant differences between CFS and healthy control groups when using a visual probe task to investigate attentional bias in CFS. Their sample size included 11 CFS and 17 control participants. The effect size found by Hou *et al.* was estimated to be Cohen's $d = 1.16$ for word stimuli and $d = .87$ for pictures signifying a

large effect size (Cohen, 1988, p. 355). The effect size for the ANOVA tests in Hou *et al*'s study was estimated $f = .57$ for words, and $f = .42$ for pictures, exceeding $f = .40$, signifying a large effect size for ANOVA tests (Cohen, 1988, p. 355). All effect sizes were calculated using the Excel-based Effect Size Calculator developed for the purposes of meta-analyses (Lipsey & Wilson, 2000).

Attention Bias - A Priori analysis

The necessary sample size was calculated on the basis of the above effect sizes in order to have the power of at least 80% chance (a value less than that increases the chance of committing a Type II error by an unacceptable degree) of detecting a medium to large effect size at $p < .05$ and $p < .01$ as recommended by Cohen for the statistics testing key hypotheses (Cohen, 1992).

For the independent *t*-tests of attentional bias indices (engagement and disengagement) to detect an effect size of $d = .80$, with a significance set at .05 a sample of at least 52 participants, 26 in each group would be needed, and a total sample of 78, when significance is set at .01. Additionally, a total sample size of 128 participants would be needed to detect a medium effect size $d = .50$ with significance set at .05.

For the ANOVA repeated measures, within-between interaction statistical tests, main effects and interactions of interest Group (CFS, Control) x Induction (Rumination, Distraction) x Word Type (Illness, Social Threat, Neutral), a total sample size of 36 participants would be needed to obtain an effect size Cohen's $f = .40$, and 72 participants for the medium effect with a significance criterion set at .05.

For the mood changes following a cognitive state induction to detect a large effect size for the 2x2x2 ANOVA of Group (CFS, Control) by Induction (Rumination, Distraction) by Time (Pre-induction, Post-induction), a total sample size of 48 participants would be needed to detect a medium effect size $f = .25$.

Equipment

The computer tasks were run on a desktop computer (CTX Model: PR711T, CTX Ultra Screen Monitor, 17 inch screen) and a Toshiba Satellite A100 laptop (15.4 inch screen). The presentation of the task and data collection was conducted using E-Prime software version 1.1 (SP3) (1.1.4.4). Participants sat in a comfortable position in front of the computer screen. The distance between the participant and the screen was approximately 50cm. Previous research suggested that any variation in distance between the participant and computer

screen had no significant influence on the effect (Owens, Asmundson, Hadjistavropoulos, & Owens, 2004).

Procedure

Participants were tested alone in a single session lasting approximately one hour. Sessions took place at the Department of Experimental Psychology in a standard testing room specifically set up for experimental purposes, and alternatively in Wolfson College, Oxford in a room designated for study purposes. The college was chosen as a location with convenient parking, which allows access for people with restricted mobility. Each room was quiet with minimal distraction for participants and fit the requirements for testing.

The study procedure was outlined and explained by the investigator in addition to participants reading an information sheet (Appendix A.1) about the study. All questions were addressed prior to obtaining the written informed consent from participants before they took part in the study (Appendix A.3).

The steps of the procedure are presented below in order:

1. Information and consent
2. Participants filled out a VAS mood measure (Time1)
3. Participants underwent induction into the cognitive state to which they were allocated: Rumination or Distraction.
4. Participants filled out a VAS mood measure (Time2)
5. Participants completed an attentional task: Exogenous Cueing
6. Participants filled out a VAS mood measure (Time3)
7. Participants took a 20-minute break to relax and rest outside of the testing room. This would allow the effects of the cognitive state induction to dissipate before participants continued to the next stage of the study (described in Chapter 5). The literature does not specify how long the cognitive state induction effect can last (Watkins & Teasdale, 2004). In comparison, a mood induction effect can last between 25 – 35 minutes (Sinclair, Mark, Enzle, Borkovec, & Cumbleton, 1994). When participants started the second computer task, all of them were past the 30-minute mark, counting from the end of the Induction procedure to the beginning of the second computer task, which measured interpretation, the Lexical Decision task.
8. Participants filled out a VAS mood measure (Time 4)
9. Participants completed an interpretation task: Lexical decision (details are outlined in Chapter 3: Interpretation).

10. Participants completed questionnaire measures in the following order:

Demographic questions: age, gender, education

Social desirability questionnaire (SDS)

Ruminative responses scale (RRS)

Depression/Anxiety questionnaire (HADS)

Health questions

Fukuda CFS diagnostic criteria

10. Participants filled out a VAS mood measure (Time5) to check for lasting effects of negative mood for ethical reasons.

11. Participants were fully debriefed, their questions were answered, and they received their payment for taking part in the study (5 pounds).

The flowchart of the study is presented below in *Figure 2.*

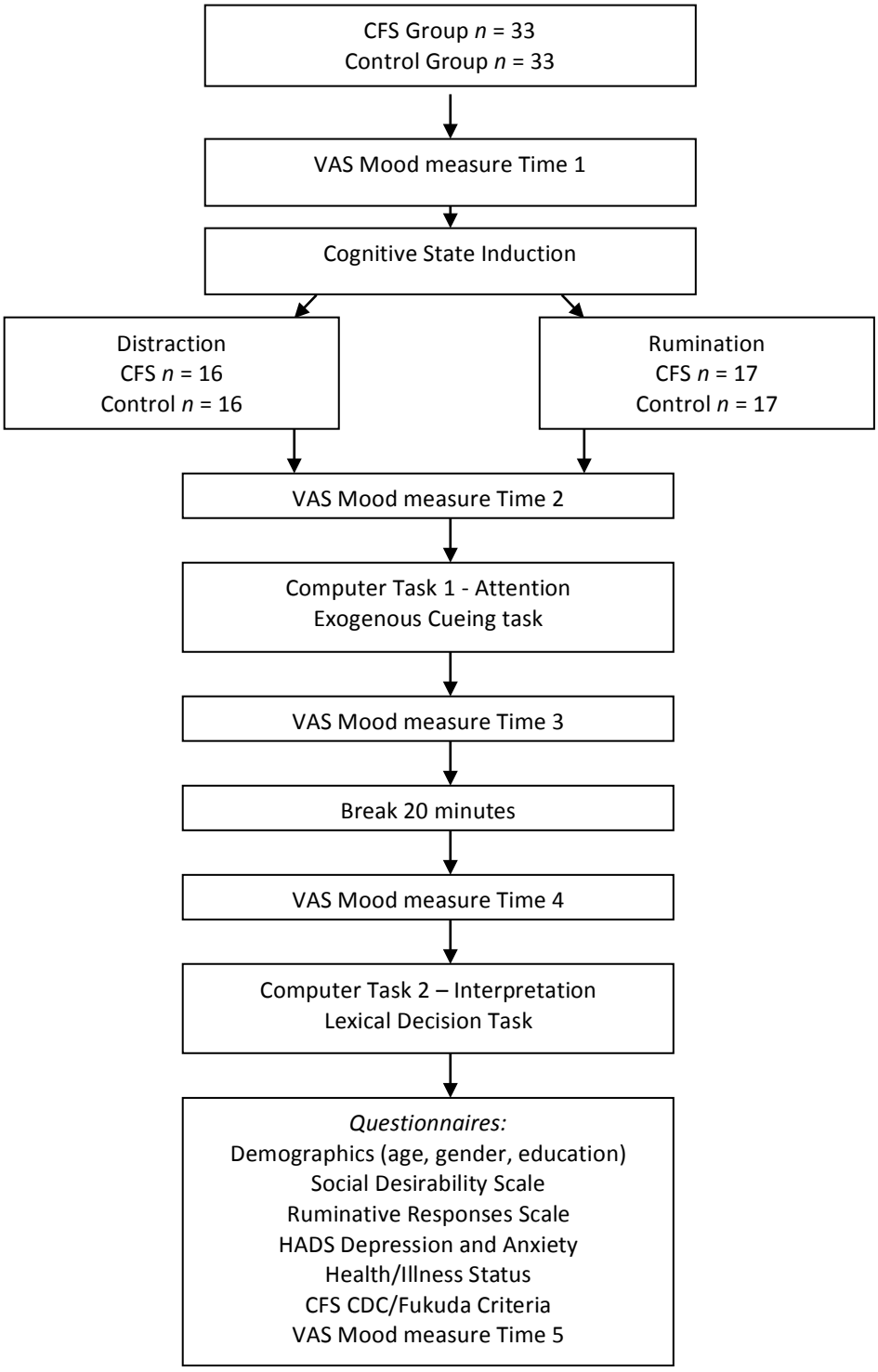


Figure 2. Full procedure for Study 1 consisting of two experimental components investigating: 1) Rumination and Attention, 2) Interpretation.

Statistical analysis

Statistical analyses were performed using Statistical Package for Social Science (SPSS) software version 17.0. Chi-square and univariate ANOVA tests were used to compare the groups on demographic characteristics (gender, education, age), and self-report measures of depression and anxiety (HADS), rumination tendency (RRS) and social desirability (SDS). Pearson correlations were carried out within the CFS group to investigate the association between self-reported illness measures (CFS symptom duration and number) and HADS and RRS subscales.

There is no standard procedure to check the effect of the Rumination and Distraction induction in the literature. Mood measures can be used to check whether a change in a mood state occurred under the influence of the induction (Watkins & Teasdale, 2001, 2004). The effect of cognitive state manipulation was checked via two methods. In the first method, Pearson correlations were used to check the strength of the relationship between VAS mood scores and RRS subscales within Rumination and Distraction conditions separately, pre- and post- induction. In order to compare the two dependent correlation coefficients with the two correlations sharing one variable in common (RRS, Mood at Time 1, Mood at Time 2, with the RRS being the variable in common) z-scores were calculated and compared using two-tailed tests of significance (Lee & Preacher, 2013).

In the second method, the effect of induction on VAS mood scores was assessed by conducting a 2 x 2 x 2 x 5 factorial analysis of variance (ANOVA). In the analysis, Group 2 (CFS, Control) and Induction 2 (Rumination, Distraction) were the between-subjects independent variables. Time 2 (Pre-induction, Post-induction) and Mood 5 (Sad, Anxious, Angry, HappyREV, CalmREV) were within-subjects repeated measures. Post-hoc pairwise comparisons (Bonferroni method was used to adjust for multiple comparisons) were used to clarify significant results. Independent samples *t*-tests were used to compare VAS mood scores between Distraction and Rumination conditions for CFS and control groups to clarify significant interactions.

HADS, RRS subscales, Social Desirability, and demographic variables (age, education) were entered as covariates into the above 2 x 2 x 2 x 5 ANOVA to check if the effect was not due to underlying differences on those variables, particularly accounting for the significant difference on HADS Depression between CFS and control groups. For the CFS group only, the number of self-reported symptoms was entered as a covariate into 2 (Induction:

Rumination, Distraction) by 2 (Time: Pre-induction, Post-induction) by 5 (Mood: Sad, Anxious, Angry, HappyREV, CalmREV) ANOVA with the Time and Mood as within-subjects measures.

Independent samples *t*-test compared the number of symptoms reported by the participants with CFS in the Rumination condition to the number reported by participants with CFS in the Distraction condition. Pearson correlations were used to assess the relationship between mood and the number of symptoms reported by participants with CFS in the Rumination or Distraction conditions. In order to compare the two dependent correlation coefficients with the two correlations sharing one variable in common (Number of symptoms, Mood at Time 1, Mood at Time 2, with the number of symptoms being the variable in common) z-scores were calculated and compared using 2-tailed tests of significance (Lee & Preacher, 2013).

The analysis on raw Reaction Time (RT) data from the exogenous cueing task was conducted to investigate a potential interaction effect between group, cognitive state induction, word stimuli type, and trial type and to check the validity of the experimental procedure. Reaction times were entered into a 2 x 2 x 3 x 2 mixed ANOVA. Group 2 (CFS, Control) and Induction 2 (Rumination, Distraction) were the between-subjects measures. Word type 3 (Illness, Social Threat, Neutral) and Trial type 2 (Valid, Invalid) were the within-subjects independent variables.

Attentional bias scores were entered into 2 x 2 x 3 mixed ANOVA with Group 2 (CFS, Control) and Induction 2 (Rumination, Distraction) as between-subjects independent variables and Word type 3 (Illness, Social Threat, Neutral) as within-subjects independent variable. Paired samples *t*-tests were used to compare Illness bias and Social Threat bias scores to the Neutral bias scores baseline separately for each group (CFS, Control) within each condition (Rumination, Distraction).

Attentional Engagement and Disengagement scores were entered into four 2 x 2 ANOVAs, where Group (CFS, Control) and Induction (Rumination, Distraction) were the between-subjects independent variables. The four indices: Illness engagement, Illness disengagement, Social Threat engagement and Social Threat disengagement were the dependent variables.

To investigate the relationship between attentional bias and the number of reported CFS symptoms, a 3 x 2 x 3 ANOVA factorial design was conducted. The between-subjects independent variables were Group 3 (CFS Low number of symptoms; CFS High number of symptoms; Control) and Induction 2 (Rumination, Distraction). Word type 3 (Illness, Social

Threat, Neutral) was the within-subjects independent variable. Attentional bias scores were the dependent measure. Pearson correlations were carried out within the CFS group to explore the relationship between attentional indices and the self-reported number of CFS symptoms, HADS, RRS subscales, and Social Desirability.

Results

Demographic and Questionnaire Measures

CFS and control groups did not differ significantly in age, gender, or education, all $p > .05$ (see Table 4). CFS group scored significantly higher on HADS Depression, compared to the control group $F(1,62) = 8.49$, $p = .005$, $\eta_p^2 = .120$. None of the other differences in scores on self-report measures were significant, all $p > .05$. Therefore, hypothesis 4 predicting that the CFS group would score higher on Ruminative Responses than the control group was not supported.

Table 4

Demographic and Questionnaire Measures for CFS and Healthy Control Groups

	CFS *(n = 33)*	Control *(n = 33)*		
	***n* (%)**	***n* (%)**	*χ2*	*p*
Gender (female)	22 (67%)	17 (52%)	1.57	*ns*
Education (Degree)	26 (78%)	31 (93 %)	3.21	*ns*
	***M* (SD)**	***M* (SD)**	*F*	*p*
CFS symptoms duration (years)	9.7 (11.9)	–		
Time since diagnosis (years)	7.6 (6.7)	–		
Number of CFS symptoms	4.8 (1.9)	–		
Current treatment	10 (30%)			
Treatment: medication	7 (21%)			
Treatment: pacing	2 (6%)			
Treatment: CBT	1 (3%)			
Age	38.1 (16.1)	32.3 (9.2)	3.34	*ns*
Social Desirability Scale	15.3 (5.3)	16.4 (5.5)	0.33	*ns*
HADS Depression	6.1 (3.5)	3.3 (2.5)	13.40	.001
HADS Anxiety	8.3 (3.6)	8.1 (3.2)	0.04	*ns*
RRS Depressive	26.9 (6.2)	26.6 (6.1)	0.03	*ns*
RRS Reflective	11.0 (3.4)	11.7 (3.5)	0.52	*ns*
RRS Brooding	10.4 (2.7)	10.2 (2.7)	0.06	*ns*

Note: HADS - Hospital Anxiety and Depression Scale;
RRS - Ruminative Responses Scale.
Treatment medication included: antivirals, antidepressants, antibiotics, painkillers
Number of CFS symptoms is out of 8 additional symptoms in the CDC/Fukuda criteria

CFS: Correlation between Illness measures and self-report measures

Correlational analysis within the CFS group was conducted on 30 people, due to missing questionnaires data from three participants following the listwise exclusion. A higher self-reported number of CFS symptoms was significantly correlated with higher scores on RRS Depressive subscale $r(30) = .41$, $p = .025$. All other correlations between psychological measures and CFS symptom measures were non-significant, all $p > .05$.

Manipulation Check: Rumination or Distraction Induction

Results of the correlational analysis conducted separately for Distraction and Rumination groups, pre- and post-induction, are presented in Table 5**.** Following Distraction induction, the positive correlations between negative mood and Ruminative Responses weakened. The test of the difference between two dependent correlations showed that the relationship between Depressive rumination and Sad mood weakened significantly after the Distraction induction, $z = 1.74$, $p = .041$. Differences between other correlations were non-significant, $p > .05$.

Following Rumination induction, the relationship between negative mood and Ruminative Responses strengthened with significant correlations detected between Depressive rumination and Sadness, Anxiety, and Happiness (reverse scored); and Brooding rumination and Anger. The test of the difference between two dependent correlations showed that the correlation between HappyREV (reverse scored) and Depressive rumination was significantly stronger post-induction, $z = 1.85$, $p = .032$. That means following the rumination induction participants' happy mood might have decreased substantially while depressive tendencies increased. Pre- and post-induction differences between other correlations were non-significant, $p > .05$.

Table 5.

Correlations Between Ruminative Responses Scales and Mood

	Distraction Group Pre-Induction, *n* = 32				
	Sad	Anxious	Angry	HappyREV	CalmREV
Depressive	.466**	.423*	.283	.280	.257
Brooding	.416*	.324	.091	.059	.221
Reflective	.291	.150	.032	.187	.067
	Distraction Group Post-Induction				
	Sad	Anxious	Angry	HappyREV	CalmREV
Depressive	.317	.404*	.283	.284	.312
Brooding	.276	.363	.173	.222	.191
Reflective	.224	.160	.114	.247	.152
	Rumination Group Pre-Induction, *n* = 34				
	Sad	Anxious	Angry	HappyREV	CalmREV
Depressive	.424*	.254	.308	.163	.368
Brooding	.260	.270	.264	.064	.296
Reflective	.111	.268	.055	-.069	.037
	Rumination Group Post-Induction				
	Sad	Anxious	Angry	HappyREV	CalmREV
Depressive	.486**	.426*	.320	.358*	.291
Brooding	.369	.304	.393*	.207	.296
Reflective	.146	.034	.003	.070	-.112

Note. * p < .05, ** p < .01

Cognitive state and Mood Volatility

The third hypothesis was supported. It predicted that the CFS subgroup in the Rumination condition would experience an increase in negative mood, compared to the control group, while the CFS subgroup in the Distraction state would experience a decrease in negative mood. A significant interaction of group 2 (CFS, Control), induction 2 (Rumination, Distraction) and Time 2 (Pre-Induction, Post-induction), F (1, 62) = 5.09, p = .028, η_p^2 = .076 in the 2 x 2 x 2 x 5 ANOVA, with mood scores as the dependent variable, indicated that in the CFS group the mood scores changed significantly after the induction, compared to the control group (see *Figure* 3.)

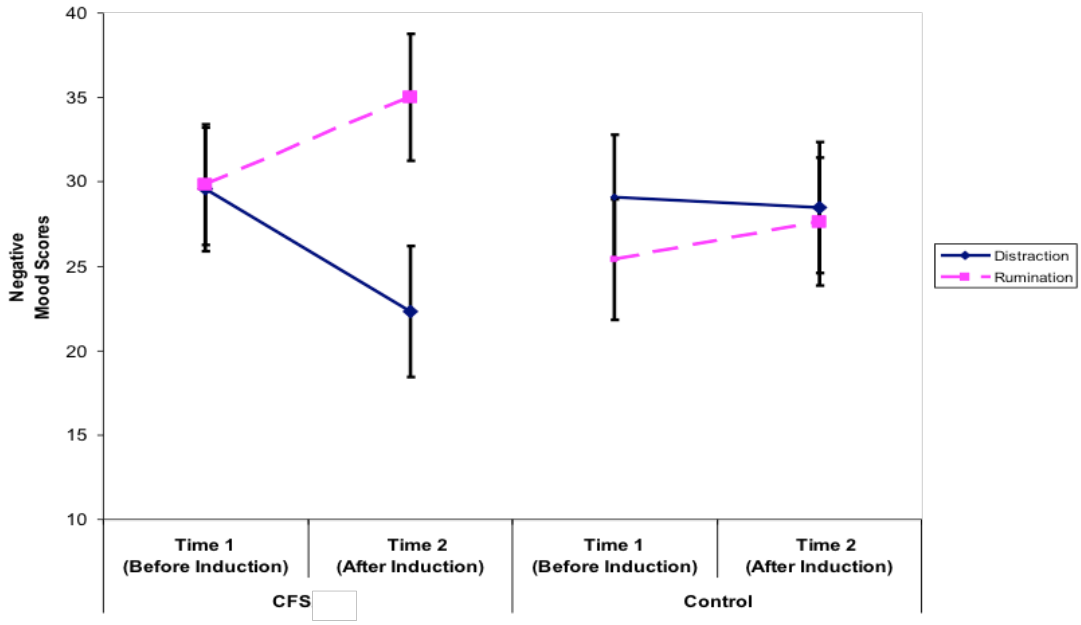


Figure 3. Mood scores (means and standard errors) for the group with CFS and the healthy control group before and after the rumination and distraction induction.

To break down the significant three-way interaction independent samples *t*-tests were conducted to compare mood scores between participants assigned to the Distraction and those assigned to the Rumination conditions, for CFS and Control groups separately.

Within the CFS group before the induction, there were no significant mood differences between subgroups assigned to Distraction (M = 29.56, SD = 15.53) and Rumination (M = 29.82, SD = 13.54) conditions, $p > .90$. After the induction, participants with CFS under the effect of Rumination (M = 35.00, SD = 15.74) had significantly higher negative mood than participants with CFS under the effect of Distraction (M = 22.31, SD = 14.13), $t(31) = 2.43$, $p = .021$. Paired samples *t*-tests demonstrated that in the CFS participants assigned to the Rumination condition the increase in negative mood was borderline significant after the induction, $t(17) = 2.05$, $p = .056$. For the participants with CFS assigned to Distraction, negative mood decreased significantly after the Distraction induction $t(16) = 4.15$, $p = .001$. Comparable analysis for the control group showed no significant differences, both $p > .50$, indicating that the mood of the healthy controls was not affected by either induction type.

In order to discover whether the underlying different levels of depression could account for the group*induction*time interaction, HADS Depression was entered into the above ANOVA as a covariate. The analysis revealed the same significant induction*time*group interaction: $F(1,59) = 4.80$, $p = .032$, $\eta_p^2 = .075$. Similarly, the

interaction remained significant after including the following covariates: Social Desirability $F(1,59) = 5.64$, $p = .021$, $\eta_p^2 = .086$; HADS Anxiety $F(1,59) = 4.45$, $p = .039$, $\eta_p^2 = .070$; or RRS subscales of Brooding, Reflecting, and Depressive $F(1,58) = 4.43$, $p = .040$, $\eta_p^2 = .07$. In addition, ANCOVA with depression, age and educational level (due to non-significant differences between groups on the last two variables) as covariates revealed comparable results, in particular, a significant three-way group*induction*time interaction $F(1,57) = 4.52$, $p = .038$, $\eta_p^2 = .074$. The induction*time interaction remained significant $F(1,30) = 13.97$, $p = .001$, $\eta_p^2 = .318$ when number of self-reported symptoms was entered as a covariate in the analysis for CFS group only. The negative mood increased significantly after the Rumination ($p = .044$), and decreased significantly after the Distraction ($p = .002$), suggesting that the effect was not underpinned by symptom number in the CFS group.

The above 2 x 2 x 2 x 5 ANOVA did not show significant main effects of Group 2 (CFS, Control), Induction 2 (Rumination, Distraction), or Time 2 (Pre-induction, Post-induction), all $p > .05$. The significant main effect of Mood 5 (Sad, Anxious, Angry, HappyREV, CalmREV) $F(4, 248) = 34.90$, $p < .001$, $\eta_p^2 = .360$ showed that all participants reported significantly lower Happy mood (HappyREV $M = 38.38$, $SD = 18.10$) than Sad ($M = 30.35$, $SD = 22.06$), Anxious ($M = 30.83$, $SD = 21.90$), Angry ($M = 11.41$, $SD = 14.19$), or Calm (CalmREV $M = 31.13$, $SD = 17.97$), all pairwise comparisons (Bonferroni adjustment) $p < .01$. Additionally, all participants scored significantly lower on Anger than on all other mood types; for all pairwise comparisons (Bonferroni adjustment) $p < .001$.

Relationship between Mood Volatility and CFS Symptom number

Correlational analysis revealed that for participants with CFS assigned to Distraction, there were no significant relationships between symptom number and VAS mood scores pre- or post-induction, all $p > .05$

For CFS participants assigned to Rumination, self-reported number of symptoms was not significantly associated with mood at Time 1 (pre-induction), all $p > .05$. In contrast, after participants with CFS were put into the ruminative state, there were significant correlations between self-reported symptom number and mood measured at Time 2 (post-induction). A higher number of symptoms was associated with more Sadness $r(17) = .51$, $p = .038$, greater Anxiety $r(17) = .73$, $p = .001$, and less Calm $r(17) = .57$, $p = .018$. This was not due to a significantly greater number of symptoms being reported by those in the rumination compared to the distraction condition, $t(31) = 1.33$, $p = .193$ (Rumination $M = 5.24$, $SD = 2.14$, Distraction $M = 4.38$, $SD = 1.50$).

The test of the difference between two dependent correlations with one variable in common showed that the difference was significant for Anxiety z = -2.34, p = .025. It demonstrated that the correlation between the number of reported symptoms and Anxiety before the Rumination induction was significantly weaker than the correlation between the number of reported symptoms and Anxiety after the Rumination induction. The differences were not significant with regard to Sadness and Calm, both p > .10.

Exogenous Cueing Task: Attentional Bias

Raw Data Analysis

The 2 x 2 x 3 x 2 ANOVA with Group 2 (CFS, Control) and Induction 2 (Rumination, Distraction) as between-measures and Word type 3 (Illness, Social Threat, Neutral) and Trial type 2 (Valid, Invalid) as within-measures did not show significant differences between groups and inductions, all showed p > .05. There were also no significant interactions involving group or induction factors all F < 1. The main effect of trial type $F(1, 62) = 128.39$, p < .001, η_p^2 = .674 demonstrated that both groups responded faster on the valid trials (M = 376.21ms, SD = 122.57) than on the invalid (M = 408.77ms, SD = 131.46), supporting the validity of the experimental premise.

Attentional Indices

Group means and standard deviations for the indices of Attentional Bias, Engagement and Disengagement within each Induction condition are presented in Table 6.

Table 6.

Mean Scores on Attentional Indices for Illness, Social Threat and Neutral Words from the Exogenous Cueing Task for CFS and Healthy Control Groups in Rumination and Distraction Conditions

	CFS		Healthy Control	
	Rumination	Distraction	Rumination	Distraction
Attentional Indices	n = 17	n = 16	n = 17	n = 16
	***M* (SD)**	***M* (SD)**	***M* (SD)**	***M* (SD)**
Attentional Bias				
Illness	34.7 (35.1)	33.9 (33.8)	29.1 (20.7)	31.7 (23.2)
Social threat	29.9 (32.6)	41.7 (29.6)	28.7 (20.7)	32.5 (21.8)
Neutral	33.7 (30.9)	35.7 (27.1)	33.1 (23.6)	26.1 (14.1)
Engagement				
Illness	-0.3 (15.7)	2.8 (21.1)	-0.5 (22.2)	0.5 (11.9)
Social threat	-2.8 (13.8)	7.9 (24.5)	0.5 (16.4)	4.1 (13.4)
Disengagement				
Illness	1.3 (17.9)	-4.5 (18.4)	-3.5 (12.4)	5.1 (20.9)
Social threat	-1.1 (14.1)	-1.8 (19.5)	-4.9 (14.5)	2.2 (14.2)

Attentional Bias

Hypothesis 1 predicting that the CFS group, compared to controls, would demonstrate an attentional bias towards illness-related words was not supported. The 2 (Group: Control, CFS) x 2 (Induction: Rumination, Distraction) x 3 (Word type: illness, social threat, neutral) ANOVA did not show significant differences between groups or inductions, and no significant interactions with group or induction factors, all $F < 1$, $p > .05$. Paired samples *t*-tests used to compare Illness and Social Threat bias scores against the baseline of Neutral bias scores did not reveal any significant differences, all $p > .05$ (see *Figure 4*).

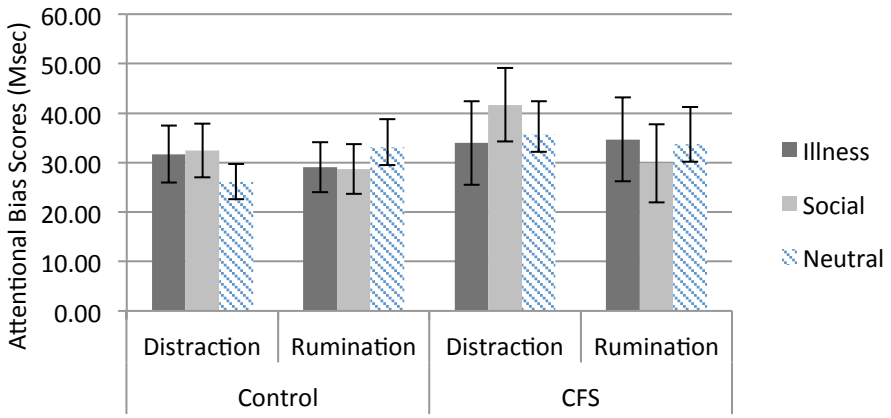


Figure 4. Attentional Bias scores, means (in Msec) and standard errors, for each word type (Illness; Social Threat; Neutral) for CFS and Control groups in two induction conditions (Rumination; Distraction).

Attentional Engagement and Disengagement

Hypothesis 2 predicting that the CFS group in a ruminative state would demonstrate attentional engagement with illness-related information, reflecting hypervigilance under the effect of self-focused rumination, (in contrast to both the CFS group under distraction and the healthy controls in either cognitive state) was not supported.

The results of four 2 x 2 ANOVAs with Group 2 (CFS, Control) and Induction 2 (Rumination, Distraction) as between measures and the four indices of attentional engagement and disengagement for Illness and Social Threat as dependent measures did not show significant main effects of group or induction, and no significant group x induction interaction; in all cases $p > .05$.

Relationship between Attentional indices and CFS symptoms measure

The CFS group was split into two groups based on the number of reported symptoms. Those who reported the minimum of 4 symptoms required by the Fukuda/CDC criteria were allocated to the Low symptom group (n = 19) while those who reported 5 symptoms and above (out of a total of 8 symptoms) were allocated to the High group (n = 14).

A 3 x 2 x 3 factorial design ANOVA with Group 2 (CFS Low; CFS High; Control) and Induction 2 (Rumination, Distraction) as between subjects measures and Word type 3 (Illness, Social Threat, Neutral) as the within-subjects measures did not reveal significant group or induction differences, and nor did it reveal a main effect of Word type, or any critical interactions with group or induction factors, all $p > .05$; thus again hypotheses 1 and 2 were not supported.

Within the CFS group, Pearson correlations between attentional indices (attentional bias, engagement and disengagement scores) and self-reported symptom number did not show significant relationships, all r in the range between -0.43 and 0.11, all $p > .05$. Similarly, no significant correlations were observed between HADS depression and anxiety and attentional indices, all showed r in the range of -0.23 and 0.34, all $p > .05$. However, a significant positive relationship was shown between Social Desirability scores and attentional bias towards Illness r (33) = .45, p = .009, bias towards Social threat r (33) = .42, p = .015, Illness Engagement r (33) = .44, p = .012 and Social threat engagement r (33) = .35, p = .045. Additionally, the analysis showed a significant negative association between Ruminative Brooding and attentional bias for Illness r (33) = -.52, p = .002.

Considering that there were no significant differences between CFS and control groups on social desirability and ruminative responses (see Table 4), analogous correlational analysis was conducted for the control group. The results were partially similar showing only a significant relationship between social desirability and Social threat bias r (33) = .36, p = .046, but not between Illness bias and social desirability or ruminative responses, with r in the range of -.27 and .13, all $p > .10$.

Discussion

The experimental component presented in this chapter used an exogenous cueing task to assess attentional bias towards illness-related information in CFS. The experiment investigated the relationship between the induced cognitive state of rumination and attentional bias, and the relationship between rumination and negative mood in CFS

compared to the healthy control group. The hypothesis that the CFS group under the state of rumination would show increased attentional bias, compared to both the CFS group under the distraction condition and the healthy controls who would show no bias, was not supported. The exogenous cueing task results did not show significant differences between CFS and control groups in attentional bias towards illness-related information, and no significant group differences on engagement or disengagement attentional indices.

Similarly, the results showed neither significant differences between participants under the effect of Rumination and those under the effect of Distraction, nor significant interaction between group and induction factors. There were no significant differences in ruminative tendencies between CFS and healthy control groups either, contrary to the fourth hypothesis. The correlational analysis showed a negative relationship between attentional bias for illness and the Brooding subscale, where more brooding appeared to be associated with reduced attentional bias, contrary to the hypothesised direction. However, the complexity of the construct of rumination, as discussed by Watkins (2008), needs to be taken into account. He proposed that repetitive thoughts, as reflected by the rumination construct, can lead to both constructive consequences (e. g. adaptive planning and health-promoting behaviours) and unconstructive ones (e.g. higher depression and anxiety, and physical health difficulties), depending on the quality of such repetitive thoughts (Watkins, 2008). Although the RSS scale is meant to separate the construct of Reflection, that is adaptive rumination, from the construct of Brooding, that is maladaptive rumination, the overlap may account for the current finding. Besides, the CFS group did not show greater tendencies to ruminate compared to the healthy control group, indicating that their type of brooding, as related to attentional bias in the current experiment, may be reflective of the more constructive type.

In support of the third hypothesis predicting the effect of self-focused rumination on negative mood, the CFS subgroup under the Rumination condition showed an increase in negative mood while the CFS subgroup under the Distraction condition showed a decrease in negative mood. There was no indication of the same effect of rumination on negative mood in the control group. The results may indicate that increasing somatic focus (e.g. by inducing a state of rumination) does not amplify attentional bias, but does increase negative mood. Conversely, while distraction does not reduce attentional bias, it does decrease negative mood in CFS. This direct relationship between rumination and negative mood is in line with most other research demonstrating that rumination enhances negative mood (Nolen-Hoeksema et al., 2008). Furthermore, the results showed a positive correlation

between reported negative mood, specifically Anxiety, and number of symptoms, if under a ruminative state. There was no evidence of the relationship between negative mood and symptom number for participants with CFS in the distraction state. Notably, that was not due to CFS participants in rumination reporting more symptoms than CFS participants under the distraction condition. Consequently, while rumination may not appear to have a direct effect on attentional bias, it may have an effect on mood, which in turn may affect subjective perception and report of symptoms. The relationship between negative mood and increased symptom reporting is in line with previous findings in healthy people (Howren & Suls, 2011).

The absence of an attentional bias here is a similar finding to the earliest attention experiment with a Stroop task (Moss-Morris & Petrie, 2003). This finding does, however, contradict another study of attention bias towards health-threat in CFS using a visual probe method, which showed the evidence of attentional bias towards health-threat in CFS group compared to healthy controls (Hou et al., 2008). The difference in the results may be due to the different methodology employed. The exogenous cueing task used in the current experiment was meant to test the early stages of attentional processing, and to be more sensitive to the initial capture of attention, than the visual probe task utilised by Hou and colleagues.

There are three methodological differences between the current and the Hou et al experiments. This study used 100 ms stimuli presentation time, presented only one word stimulus at a time, and used words that were symptom and fatigue descriptors. Conversely, Hou and colleagues employed a visual probe task that presented word or picture stimuli in pairs (one highly health-threatening and one neutral) for 500ms (longer exposure), which is thought to measure higher order strategic processing (Fox et al., 2001). Together the two studies may indicate that attentional bias in CFS occurs at the later strategic processing stage rather than in the early stage of attentional capture. The bias may emerge at the later strategic processing level, perhaps, in the form of difficulty in the disengagement of attention from threat (Koster et al., 2004; Koster et al., 2006). The current method, due to the lack of competing stimuli and short stimulus presentation time, may not be sensitive enough to identify the subtleties of the attentional disengagement process.

The fact that no attentional bias was found in the group with CFS may reflect a lack of activation of the appropriate schema. Crane and Martin (2003) found that IBS patients, when an illness schema was activated through rumination on IBS treatment and IBS-related cues, detected more symptoms, of greater severity, and attributed them to IBS, as opposed

to when a more neutral IBS schema was activated through the focus on the neutral aspects of symptoms (e.g. time of day when it occurred). Therefore, the attentional bias may manifest only when such a schema is accessed, and this means that the challenge is in choosing stimuli that reflect the content of such schema. While the current study also attempted to activate the illness schema through rumination, the procedure to induce rumination differed in that it concerned generic psychological and physical information, rather than information related specifically to CFS symptoms, as in the Crane and Martin (2003) IBS experiment.

The word stimuli in this experiment were intended to reflect the symptoms and labels that people with CFS would associate with their condition. However, people with CFS may associate their illness with more general and more threatening stimuli, as used by Hou et al. (2008), due to the scarcity of information about CFS and their beliefs in the seriousness and biophysical origin of it. This is in contrast with the more symptom-specific and fatigue-centric stimuli used in the current study or in the one by Moss-Morris and Petrie (2003). Henderson, Hagger, and Orbell (2007) showed that attention in healthy populations was influenced by stimuli that were illness-specific rather than generally threatening. Their participants showed attentional bias towards words associated with the common cold after recalling a recent experience of having a common cold. When asked to think about cardiovascular disease, the participants showed attentional bias towards words associated with cardiovascular disease, rather than common cold words

Therefore, the more general and severe threat stimuli utilised by Hou et al. (2008) may not alone account for the difference, but it is possible that they tapped into a more relevant aspect of the illness schema in CFS. The selected illness-related words in this study might not have been illness-relevant enough for the participants with CFS, and therefore might not have reflected their actual concerns. The threat level of the word stimuli in this study was lower than of the stimuli used by Hou and colleagues. The choice of stimuli for the attentional task has to be considered carefully for it to be representative of the health-threat for people with CFS. Care has to be given, for instance, to the specificity of the stimuli, its ecological validity (words, for example, may be too abstract to represent a concrete health-threat), and the severity of the threat. All these factors play important roles in the process of tapping into the subtleties of attentional processing (Henderson et al., 2007; Roelofs, Crombez, Peters, Verschuere, & Vlaeyen, 2005). Furthermore, more recent evidence of attentional bias in CFS suggested further subdivision within the CFS population. Hou and colleagues (2014) have uncovered an attentional bias for health-threat in those

participants with CFS who also demonstrated impaired attentional control, but not in those with attentional control at comparable levels to healthy controls.

There are a number of methodological limitations in this study. Firstly, the exogenous cueing is proposed as a paradigm for testing initial automatic reflexive attention, and thus initial orienting of attention towards stimuli (Fox et al., 2001). However, the task may be less sensitive to the movement of attention, due to the very fast response times recorded across all valid trials, therefore making it difficult to discern whether the attentional orientation towards threat is faster than that towards neutral stimuli (Fox et al., 2001; Mogg, Holmes, Garner, & Bradley, 2008).

Secondly, the selected stimuli may not elicit an attentional bias in the CFS group due to low relevance. The words have been rated as low to mid-relevant to health-threat and low on emotional threat. The words were chosen to reflect the feeling of fatigue and to be relevant to symptoms of CFS, as they were assessed in the study. However, participants were not asked to rate them as relevant to their own symptoms, but as generally relevant to health-threat. Likewise, Deary (2008) proposed that the health-threat in CFS may not correspond to the illness itself (as reflected by such symptom words as "tired" or "sore") but to the factors that threaten the established energy balance – that is to say, the achieved accommodation to the illness. Therefore, while the selected words might have reflected the symptoms, they might not have been regarded as a health-threat.

Another limitation of this study is the assessment of the effect of the cognitive state induction. Generally, the mood is expected not to change via the induction, because it is meant to act on the cognition. Conversely, the mood measure is an accepted procedure in studies that used cognitive state induction. The Visual analogue scale (VAS) that was used as a mood measure also has its drawbacks. Although VAS has been found to be a valid measure of mood, including in populations with cognitive impairments (Arruda, Stern, & Legendre, 1996), its reported low reliability (Couper et al., 2006) is a concern. It was chosen as a sensitive measure of short-term change in mood over more discrete measures (e.g. Positive and Negative Affect Scale) (Watson, Clark, & Tellegen, 1988); however, it may be subject to response bias (Ahearn, 1997) and the scales may be regarded differently by healthy populations, compared to psychiatric populations (e.g. treating the scale as a continuum or as discrete values, or end aversion, or alternatively choosing extreme values) (McCormack, Horne, & Sheather, 1988).

While there is no standard procedure for measuring the direct effect of induction on cognitive state, there are measures of self-focus or measures of adherence to the procedure

that have been used as manipulation checks focus, but these have not been utilised in this experiment (Watkins & Teasdale, 2001, 2004). The Ruminative Responses Scale could have been used to measure the change in rumination post-induction, but in this study, ruminative tendencies were assessed only once at the end of the study, and it therefore would not have been appropriate to measure a change in cognitive state. A recently developed measure, Momentary Ruminative Self Focus Inventory (Mor, Marchetti, & Koster, 2015), has been utilized as a measure of cognitive state manipulation and should be considered for future research (Grol, Hertel, Koster, & De Raedt, 2015).

With regard to the manipulation, there are additional shortcomings. Participants were randomly allocated through a coin toss by the investigator. The coin toss is the most basic method of randomisation, but is generally not recommended because of the high chance of achieving unequal groups, especially when working with small sample sizes (Dettori, 2010). While that has not been a limitation of the current study, there is still a possibility of randomisation being compromised. Furthermore, using such a basic method may compromise consistent implementation, and the lack of a record makes it difficult to check the randomisation procedure. A better procedure would be generation of a random sequence, and then, for example, assigning odd numbers to condition A and even numbers to condition B (Schulz & Grimes, 2002). Another limitation of the manipulation was that the investigator was not blind to the condition to which participants were allocated. The experimenter herself had conducted the induction, thus providing a source of potential bias. A second experimenter would have been required to run the sessions who would have been blind to the induction condition. Due to lack of human resources, it was not possible to have a second investigator present for all the testing sessions.

Another limitation in the study is the potential difficulty in interpreting those aspects of the results which can be viewed as null results. The inconsistent results may be due to differences in the statistical power between the studies. The post hoc power analysis showed that with the sample size of 66 and alpha set at < .001, the power to detect the critical group by threat type by induction interaction was equal to .98. This study has an estimated 98% chance of detecting a large effect size, as obtained by Hou *et al*'s study at the significance level of $p < .001$. Therefore, the lack of evidence for attentional bias in the study is unlikely to be due to lower statistical power.

It may be that the difference in the results between this study and the study by Hou et al (2008) is due to differences in assessed populations. The representativeness of the current sample needs to be considered in light of recruitment limitations. The CFS group was

recruited through community and local CFS support groups. That is similar to the recruitment method employed by Hou and colleagues in the 2008 study. However, because the severity of fatigue was not measured in this study, we cannot compare the fatigue levels of the two populations, and therefore it is possible that Hou and colleagues accessed a more severely affected population. An additional major limitation of the current study is the lack of assessment of the severity or frequency of symptoms, including fatigue. The measure of symptoms only consisted of the CDC/Fukuda criteria, where participants were asked to report the nature and the number of symptoms they experienced in the past 6 months.

The point of concern in the current study is the similarity in anxiety scores between CFS and control groups. The anxiety scores of the CFS group in the current study were comparable to the CFS group in Hou et al (2008) investigation, 8.3 and 7.7 respectively. However, the reason that the scores of the CFS group did not differ significantly from the scores of the control group is because the latter scored similarly highly on anxiety 8.1. Thus it appears that we have drawn a sample from a healthy population who were abnormally high in anxiety. There were no extreme outliers in the healthy group that would influence the mean, and the range was between 1 and 14, compared to the range in the CFS group 0 – 16. That similarity in anxiety levels may in fact account for the similarity in attentional processes, considering the strong relationship between anxiety and attentional bias, particularly in the early stages of the attentional process (Mathews & MacLeod, 2005). However, Hou et al (2008) also did not detect significant differences in anxiety scores between CFS and control groups (p = .26), even while demonstrating significant differences between the groups in terms of attentional bias scores. Their analysis of covariance showed that differences in attentional bias between groups were not due to emotional factors, including anxiety and depression.

The generalizability of the current CFS group to the clinical population is limited because the current sample is drawn from the community. In this study participants have not undergone any laboratory diagnostic tests by a physician in order to exclude other potential conditions, although all participants were assumed to have undergone the necessary laboratory tests in order to be diagnosed with CFS. The recruitment solely relied on a self-report of the CFS diagnosis, and the self-report could not be checked through participants' GPs or medical specialists. It is notable that seven participants reported fewer than four out of the eight symptoms required for CDC/Fukuda diagnosis. The major limitation in the study is that fatigue severity and degree of disability was not assessed, which precludes comparisons with CFS groups in literature. That indicates the possibility that

the current sample, rather than representing the CFS population, was instead drawn from the subclinical population suffering from chronic elevated idiopathic fatigue, rather than being currently asymptomatic CFS patients.

There was no requirement in the inclusion criteria for the study that CFS diagnosis needed to be have been received in the past 6 months, as, for example, was part of the inclusion criteria for the most recent Hou et al study (2014), investigating attentional bias in CFS. Such a requirement, however, would have greatly impeded recruitment from a community sample. Thus, any person who had reported receiving a diagnosis of CFS by their GP or at a specialist clinic since an unspecified point in time has been included in the study.

Another issue involves the assessment of comorbid conditions, and then the exclusion or inclusion of them into the analysis. The comorbidity was also assessed through self-reports by using the HADS measure and through reports of comorbid diagnoses. Comorbidity, particularly with anxiety and depression, might have jeopardized the results; however, the results when such participants were excluded were comparable to the ones where they were included. There need to be very clear guidelines on how to exclude/include/stratify those participants who report comorbid depression and/or anxiety.

Taking into account the association between the cognitive focus (rumination on or distraction from the physical and psychological state), the negative mood and the symptom report, it would be informative to look directly into the relationship between mood, attentional bias, and CFS symptoms. Methodological considerations of using exogenous cueing need to be addressed by introducing another task that would be sensitive to different aspects of attentional processes – perhaps the visual probe task for a direct comparison between methodologies. The choice of stimuli would need to be considered on the basis of complexity, threat level, and competition for attentional resources.

Chapter 3: Study 2: Attention and Mood Experiment

Introduction

A perception that one's emotional balance is threatened may lead to sustained emotional arousal, which may be perceived as part of the illness symptomology in CFS (Deary, 2008). Similarly, other theoretical accounts of medically unexplained symptoms propose that negative mood and emotional distress may lead to increased attention on symptoms, illness worry and catastrophic interpretation of the symptoms, thereby maintaining negative illness cognitions and perpetuating the symptoms (Brown, 2004; Kolk, Hanewald, Schagen, & Gijsbers van Wijk, 2003).

The study described in Chapter 2, which investigated the effect of rumination on attentional bias towards illness in CFS, demonstrated that self-focused rumination increased negative mood in CFS group, compared to the CFS group in a distracted cognitive state and compared to the healthy controls. The finding points towards possible emotional dysregulation in CFS, which is reflected in greater mood volatility as a consequence of cognitive processes, such as rumination. This is supported by the existing empirical studies of the emotional mechanisms in CFS. Caseras et al. (2008) induced a state of fatigue in CFS and healthy control groups by playing videos of real life fatiguing situations while the participants were in the scanner. The researchers observed reduced brain activation among CFS participants in the dorsolateral and dorsomedial prefrontal regions, which previously have been found to be associated with emotion regulation (Ochsner, Bunge, Gross, & Gabrieli, 2002; Phan et al., 2005). On the other hand, Caseras and colleagues (2008) observed an increased activation in cerebellum, occipito-parietal regions and posterior cingulate cortex in response to fatigue provoking videos in CFS group, compared to healthy controls. These brain regions have been implicated in the processing of aversive or threatening emotional stimuli (Garrett & Maddock, 2006; Pourtois, Schwartz, Seghier, Lazeyras, & Vuilleumier, 2006).

On the basis of the theories and empirical evidence discussed above we would predict that if people with CFS experienced high emotional distress it would increase the attentional vigilance towards symptoms. However, in the study described in Chapter 2, ruminative self-focus increased negative mood, but did not lead to increased attentional focus on illness. Despite what one might expect, the evidence suggests that negative mood plays little role in attentional bias in CFS. Hou and colleagues (2008) did not observe a relationship between attentional bias and depression or anxiety in CFS. Similarly, Hou and colleagues (2014) study has not shown a relationship between attentional bias in CFS and depression. Likewise, in

spite of the rumination increasing negative mood in the experiment described in Chapter 2, no attentional bias was detected. The explanation for the latter may be that mood may not exert an influence at such early preconscious reflexive attention, as measured by the exogenous cueing task with only a very short duration (100ms) of threat stimuli presentation. Additionally, while there is a scarcity of evidence in the case of depression for an attentional bias towards threat in the early attentional stage, it is argued that the attentional process in depression is in fact more likely to be disrupted during the later conscious elaborative stages (Gotlib & Joormann, 2010).

The evidence from Hou and colleagues (2008, 2014) indicates that in CFS attentional bias may be pervasive regardless of the mood state. Thus, one would expect to observe attentional bias in both neutral and depressive moods in the CFS group. However, depressed mood may lead to the increased magnitude of attentional bias, and specifically in the later stages of the attentional process, with regards to a difficulty in disengaging from threatening stimuli, as evidenced by the studies in depression and attention (Gotlib & Joormann, 2010).

The absence of attentional bias being found in the study on attention and rumination described in Chapter 2 may also be due to the methodology. First, the exogenous cueing task and short stimulus presentation (100ms) might have been less suitable to measuring elaborative voluntary attentional stage. Second, the stimuli reflected feelings of fatigue specifically which might have been seen as low threat, rather than the high level health-threat that would reflect the serious consequences of an illness. The fact that the stimuli were of low health-threat level might have also resulted in the lack of attentional bias demonstrated by the CFS group. Therefore, the current study had a number of methodological modifications, which aimed to activate a negative illness schema and to tap into the later stages of attentional process.

In order to investigate the direct effect of mood on attention, the current experiment employed the Velten mood induction procedure. Participants were allocated to undergo either depressive or neutral mood induction before completing attentional tasks (Velten, 1968). In the tasks the stimulus presentation was lengthened to 500ms, which allowed the measurement of conscious attentional processing and the voluntary allocation of attention. Current evidence from Hou and colleagues (2008, 2014) points to the likelihood that attentional bias in CFS occurs at the later strategic processing stage. Therefore, one would expect to observe an attentional bias towards health-threat in the CFS group which would be given longer stimulus presentation time.

Moreover, one would also expect to observe biased processing in both the attentional capture, as measured by the index of attentional engagement, and in the later attentional disengagement stage that reflects difficulty in shifting attention away from threat stimuli. This is in accordance with the argument presented by Mogg et al. (2008), who re-examined the findings from the exogenous cueing task. Fox and colleagues (2001) proposed that the exogenous cueing task would be more sensitive to differentiating between attentional capture and attentional disengagement, and this would be achieved by measuring reflexive attention to noncompeting stimuli presented out of central field of vision. Consequently, Fox et al successfully demonstrated evidence of difficulty in attentional disengagement, rather than the speeded up attentional capture that has been shown by previous studies.

Mogg and colleagues (2008), however, identified a potential problem with interpreting the results of the exogenous cueing task. The issue involved a slowing down of reaction time because of the threatening nature of the stimuli (a sort of freeze response). Adjusting reaction times to account for the effect of a slowed-down response can lead to conflicting conclusions. Therefore, it remains unclear whether the bias lies in the attentional orientation to threat or in the difficulty in disengaging attention (Mogg et al., 2008). Evidence from the exogenous cueing task as used with people with Irritable Bowel Syndrome showed an attentional engagement with pain words in people with IBS, compared to healthy controls (Chapman & Martin, 2011a). On the other hand, impairment in attentional disengagement was detected in healthy individuals high on state anxiety using exogenous cueing task and stimuli presentation time under 500ms (Fox et al., 2001). The evidence from a dot-probe task also showed a difficulty in disengaging attention in people with chronic pain (Dehghani, Sharpe, & Nicholas, 2003; Roelofs, Peters, Fassaert, & Vlaeyen, 2005) and in healthy populations in response to highly and mildly- threatening pictures presented for 500ms (Koster et al., 2004).

Another experimental modification concerned the task difficulty and demand on cognitive load. The rumination and attention study in Chapter 2 attempted to tap into the negative illness schema in CFS hypothesised to bias information processing towards health-threat, contributing to the symptom perpetuation (Knoop et al., 2010). On that note, Moss and DiCaccavo (2005) suggested, under the assumption that cognitive resources are limited, that an illness schema would become evident through preferential processing of the stimuli consistent with that schema, if such cognitive resources are stretched when under a high mental load or when undertaking a difficult task.

In a visual probe task used by Hou et al. (2008), neutral and health-threat stimuli were presented together, and thereby were competing for cognitive resources; the results showed preferential processing of the health-threat by people with CFS. The exogenous cueing task employed in the Attention and Rumination study in this thesis lacked the competing stimulus and attentional resources were not stretched; thus the preferential processing may not have occurred. Taking into account the evidence for the nature of cognitive dysfunction in CFS such as slower processing speed and reduced efficiency of information processing (Majer et al., 2008), people with CFS might be expected to demonstrate preferential processing of the information consistent with the illness schema, if their cognitive resources are over-tasked. Due to its higher difficulty, the visual probe may put greater cognitive burden on the participants, thereby stretching their mental resources (Mogg & Bradley, 1999). The current experiment utilised the visual probe and the exogenous cueing tasks to investigate the attentional bias in CFS under the high and low cognitive load conditions. One would expect to see attentional bias towards health threat in the performance of the CFS group on the visual probe task.

Another important matter concerns threat severity and relevance to current illness concerns. People with more specific illnesses demonstrate attentional biases particular to their illness. People with social phobia showed attentional bias towards specific phobia-related words, in comparison to those with generalized anxiety, who showed broad-spectrum attentional bias towards all non-specific threat (Becker, Rinck, Margraf, & Roth, 2001). Stimuli that are highly relevant to individual concerns in specific disorders would activate an illness schema that would be congruent with the threat stimuli leading to attentional bias (Martin, Williams, & Clarke, 1991; Williams, Watts, Macleod, & Mathews, 1997). Henderson et al. (2007) showed that even healthy people, if primed with a specific illness schema (e.g. cardiovascular disease), demonstrated attentional bias towards the health-threat stimuli directly relevant to that specific illness schema, cardiovascular as opposed to common cold. The word and picture stimuli used by Hou and colleagues (2008) might have reflected the concerns of people with CFS, in spite of being a non-specific health-threat. People with CFS tend to have strong beliefs in the seriousness and the biomedical nature of their condition, and attribute a wide range of symptoms to CFS (Moss-Morris & Chalder, 2003). The range of symptoms associated with CFS is quite wide: from physiological, to cognitive and emotional, they encompass the entire spectrum of human functioning. CFS is a deeply pervasive condition, so it is more likely that general health-threat would activate the illness schema in CFS.

This study used the same word stimuli as by Hou and colleagues (2008). Also replicating their experimental set-up, health-threat pictures were incorporated into attention tasks. Pictures were suggested to be more relevant than words for illness groups (Moss-Morris & Petrie, 2003). There is a concern over the ecological validity of words, which may be too limited in context and meaning (Mogg & Bradley, 1999). Another problem with linguistic stimuli is the varying degree of familiarity participants have with the words, even if they are matched on frequency of use; this is a problem that doesn't apply to pictures (Mogg & Bradley, 1999). It should be noted though that Hou et al. (2008) study did not show group differences in response to words and pictures. In a pilot study for the current experiment, people with CFS or asthma and healthy controls were asked to rate word and picture stimuli on relevance to health-threat. The pictures were not regarded as more relevant to health-threat than the words were. Consequently, the prediction for the current study would be that reaction times to words and pictures would not differ significantly.

The final methodological modification was the addition of a comparison group with a different chronic illness, asthma, to investigate whether biased attentional processing may be characteristic of a chronic illness in general, rather than CFS in particular. Symptom monitoring can be an adaptive response aiming to manage the chronic condition. Asthma, for example, requires adherence to a daily medication regime or an early and quick detection of symptom escalation to prevent an asthma attack. However, De Peuter and colleagues (2007) suggested that over-perception of symptoms by those with a chronic illness may be one of the risk factors for negative health outcomes and symptom perpetuation; in asthma specifically, over-perception of symptoms may contribute to a lack of control over asthma symptoms. It was shown that external and internal cues may lead to increased sensitivity to symptoms (e.g. breathlessness) and amplified perception of symptoms in the absence of any physiological changes, within the asthma population (De Peuter, Lemaigre, et al., 2007). Rietveld (2003) suggested that emotional arousal may contribute to over-perception, though he did not specify what type of emotional arousal. Similarly, Janssens and colleagues (2009) proposed that high threat-level and depressed mood would lead to increased attentional vigilance in asthma; in contrast, neutral mood and low threat level were more likely to lead to avoidance. Even though the health-threat stimuli used in the current study could be considered high threat, they may be less relevant to people with asthma who would be more concerned with specific respiratory symptoms; people with asthma seemed to show more interference when responding to asthma-related words rather than general negative words (Jessop et al., 2004; Martinez-Moragon et al.,

2003). In asthma, though, empirical findings support the reciprocal relationship between attention and mood. While no difference was found between asthma individuals and healthy controls in their reaction to asthma-related words in a visual probe task, within the asthma group increased attentional vigilance for asthma-related health-threat was related to increased negative affect (De Peuter, Lemaigre, et al., 2007). Similarly, greater negative affect, such as depression and anxiety, was found to be related to increased perception of dyspnea in people with asthma (Martinez-Moragon et al., 2003). Therefore, one would expect to observe attentional bias in asthma only in depressive mood. Meanwhile, the CFS group would demonstrate attentional bias to general health threat regardless of mood, because their attentional focus on symptoms would be more extensive and pervasive, and less subject to variations in mood, compared to people with asthma.

Therefore, the first aim of the comparison with the asthma group in the current study was to check whether a pattern of over-monitoring and attentional vigilance would be typical of CFS population alone, or if this pattern would also be characteristic of other populations with chronic illnesses. The second aim was to compare the interaction between negative mood and attentional processes. In CFS, attentional bias would be expected to occur regardless of the mood, while in the asthma group only the state of negative mood would lead to increased attentional vigilance for threat.

Attentional bias in CFS is hypothesized to be pervasive and profound (Knoop et al., 2010; Moss-Morris, 2005), thus it would be expected to occur both in the engagement component, orienting and focusing attention on health-threat, and in the disengagement component, shifting attention away from health-threat. Attentional bias in CFS should occur regardless of the mood, in neutral and depressive mood states. While attentional bias may be observed in the easier exogenous cueing task, the more difficult task with higher cognitive load would be more likely to activate a negative illness schema, and therefore bias would be more likely to manifest in the visual probe task.

The hypotheses tested in the current studies are summarized in Table 1 for clarity.

Table 1.

The Summary of Hypotheses with Regard to Attentional Bias Under the Effect of Mood

#	Hypotheses	Task	Group	Mood	Prediction
1	In the exogenous cueing task, on account of the longer stimulus duration (500ms) and the high level of threat, the CFS group will demonstrate attentional bias towards health-threat in both neutral and depressive moods, compared to the healthy control and asthma groups. In comparison, the asthma group will demonstrate attentional bias towards health-threat only under the influence of a depressive mood.	Exogenous Cueing	CFS	Neutral and Depressive	significantly higher attentional bias scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional bias scores than Control
2	In the visual probe task, on account of the illness schema being activated under the high cognitive load, high level of threat, and long stimulus duration, the CFS group will demonstrate attentional bias towards health-threat in both neutral and depressive moods, compared to the asthma and healthy control group. In comparison, the asthma group will demonstrate attentional bias towards health-threat only under the influence of a depressive mood.	Visual probe	CFS	Neutral and Depressive	significantly higher attentional bias scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional bias scores than Control
3	In the exogenous cueing task, the CFS group will demonstrate attentional engagement when in either a neutral or a depressive mood, reflecting hypervigilance for threat, compared to asthma and control groups. The asthma group will demonstrate attentional engagement if in depressive mood, reflecting increased attention to health-threat under the effect of negative mood.	Exogenous Cueing	CFS	Neutral and Depressive	significantly higher attentional engagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional engagement scores than Control
4	In the visual probe task, the CFS group will demonstrate attentional engagement if in neutral or depressive mood, reflecting hypervigilance for threat. The asthma group will demonstrate attentional engagement only when in a depressive mood, reflecting hypervigilance for threat.	Visual probe	CFS	Neutral and Depressive	significantly higher attentional engagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional engagement scores than Control
5	In the exogenous cueing task, the CFS group will demonstrate attentional disengagement when in neutral or depressive mood, compared to the asthma and control groups. The asthma group will show attentional disengagement only when in depressive mood.	Exogenous Cueing	CFS	Neutral and Depressive	significantly higher attentional disengagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional disengagement scores than Control
6	In the visual probe task, the CFS group will demonstrate attentional disengagement when in neutral and depressive mood, as compared to the asthma and control groups. The asthma group will show attentional disengagement only when in a depressive mood.	Visual probe	CFS	Neutral and Depressive	significantly higher attentional disengagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional disengagement scores than Control

Method

Study Design

The study had a quasi-experimental design with two between-subjects independent variables. The first between-subjects factor was group: people with a CFS diagnosis were compared to age- and gender- and education-matched people with asthma and healthy controls. The second between-subjects factor was mood state: within each group (CFS, Asthma, Control) participants were randomly allocated to undergo either Depressive or Neutral mood state induction (Slyker & McNally, 1991; Velten, 1968).

Random allocation was achieved by randomizing a list of numbers and assigning odd numbers to Depressive mood and even numbers to Neutral mood. The same investigator conducted the induction and the rest of the study procedure, which included two computer tasks and questionnaire measures. It was not possible to have a second person conducting the testing, therefore blind testing by the experimenter was not achieved.

The within-subjects factor for the two attentional tasks included three types of stimuli (Health-Threat, Activity, Neutral). In this chapter, the analysis of Health-Threat stimuli is presented in comparison to Neutral stimuli. The analysis of Activity stimuli, as compared to Neutral, is presented in Chapter 4: Attention and Activity.

The main dependent variable was Reaction Times (RTs) on the exogenous cueing and visual probe tasks. RTs were converted into attentional indices such as attentional bias, engagement, and disengagement scores, which were the main variables of interest. Another dependent variable was mood scores, used to check the effect of mood state induction. Additional dependent variables included questionnaire measures to obtain the descriptive information about participants.

This study has been reviewed by and received ethics clearance through the University of Oxford Central University Research Ethics Committee (CUREC), assigned reference number: MSD/IDREC/C1/2009/42 (Appendix B.2).

Participants

People with CFS were included in the study if they:

1. Reported a primary CFS diagnosis by a qualified medical practitioner (GP, referred specialist). Any person who had received a diagnosis of CFS by their GP or at a specialist clinic in the past unspecified period of time was considered for inclusion into the study.

AND

2. Met the CDC/Fukuda criteria for the presence of current primary unexplained, persistent or relapsing fatigue, which is not relieved by rest and results in significant reduction of activities for the last 6 months (Fukuda et al., 1994).

AND

3. Reported four concurrent symptoms from the eight outlined by the CDC/Fukuda criteria: impairment in short-term memory/concentration, sore throat, tender lymph nodes, muscle pain, multi-joint pain, headache, unrefreshing sleep, post-exertional malaise more than 24 hours. For the diagnosis of CFS based on CDC/Fukuda criteria the minimum number of additional symptoms required is four symptoms experienced in the past 6 months.

Participants with CFS rated the frequency of their symptoms in the past 6 consecutive months (8 symptoms according to the Fukuda/CDC criteria) on a scale from 0 (never experience) to 4 (experience all of the time). The range of reported symptom frequency was between 12 and 26. The maximum score of 32 would suggest that an individual experienced all 8 symptoms all of the time – 4, multiplying 8 by 4. The minimum score of 12 in the CFS group was due to participants' experiencing minimum of 4 symptoms "most of the time" with an assigned score of 3, multiplying 3 by 4 led to the score of 12. Therefore, all participants in the CFS group met the CDC/Fukuda criteria and had been experiencing symptoms in the past 6 months. All participants with CFS reported experiencing the symptom of post-exertional malaise.

Participants were excluded if they reported

1. A current acute or chronic primary medical or psychiatric diagnosis that may be the cause of extreme fatigue and would preclude the diagnosis of CFS, for example any diagnosis of the conditions outlined by CDC/Fukuda (1994), Reeves et al (2003; 2005), or NICE (2007) guidelines.

2. A current diagnosis of primary depression, i.e. depression that was diagnosed in the past 5 years prior to receiving a CFS diagnosis, as recommended by Reeves and colleagues (2003; 2005).

Due to reported comorbidity of CFS and depression, the history of depression and anxiety was checked (Mccue et al., 2006). Three participants with CFS reported a previous diagnosis of depression and anxiety. Two of them reported a depression diagnosis after receiving their CFS diagnosis. One participant reported comorbid anxiety and depression after receiving their CFS diagnosis. These participants were included in the study because their depression/anxiety had not precluded their diagnosis of CFS.

Depression and anxiety have also been assessed using Hospital Anxiety and Depression scale (HADS) (Zigmond &Snaith, 1983). The recommended cut-off scores for the CFS population are 9-10 points (Morriss & Wearden, 1998). Six participants with CFS scored above 9 on HADS Depression and eight scored above 9 on HADS Anxiety. Crosschecking revealed that one person had a high score due to their reported comorbid depression diagnosed after receiving a CFS diagnosis; this individual was included in the study because their depression had not precluded their diagnosis of CFS. Other participants were included because of the absence of psychiatric comorbidity or a history of psychiatric disorder.

Participants in the asthma group were included in the study if they reported:

1. A primary asthma diagnosis by a qualified medical practitioner (their GP, or referred specialists).

AND

2. Current experience of asthma symptoms.

AND

3. Current use of medication to manage their asthma (e.g. preventer/reliever medication, inhaled corticosteroids).

Asthma duration was measured by the number of years since symptoms started and since a diagnosis by a physician. Asthma severity was rated on a three-point scale corresponding to mild, moderate and severe. The level of interference that asthma had on an individual's daily functioning was rated on a scale from 0 (not at all) to 10 (extremely) (Brooks et al., 1989).

Participants with asthma were excluded if they reported current acute or another chronic medical or psychiatric diagnosis. Three participants with asthma reported a diagnosis of depression and anxiety in the past. Two of them reported a history of depression diagnosis after receiving an asthma diagnosis, and one reported comorbid anxiety after receiving an asthma diagnosis. These participants were included into the study because their depression/anxiety did not preclude their diagnosis of asthma.

Potential depression and anxiety in the asthma group have also been assessed using HADS (Zigmond & Snaith, 1983). The recommended cut-off scores for the general population are 8-10 points (Herrmann, 1997; Zigmond & Snaith, 1983). Six participants with asthma scored above 8 on HADS Depression and eight participants scored above 8 on HADS Anxiety. Crosschecking revealed that one person had a high score due to their reported history of anxiety; this individual was included in the study because their anxiety had not precluded

their diagnosis of asthma. Other participants were included because of the absence of psychiatric comorbidity or history of psychiatric disorder.

Additional inclusion criteria for all participants specified 18 years of age, normal or corrected-to-normal vision, good hearing, good manual dexterity, and English at the standard of a native speaker. Healthy control participants were excluded if they reported current acute or chronic medical or psychiatric diagnosis. One control participant reported diagnosed depression in the past (longer than five years ago). They were included into the study, because their depression had been absent in the past five years.

The final sample consisted of 16 people with CFS, 25 with Asthma, and 28 healthy controls matched on age, gender, and education. People with CFS were recruited primarily from Oxford and Oxfordshire CFS support and self-help groups, from among the staff and students of the University of Oxford, through local advertisement via the Internet (Facebook, local health forums), complementary and alternative medicine (CAM) clinics, Oxford-based printed and online information sheets (DailyInfo, Gumtree), and newspaper advertisements and posters distributed in the community.

Participants with asthma were recruited through similar means as the CFS group, through contacting local support and self-help groups, complementary and alternative medicine (CAM) clinics, via online and newspapers advertisements, and local posters. Healthy controls were recruited via advertisement among the staff and students of the University of Oxford, the local communities of Oxford and its surrounds. Participants were compensated for their time, including their traveling expenses (up to £10).

Materials

Mood state induction

The procedure for the mood induction was adopted from previous studies of the influence of emotion on cognitive processing (Moore & Oaksford, 2002) and of the effectiveness of mood induction (Martin, 1990; Slyker & McNally, 1991). The research suggested that the most effective way to induce a mood is to include explicit instructions, music, and Velten statements (Velten, 1968).

In the depressive mood condition, participants were asked explicitly to change their mood and think about sad and negative things, while reading a list of statements and listening to a piece of music (Barber, Adagio for Strings), same as used by Moore and Oaksford (2002). The statements in the depressive mood condition described feelings of sadness, loneliness, discouragement, unhappiness, and the like.

In the neutral mood induction, participants were explicitly instructed to try and feel calm and think about neutral things unrelated to themselves, while reading through a list of statements and listening to a piece of music (Brahms 2nd movement from the 3rd symphony, as in the study by Moore and Oaksford (2002). In the neutral mood condition the statements contain neutral historical facts or various trivia.

The induction procedure took place before the computer tasks, and was therefore the first step in the procedure. Participants were randomly allocated either to depressive or neutral mood induction. In each condition, participants were instructed to read through a list of statements for eight minutes while at the same time listening to music. They were asked to read slowly to themselves, and to use their imagination and concentration to focus on each of the ideas presented in the sentences, and to visualize each item (see Appendix B.5 for the full induction procedure).

The induction procedure took eight minutes. The effect of the induced mood was expected to last for the duration of the two computer tasks that is a minimum of 25 minutes (Frost & Green, 1982; Sinclair et al., 1994). Participants' mood was assessed via a self-report measure prior to and instantly after the induction. Participants started the first computer task immediately after the induction.

Exogenous Cueing Task

Exogenous cueing methodology was adopted from a study on anxiety (Fox et al., 2001) and attentional bias in IBS (Martin & Chapman, 2010). It is a valid measure of attentional processing for assessing the earlier stages of spatial allocation of attention and the orientation of attention, in accordance with eye-tracking research that suggested a good degree of correspondence between gaze and attention (Armstrong & Olatunji, 2012; Fox et al., 2001). A single cue (neutral or threat word) was presented either on the left or on the right side of a computer screen for the duration of 500 milliseconds (ms). Immediately after the cue disappeared, a target (the dot) was presented in one of the two locations, either in the same location as the preceding cue (a valid trial) or on the opposite side of the screen (an invalid trial). Participants were instructed to respond as quickly as possible to the appearance of the dot and press the button indicating whether it appeared on the left or on the right. The reaction times were the dependent variable measured.

An experimental trial started with a presentation of a central fixation cross (size 14 mm x 14 mm) on a computer screen for 500ms, followed by a stimulus (word or picture) presented for 500ms either on the left or on the right of the fixation cross. The words varied

in size depending on their length; the length range was 40 – 95 mm, the height 6 – 10 mm. Their distance from the fixation point was 46mm. The pictures measured 70mm in height and 96mm in length. The distance from the fixation point to the inner edges of the pictures was 46mm. The picture size and positioning were replicated from experiments into attentional bias in individuals with anxiety (Lees, Mogg, & Bradley, 2005) and CFS (Hou et al., 2008).

The stimulus was followed by a 50ms blank mask. Then the dot (1mm in diameter) appeared either on the left or on the right side of the screen, 46mm from the fixation point, and stayed on the screen until participant responded or for 2500ms. Inter-trial interval was 1000ms. *Figure 1* presents a graphic representation of two types of experimental trial, valid and invalid.

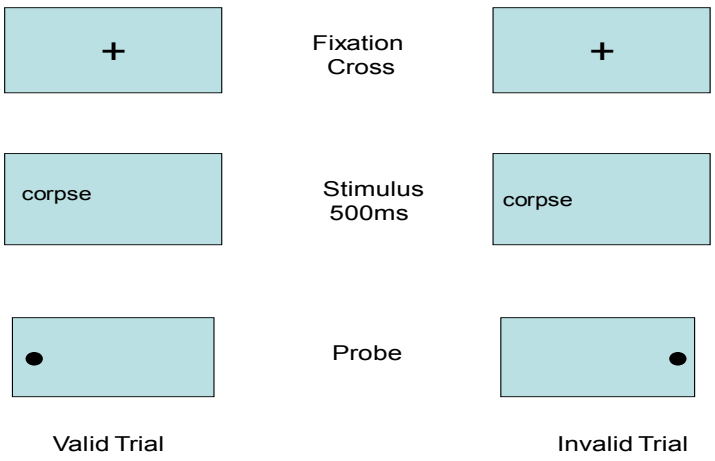


Figure 1. The sequence of stimuli presentation in the exogenous cueing task on valid and invalid trials.

Instructions

The instructions given to the participants included: to look at the fixation cross on the monitor and when they saw a dot appear on the left or on the right side of the screen press a key on a computer keyboard to indicate whether it appeared on the left (**z** key) or on the right (**m** key) side of the screen. Participants were instructed to concentrate on locating the dots and not the words or pictures (which might have preceded the dots), to be as fast and as accurate as possible, and to maintain their gaze on the fixation cross at the centre of the screen.

Participants received instructions and completed a practice block (16 trials, 8 word and 8 picture trials), after which they had the opportunity to ask any questions or rerun the

practice. Each stimulus was presented four times, in two positions (left and right) and in two trial types (valid and invalid), and therefore the presentation of 16 Health-threat, 16 Activity, and 16 Neutral words produced 192 experimental word trials in total. Similarly, there were 192 picture trials. Participants completed a total of 384 experimental trials. The presentation of trials was randomized. An additional 24 catch trials, where just the dots appeared without being preceded by a word, were used to ensure participants focused on the dots and not the words. The task took about 13 minutes to complete.

Exogenous Cueing task stimuli

Words

Three types of words used in the task included: Health-Threat (e.g. funeral), Activity (e.g. jogging), and Neutral (e.g. keyhole) (see Table 2). The health-threat words were selected from the previous study on attentional bias in CFS (Hou et al., 2008). Activity words represented two types of activities: domestic chores (e.g. washing), and mild exercise (e.g. jogging). The aspect of the methodology concerning word selection and rating is described in the section, Stimuli Ratings.

Sixteen words of each type were used, which varied in length (5 to 12 letters) and frequency. Frequency ratings were based on Carroll, Davies, and Richman (1971) norms (U - *estimated frequency* of a word in print *per million tokens*). All three types of words were matched on word length $p > .99$, and frequency $p > .98$ (see Table 2).

Table 2.

Word Stimuli Lengths and Frequencies for the Exogenous Cueing Task

Health threat	Freq U	Length	Activity	Freq U	Length	Neutral	Freq U	Length
cancer	4.26	6.00	hurrying	10.00	8.00	flute	3.59	5.00
casualty	0.08	8.00	dusting	1.50	7.00	ballot	1.40	6.00
coffin	3.16	6.00	washing	24.00	7.00	ribbon	18.80	6.00
collapse	2.44	8.00	sweeping	15.20	8.00	perfume	8.90	7.00
coronary	0.23	8.00	skipping	6.00	8.00	valiantly	0.58	9.00
corpse	1.82	6.00	jogging	0.48	6.00	thymine	0.05	7.00
diseased	1.40	8.00	bicycles	0.30	8.00	quartet	1.40	7.00
dying	14.20	6.00	cleaning	14.00	8.00	stripe	0.86	6.00
fatal	5.68	5.00	swimmer	4.29	7.00	waterproof	1.40	10.00
funeral	4.58	7.00	gymnasium	3.30	9.00	cobblestone	0.43	11.00
hospitalised	0.17	12.00	ironing	1.00	7.00	element	40.00	7.00
illness	10.75	7.00	wiping	3.10	6.00	granite	8.80	7.00
infectious	1.17	10.00	gardening	0.90	9.00	quadrangle	0.18	10.00
operation	32.18	9.00	vacuuming	0.10	9.00	grapefruit	2.40	10.00
paralysed	2.76	9.00	mopping	0.40	7.00	aisle	1.70	5.00
spasm	0.32	5.00	lifting	11.00	7.00	keyhole	0.19	7.00
	5.32	**7.50**		**5.97**	**7.56**		**5.67**	**7.50**

Note: Words were matched for length and frequency
using Carrol, Davies and Richman's 1971 norms
U - estimated frequency per million tokens

Pictures

Some of the picture stimuli were selected from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2008). The rest of the images were obtained from public online image depositories. The images were found through Google image search using key words describing the content of the pictures, such as paralysed to search for an image of a person in a wheelchair. All images were converted into black and white. The content of each experimental image matched the meaning of the word stimuli accordingly: 16 Health-Threat images (e.g. picture of a person in a hospital bed to match the word 'hospitalised'), 16 Activity images (a picture of a person sweeping the floor to match the word 'sweeping'), and 16 Neutral images (a picture of a ribbon to match the word "ribbon"). Not all neutral images matched the neutral words exactly for two reasons: firstly, because of the difficulty of matching images to particular words, e. g "valiantly"; secondly, because of the necessity of matching neutral images to Health-Threat images in content and complexity. The Health-Threat images used in the Exogenous Cueing task are presented in Appendix B.6.1, the Activity images in Appendix B.6.2, and Neutral in B.6.3. In total, there were 16 Health-Threat, 16 Activity, and 16 Neutral experimental pictures. An additional eight neutral pictures were used for the practice trials.

Exogenous Cueing Task Data Preparation

The Reaction Time (RT in milliseconds) data from the exogenous cueing task were filtered by removing RTs for incorrect answers, and for responses below 100ms (considered an anticipatory response) and above 1500ms (considered a miss), as well as those at more than 2 *SDs* away from that participant's mean (Asmundson & Hadjistavropoulos, 2007; Fox et al., 2001). The three groups (CFS, Asthma, Controls) did not differ on accuracy rates, number of outliers, and amount of data included into the analysis (all $p > .30$). Statistical analyses were performed using filtered data.

Attentional bias scores were calculated for each word type by subtracting valid trials' RTs from invalid trials' RTs (Asmundson & Hadjistavropoulos, 2007). If RTs on invalid trials were longer than RTs on the valid trials, the resulting positive values would indicate an attentional bias towards particular stimuli type. Meanwhile, if RTs on invalid trials were shorter than on valid trials, then the resulting negative values would indicate a pattern of avoidance.

Attentional indices of Engagement and Disengagement were calculated for each word type: Health-Threat, Activity and Neutral following the procedure outlined in previous studies (Koster et al., 2006). The Attentional Engagement index was computed by subtracting RTs on valid Health-Threat or Activity trials from valid Neutral trials ($RT_{\text{valid neutral}}$ - $RT_{\text{valid threat}}$). Positive values on the Engagement Index would suggest that threat words captured participants' attention, indicated by quicker responses towards threat on a valid trial than towards neutral stimuli.

The Disengagement index was calculated by subtracting RTs on invalid Neutral trials from invalid Health-Threat or Activity trials ($RT_{\text{invalid threat}}$ - $RT_{\text{invalid neutral}}$). Positive scores on the disengagement index would demonstrate difficulties disengaging from threat, due to quicker response on an invalid Neutral trial and slower response on an invalid threat trial, indicating a difficulty in switching attention from a threat towards the dot appearing in another location.

Visual Probe Task

The visual probe task presentation was adopted from the previous attentional bias experiments in CFS (Hou et al., 2008; Lees et al., 2005). It is a valid widely-used measure of attentional processing for assessing attentional allocation in the presence of emotionally threatening information in healthy populations (Murphy & Isaacowitz, 2008), in groups with anxiety (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007) and in

groups experiencing chronic pain (Schoth et al., 2012). Findings from eye-tracking research correspond to findings from studies using reaction times as measure of attention, such as visual probe, thus supporting its validity (Armstrong & Olatunji, 2012)

In the visual probe task, a stimulus pair (word- or picture-pair), one above and one below the fixation point was presented for the duration of 500ms on a computer screen. The stimulus pair consisted of one threat cue (word or picture) and one matched neutral cue (word or picture). After the stimulus pair disappeared, a visual probe (an arrow) appeared in one of the two locations, either in the same location as a threat cue or in the same location as a neutral cue. Participants indicated whether the arrow pointed to the left or to the right by pressing a button. Measured reaction times were the dependent variable.

An experimental trial started with a presentation of a central fixation cross (size 14 mm x 14 mm) for 500ms on a computer screen. It was followed by a word- or picture-pair presented for 500ms, with one cue above the fixation point and another cue below. For the word pairs, their vertical distance from the fixation point was 50mm, so the distance between their inner edges was 100mm. The words varied in size depending on their length, ranging in length 40 – 95mm and height 6 – 10mm. The picture size and positioning were replicated from the previous experiments in anxiety (Lees et al., 2005) and CFS (Hou et al., 2008). The pictures measured 70mm in height and 96mm in length. The distance between their inner edges was 50mm.

The stimulus pair was followed by a 50ms blank mask. Then the arrow (length 15 mm) appeared either above or below the fixation point (vertical distance from the fixation point was 46mm), and stayed on the screen either until participants responded or for 2500ms. The inter-trial interval was 1000ms. Figure 2 presents a graphic representation of two types of an experimental trial, probe replacing a threat stimulus and probe replacing a neutral stimulus.

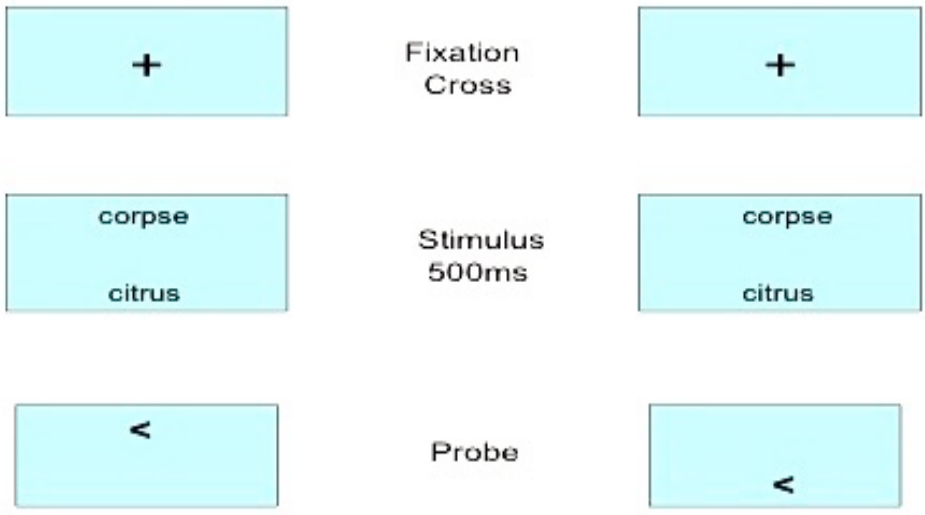


Figure 2. The sequence of stimuli presentation in the Visual Probe task

The following instructions were given to the participants: to look at the fixation cross on the monitor, and when an arrow appeared on the top or bottom half of the screen press, a key on the computer keyboard to indicate whether the arrow pointed to the left (**z** key) or to the right (**m** key). Participants were instructed to concentrate on detecting the arrows and not the words or pictures, which might have preceded them. They were asked to be as fast and as accurate as possible and maintain their gaze at the centre of the screen.

Participants received instructions and completed a practice block (16 trials, 8 word and 8 picture trials), after which they had the opportunity to ask any questions or rerun the practice. Each experimental word or picture pair was presented four times, so that each threat cue was presented in two positions (above and below the fixation point) and the arrow replaced the threat cue (valid trial) or the neutral word (invalid trial). Therefore the presentation of the 48 pairs (16 of each: Health Threat- Neutral, Activity – Neutral, Neutral - Neutral) produced 192 experimental word trials and 192 pictures trials; in total, 384 experimental trials. Of those trials, half had the arrow pointing left, and half had the arrow pointing right. Trials were presented in a random order. The task took on average 13 minutes to complete.

Visual Probe Task Stimuli

Words

The three types of word stimuli used in the visual probe task were the same as in the exogenous cueing task. However, in the visual probe task, word stimuli were presented as word-pairs. One word in a pair was a threat word – either Health-Threat or Activity. The

second word in a pair was a Neutral word. There were 16 word-pairs of each type: Health-Threat and Neutral (e.g. cancer – feline), Activity and Neutral (e.g. jogging – chrome), and Neutral-Neutral (e.g. flute – flint), making a sum of 48 word-pairs. An additional eight Neutral-Neutral pairs were used for practice trials.

The parings of a Health-Threat word with a Neutral one were replicated from the previous study in CFS (Hou et al., 2008) with several substitutions among the neutral stimuli. Neutral words, such as 'rowing', 'performances', and 'leisurely', were substituted with other words unrelated to activity or leisure so that they would not conflict with the Activity stimuli. Health-Threat and Neutral words were matched on length and frequency (frequency per million – U according to Carroll et al. (1971) norms), both $p > .99$ (see Table 3). Activity word-pairs were similarly matched on length and frequency, both $p > .99$ (see Table 4). Neutral-Neutral pairs used to measure the baseline were also matched on length and frequency, both $p > .99$ (see Table 5).

All six groups of words were matched on Carroll et al. (1971) frequency, $p > .999$. The methodology concerning stimuli selection and rating is described in section, Stimuli ratings.

Table 3.

Visual Probe, Health Threat Words - Lengths and Frequencies

Health threat	Freq U	Length	Freq U	Neutral
cancer	4.26	6.00	0.11	feline
casualty	0.08	8.00	3.75	tractors
coffin	3.16	6.00	6.50	fabric
collapse	2.44	8.00	1.85	farmyard
coronary	0.23	8.00	2.63	dwelling
corpse	1.82	6.00	3.20	citrus
diseased	1.40	8.00	6.22	bathroom
dying	14.20	6.00	14.00	kettle
fatal	5.68	5.00	1.58	manor
funeral	4.58	7.00	12.74	cottage
hospitalised	0.17	12.00	8.50	architecture
illness	10.75	7.00	0.25	flowery
infectious	1.17	10.00	0.54	coniferous
operation	32.18	9.00	6.30	livestock
paralysed	2.76	9.00	5.80	moccasins
spasm	0.32	5.00	11.26	woven
	5.32	**7.50**	**5.33**	

Note: Words were matched for length and frequency
using Carrol, Davies and Richman's 1971 norms
U - estimated frequency per million tokens

Table 4.

Visual Probe, Activity Words - Lengths and Frequencies

Activity	Freq U	Length	Freq U	Neutral
hurrying	10.00	8.00	6.00	gleaming
dusting	1.50	7.00	2.50	viewing
washing	24.00	7.00	24.70	whistle
sweeping	15.20	8.00	15.40	touching
skipping	6.00	8.00	6.40	markings
jogging	0.48	6.00	1.80	chrome
bicycles	0.30	8.00	0.30	ringlets
cleaning	14.00	8.00	9.60	envelope
swimmer	4.29	7.00	4.20	terrain
gymnasium	3.30	9.00	3.30	spaghetti
ironing	1.00	7.00	1.00	ruffles
wiping	3.10	6.00	2.60	gazing
gardening	0.90	9.00	2.20	crouching
vacuuming	0.10	9.00	0.30	sprinkler
mopping	0.40	7.00	0.30	hydrant
lifting	11.00	7.00	14.50	grazing
	5.97	**7.56**	**5.94**	

Note: Words were matched for length and frequency
using Carrol, Davies and Richman's 1971 norms
U - estimated frequency per million tokens

Table 5.

Visual Probe, Neutral Words - Lengths and Frequencies

Neutral	Freq U	Length	Freq U	Neutral
Flute	3.59	5.00	3.59	Flint
Ballot	1.40	6.00	1.40	Stereo
Ribbon	18.80	6.00	18.60	Statue
Perfume	8.90	7.00	8.90	Coconut
Valiantly	0.58	9.00	0.99	Stainless
Thymine	0.05	7.00	1.62	Aquatic
Quartet	1.40	7.00	1.40	Codfish
Stripe	0.86	6.00	0.88	Porter
Waterproof	1.40	10.00	4.10	Watermelon
Cobblestone	0.43	11.00	0.45	Coefficient
Element	40.00	7.00	42.00	Quarter
Granite	8.80	7.00	1.60	Dictate
Quadrangle	0.18	10.00	3.30	Stagecoach
Grapefruit	2.40	10.00	0.02	Gramophone
Aisle	1.70	5.00	2.40	Satin
Keyhole	0.19	7.00	0.23	Keynote
	5.67	**7.50**	**5.72**	

Note: Words were matched for length and frequency
using Carrol, Davies and Richman's 1971 norms
U - estimated frequency per million tokens

Pictures

The Health-Threat and Neutral pictures used in the visual probe task were the same as in the exogenous cueing task. The main modification for the purposes of the visual probe task concerned the pairing of the threat and neutral images. The picture pairs are presented in Appendices B.6.1 – B.6.3. The Neutral halves of the picture-pairs were chosen to match the threat picture in content and complexity; for example, a picture of a group of doctors performing surgery (to match the word ‘operation’) was paired with a picture of a group of people playing a board game. Sixteen additional Neutral images were matched to the ones used in the exogenous cueing task aiming to keep consistency between the neutral words and images, but also meeting the requirement of matching image content and complexity. Overall there were 48 picture pairs, and an additional eight pairs for the practice trials. The aspect of the methodology concerning stimuli selection and rating is described in the section, Stimuli Ratings.

Visual Probe Task Data Preparation

The Reaction Time (RT) (in milliseconds) data from the visual probe task were filtered by removing RTs for incorrect answers, and for responses below 200 and above 2000ms, as well as those at more than 2 *SDs* from that participant's mean (Hou et al., 2008; Lees et al., 2005). The three groups (CFS, Asthma, Controls) did not differ on accuracy rates and amount of data included in the analysis, all $p > .30$. Statistical analyses were performed on the filtered data.

Attention Bias scores were calculated for the visual probe task following the formula ((TUDL – TLDL) + (TLDU – TUDU))/2. In the formula T denoted Threat and N - neutral stimulus, and the letters U-upper and L-lower denoted the position above or below the fixation cross respectively, D was the target arrow (Asmundson & Hadjistavropoulos, 2007). RTs on the valid trials were subtracted from the RTs on the invalid trials. If RTs on invalid trials were longer than RTs on the valid trials, then the resulting positive values would indicate an attentional bias towards a particular type of stimuli. If RTs on invalid trials were shorter than on valid trials, the resulting negative values would indicate avoidance.

Attentional indices of Engagement for the visual probe task followed the formula ((NUDU + NUDL + NLDU + NLDL)/4) - ((TUDU + TLDL)/2) (Asmundson & Hadjistavropoulos, 2007). The procedure involved subtracting RTs on valid threat trials from those recorded on the neutral trials. Positive values on the Engagement Index would suggest that threat stimuli captured participants' attention, indicating a faster reaction towards threat on valid trials.

Disengagement scores for the visual probe task were calculated by subtracting RTs on invalid neutral trials from invalid threat trials, following the formula ((TUDL + TLDU/2) – ((NUDU + NUDL + NLDU + NLDL)/4)). Positive scores on the Disengagement Index would demonstrate difficulties disengaging from threat, since they would reflect a faster reaction on trials following neutral stimuli and a slower reaction on an invalid trials following a threat word, thus indicating a difficulty in switching attention from a threat towards the arrow appearing in an uncued location.

Health-Threat Stimuli Ratings

Words and Pictures

On separate occasions, independent judges (6 CFS, 15 Asthma, 17 Healthy Control) were asked to rate the relevance of pictures and words to health-threat on an 11-point scale (0 – not at all relevant, 10 – extremely relevant). The words and pictures for Health-Threat were presented separately in a random order, while being interspersed with neutral words

and pictures. Participants were drawn from those who volunteered but could not participate in the laboratory-based experiments due to their low mobility or long distance. The means and standard deviations for Health-Threat stimuli are presented in Table 6 – Words and Table 7 - Pictures. The mean rating of relevance to health-threat for Neutral words was 0.47 (*SD* = 0.28), and for Neutral pictures was 0.84 (*SD* = 0.33).

Table 6.

Mean Relevance Ratings for Health Threat Words by Independent Raters
6 CFS, 15 Asthma, 17 Controls

	Health Threat	Mean	SD
1	cancer	6.83	3.40
2	casualty	7.39	2.40
3	coffin	6.00	3.76
4	collapse	6.56	1.98
5	coronary	7.56	2.45
6	corpse	6.67	2.81
7	diseased	7.33	2.14
8	dying	8.67	1.75
9	fatal	7.78	3.08
10	funeral	5.89	4.10
11	hospitalised	7.00	2.47
12	illness	7.44	1.85
13	infectious	7.17	2.26
14	operation	6.94	2.98
15	paralysed	7.22	2.46
16	spasm	3.67	2.59
		6.88	**1.09**

Note. The words were rated on an 11 point scale
(0 Not at all - 10 Extremely)

Table 7.

Relevance Ratings for Health-Threat Pictures by Independent Raters
CFS n = 6, Asthma n = 15, Healthy Controls n = 17

	Health Threat	Mean	SD
1	cancer	4.73	2.69
2	casualty	4.80	2.65
3	coffin	7.27	2.79
4	collapse	5.93	2.15
5	coronary	7.33	1.50
6	corpse	7.67	2.32
7	diseased	6.13	2.53
8	dying	7.20	2.08
9	fatal	6.73	3.24
10	funeral	6.33	3.64
11	hospitalised	7.73	1.98
12	illness	7.00	1.93
13	infectious	5.67	2.29
14	operation	7.07	2.15
15	paralysed	4.73	2.31
16	spasm	3.53	2.07
		6.24	**1.25**

Note. The pictures were rated on an 11 point scale (0 Not at all - 10 Extremely)

Two one-way ANOVAs separately for words and pictures did not show significant differences in mean ratings between the three groups (all $p > .10$) (see Table 8).

Table 8.

Mean Ratings of Health Threat Stimuli for Each Group (CFS, Asthma, Control)

	CFS *n = 6*	Asthma *n = 15*	Control *n = 17*
	M (SD)	*M* (SD)	*M* (SD)
Health Threat words	6.7 (2.9)	7.5 (1.1)	6.5 (1.5)
Health Threat pictures	7.3 (1.9)	5.9 (1.6)	6.3 (1.8)

Note. Stimuli were rated on an 11 point scale (0 Not at all - 10 Extremely)

Questionnaires

All self-report measures of demographic and illness characteristics, as well as the following questionnaires (Appendix B.4), were completed at the end of the study after the computer tasks.

The Hospital Anxiety and Depression Scale (HADS) consists of 14 items that measure anxiety and depression in populations with non-psychiatric medical conditions, in such a way that the scores are not affected by the physical symptoms these populations may be experiencing (Zigmond & Snaith, 1983). The range of scores is 0-21 for each subscale, with a higher score indicating greater severity. The developers suggest the following classification of cases based on the scores: normal range (0 – 7), mild (8-10), moderate (11-15), and severe (16 or higher). For people with CFS, a cut-off score of 9-10 is recommended to distinguish patients with elevated anxiety or depression (Morriss & Wearden, 1998). The scale has good internal consistency Cronbach's α 0.87 for the Anxiety subscale; and Cronbach's α 0.79 for the Depression subscale (Mccue et al., 2006) and has been validated in different medical settings (Bjelland et al., 2002; Mondolo et al., 2006). In the current sample, Cronbach's α for Depression subscale was 0.81 and for Anxiety 0.81. The scale was used to assess psychiatric comorbidity in the CFS group. Depression and anxiety may exert an influence on attentional processes (Gotlib & Joormann, 2010; Mogg, McNamara, et al., 2000), and therefore HADS scores were used as covariates in the statistical analysis of attentional bias scores.

Positive and Negative Affective Schedule (PANAS) is a 20-item mood measure (Watson et al., 1988) of positive and negative affect, using 10 adjectives of each of these two kinds. Participants were asked to read each item and indicate to what extent they were feeling that way right now, using a 5-point scale (1- very slightly or not at all to 5 – extremely). The range of scores for each subscale is 10 – 50. The scale is widely used in different settings to measure mood, and has good validity and Cronbach's α of 0.89 for the Positive Affect (PA) subscale and 0.85 for the Negative Affect (NA) (Crawford & Henry, 2004). In the current sample, the Cronbach's α was 0.88 for PA subscale and 0.75 for the NA subscale. The advantage of PANAS is that it is a good measure of within- and between-subjects individual differences, suitable for the measure of change in mood within participants and between the groups (Rossi & Pourtois, 2012).

The PANAS was administered four times during the study: 1) before the mood induction, 2) after the mood induction and before the first computer task, 3) after the first computer task and before the second computer task, 4) after the second computer task. It is an easy, quick and efficient measure of a current mood without increasing the burden on participants. PANAS has been used previously to measure the effect of mood induction (Broderick, 2005; Gadea, Gomez, Gonzalez-Bono, Espert, & Salvador, 2005).

Brief Fatigue Inventory (BFI) is a uni-dimensional measure assessing the severity of fatigue. The main advantage of the measure for the current study was that it allowed assessment of the level of fatigue at that moment in time, the usual and worst levels of fatigue in the past 24 hours, and the degree by which fatigue interfered with the range of routine activities (e.g. walking ability, work, relations with other people, enjoyment of life) in the past 24 hours. BFI was developed to measure fatigue in people with cancer suffering from cancer-related fatigue (Mendoza et al., 1999). BFI has not been used to measure fatigue in people with CFS before, but it is a quick unidimensional measure of fatigue, that is both valid and reliable, making it suitable for screening purposes (Dittner, Wessely, & Brown, 2004; Whitehead, 2009). The advantages of the instrument include its shortness (9 items), the speed and ease with which it can be administered and scored, and its face validity. It demonstrated good internal consistency, with Cronbach's α at 0.96. Participants were asked to rate their fatigue on a scale from 0 (no fatigue) to 100 (as bad as you can imagine). The scores for fatigue interference (rated on a scale from 0 – does not interfere to 100 – completely interferes) were computed, with higher scores meaning the fatigue interfered to a greater extent with functioning. In the current sample, the Cronbach's α was 0.95 for the interference subscale.

Power Analysis

Sample size for the current study was determined based on the large effect sizes observed in a comparable study by Hou and colleagues (2008) with 11 CFS and 17 control participants. The effect sizes were calculated for previously reported studies using G*Power, version 3.1.3 (Faul, Erdfelder, Buchner, & Lang, 2009; Faul, Erdfelder, Lang, & Buchner, 2007). For the parameters of the power set at .80 and alpha set at .05, according to Cohen's convention, a total sample size of 30 participants would be needed to detect an effect size of Cohen's f = .40 for the ANOVA of bias scores 2 way interaction Group (Control, CFS, Asthma) x Stimulus Type (Health Threat, Activity, Neutral), and total sample size of 69 participants for the medium effect size (Cohen, 1992). For the ANOVA of bias scores 3-way interaction Group (Control, CFS, Asthma) x Induction (Depressive, Neutral) x Stimulus Type (Health threat, Activity, Neutral), a total sample size of 42 participants would be needed to detect a large effect size, and 96 to detect a medium effect size.

Equipment

Computer tasks were run on a desktop computer (CTX Model: PR711T, CTX Ultra Screen Monitor, 17 inch screen) and a Toshiba Satellite A100 laptop (15.4 inch screen). The presentation of the task and the data collection were conducted using E-Prime software version 2.0 (SP3) (2.0.8.74). Participants sat in a comfortable position in front of the computer screen. The distance between the participant and the screen was approximately 50cm. Previous research suggested that any variation in distance between the participant and computer screen had no significant influence on the effect (Owens et al., 2004).

Procedure

Participants were tested alone in a single session lasting approximately one hour. Sessions took place at the Department of Experimental Psychology in a standard testing room specifically set up for experimental purposes, or alternatively in Wolfson College, Oxford in a room designated for study purposes. The college was chosen as a location with convenient parking, which would allow access for people with restricted mobility. Each room was quiet with minimal distraction for participants, and fitting the requirements for testing.

The study procedure was outlined and explained by the investigator, and participants read an information sheet (Appendix B.1) about the study. Any questions were addressed, and then the participants were invited to give written informed consent, which was required before they could take part in the study (Appendix B.3).

The steps of the procedure in order are presented below.

1. Participants filled out a PANAS measure (Time1)

2. Participants underwent the induction into the mood state to which they were allocated, either Depressive or Neutral.

3. Participants filled out a PANAS measure (Time2)

4. Participants completed an attentional task: Exogenous Cueing/Visual probe.

5. Participants filled out a PANAS measure (Time3)

6. Participants completed an attentional task: Visual probe/Exogenous Cueing

7. Participants filled out a PANAS measure (Time4)

8. Participants completed questionnaire measures in the following order:

    Demographic questions: age, gender, education

    Brief Fatigue Inventory (BFI)

    Depression/Anxiety questionnaire (HADS)

    Health questions

    CDC/Fukuda CFS diagnostic criteria

10. Participants were fully debriefed, their questions were answered, and they received their payment for the study (10 pounds). Those participants who wished to underwent a positive mood induction to remove the effects of the depressive mood induction.

The order in which the two attention tasks were presented was varied equally across the participants, so that in each group half of the participants completed the Visual probe task first, and half of the participants completed the Exogenous Cueing task first. The session took on average 60 minutes, but the length varied among participants. The method flowchart is presented in the *Figure 3* below.

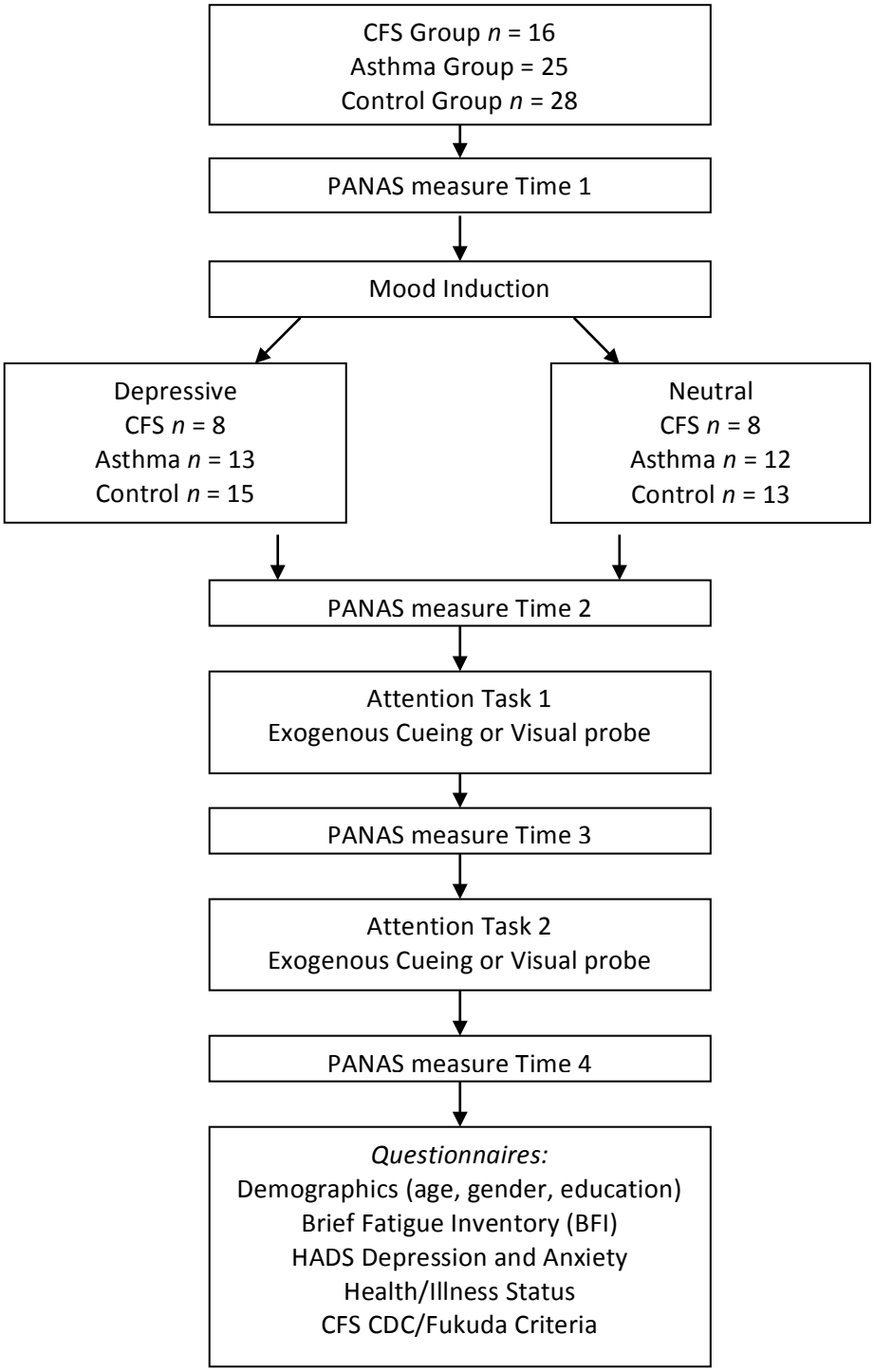


Figure 3. Full experimental procedure for the Attentional Bias and Mood study.

Statistical Analysis

Statistical analyses were performed using Statistical Package for Social Science (SPSS) software version 20.0. Chi-square and univariate ANOVA tests were used to compare the groups on demographic characteristics (gender, education, age), HADS Depression and Anxiety, and Brief Fatigue Inventory.

The effect of mood state manipulation on PANAS scores was checked by conducting two 2 x 2 ANOVAs. Induction 2 (Depressive, Neutral) was the between subjects independent variable. Time 2 (Pre-induction, Post-induction) was within-subjects repeated measure. Positive affect scores were the dependent variable in one ANOVA, and Negative affect scores in another. Independent samples *t*-tests were used to compare PANAS scores between Depressive and Neutral conditions to clarify significant interactions. To check if the induction affected each group differently an ANOVA analysis was conducted: Group 3 (CFS, Control, Asthma) x Induction 2 (Depressive, Neutral) x Time 2 (Pre-Induction, Post-Induction) ANOVA factorial design with Group and Induction as between-subjects measures and Time as repeated measures. Positive and negative PANAS scores were the dependent measures for each analysis.

The Health-Threat attentional bias, Engagement and Disengagement scores from exogenous cueing and from visual probe tasks were entered into separate 3 x 2 x 2 factorial design ANOVAs. Group 3 (CFS, Asthma, Control) and Induction 2 (Depressive, Neutral) were the between-subjects independent variables. Stimulus 2 (Words, Pictures) was a within-subject independent variable. The Health-Threat bias, engagement and disengagement scores from the two tasks were the dependent variables. In the analysis of Health-Threat bias scores the Neutral trials' scores were entered as covariates in accordance with the analysis performed by Hou and colleagues (2008). Independent samples *t*-tests were used to clarify significant interactions for planned comparisons in accordance with hypotheses to compare the CFS group with the asthma and control groups, and to compare the asthma group with the control. The Bonferroni method of correction was used to take into account the possibility of Type I error and to adjust the significance value for multiple comparisons; thus, the value of 0.05 was divided by the number of tests performed on the data set to adjust the significance value.

Results

Demographic and Questionnaire Measures

CFS, Asthma and control groups did not differ significantly in age, gender, or education, in all cases $p > .10$. Table 9 presents demographic measures, mean group scores on questionnaires, and illness measures for CFS and Asthma groups.

Table 9.

Demographic and Questionnaire Measures for CFS, Asthma, and Healthy Control Groups

	CFS *(n = 16)*	Asthma *(n = 25)*	Control *(n = 28)*				
	***n* (%)**	***n* (%)**	***n* (%)**	*χ2*	*p*		
Gender (female)	14 (87%)	15 (60%)	16 (57%)	4.61	*ns*		
Education (Degree)	11 (69%)	19 (76%)	22 (78%)	0.54	*ns*		
	***M* (SD)**	***M* (SD)**	***M* (SD)**				
Symptoms duration (years)	10.3 (6.9)	23.9 (15.1)					
Time since diagnosis (years)	7.1 (6.4)	23.4 (15.2)					
CFS symptom frequency (past 6 months)	18.7 (4.8)						
	***n* (%)**						
Received treatment	11 (68%)						
Treatment: medication	3 (19%)						
Treatment: CAM	4 (25%)						
Treatment: CBT	2 (13%)						
Treatment: GET	2 (13%)						
Current Treatment	8 (50%)						
Asthma severity (0-100		40.4 (28.9)					
Asthma interfere (0-100		25.2 (24.6)					
	***M* (SD)**	***M* (SD)**	***M* (SD)**	*F*	*p*	Pairwise comparisons	*p*
BFI Fatigue NOW	6.1 (1.7)	3.9 (2.5)	3.9 (2.1)	6.3	.003	CFS vs C	.006
						CFS vs A	.007
BFI Fatigue USUAL within past 24 hr	5.7 (1.9)	2.9 (2.1)	3.4 (2.1)	8.9	< .001	CFS vs C	.003
						CFS vs A	< .001
BFI Fatigue WORST within past 24 hr	7.4 (2.1)	5.2 (2.8)	5.1 (2.3)	5.4	.007	CFS vs C	.010
						CFS vs A	.018
BFI Fatigue Interference	36.4 (15.7)	12.9 (11.5)	13.6 (11.1)	21.1	< .001	CFS vs C	< .001
						CFS vs A	< .001
BFI Total score	6.8 (3.4)	2.7 (1.9)	2.9 (1.8)	18.8	< .001	CFS vs C	< .001
						CFS vs A	< .001
Age	41.0 (15.3)	32.1 (11.9)	37.3 (15.3)	2.3	*ns*		
HADS Depression	8.8 (4.5)	5.6 (4.1)	4.3 (3.4)	6.7	.002	CFS vs C	0.002
						CFS vs A	0.041
HADS Anxiety	8.5 (4.6)	6.1 (4.4)	6.4 (3.3)	2.1	*ns*		

Note. BFI - Brief Fatigue Inventory measured severity of fatigue
HADS - Hospital Anxiety and Depression Scale

Manipulation Check: Depressive or Neutral Mood Induction

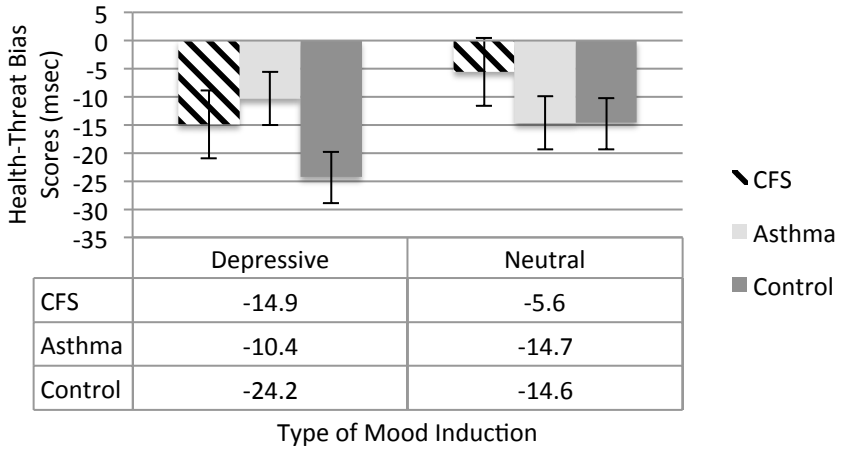
The analysis comparing Negative Affect scores pre- and post-Induction demonstrated a significant Induction x Time interaction $F(1,67) = 8.43$, $p = .005$. Negative affect significantly increased after the Depressive induction $t(35) = 2.11$, $p = .042$, and significantly decreased after the Neutral induction $t(32) = 2.25$, $p = .031$.

The analysis comparing Positive Affect scores also showed a significant Induction x Time interaction $F(1,67) = 6.49$, $p = .013$. Positive affect decreased significantly if participants were put into a depressive state; the mean difference was 5.89 ($SD = 5.88$), $t(35) = 5.99$, $p < .001$. Positive affect also decreased significantly if participants were put into the neutral mood state, but to a lesser degree; the mean difference was 2.52 ($SD = 5.02$), $t(32) = 2.88$, $p = .007$.

The ANOVA with the added Group factor did not demonstrate a significant three-way interaction Group x Induction x Time, with $p > .77$ for Positive, and $p > .59$ for Negative affect, indicating the induction had the same effect on each group.

Exogenous Cueing – Health Threat bias - Tests of Hypothesis 1

The 3 x 2 x 2 ANOVA comparing Health-threat bias scores did not reveal any significant differences between the Groups 3 (CFS, Asthma, Controls), or Inductions 2 (Depressive, Neutral), and no significant Group x Induction interaction; in all cases $p > .18$. No significant main effect of stimulus 2 (Words, Pictures) was shown, and no interactions between stimulus and between-subjects factors, all $p > .05$ (See *Figure 4* and Table 10 for means and standard deviations for three groups in mood induction).



	Depressive	Neutral
CFS	-14.9	-5.6
Asthma	-10.4	-14.7
Control	-24.2	-14.6

Figure 4. Means and Standard errors of Health-Threat Bias scores on the Exogenous Cueing task for the three groups (CFS, asthma, control) within each mood induction (Depressive, Neutral).

Table 10.

Attentional Indices for Health-Threat from the Exogenous Cueing and Visual Probe tasks for CFS, Asthma and Healthy Control Groups

	Depressive			Neutral		
	CFS	Asthma	Control	CFS	Asthma	Control
	M (SD)	*M* (SD)	*M* (SD)	*M* (SD)	*M* (SD)	*M* (SD)
Exogenous Cueing	*n* = 8	*n* = 13	*n* = 15	*n* = 8	*n* = 12	*n* = 13
Word Bias	-7.7 (40.4)	-18.3 (30.9)	-19.9 (32.9)	-11.8 (34.5)	-20.5 (24.3)	-23.9 (23.4)
Picture Bias	-2.1 (30.7)	-3.6 (22.3)	-20.4 (20.9)	-14.5 (47.2)	-8.7 (17.9)	-16.5 (23.6)
Word Engagement	3.9 (14.9)	-5.3 (14.3)	-4.2 (23.1)	13.3 (21.6)	-0.6 (21.4)	-3.3 (23.7)
Picture Engagement	2.2 (27.9)	-6.3 (13.3)	-16.2 (27.1)	-12.3 (34.5)	-7.7 (12.5)	-11.2 (16.3)
Word Disengagement	-2.5 (26.1)	11.3 (20.9)	0.3 (19.2)	10.4 (22.9)	1.5 (14.3)	4.2 (13.1)
Picture Disengagement	-13.7 (19.4)	6.2 (15.5)	-4.6 (18.9)	8.2 (28.6)	3.5 (14.5)	10.7 (13.5)
Visual Probe						
Word Bias	-13.4 (29.7)	2.5 (17.1)	0.9 (15.9)	6.7 (10.3)	-0.9 (19.1)	9.4 (20.6)
Picture Bias	14.9 (50.3)	6.8 (14.4)	2.2 (21.2)	6.2 (13.4)	-12.3 (9.2)	1.4 (19.2)
Word Engagement	-16.8 (49.9)	-0.4 (14.9)	-1.7 (14.8)	-6.4 (9.1)	-1.9 (13.6)	7.7 (17.1)
Picture Engagement	-12.1 (26.4)	-3.3 (18.2)	-9.5 (15.9)	-2.9 (24.6)	-10.7 (10.6)	-0.9 (17.2)
Word Disengagement	3.4 (42.5)	2.8 (22.2)	2.7 (17.1)	13.2 (12.2)	0.9 (13.9)	1.7 (19.7)
Picture Disengagement	27.1 (39.6)	10.1 (19.2)	11.6 (13.6)	91. (15.7)	-1.6 (9.6)	2.3 (20.3)

Note. Positive bias scores reflect attentional approach, negative bias scores reflect attentional avoidance
Positive engagement scores reflect attentional capture by threat stimuli
Positive disengagement scores reflect difficulty in disengaging attention from threat

Exogenous Cueing – Health-Threat Engagement – Test of Hypothesis 3

The 3 x 2 x 2 ANOVA comparing Health-Threat Engagement scores did not reveal any significant differences between the Groups 3 (CFS, Asthma, Controls), or Inductions 2 (Depressive, Neutral), and there was no significant Group x Induction interaction; in all cases $p > .05$ (see *Figure* 5). The analysis revealed a significant effect of Stimulus F (1, 63) = 5.96, p = .017, η_p^2 = .086, indicating that all groups' attention was more likely to be captured by the Word stimuli (M = 0.68, SE = 2.54) than by the Picture stimuli (M = -8.58, SE = 2.76), but there were no significant interactions involving Stimulus factor; all $p > .10$.

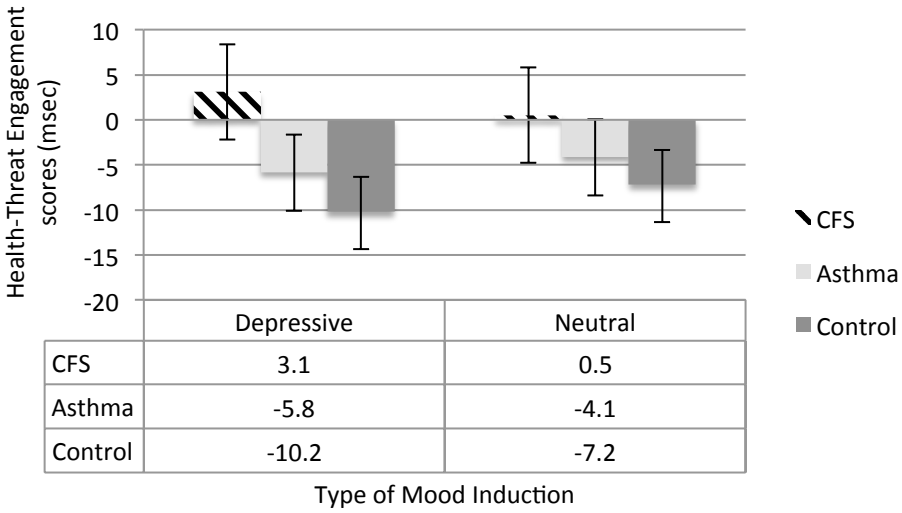


Figure 5. Means and Standard errors of Health-Threat Engagement scores on the Exogenous Cueing task for the three groups (CFS, asthma, control) within each mood induction (Depressive, Neutral).

Exogenous Cueing – Health Threat Disengagement – Test of Hypothesis 5

The 3 x 2 x 2 ANOVA comparing Health-Threat Disengagement scores did not show significant differences between Groups 3 (CFS, Asthma, Controls), or Inductions 2 (Depressive, Neutral), both $p > .07$. Nor was there a main effect of Stimulus (Words, Pictures), $p > .10$. The analysis revealed a significant Group x Induction interaction $F(2,63) = 3.29$, $p = .044$, $\eta_p^2 = .095$. (see *Figure 6.*).

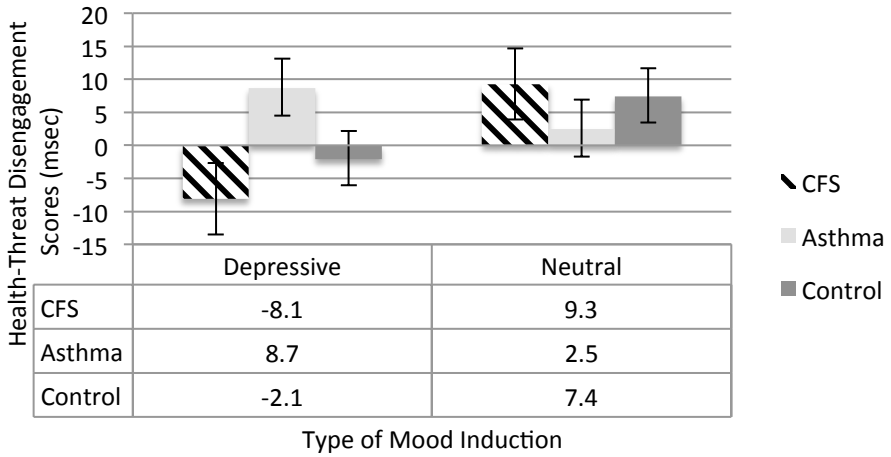


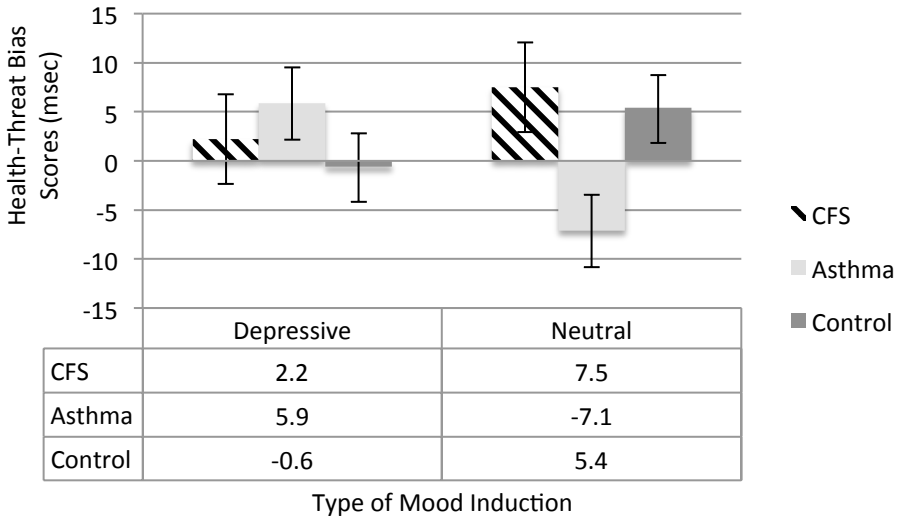
Figure 6. Means and Standard errors of Health-Threat Disengagement scores on the Exogenous Cueing task for the three groups (CFS, asthma, control) within each mood induction (Depressive, Neutral).

Hypothesis 5 stated that in the exogenous cueing task, the CFS group would demonstrate attentional disengagement if in a neutral or depressive mood, compared to the asthma and control groups. The asthma group was predicted to show attentional disengagement only when in a depressive mood. In view of the significant Group by Induction interaction in order to test the hypothesis, the means for the three groups were compared using independent samples *t*-tests. For the neutral mood the two planned comparisons (CFS vs Asthma, CFS vs Control) showed non-significant results, both $p > .20$ (see Table 10 and *Figure 6*).

The analysis within Depressive mood state showed a significant difference between CFS and Asthma groups $t(19) = 2.43$, $p = .025$. When in a depressive mood, the asthma group obtained a positive value which showed a difficulty in disengagement from Health-threat $M = 8.71$, ($SD = 11.7$). Meanwhile, the CFS group obtained a negative value, which demonstrated avoidance $M = -8.11$ ($SD = 20.18$). The negative value for CFS group indicated that the RTs were faster on invalid trials, meaning the individuals with CFS were quicker to switch from the threat stimulus to a different location. A Bonferroni correction, applied to adjust for multiple comparisons, where 0.05 was divided by 6, the number of performed tests on the single dataset (Bland & Altman, 1995), showed that the *p* value should be below .008 to demonstrate significance. The *p* value of .025 is above that value, so the chance of committing type I error was too high to firmly conclude significance. The differences between the CFS and healthy control groups, and between the asthma and healthy control groups were non-significant, $p > .45$.

Visual probe – Health Threat bias – Test of Hypothesis 2

The 3 x 2 x 2 ANOVA comparing Health-Threat bias scores did not show significant differences between Groups 3 (CFS, Asthma, Controls) or Inductions 2 (Depressive, Neutral), both $p > .18$. No significant main effect of Stimulus 2 (Words, Pictures) was shown, but there was a significant Induction x Stimulus interaction $F(1,61) = 5.12$, $p = .027$, $\eta_p^2 = .077$. When in a depressive mood, participants showed stronger attentional bias towards the pictures ($M = 8.09$, $SD = 27.97$) than to the words ($M = -3.08$, $SD = 20.47$), $t(36) = -2.87$, $p = .007$. No significant difference in attention towards words or pictures was observed in neutral mood, $p > .05$. The 3 x 2 x 2 ANOVA also revealed a significant Group x Induction interaction $F(2,61) = 4.06$, $p = .022$, $\eta_p^2 = .118$ (see *Figure 7*).



	Depressive	Neutral
CFS	2.2	7.5
Asthma	5.9	-7.1
Control	-0.6	5.4

Figure 7. Means and Standard errors of Health-Threat Bias scores on the Visual Probe task for the three groups (CFS, asthma, control) within each mood induction (Depressive, Neutral).

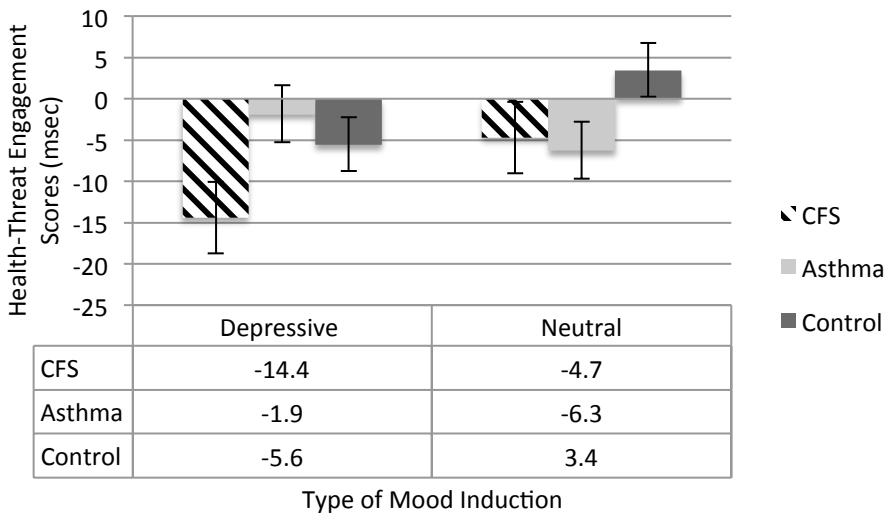
Hypothesis 2 stated that in the visual probe task, the CFS group would demonstrate attentional bias towards health-threat in both the neutral and depressive moods, compared to the asthma and healthy control groups. In contrast, the asthma group would demonstrate attentional bias towards health-threat only under the influence of depressive mood.

To test the hypothesis, the means for the three groups were compared using independent samples *t*-tests. The two planned comparisons in the neutral mood (CFS vs Asthma, CFS vs Control) indicated that CFS group showed significantly greater attentional bias towards Health-Threat M = 6.45 (SD = 8.11) than Asthma M = -6.63 (SD = 10.43), who demonstrated avoidance, $t(18) = 2.99$, $p = .008$. The difference between the CFS and the control groups was not significant, $p > .80$. The Bonferroni correction applied to all five tests suggested that the p value should be below .01 to indicate significance. Thus the difference between the CFS and asthma groups within neutral mood remained significant.

For the depressive mood all three planned comparisons (CFS vs Asthma, CFS vs Control, Asthma vs Control) showed non-significant results, all $p > .50$.

Visual probe – Health Threat engagement - Test of Hypothesis 4

The 3 x 2 x 2 ANOVA comparing Health-Threat engagement scores did not reveal any significant differences between Groups 3 (CFS, Asthma, Controls), or Inductions 2 (Depressive, Neutral), and no Group x Induction interaction, all $p > .09$. Main effect or interactions with other factors for the repeated measure of Stimulus 2 (Words, Pictures) were not significant either, all $p > .10$ (see *Figure 8*).



	Depressive	Neutral
CFS	-14.4	-4.7
Asthma	-1.9	-6.3
Control	-5.6	3.4

Figure 8. Means and Standard errors of Health-Threat Engagement scores on the Visual Probe task for the three groups (CFS, asthma, control) within each mood induction (Depressive, Neutral).

Visual probe – Health Threat Disengagement – Test of Hypothesis 6

The 3 x 2 x 2 ANOVA comparing Health-Threat Disengagement scores did not reveal any significant differences between Groups (CFS, Asthma, Controls), Inductions (Depressive, Neutral), both $p > .16$, or a significant Group x Induction interaction $p > .90$ (see *Figure 9*). The main effect or interactions with group factor for the repeated measure of Stimulus (Words, Pictures) were not significant either, all $p > .10$. However the interaction Induction x Stimulus was significant $F(1,63) = 7.21$, $p = .008$, $\eta_p^2 = .103$. Independent samples *t*-tests showed that in the Depressive induction all participants had greater difficulty in disengaging their attention from pictures ($M = 15.89$, $SD = 23.67$) than from words ($M = 2.81$, $SD = 25.43$), $t(36) = 3.07$, $p = .004$. The difference in the Neutral mood induction was not significant, $p > .86$.

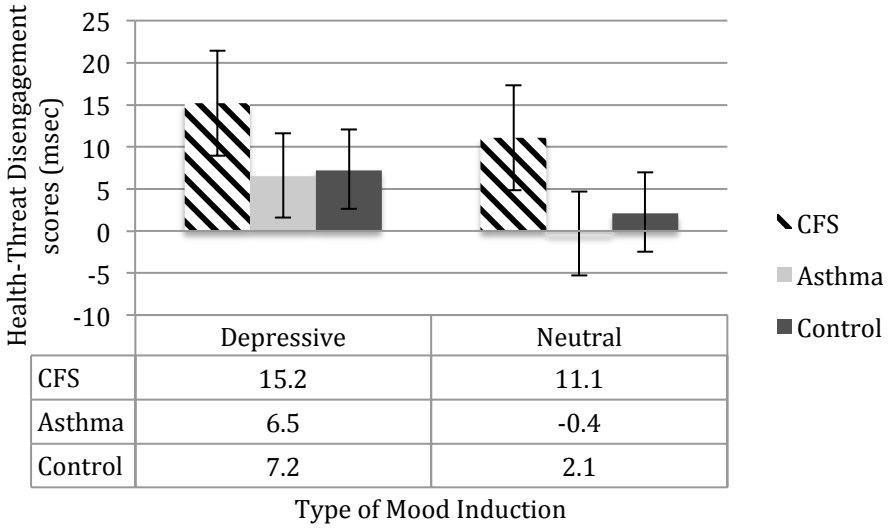


Figure 9. Means and Standard errors of Health-Threat Disengagement scores on the Visual probe task for the three groups (CFS, asthma, control) within each mood induction (Depressive, Neutral).

Discussion

The study investigated the effect of neutral or depressive mood on attentional bias for health-threat in people with CFS, compared to people with asthma and to healthy controls. The exogenous cueing task was used to measure attentional bias under low cognitive load and a visual probe task to explore attentional bias under high cognitive load.

The first hypothesis was not supported. The prediction stated that in the exogenous cueing task the CFS group would demonstrate an attentional bias to health-threat in both neutral and depressive mood, compared to asthma and control groups. The analysis of attentional bias scores in the exogenous cueing task (with its low cognitive load) showed the absence of significant group differences, mood state differences or a significant interaction between group and induced mood. The results similarly did not support the prediction that the asthma group would show the attentional bias under the effect of depressive mood.

All participants, regardless of the illness status or mood state, obtained negative values on the attentional bias index, suggesting their reaction times were quicker on the *invalid* threat trials than on the *valid* threat trials, a reverse of the pattern that would be expected on the exogenous cueing task. This may be due to the time between the presentation of the stimulus and the presentation of the target, the stimulus onset asynchrony (SOA). The finding of longer responses on the invalid trials in this study is in line with previous research showing that if the SOA is longer than 250ms (in the current task the SOA was 500ms), a phenomenon known as Inhibition of Return (IOR) occurs (Lupianez, Klein,

& Bartolomeo, 2006; Posner, Rafal, Choate, & Vaughan, 1985). It involves a prevention of attention returning to the location that has already been attended to, ensuring that the attentional system remains alert to novel events in the environment. In other words in the period of 500ms the attention of participants may have time to wander off from the cued location. When the probe appears in the cued location (*valid* trial) the attention is inhibited from returning back to that familiar location, but when the probe appears in a new location (*invalid* trial) the attention is speeded up (Lupianez et al., 2006; Posner et al., 1985). IOR is considered to be a healthy adaptive response of the attentional system, and abnormal patterns of IOR have been observed in Parkinson's and Alzheimer's (Lupianez et al., 2006). The similarities of responses among all participants in this study suggest an absence of cognitive deficits in terms of spatial attention allocation in the groups with CFS and with asthma.

Alternatively, negative bias scores on the exogenous cueing task may indicate attentional avoidance. The results of the exogenous cueing task may indicate that at the early stage, prior to the voluntary manipulation of attention, all participants, regardless of any mood or illness state, show marked preference for avoidance of the health threat. That avoidance pattern may be due to the low severity of health-threat; literature showed that when severity is deemed low enough an avoidant response may occur in low anxious and high anxious people (Mathews & MacLeod, 2005). Avoidance may also be part of the mechanism of mood repair or mood regulation mechanisms, attending away from unpleasant stimulus may either prevent mood deterioration or change the mood state from negative to a more pleasant state (Bless & Fiedler, 2006; Goldman, Kraemer, & Salovey, 1996; Todd, Cunningham, Anderson, & Thompson, 2012). Though that would be an unlikely explanation for the CFS group, considering the probable impairments in mood regulation mechanisms in CFS (Caseras et al., 2008).

The second hypothesis predicted that in the visual probe task (on account of illness schema being activated under the high cognitive load, high level of threat, and long stimulus duration) the CFS group would demonstrate attentional bias towards health-threat in both neutral and depressive moods, compared to the healthy control group. In comparison, it was predicted that the asthma group would demonstrate attentional bias towards health-threat only under the influence of depressive mood. The second hypothesis received mixed support. Under the effect of neutral mood, as predicted, the CFS group showed attentional bias towards health-threat only in comparison to the asthma group who demonstrated

significant avoidance. CFS and the control groups did not differ significantly in attention towards health-threat in neutral mood.

In accordance with the hypothesis that the negative mood would have an effect on attentional bias in the asthma group, participants with asthma showed attentional avoidance when in the neutral mood, and attentional approach when in the depressive mood. That is in line with previous findings, showing that attentional bias in asthma is associated with negative affect (De Peuter, Lemaigre, et al., 2007; Martinez-Moragon et al., 2003). However, no significant group differences were detected in depressive mood, indicating that attentional bias towards health-threat in negative mood is not unique to asthma.

The differences in the results of exogenous cueing and visual probe tasks may have to do with the task difficulty, cognitive load, and allocation of cognitive resources (Mogg & Bradley, 1999). Taking into account the evidence for the difficulties in concentration and sustained attention reported by people with CFS, including both the effect of mental fatigue on cognitive performance (Capuron et al., 2006; Cockshell & Mathias, 2010), and the slowed information processing present in CFS (Glass, 2006; Majer et al., 2008; Moss-Morris, Petrie, Large, et al., 1996), then the difficulty of the task may be the factor influencing attention. Exogenous cueing is an easier task than visual probe, and therefore should put less of a burden on cognitive resources and demand less mental effort and concentration (Mogg & Bradley, 1999). Subsequently, the participants might have found it easier to keep their focus on the task relevant information, and ignore the health threat stimuli as irrelevant, particularly if they found that irrelevant stimuli were unpleasant. The visual probe task places higher demand on sustained attention and concentration, putting a strain on cognitive resources. This would activate the illness schema for guiding information processing preserving cognitive resources (Moss & DiCaccavo, 2005). Thus attentional shift towards health-threat may be more evident in performance on the visual probe task than on the exogenous cueing one.

The third and fourth hypotheses predicting that the CFS group would show attentional engagement with health-threat when in both neutral and depressive mood, as compared to asthma and control groups, were not supported. The analysis of attentional engagement scores in both tasks showed the absence of significant group differences or any interaction with mood. The fact that the visual probe task also showed negative scores on the Attentional Engagement index, similar to the scores in the exogenous cueing task, may indicate the possibility that avoidant cognitive processing occurs at earlier attentional

stages. This suggests that it is not only the direction and properties of attention that play a role in illness perception, coping, and outcomes, but attentional control itself may also be involved (Beevers, Clasen, Stice, & Schnyer, 2010; Eysenck & Derakshan, 2011; Eysenck, Derakshan, Santos, & Calvo, 2007; Sanabria et al., 2011). The importance of attentional control was demonstrated in the most recent finding that attentional bias towards health-threat was present in people with CFS with poor executive control, but not in the ones who did not show any impairment in cognitive control (Hou et al., 2014).

The current study was the first to investigate the degree of attentional disengagement from health-threat present in CFS, as demonstrated by the impairment in the attentional maintenance process and the longer dwell time on health threat. It was hypothesised that in the CFS group, attentional bias would manifest also in the difficulty in disengaging attention from health threat. The results of the exogenous cueing task did not show significant group or mood differences, but showed a significant group by mood interaction. However, the planned comparisons to clarify the interaction, where CFS group was compared with the asthma and control groups within neutral and within depressive state, did not support the hypothesis. In the neutral mood, the CFS group did not differ significantly from the healthy controls or the asthma group in their attentional disengagement scores. When in the depressive mood, a significant group difference was detected between the CFS and asthma groups, suggesting a greater difficulty in disengaging from health-threat for the asthma group, and greater avoidance for the CFS group. However, applying the Bonferroni correction for multiple comparisons to prevent Type I error, reduced the difference to non-significant. Most importantly, the asthma group did not differ significantly from the control group. Therefore, the fifth hypothesis was not supported. The results of the visual probe task did not show a significant effect of mood on group differences in attentional disengagement, and thus the sixth hypothesis was not supported.

Overall, the current experiment did not replicate the results of Hou and colleagues (2008) study of attentional bias in CFS. The main difference between the current experiment and the Hou *et al*'s study was the mood manipulation. The results of the current study, in support of Hou *et al's* findings, suggest that attentional process in CFS is not underpinned by changes in negative mood, because depressive mood has not exerted an influence on the attentional bias in CFS.

Importantly, the difference in the results might be due to sampling from different CFS subpopulations. However, the inclusion criteria for the current study were similar to Hou and colleagues' 2008 study: that study employed a small sample, recruited from wider

community and support groups on the basis of a self-reported diagnosis of CFS, and self-reported CDC/Fukuda criteria. A major limitation of the current study was that the diagnosis of the participants with CFS was only reported and no other diagnostic measures were performed, which contributes to greater intra and inter-individual variability within the CFS group. On the other hand, Hou et al (2014) study also did not show attentional bias in their total CFS group; the bias manifested only in those people with CFS who showed impaired executive control. Their sample was much more carefully selected: from a specialist CFS clinic, diagnosed by a specialist medical practitioner, and diagnosed more recently within the last 6 months. What it may suggest is that the attentional focus may play a smaller role so early in the diagnosis, but as the illness progresses, increasing attentional bias may contribute to symptom perpetuation. That may explain the differences in the results between Hou et al (2008) and Hou et al (2014), but not why the current experiment failed to demonstrate attentional bias.

The level of functioning of the selected sample of people with CFS is also an issue, even though the assessment of fatigue showed greater fatigue and its interference with functioning in the CFS group, when compared to asthma and control groups. Firstly, the measure of fatigue used in the study, while a valid measure of current fatigue, may not be an appropriate measure to assess fatigue in CFS specifically, which may be qualitatively different from the fatigue sensation experienced by other populations or the transitory fatigue sensation experienced after performing a task. Additionally, it prevents comparability with other studies of CFS and precludes generalizability from the current sample. In terms of functioning, current participants were well enough to travel back and forth from home and participate in the study, indicating a comparatively high level of functioning. Thus, the sample of the most severely affected individuals remains elusive.

Most importantly, considering a more complex design, with two rather than one between group factors being measured (group and mood), the current study suffers from a severe limitation of a small sample size (total CFS n = 16). After the allocation of CFS participants to each induction the two subgroup sample sizes were n = 8. Comparatively Hou et al (2014) had 13 people in their subgroups, and their inclusion criteria was more stringent (recruited from specialist clinic, diagnosed in the previous 6 months, high scoring on a valid and reliable Chalder Fatigue Scale (Chalder et al., 1993).

The small size of the current sample resulted in high variability, reflected by the large standard deviations and standard errors. The number of comparisons needed to be performed for the data generated by the two attention tasks exceeds the capabilities of the

current sample, preventing deeper exploration of attentional patterns in CFS. It has also limited the kind of correlational analyses that can be performed because it would be inappropriate to conduct such analysis on a group consisting of eight people, if different mood inductions are also taken into account.

This raises an important question of recruitment strategies for investigating the nature of CFS. The fact that it is a complex, multi-system and heterogeneous condition, contributes to the problem of comparability between different studies and generalizability from each study to the wider population. As demonstrated by the differences between Hou et al (2008), Hou et al (2014) and the studies described in the thesis so far, one of the explanations for varying results may be that the samples were recruited from different populations. Therefore, even the use of the same methodology (visual probe task) precludes comparison between studies.

The main problem, though, is the size of the sample. The current sample size overall is comparable to other studies, but taking into consideration the added complexity of the design reduces its power. This is reflective of the difficulty in participant recruitment. The studies described in the thesis set out to investigate people with CFS recruited from a wider community sample in accordance with the need for more community-based studies of CFS (Jason, Richman, et al., 1999). Mainly, the studies investigate people in the context of specialist clinics, in primary care or hospital settings. On one hand, that allows access to participants and assures the validity of the diagnosis; on the other hand, populations investigated after they have already being referred to a specialist clinic may also reflect referral or selection bias. However, working with a specialist CFS clinic allows access to CFS population, which is highly important for recruiting participants. The issue with community-based studies is that they require significantly greater numbers of participants, who then could be classified into diagnostic categories (e.g. primarily CFS, primarily ME, subclinical). The research within different community settings would add to the research conducted in specialist care settings. However, recruitment from the community is fraught with difficulties.

The experience of conducting the current study demonstrated several problems. Firstly, there is a distrust towards psychological research in CFS. This is reflected in the number of debates reviewed in Chapter 1: Introduction concerning theories and treatment of CFS. The majority of people contacted declined to participate in the study when they were informed that it was to be conducted in a psychology department. Secondly, the methods for recruiting from the community (e.g. newspapers and online advertisement, posters)

simply may not reach the CFS population. Individuals with CFS may be house-bound, may not spend a lot of time on the internet due to high levels of mental fatigue and difficulties in sustained attention and concentration, or they may be generally restricted in activities. Thirdly, any laboratory study involves a high degree of involvement, effort, travel and time, which may prevent people from deciding to take part in it. In this case, assessing people in a specialist clinic where they come for diagnostic tests or treatment means that they do not need to put any more effort and time into participating in the study. Fourthly, recruiting from a community sample without involvement of clinicians means there would be great differences in how, when, by whom and using what criteria people were diagnosed with CFS.

What are the ways to rectify these limitations? Conducting research on just populations from specialist clinics may reduce generalizability and prevent access to subclinical populations, including those who may experience a large degree of suffering but may not fall into any diagnostic category, and those underrepresented and/or severely affected populations who are unable to access the clinics. Conducting research on a wider community leads to too much heterogeneity, and may include people who might have been misdiagnosed, and results in severe methodological shortcomings.

Firstly, CFS research, particularly as it is a deeply multi-faceted disease, requires a great degree of collaboration, not just between researchers from different fields, but between researchers and clinicians, and most importantly between researchers, clinicians and patients. The conflict between clinicians and patients may start as early as diagnosis (Banks & Prior, 2001; Deale & Wessely, 2001; Picariello et al., 2015). The lack of trust between physicians and patients then transfers to mistrust of the research.

Collaboration between the psychology and physiology fields would allow for greater patient involvement, meaning that the patients might be less likely to be put off by the psychological nature of the research. Specialist clinics would be a more appropriate source of participants, compared to community recruitment, because the sample drawn from specialist clinics would be better defined and more homogeneous, both in terms of their diagnostic criteria and the diagnostic tests performed to rule out other diagnoses. Recruitment from specialist clinics also allows access to bigger samples, thus improving research, as demonstrated by Hou et al (2014). For that matter, the CFS population can always be stratified into those meeting different criteria, and these different subpopulations can be compared to each other, similar to the method in the PACE trial (White et al., 2011). They may also be compared on the basis of recruitment: those recruited from a community

and those from specialist clinics; or on the basis of recency of the diagnosis: people with a current versus people with an older diagnosis.

Web-based methods of assessment would also help increase the capabilities of community recruitment, and may allow access to more severely affected groups. The drawback is that web-based methods have even less control over the diagnostic process, as the people who participate in an online study would not be able to go through the battery of tests to confirm their CFS diagnosis, and the study would have to rely on self-reports. However, web-based methods can be used if participants are recruited from a specialist clinic, so that the methods of their diagnosis are uniform and the diagnosis is confirmed. Web-based methods are also a good way to compare different populations from multiple specialist clinics and community settings across the country, and this applies similarly for cross-national research. Therefore, future research should utilise online resources for conducting studies on such a hard-to-access population as people with CFS.

The current study was the first to investigate the direct effect of mood on attention in CFS. The mood induction was successful as demonstrated by the positive and negative affect scores; the former decreased following the neutral induction and the latter increased following the depressed induction. The study, however, lacked the emotional assessment of the health-threat stimuli. The words and pictures were rated on relevance to health-threat in the pilot study, but not on their emotional impact. Therefore the degree of emotional impact of the stimuli on attention could not be assessed. Additionally, the ratings provided by healthy people and the people with asthma and CFS were around the middle of the scale, and therefore the use of stimuli of varying degrees of severity would provide a more detailed account of attentional bias in CFS. The study needs replication with a larger sample size, using the visual probe task and utilizing stimuli of varying threat levels and varying specificity to investigate in more depth negative illness schema and attentional processes in CFS. Considering that CFS presents as a condition of dysregulation, as discussed in more detail in Chapter 1: Introduction, pp. 22 - 23, the research direction of investigating attentional control and its role in biased information processing as conducted by Hou and colleagues (2014) appears promising.

Chapter 4: Study 3: Attention and Activity Experiment

Introduction

According to the Self-Regulation theory by Leventhal et al. (2008) the cognitive-emotional representations of the illness and symptoms, and consequently the cognitive processes that underpin them, determine the choice of responses to stress and illness, which in turn lead to health outcomes. Within the framework of the Self-Regulation theory, Deary (2008) proposed that the illness representations that an individual with CFS develops may not be of the illness itself, but of the events that are perceived as dangerous to an established physiological, affective, cognitive, and behavioural balance. In CFS activity may be regarded as threatening to that balance established between the energy levels and the functioning. Activity demands (e.g. standing up, moving, walking, household chores, exercise, social activities) may be perceived as causing a depletion of energy, and a consequent increase in symptoms. Thus, people with CFS may view activity, because it precipitates increased symptom severity, as health-threatening in the same way that they would view a serious illness as health-threatening. Vercoulen and colleagues (1997) showed that cognitions about activity, such as expectations that it would result in high fatigue, were significantly more related to actual activity levels in people with CFS than in people with Multiple Sclerosis (MS). Additionally, even though the objectively measured activity levels were similar for CFS and MS, only in CFS group higher activity was related to higher fatigue. The latter attributed their fatigue to being active and expected that activity would lead to elevated fatigue more than the MS group (Vercoulen et al., 1997). Expectation of harm from the exercise may thus increase attentional focus on activity and on its consequences for the organism. These catastrophising expectations may reinforce over-monitoring strategies, which may lead to the amplification of sensation of illness and fatigue. Thereby, the aim of the current study was to investigate the cognitive processing of activity-related information in CFS, starting with the attentional bias towards linguistic and pictorial stimuli representing activity.

Prior research concerning activity monitoring and perception of exertion documented a curious discrepancy between the objective measurement and subjective perception of activity and fatigue levels in the CFS population. Fry and Martin (1996a) demonstrated a discrepancy between the objective measures and self-report ratings of activity in children with CFS, which involved an underestimation of one's own functioning (compared to the objective measures of one's activity), and an overestimation of functioning in others (Fry &

Martin, 1996a). A similar pattern was observed in adults with CFS regarding cognitive functioning (Metzger & Denney, 2002).

Fry and Martin (1996b) explained such a discrepancy through distorted cognitive processing, and enhanced perception of body sensations and fatigue, combined with the unrealistic expectations that people with CFS have of the functioning of themselves and others – expectations they feel that they constantly fall short of. People with CFS perceive their fatigue as disproportionate to the amount of exertion, and perceive their exertion as disproportionate to the amount of activity performed, indicating a distortion in the processing and evaluation of fatigue, exertion, and activity information (Fry & Martin, 1996b). Enhanced attention towards their bodies as they perform activity may explain their feeling that their exertion is far greater than the amount of activity they have performed.

Cook and colleagues (2003) compared the physical exercise capacity in Gulf war veterans with CFS to healthy controls, and found they performed similarly in physical exercise and on measured physiological variables (e.g. oxygen consumption, respiratory rate). However, the CFS group rated their exertion during each minute of the exercise and at each level of increased intensity as significantly higher than the controls (Cook et al., 2003). Similarly, Fulcher and White (2000) found that a CFS group had a comparable level of fitness to a sedentary but healthy comparison group, but the CFS group rated their exertion as significantly higher, which was similar to the comparison group with depression. Moreover, in spite of similar fitness levels, the CFS group was not able to perform as well as the healthy controls on the physical exercise test and scored lower on physiological measures (e.g. maximal heart rate, aerobic capacity); this was also similar to the group with depression (Fulcher & White, 2000). That may suggest that negative mood may play a role in perception of activity, exertion and fatigue. Negative mood may amplify attentional bias towards threat through activating negative illness schema; in this case, the threat would be the activity.

Negative illness schema may not only amplify and bias attention towards symptom-related and illness-related health threat (Knoop et al., 2010; Moss-Morris, 2005), but also bias cognitive processing of functioning and activity in relation to health and illness. Identifying a potential attentional bias towards activity-related information, similar to the attentional bias towards health-threat and somatic information, may have implications for the treatment of CFS. Reducing the focus on fatigue via cognitive-behavioural treatments leads to lower fatigue and improved functioning (Wiborg et al., 2011). Reducing the focus on activity and its catastrophic interpretations, such as regarding it as health-threatening and harmful, may also aid the treatment, increase the effect of exercise-based treatments and

perhaps aid in adherence to Graded Exercise Therapy (GET). Notably, if attention towards activity itself is amplified in people with CFS, that may help in explaining the discrepancies between their perception of their level of activity and objective measurements of their activity.

To explore the attentional patterns with regard to activity, the current study used two tasks, the exogenous cueing and the visual probe, to investigate the attentional bias towards health-threat in CFS, as represented by activity. The tasks utilised words and images describing exercise, movement, exertion, and concepts related to being active. The choice of word and picture stimuli for the measurement of attentional bias in relation to exertion and activity included combined types of stimuli reflecting exercise and domestic daily chores. Stimuli were chosen based on their relevance to CFS participants and their concerns over energy preservation and sustained levels of functioning. The exercise-related stimuli were judged to be relevant for CFS, because they may be part of a graded-exercise treatment. Similarly, stimuli reflecting daily chores and housekeeping were thought to be relevant, because these are daily, necessary, and energy-demanding activities.

The CFS group was compared to a healthy control and an asthma group in order to explore the differences in the way ill and healthy populations perceive activity, and in the way different illness groups attend to activity and exertion. Exercise has long been recognised as a potential trigger for inducing asthma symptoms or an asthma attack (Parsons & Mastronarde, 2009). Similar to CFS, people with asthma may perceive exercise as a health-threat, as a potential source of danger to the established health/illness balance and their management of asthma symptoms. Also like CFS, asthma has a long varying intermittent course of illness, with symptomatic highs and lows, difficult to characterize and predict (Gershon, Guan, Victor, Wang, & To, 2012). Again similar to CFS, activity, particularly exercise, is associated with fear cognitions in people with asthma (Emtner, Herala, & Stålenheim, 1996). Physical activity has direct relevance and may be highly salient to people with asthma, and therefore an attentional bias towards activity as health-threat could be expected to occur. However, as reviewed in the Introduction to Chapter 3, attentional biases for health-threat in asthma are strongly linked to negative affect (De Peuter, Lemaigre, et al., 2007; Martinez-Moragon et al., 2003), and attentional vigilance in asthma is thought to increase if people are in a state of depressed mood (Janssens et al., 2009). Therefore, one would expect to observe attentional bias in an asthma group only under the condition of negative mood. In comparison, the attentional bias would be pervasive in the CFS group, and would occur in both neutral and negative moods. Hou et al (2008, 2014) showed that

attentional bias in CFS is independent of mood state, and therefore the expectation would be that the CFS group would also demonstrate bias when in a neutral mood.

The current study investigated an attentional bias towards activity, based on the theory that activity may be perceived as health-threat in CFS (Deary, 2008). The hypotheses tested in the experiment are presented in Table 1 for clarity.

Table 1.

The Summary of Hypotheses with regard to Attentional Bias towards Activity under the Effect of Mood

#	Hypotheses	Task	Group	Mood	Prediction
1	In the exogenous cueing task, the CFS group will demonstrate attentional bias towards activity words and pictures in both neutral and depressive moods, compared to the healthy control and asthma groups. In comparison, the asthma group will demonstrate attentional bias towards activity only under the influence of depressive mood.	Exogenous Cueing	CFS	Neutral and Depressive	significantly higher attentional bias scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional bias scores than Control
2	In the visual probe task, the CFS group will demonstrate attentional bias towards activity words and pictures in both neutral and depressive moods, compared to the asthma and healthy control groups. In comparison, the asthma group will demonstrate attentional bias towards activity only under the influence of depressive mood.	Visual probe	CFS	Neutral and Depressive	significantly higher attentional bias scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional bias scores than Control
3	In the exogenous cueing task, the CFS group will demonstrate attentional engagement with activity words and pictures in neutral mood and depressive mood, reflecting hypervigilance for threat, compared to asthma and control groups. The asthma group will demonstrate attentional engagement if in depressive mood, reflecting increased attention to activity under the effect of negative mood.	Exogenous Cueing	CFS	Neutral and Depressive	significantly higher attentional engagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional engagement scores than Control
4	In the visual probe task, the CFS group will demonstrate attentional engagement with activity words and pictures if in neutral or depressive mood, reflecting hypervigilance for threat. The asthma group will demonstrate attentional engagement only in depressive mood, reflecting hypervigilance for threat.	Visual probe	CFS	Neutral and Depressive	significantly higher attentional engagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional engagement scores than Control
5	In the exogenous cueing task, the CFS group will demonstrate greater difficulty in attentional disengagement from activity words and pictures in neutral and depressive moods, compared to asthma and control. The asthma group will show attentional disengagement only in depressive mood.	Exogenous Cueing	CFS	Neutral and Depressive	significantly higher attentional disengagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional disengagement scores than Control
6	In the visual probe task, the CFS group will demonstrate greater difficulty in attentional disengagement from activity words and pictures in neutral and depressive moods, compared to asthma and control groups. The asthma group will show attentional disengagement only in depressive mood.	Visual probe	CFS	Neutral and Depressive	significantly higher attentional disengagement scores than Asthma and Control
			Asthma	Depressive	significantly higher attentional disengagement scores than Control

Method

Study Design

The data presented in this chapter has been collected in the study described fully in the Method section of Chapter 3: Attention and Mood. Relevant information is replicated in this chapter for clarity.

The study had a quasi-experimental design with two between-subjects independent variables. The first between-subjects factor was group: CFS group was compared to asthma and healthy control groups matched on age, gender, and education. The second between-subjects factor was mood state: within each group (CFS, Asthma, Control) participants were randomly allocated to undergo either Depressive or Neutral mood state induction (Slyker & McNally, 1991; Velten, 1968). Within-subjects factor for the two attentional tasks included three types of stimuli (Health-Threat, Activity, Neutral). Chapter 3 presented the analysis of Health-threat stimuli. The current chapter presents the analysis of Activity stimuli.

The main dependent variable was Reaction Times (RTs) on the exogenous cueing and visual probe tasks. RTs were converted into attentional indices such as attentional bias, engagement, and disengagement scores; these were the main variables of interest. Another dependent variable was mood scores, used to check the effect of mood state induction. Additional dependent variables included questionnaire measures to obtain the descriptive information about participants.

This study has been reviewed by and received ethics clearance through the University of Oxford Central University Research Ethics Committee (CUREC), assigned reference number: MSD/IDREC/C1/2009/42 (Appendix B.2).

Participants

Participants who contributed the data described in the current chapter are the same people who contributed the data to the experiment on attentional bias and mood described in Chapter 3. The inclusion and exclusion criteria for the participants with CFS, Asthma, and for the healthy controls were described fully in Chapter 3, Method, section on *Participants* p. 75. Comorbidity assessment and recruitment strategy were also described in Chapter 3, p. 76-77.

Materials

The mood state induction, which participants had undergone at the beginning of the study, was described in Chapter 3, Method, Materials section, pp. 115 – 116.

Exogenous Cueing Task

Methodology for exogenous cueing task was described fully in Chapter 3, Method, Materials, Exogenous Cueing Task, pp. 116 – 118. Relevant information is replicated here for clarity.

Participants received instructions and completed a practice block (16 trials, 8 word and 8 picture trials), after which they had the opportunity to ask any questions or rerun the practice. Each stimulus was presented four times, in two positions (left and right) and in two trial types (valid and invalid), therefore the presentation of 16 Health-Threat, 16 Activity, and 16 Neutral words produced 192 experimental word trials. Similarly, there were 192 picture trials. Participants completed total of 384 experimental trials, which were randomized in one block. An additional 24 catch trials, where just the dots appeared without being preceded by a word, were used to ensure participants focused on the dots and not the words. The task took about 13 minutes to complete.

Exogenous Cueing Task Stimuli

Full description of the stimuli used in the Exogenous Cueing task (presented in Chapter 3, Method, Materials, Exogenous Cueing Task stimuli, pp. 118 – 119) demonstrated the length and frequency matching between words and pictures of different types selected for the study. The aspect of the methodology concerning Activity word selection and rating is described in section Stimuli Ratings below. Relevant information is replicated here for clarity.

Words

The three types of words used in the task included: Health-Threat (HT) (e.g. funeral), Activity (A) (e.g. jogging), and Neutral (N) (e.g. keyhole). Sixteen words were used as the Activity stimuli, representing two types of activities: domestic chores (e.g. washing) or mild exercise (e.g. jogging). Words varied in length (5 to 12 letters) and frequency. Frequency ratings were based on Carroll, Davies, and Richman's (1971) norms (U - *estimated frequency* of a word in print *per million tokens*). Activity words were matched to health-threat and

neutral words on length $p > .99$, and frequency $p > .98$. The list of words, their lengths and frequencies were presented in Chapter 3, Table 2, p. 119.

Pictures

All images were black and white. Each experimental image matched the type of word accordingly: 16 Activity images (a picture of a person sweeping the floor to match the word 'sweeping'), and 16 Neutral images (a picture of a ribbon to match the word "ribbon"). Not all neutral images matched the neutral words exactly for two reasons: firstly, because of the difficulty of matching images to particular words (e. g valiantly); secondly, because of the necessity of matching neutral images to Activity images in content and complexity. The Activity images used in the experiment are presented in Appendix B.6.2. There were 16 Activity images matched with 16 Neutral images.

Exogenous Cueing Task Data Preparation

The Reaction Time (RT in milliseconds) data from the exogenous cueing task were filtered by removing RTs for incorrect answers, and responses that were below 100ms (considered an anticipatory response) above 1500ms (considered a miss), and greater than 2 *SDs* away from that participant's mean (Asmundson & Hadjistavropoulos, 2007; Fox et al., 2001). The percentage of data exluded form the analysis did not differ between the three groups (CFS, Asthma, Control), $p > .30$.

Activity bias scores were calculated for each word type by subtracting valid trials' RTs from invalid trials' RTs (Asmundson & Hadjistavropoulos, 2007). If RTs on invalid trials were longer than RTs on the valid trials, then positive values were obtained and these indicated attentional bias towards a particular stimuli type. If RTs on invalid trials were shorter than on valid trials, negative values were obtained and indicated avoidance.

Attentional indices of Activity Engagement and Disengagement were calculated for Activity stimuli in the same way as for Health-Threat stimuli following the procedure outlined in previous studies (Koster et al., 2006). The Attentional Engagement index was computed by subtracting RTs on valid Activity trials from valid Neutral trials ($RT_{\text{valid neutral}} - RT_{\text{valid threat}}$). Positive values on the engagement index demonstrated a faster reaction towards threat on a valid trial, suggesting that Activity words captured participants' attention.

The Disengagement index was calculated by subtracting RTs on invalid Neutral trials from invalid Activity trials ($RT_{\text{invalid threat}} - RT_{\text{invalid neutral}}$). Positive scores on the disengagement index demonstrated difficulties disengaging from threat, because of a faster reaction on an

invalid Neutral trial and slower response on an invalid threat trial. This would indicate a difficulty in switching attention from a threat towards a dot appearing in another location.

Visual Probe Task

Methodology for the visual probe task was described fully in Chapter 3, Method, Materials, Visual Probe Task, pp. 120 – 122. Relevant information is replicated here for clarity.

Participants received instructions and completed a practice block (16 trials, 8 word and 8 picture trials), after which they had the opportunity to ask any questions or rerun the practice. Each experimental pair was presented four times, so that each threat cue was presented in two positions (above and below the fixation point) and the arrow replaced the threat cue (valid trial) or the neutral word (invalid trial). Therefore, the presentation of the 16 pairs Activity-Neutral produced 64 experimental Activity word trials. Of those trials half had the arrow pointing left, and half had the arrow pointing right. In a similar way, there were 64 Activity picture trials, resulting in 128 experimental trials presenting Activity stimuli. Trials were presented randomly. The task took on average 13 minutes to complete.

Visual Probe Task Stimuli

Full description of the stimuli used in the Visual Probe task was described in Chapter 3, Method, Materials, Visual Probe Task Stimuli, pp. 122 – 125. The aspect of the methodology concerning word selection and rating is described in section Stimuli Ratings below. Relevant information is replicated here for clarity.

Words

In the visual probe task, word stimuli were presented as word-pairs. One word in a pair was a threat word - Activity. The second word in a pair was a Neutral word. There were 16 Activity-Neutral pairs (e.g. jogging - chrome). All activity and neutral words were matched on length $p > .99$ and frequency $p > .98$ per Carroll et al. (1971) norms.

The words, lengths, frequencies, and mean frequencies for the stimuli were presented in Chapter 3, Tables 4, 5, and 6, pp. 124 – 127. Overall, all six (Health-Threat, Activity, Neutral, and their respective Neutral pairs) groups of words were matched on $p > .99$. The aspect of the methodology concerning stimuli selection and rating is described in section Stimuli ratings below.

Pictures

Activity and Neutral pictures used in the visual probe task were the same as in the exogenous cueing task. The main modification for the purposes of the visual probe task concerned the pairing of the threat and neutral images. The picture-pairs are presented in Appendices B.6.2. Neutral halves of the picture-pairs were chosen to match the threat picture in content and complexity, for example a picture of a person gardening was matched with a picture of a person wearing similar clothes gazing at a small pond. There were 16 Activity picture-pairs.

Visual Probe Task Data Preparation

The Reaction Time (RT) (in milliseconds) data from the visual probe task were filtered by removing RTs for incorrect answers, as well as responses that were below 200ms, above 2000ms, or greater than 2 *SDs* from that participant's mean (Hou et al., 2008; Lees et al., 2005). The percentage of data excluded from the analysis did not differ between the three groups (CFS, Asthma, Control), $p > .30$.

Activity Bias scores were calculated for the visual probe task following the formula ((TUDL – TLDL) + (TLDU – TUDU))/2, where T is threat and N is neutral stimulus, and the letters U-upper and L-lower denote the position above or below the fixation cross respectively, D is the target arrow (Asmundson & Hadjistavropoulos, 2007). The RTs on the valid trials were subtracted from the RTs on the invalid trials (Asmundson & Hadjistavropoulos, 2007). If RTs on invalid trials were longer than RTs on the valid trials, positive values were obtained and these indicated attentional bias towards a particular type of stimuli. If RTs on invalid trials were shorter than on valid trials, negative values were obtained, which indicated avoidance.

Attentional indices of Engagement for the visual probe task followed the formula ((NUDU + NUDL + NLDU + NLDL)/4) - ((TUDU + TLDL)/2). The procedure involved subtracting RTs on valid threat trials from valid neutral trials. Positive values on the engagement index reflected faster reaction towards threat on valid trials, indicating that threat stimuli captured participants' attention.

Disengagement scores for the visual probe task were calculated by subtracting RTs on invalid neutral trials from invalid threat trials, following the formula ((TUDL + TLDU/2) – ((NUDU + NUDL + NLDU + NLDL)/4)). Positive scores on the disengagement index demonstrated difficulties disengaging from threat, due to a slower reaction on the invalid trials following a threat word, compared to faster reaction on invalid trials following neutral

stimuli. This would suggest a difficulty in switching attention from a threat towards an arrow appearing in an uncued location.

Activity Word and Picture Stimuli Ratings

On separate occasions, independent judges (6 CFS, 15 Asthma, 17 Control) were asked to rate how relevant pictures or words were to activity on an 11-point scale (0 – not at all, 10 – extremely relevant). These were the same people as described in Chapter 3, Method, Stimuli Ratings, pp. 126 – 128, who provided ratings for the Health-Threat stimuli in Chapter 3 and the Activity stimuli in the current chapter.

Activity words and pictures were presented separately in random order interspersed with neutral words and pictures. The means and standard deviations for Activity stimuli are presented in Table 2 – Words and Table 3 - Pictures. Mean ratings for neutral words were 1.34 (*SD* = 0.44) and for neutral pictures 1.01 (*SD* = 0.37).

Table 2.

Relevance Ratings for Activity Words by Independent Raters
CFS n = 6, Asthma n = 15, Healthy Controls n = 17

	Activity	Means	SD
1	bicycles	7.76	1.73
2	cleaning	4.90	2.84
3	wiping	4.05	2.65
4	gardening	5.95	2.46
5	gymnasium	8.48	1.81
6	hurrying	6.14	2.95
7	ironing	4.67	2.27
8	jogging	7.90	2.43
9	lifting	6.52	2.34
10	mopping	5.29	2.59
11	skipping	5.95	2.89
12	sweeping	4.95	2.40
13	swimmer	7.90	1.87
14	vacuuming	4.71	2.22
15	washing	4.38	2.58
16	dusting	4.57	2.68
	TOTAL	**5.88**	**1.44**

Note. The words were rated on an 11 point scale
(0 Not at all - 10 Extremely)

Table 3.

Relevance Ratings for Activity Pictures by Independent Raters
CFS n = 6, Asthma n = 15, Healthy Controls n = 17

	Activity	Means	SD
1	bicycles	8.00	2.07
2	cleaning	4.73	2.43
3	wiping	6.00	2.07
4	gardening	6.73	1.71
5	gymnasium	7.73	2.46
6	hurrying	5.07	2.28
7	ironing	4.53	2.26
8	jogging	7.93	2.12
9	lifting	6.33	1.80
10	mopping	5.53	1.85
11	skipping	7.13	2.29
12	sweeping	5.33	2.32
13	swimmer	7.27	2.46
14	vacuuming	5.93	2.22
15	washing	5.00	2.33
16	dusting	4.73	2.19
	TOTAL	**6.13**	**1.21**

Note. The pictures were rated on an 11 point scale (0 Not at all - 10 Extremely)

Two one-way ANOVAs for words and pictures separately did not show significant differences in mean ratings between the three groups, all $p > .10$ (see Table 4).

Table 4.

Mean Ratings of Activity Stimuli for Each Group (CFS, Asthma, Control)

	CFS *n = 6*	Asthma *n = 15*	Control *n = 17*
	M (SD)	*M* (SD)	*M* (SD)
Activity words	6.9 (2.3)	5.6 (1.2)	5.7 (0.8)
Activity pictures	7.5 (3.4)	6.6 (0.4)	5.5 (1.2)

Note. Stimuli were rated on an 11 point scale (0 Not at all - 10 Extremely)

Questionnaires

All self-report measures of demographic and illness characteristics and the following questionnaires (Appendix B.4) were completed at the end of the study after the computer tasks. The full description of self-report measures has been presented in Chapter 3, Method, Questionnaires, pp. 128 – 130.

Self-report measures included the Hospital Anxiety and Depression Scale (HADS), the Positive and Negative Affect Schedule (PANAS), and the Brief Fatigue Inventory (BFI).

Power Analysis

The sample size for the current study was determined based on the effect sizes observed in a comparable study by Hou and colleagues (2008) with 11 CFS and 17 control participants. The effect size for the experiment with Activity stimuli however is unknown, because activity stimuli have not been used before in the study of attentional bias in CFS. In the absence of the relevant research using activity stimuli, it was thought that the best way to determine the sample size required was to use the same power analysis employed in Chapter 3, p. 130.

Equipment

The computer tasks were run on a desktop computer (CTX Model: PR711T, CTX Ultra Screen Monitor, 17 inch screen) and a Toshiba Satellite A100 laptop (15.4 inch screen). The presentation of the task and data collection was conducted using E-Prime software version 2.0 (SP3) (2.0.8.74). Participants sat in a comfortable position in front of the computer screen. The distance between the participant and the screen was approximately 50cm. Previous research suggested that any variation in distance between the participant and computer screen had no significant influence on the effect (Owens et al., 2004).

Procedure

For clarity the study procedure is replicated here from Chapter 3. Participants were tested alone in a single session lasting approximately one hour. Sessions took place at the Department of Experimental Psychology in a standard testing room specifically set up for experimental purposes, or alternatively in Wolfson College, Oxford in a room designated for study purposes. The college was chosen as a location with convenient parking, which allowed access for people with restricted mobility. Each room was quiet with minimal distraction for participants and fit the requirements for testing.

The study procedure was outlined and explained by the investigator in addition to participants reading an information sheet (Appendix B.1) about the study. All questions were addressed prior to written informed consent being obtained from participants before they took part in the study (Appendix B.3). The steps of the procedure are presented in order below.

1. Participants filled out a PANAS measure (Time1)

2. Participants underwent induction into the mood state to which they were allocated: Depressive or Neutral.

3. Participants filled out a PANAS measure (Time2)

4. Participants completed an attentional task: Exogenous Cueing/Visual Probe.

5. Participants filled out a PANAS measure (Time3)

6. Participants completed an attentional task: Visual Probe/Exogenous Cueing

7. Participants filled out a PANAS measure (Time4)

8. Participants completed questionnaire measures in the following order:

Demographic questions: age, gender, education

Brief Fatigue Inventory (BFI)

Depression/Anxiety questionnaire (HADS)

Health questions

Fukuda CFS diagnostic criteria

10. Participants were fully debriefed, their questions were answered, and they received their payment for the study (10 pounds). Participants were offered a positive mood induction to counteract the effects of the depressive mood induction, and some took up the offer.

The order in which the attention tasks were presented was systematically varied across the participants, such that in each group half of the participants completed the Visual Probe task first, and half of the participants completed the Exogenous Cueing task first. The session took on average 60 minutes, the length of time varied among participants.

Data Analysis

Statistical analyses were performed using Statistical Package for Social Science (SPSS) software version 20.0.

The Activity attentional bias scores, and Engagement and Disengagement scores from exogenous cueing and from visual probe tasks were entered into separate 3 x 2 x 2 factorial design ANOVAs. Group 3 (CFS, Asthma, Control) and Induction 2 (Neutral, Depressive) were the between-subjects independent variables. Stimulus 2 (Words, Pictures) was a within-subject independent variable. The Activity bias, engagement and disengagement scores from the two tasks were the dependent variables. In the analysis of Activity Bias scores, the scores on Neutral trials were entered as covariates in accordance with the analysis performed by Hou and colleagues (2008). Independent samples *t*-tests were used to clarify significant

interactions in accordance with the hypotheses, to compare the CFS, asthma and control groups. Bonferroni method of correction was used to take into account Type I errors and to adjust the significance value for multiple comparisons, the value of 0.05 was divided by the number of tests performed on the data set to adjust the significance value.

Results

Demographic and Questionnaire Measures

CFS, Asthma and control groups did not differ significantly in age, gender, or education, in all cases $p > .10$. Table 9 from Chapter 3, p. 135. presenting demographic measures, mean group scores on questionnaires, and illness measures for CFS and Asthma groups is replicated here for clarity (see Table 5).

Table 5.

Demographic and Questionnaire Measures for CFS, Asthma, and Healthy Control Groups

	CFS *(n = 16)*	Asthma *(n = 25)*	Control *(n = 28)*				
	***n* (%)**	***n* (%)**	***n* (%)**	*χ2*	*p*		
Gender (female)	14 (87%)	15 (60%)	16 (57%)	4.61	*ns*		
Education (Degree)	11 (69%)	19 (76%)	22 (78%)	0.54	*ns*		
	***M* (SD)**	***M* (SD)**	***M* (SD)**				
Symptoms duration (years)	10.3 (6.9)	23.9 (15.1)					
Time since diagnosis (years)	7.1 (6.4)	23.4 (15.2)					
CFS symptom frequency (past 6 months)	18.7 (4.8)						
	***n* (%)**						
Received treatment	11 (68%)						
Treatment: medication	3 (19%)						
Treatment: CAM	4 (25%)						
Treatment: CBT	2 (13%)						
Treatment: GET	2 (13%)						
Current Treatment	8 (50%)						
Asthma severity (0-100		40.4 (28.9)					
Asthma interfere (0-100		25.2 (24.6)					
	***M* (SD)**	***M* (SD)**	***M* (SD)**	*F*	*p*	Pairwise comparisons	*p*
BFI Fatigue NOW	6.1 (1.7)	3.9 (2.5)	3.9 (2.1)	6.3	.003	CFS vs C	.006
						CFS vs A	.007
BFI Fatigue USUAL within past 24 hr	5.7 (1.9)	2.9 (2.1)	3.4 (2.1)	8.9	< .001	CFS vs C	.003
						CFS vs A	< .001
BFI Fatigue WORST within past 24 hr	7.4 (2.1)	5.2 (2.8)	5.1 (2.3)	5.4	.007	CFS vs C	.010
						CFS vs A	.018
BFI Fatigue Interference	36.4 (15.7)	12.9 (11.5)	13.6 (11.1)	21.1	< .001	CFS vs C	< .001
						CFS vs A	< .001
BFI Total score	6.8 (3.4)	2.7 (1.9)	2.9 (1.8)	18.8	< .001	CFS vs C	< .001
						CFS vs A	< .001
Age	41.0 (15.3)	32.1 (11.9)	37.3 (15.3)	2.3	*ns*		
HADS Depression	8.8 (4.5)	5.6 (4.1)	4.3 (3.4)	6.7	.002	CFS vs C	0.002
						CFS vs A	0.041
HADS Anxiety	8.5 (4.6)	6.1 (4.4)	6.4 (3.3)	2.1	*ns*		

Note. BFI - Brief Fatigue Inventory measured severity of fatigue
HADS - Hospital Anxiety and Depression Scale

Attentional Indices

The means and standard deviations for the attentional indices regarding Activity stimuli for three groups (CFS, Asthma, Control) in two types of mood induction (Neutral, Depressive) are presented in Table 6.

Table 6.

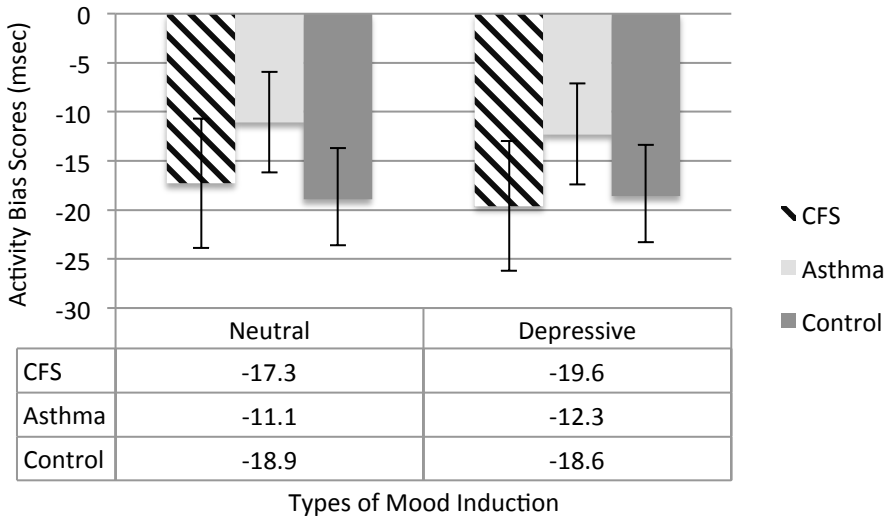
Attentional Indices for Activity Stimuli from the Exogenous Cueing and Visual Probe Tasks for CFS, Asthma and Healthy Control Groups

	Neutral			Depressive		
	CFS	Asthma	Control	CFS	Asthma	Control
	M (SD)	*M* (SD)	*M* (SD)	*M* (SD)	*M* (SD)	*M* (SD)
Exogenous Cueing	*n* = 8	*n* = 12	*n* = 13	*n* = 8	*n* = 13	*n* = 15
Word Bias	-22.9 (46.9)	-19.8 (19.6)	-27.6 (31.4)	-18.2 (31.7)	-18.5 (31.9)	-24.7 (34.7)
Picture Bias	-26.7 (51.9)	-2.4 (26.9)	-23.3 (23.9)	0.6 (24.4)	-6.7 (22.3)	-4.2 (26.8)
Word Engagement	11.4 (25.5)	-0.3 (28.9)	-0.2 (19.1)	-4.4 (15.5)	0.5 (8.8)	-9.5 (26.9)
Picture Engagement	-13.2 (24.8)	0.1 (12.9)	-11.1 (15.6)	10.1 (13.5)	-5.9 (13.4)	-0.8 (10.1)
Word Disengagement	1.2 (17.7)	2.1 (18.1)	-2.5 (15.4)	-4.6 (30.5)	5.3 (15.4)	0.9 (15.6)
Picture Disengagement	-3.1 (17.7)	2.1 (14.5)	3.7 (15.8)	-18.9 (24.5)	2.5 (19.7)	-3.8 (9.1)
Visual Probe						
Word Bias	6.1 (17.9)	-3.1 (13.7)	6.1 (23.8)	-28.5 (44.7)	-0.5 (12.7)	-28.5 (44.6)
Picture Bias	-6.7 (16.1)	-2.6 (22.4)	0.4 (19.5)	-1.3 (48.9)	-6.1 (14.6)	-1.4 (48.9)
Word Engagement	5.2 (15.9)	-4.3 (12.1)	8.9 (20.3)	-23.5 (37.4)	2.8 (19.6)	-23.5 (37.4)
Picture Engagement	-10.8 (13.7)	-5.8 (18.3)	-3.1 (11.9)	-14.6 (28.4)	-12.4 (10.3)	-14.6 (28.4)
Word Disengagement	0.9 (13.5)	1.3 (14.1)	-2.9 (12.5)	-5.1 (33.3)	-3.3 (17.4)	-5.1 (33.3)
Picture Disengagement	4.1 (22.9)	3.2 (10.1)	3.5 (16.7)	13.2 (47.1)	6.3 (16.4)	13.2 (47.1)

Note. Positive bias scores reflect attentional approach, negative bias scores reflect attentional avoidance
Positive engagement scores reflect attentional capture by threat stimuli
Positive disengagement scores reflect difficulty in disengaging attention from threat

Exogenous Cueing Task – Activity Bias – Test of Hypothesis 1

The 3 x 2 x 2 ANOVA comparing Activity bias scores did not reveal any significant differences between the Groups 3 (CFS, Asthma, Controls) or Inductions 2 (Neutral, Depressive), and no significant Group x Induction interaction, in all cases $p > .18$. No significant main effect of Stimulus 2 (Words, Pictures) was detected, and no interactions with between-subjects factors and stimulus, all $p > .10$ (see *Figure 1* and Table 5).



	Neutral	Depressive
CFS	-17.3	-19.6
Asthma	-11.1	-12.3
Control	-18.9	-18.6

Figure 1. Means and Standard errors of Activity Bias scores on the Exogenous Cueing task for the three groups (CFS, Asthma, Control) within each mood induction (Neutral, Depressive).

Exogenous Cueing Task – Activity Engagement – Test of Hypothesis 3

The 3 x 2 x 2 ANOVA comparing Activity Engagement scores did not reveal any significant differences between the Groups 3 (CFS, Asthma, Controls), or Inductions 2 (Neutral, Depressive), and no significant Group x Induction interaction, in all cases $p > .20$. The analysis of the repeated measures revealed a significant Group x Induction x Stimulus type interaction F (2, 63) = 3.34, p = .042, η_p^2 = .096 (see *Figure 2*.)

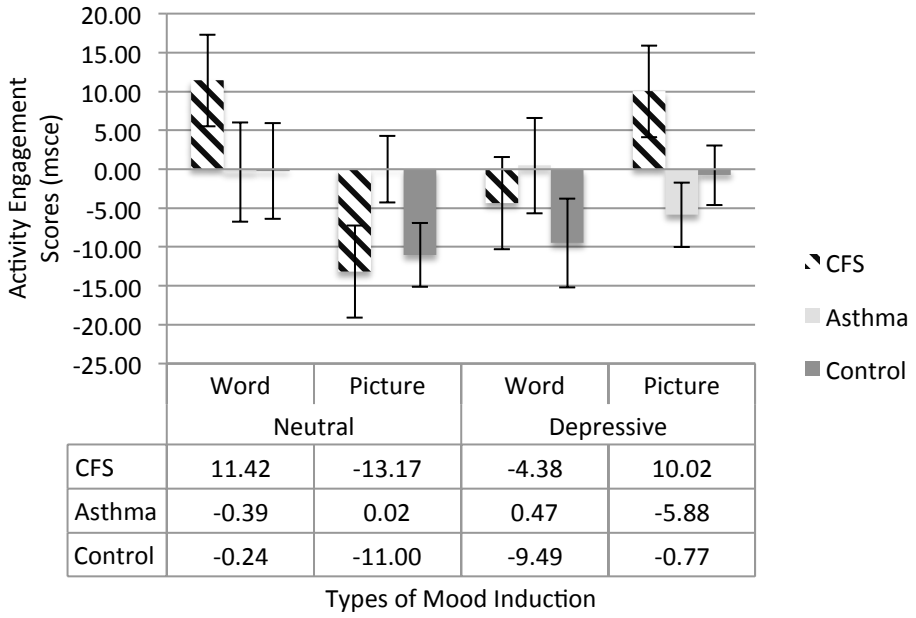


Figure 2. Means and Standard errors of Activity Engagement scores on the Exogenous Cueing task for the three groups (CFS, Asthma, Control) within each mood induction (Neutral, Depressive) for each Stimulus type (Word, Picture).

Hypothesis 3 predicted that in the exogenous cueing task, the CFS group would demonstrate attentional engagement with Activity stimuli when in either a neutral or depressive mood, compared to asthma and control groups. Asthma group will demonstrate Attentional engagement only in depressive mood, compared to the control group. To test the hypothesis, independent samples *t*-tests were used to separately compare the means of the three groups with regard to Neutral and Depressive moods, and also with regard to each stimulus type.

Within neutral mood, the planned comparisons of CFS vs Control and CFS vs Asthma did not show any significant differences in responses to words, both *t*-tests $p > .20$, or to pictures, both *t*-tests $p > .10$.

Within depressive mood, the comparisons between CFS and control, CFS and asthma, and asthma and control groups did not show significant differences in responses to words, three *t*-tests $p > .25$.

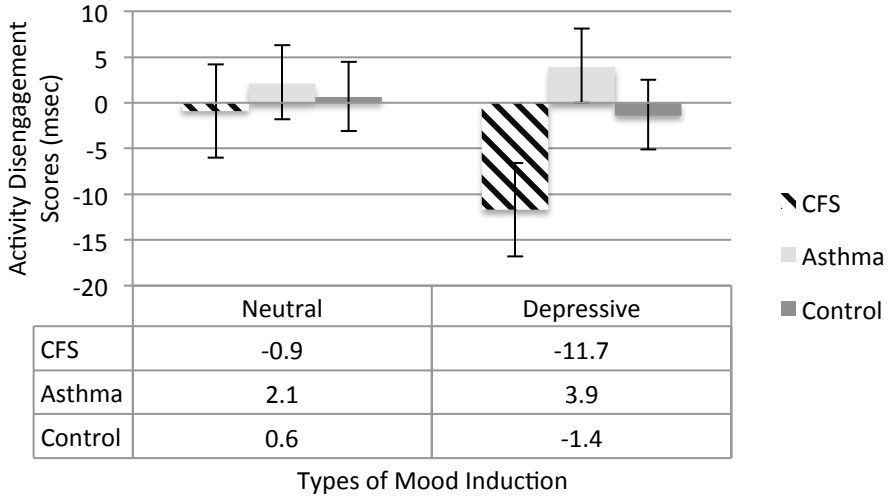
Within depressive mood, the CFS group showed greater attentional engagement with Activity pictures $M = 10.10$ ($SD = 13.5$) than control group $M = -0.77$ ($SD = 10.11$) $t(21) = 2.17$, $p = .041$, and the Asthma group $M = -5.88$ ($SD = 13.45$), $t(19) = 2.63$, $p = .016$. The difference between the control and asthma groups in response to Activity pictures, when in depressive mood was not significant $p > .20$. To correct for multiple comparisons, the Bonferroni

method was applied, and the significance set at 0.05 was divided by the number of tests performed on this particular data set (3 *t*-tests), giving a critical significance level of 0.016. The significant difference between the CFS and control groups was above that value, while the significant difference between the CFS and asthma groups was borderline.

An even more stringent criteria could be applied by dividing 0.05 by the number of tests performed on the entire data set (four within neutral and six within depressive mood), which therefore set the critical significance at .005. Thus, the likelihood of committing type I error was high in the current analysis.

Exogenous Cueing task – Activity Disengagement – Test of hypothesis 5

The 3 x 2 x 2 ANOVA comparing Activity Disengagement scores did not reveal any significant differences between Groups 3 (CFS, Asthma, Controls) or Inductions 2 (Neutral, Depressive), and no significant Group x Induction interaction, all $p > .14$. For the Stimulus type 2 (Words, Pictures), the main effect and interactions with the group and induction factors were also non-significant, all $p > .09$ (see *Figure 3*).



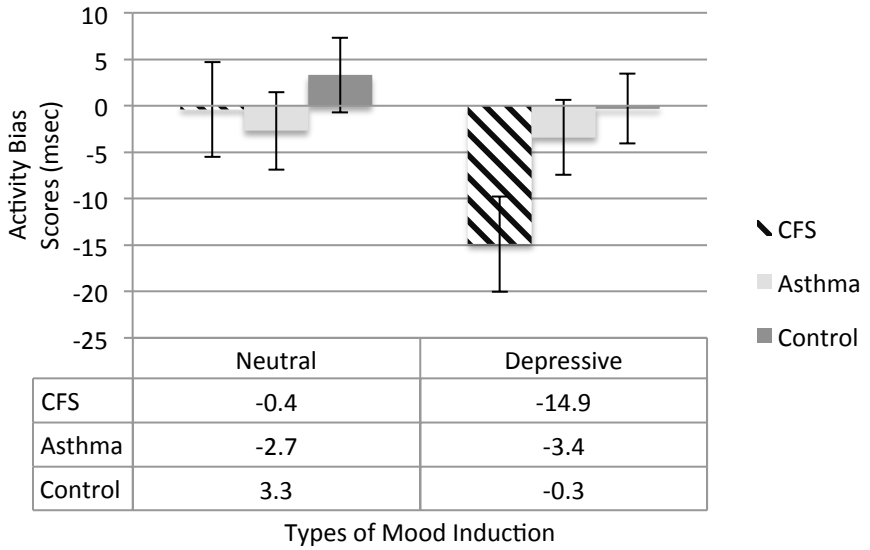
	Neutral	Depressive
CFS	-0.9	-11.7
Asthma	2.1	3.9
Control	0.6	-1.4

Figure 3. Means and Standard errors of Activity Disengagement scores on the Exogenous Cueing task for the three groups (CFS, Asthma, Control) within each mood induction (Neutral, Depressive).

Visual probe task – Activity Bias – Test of Hypothesis 2

The 3 x 2 x 2 ANOVA comparing Activity bias scores did not reveal any significant differences between the Groups 3 (CFS, Asthma, Controls), Induction types 2 (Neutral, Depressive), or the interaction between Group and Induction, all $p > .08$. No significant main

effect of Stimulus 2 (Words, Pictures) was shown, and no interactions concerning between-subjects factors and stimulus, all $p > .05$ (see *Figure 4*).



	Neutral	Depressive
CFS	-0.4	-14.9
Asthma	-2.7	-3.4
Control	3.3	-0.3

Figure 4. Means and Standard errors of Activity Bias scores on the Visual Probe task for the three groups (CFS, Asthma, Control) within each mood induction (Neutral, Depressive).

Visual probe task – Activity Engagement – Test of Hypothesis 4

The 3 x 2 x 2 ANOVA comparing Activity engagement scores revealed a significant difference between Groups 3 (CFS, Asthma, Controls), $F(2,63) = 3.82$, $p = .027$, $\eta_p^2 = .108$. Pairwise comparisons with Bonferroni corrections indicated that CFS group $M = -10.91$ ($SD = 3.21$) showed significantly greater attentional avoidance than the control group $M = 0.11$ ($SD = 2.43$), $p = .024$. No other group differences were significant, both comparisons (CFS vs Asthma, Asthma vs Control) $p > .40$ (see *Figure 5*).

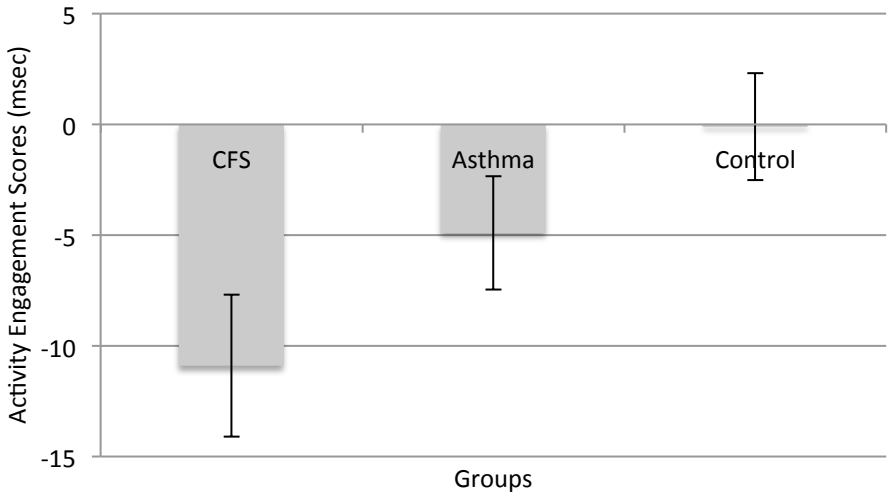


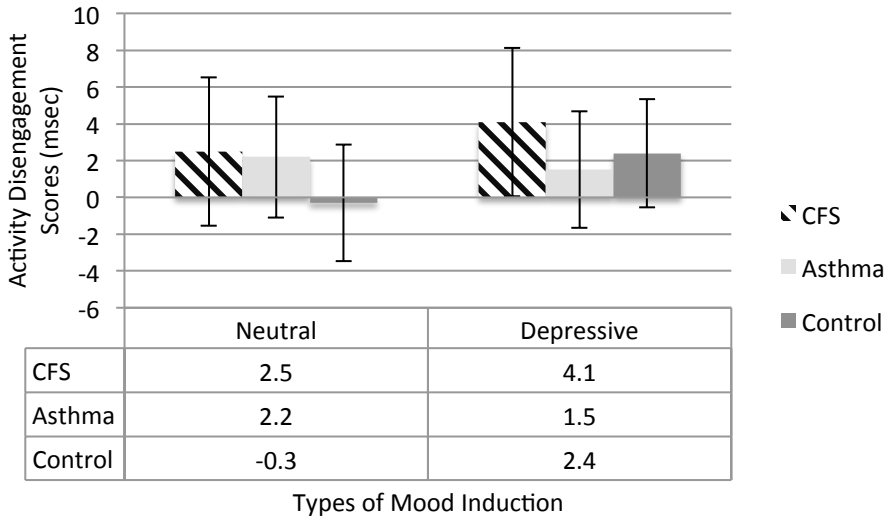
Figure 5. Means and Standard errors of Activity Engagement scores on the Visual Probe task for the three groups (CFS, Asthma, Control).

A significant difference between Induction types (Neutral, Depressive) $F(2,63) = 5.13$, $p = .027$, $\eta_p^2 = .075$ showed that the three groups were more avoidant of Activity stimuli in Depressive mood $M = -8.83$ ($SD = 2.21$) than in Neutral $M = -1.64$ ($SD = 2.28$). The main effect of Stimulus 2 (Word, Picture) and all the interactions with group and induction type factors were not significant, all $p > .05$.

Visual probe – Activity Disengagement – Test of Hypothesis 6

The 3 x 2 x 2 ANOVA comparing Activity Disengagement scores showed no significant Group 3 (CFS, Asthma, Controls) or Induction 2 (Neutral, Depressive) differences, both $p > .70$, and no significant Group x Induction interaction $p > .80$ (see *Figure 6*).

The significant main effect of Stimulus 2 (Words, Pictures) showed greater attentional disengagement difficulty for pictures of activity $M = 6.34$ ($SE = 2.62$) than for words $M = -2.02$ ($SE = 2.29$), $F(1,63) = 4.33$, $p = .041$, $\eta_p^2 = .064$. No significant interactions with group or induction type factors were detected, all $p > .25$.



	Neutral	Depressive
CFS	2.5	4.1
Asthma	2.2	1.5
Control	-0.3	2.4

Figure 6. Means and Standard errors of Activity Disengagement scores on the Visual Probe task for the three groups (CFS, Asthma, Control) within each mood induction (Neutral, Depressive).

Discussion

The study investigated the effect of neutral or depressive mood on attentional bias for information related to activity in a CFS group, compared to an asthma and a healthy control group. The exogenous cueing task measured attentional bias under low cognitive load and the visual probe task assessed attention under high cognitive load.

The first hypothesis predicting that in the exogenous cueing task, the CFS group would demonstrate attentional bias for activity in both neutral and depressive mood, as compared to asthma and control groups was not supported. The analysis did not show significant group differences or the predicted significant interaction between group and induced mood. Similarly, the asthma group did not show attentional bias under the effect of depressive mood.

All participants showed negative values on the attentional bias index in relation to activity, indicating their reaction times were quicker on the *invalid* Activity trials than on the *valid* Activity trials. Similar to health-threat trials described in the Chapter 3, an Inhibition of Return effect may have occurred, due to the long stimulus duration of 500ms in the exogenous cueing task (Lupianez et al., 2006; Posner et al., 1985). The implication is that, given a long duration between the presentation of the stimulus and the presentation of the target (stimulus onset asynchrony), our attention seeks out novel information and is

inhibited from returning to a previously attended location (Sanabria et al., 2011). Hence the responses on the invalidly cued trials were quicker (because these presented novel stimuli), while the responses on validly cued trials were slower (because the target appearing in the cued location was not novel and failed to capture attention). In response to Activity stimuli, the CFS group, along with the asthma and healthy control groups, demonstrated a healthy attentional pattern, unlike the impairment of IOR found among Parkinson's and Alzheimer's patients (Lupianez et al., 2006).

Alternatively, the groups' responses in the exogenous cueing task can be interpreted as attentional avoidance, where attention is not simply inhibited from returning to the place previously attended to, but is inhibited from returning to that place due to the unpleasant nature of the stimulus. Pervasive cognitive avoidance in the healthy group fits evidence from Khatibi, Dehghani, Sharpe, Asmundson, and Pouretemad (2009) study where healthy people demonstrated attentional avoidance of happy faces and faces in pain, that is of the affectively pleasant and unpleasant stimuli. Cognitive avoidance in the CFS and asthma groups may be due to the unpleasantness of the Activity stimuli. Alternatively, activity may have lost its novelty or excitement, thus inhibiting attentional return, a mechanism that may underlie a loss of motivation to continue engaging in activity or exercise.

The second hypothesis, predicting attentional bias towards activity in the CFS group regardless of their mood state, and attentional bias in the asthma group only when in a depressive mood state in the visual probe task, was not supported either. Similar to the exogenous cueing task, the means from the visual probe showed negative values for CFS group, which in this case may point towards attentional avoidance, because the inhibition of return effect is not expected to occur in a visual probe task.

The evidence for possible cognitive avoidance is in line with the evidence of behavioural avoidance in CFS. People with CFS tend to avoid engaging in activity in an attempt to prevent the consequent increase in fatigue and pain that follows activity periods, a symptom of 'post-exertional malaise' in CFS (Bazelmans et al., 2006; Nijs et al., 2013). However, this cognitive avoidance is not unique to the CFS group, since it was also shown in the healthy group and the people with asthma.

The third hypothesis predicting that in the exogenous cueing task the CFS group would show attentional engagement with activity in neutral and in depressive mood, as compared to asthma and control groups, received mixed support. Groups did not differ in their attention towards activity in the neutral mood state. In depressive mood, groups did not differ in their attention towards word stimuli. However, in depressive mood the CFS group

showed greater attentional engagement with pictures of activity than did the control or asthma groups. Taking into account the adjustment for multiple comparisons, however, points to the possibility that the finding may be spurious rather than indicative of attentional biases. On the other hand, the finding fits the evidence from Hou et al (2008) for attentional bias for health-threat, and Deary's (2008) proposal that events that threaten the established balance can be perceived as health-threatening.

The undetermined aversive and emotional nature of the pictorial and linguistic representations of activity makes it difficult to speculate on the difference in the CFS group's response to words and pictures in the exogenous cueing task. If the attentional process measured by the exogenous cueing task is independent of higher cognition (Fox et al., 2001), then it is the emotional content of the stimuli that may influence the attentional direction (Krompinger, Moser, & Simons, 2008). Arguably, the pictures may have a greater emotional impact, as for example found in anxiety (Reinholdt-Dunne, Mogg, & Bradley, 2009). Depressed mood may put people with CFS in a hypervigilant state towards potential threats to health, which here are represented by the images representing exertion, and the exogenous cueing task is considered to be sensitive to detecting a hypervigilant attentional pattern (Mogg et al., 2008).

The fourth hypothesis predicting greater attentional engagement in the CFS group in the visual probe was not supported. Significant group difference showed that the CFS group demonstrated substantially greater attentional avoidance of Activity stimuli (words and pictures) independent of the mood state, compared to the control group. The result was directly opposite to the prediction that the CFS group would demonstrate attentional engagement with activity. As discussed above, this process of cognitive avoidance of activity-related stimuli may parallel that of behavioural avoidance of activity and exercise due to fear of exacerbating fatigue and pain (Bazelmans et al., 2006; Nijs et al., 2013). The evidence of attentional avoidance by the CFS group from the visual probe task is in opposition to the evidence of attentional engagement with activity images if in depressive mood from the exogenous cueing task. This difference may be explained by the effect of mood and cognitive load. Under a higher cognitive load in the visual probe task, people with CFS may opt for the strategy of avoidance of stimuli that is related to exertion, a cognitive avoidance strategy parallel to behavioural avoidance. When the cognitive load is lighter, as in the exogenous cueing task the mood state may exert its influence and attention is directed towards the activity information.

The results did not support the fifth and sixth hypotheses that the CFS group would demonstrate difficulty in attentional disengagement from activity, compared to the asthma and control groups. Similarly, depressive mood did not lead to greater difficulty in attentional disengagement in the asthma group. If the results so far point towards attentional avoidance of activity stimuli, rather than engagement with it, then it would be unlikely that we found difficulty in attentional disengagement, which is characterized by an increased dwelling time on the information and difficulty in switching the attentional focus to something else.

This is the first study that has undertaken the task of putting together a pattern of attention in relation to activity-related information in CFS. The results across the two tasks indicated a potential cognitive avoidance of the Activity stimuli in people with CFS when they were subjected to higher mental load. Mood did not appear to influence attention, whether towards or away from activity, either in people with a chronic illness or in the healthy control group.

The results may indicate that avoidant processing of activity is characteristic of attentional process regardless of an individual's health status. Such a finding needs to be considered within the general framework of research focused on the promotion of physical activity. If behavioural avoidance of activity is related to avoidant and fear cognitions about activity (Leeuw et al., 2007; Wouters et al., 2012), which may be underpinned by avoidant tendencies in the underlying cognitive processing, then an intervention to increase activity in CFS needs to take into account the cognitive perception of exercise, body movement, exertion. The intervention would restructure this pattern of avoidance and redirect the attentional process towards the activity information to facilitate positive and meaningful processing (Hadjistavropoulos et al., 1998; Mullen & Suls, 1982).

The nature of the activity stimuli needs to be considered in light of the above results. In both paradigms, the stimulus hypothesised to be at the core of the impaired processing was expected to be unpleasant, fearful, or threatening. In the pilot study, the stimuli were rated for relevance to the concept of being active, but not for their emotional impact, or for their relevance to health-threat. It was hypothesised that activity information would be viewed as threat-related by CFS participants, because it represents the danger to their established balance, the physiological, cognitive, affective and behavioural homeostasis (Deary, 2008). However, that does not rule out the opposite possibility that activity stimuli were pleasant. However, if that were the case why would the attentional patterns in this study reflect avoidance? Avoidance of pleasant stimuli has been detected before in a group

of chronic pain patients, who attended away from happy faces, but towards pain faces (Khatibi et al., 2009). It may be an attempt at mood regulation, to prevent the emotional distress due to the inability to engage in pleasant activities, or to avoid experiencing the fear with regard to activity.

The major limitation of this part of the experiment is the lack of emotional ratings of the activity words and pictures. A future experiment should take into account the emotional impact of the pictures: activity pictures could be separated into either pleasant or unpleasant, and depicting either low or high intensity activity. This is particularly important when one takes into consideration previous findings where meaningful activities were associated with higher functioning and lower fatigue, while tiring and high intensity activities were associated with higher fatigue (Jason, Timpo, et al., 2009; Nijs, Meeus, Heins, et al., 2012). The activity stimuli for this experiment were chosen to be mildly threatening, because extreme activity would potentially have the same effect on all participants, even healthy people may be fearful of extreme activities. A milder threat would be more likely to tease out the differences in attention towards activity between the illness groups and the healthy group, because for people with CFS it is the daily chores and mild exercise that present great difficulties.

In the future, it may be informative to have CFS participants perform an attentional task with activity stimuli before, during and after low and high intensity exercise. That may demonstrate the mechanisms behind the discrepancy in subjective and objective measures of functioning, and how attentional focus on exertion and resulting fatigue may increase or decrease the effectiveness of Graded Exercise Therapy.

Finally, the main limitation of the study was the small size of CFS group. Taking into account the degree of fluctuations within the CFS group as demonstrated by large standard deviations, the stability and generalizability of these results remain under question. This limitation has been discussed in depth in Chapter 3 (pp. 146 – 148), including the ways of addressing the problem of recruitment for studies of CFS that investigate primarily cognitive-behavioural factors. To address that limitation, the next study described in this chapter utilised a web-based method of data collection investigating the relationship between fear cognitions in relation to movement, activity levels, fatigue and functioning.

Chapter 4B: Pilot Study: Activity Survey

Introduction

CFS is accompanied by significant reduction in activity (Fukuda et al., 1994). A recent finding, however, showed that following a CBT intervention, fatigue was reduced, but it was not necessarily accompanied by an increase in activity (Wiborg et al., 2010). Mediation analysis for a CBT trial showed that the treatment did not lead to a change in activity levels, higher activity was not associated with lower fatigue, and the effect of CBT was not attributed to change in activity but to the decreased focus on fatigue (Wiborg et al., 2011). Two main questions arise from the above finding. The first question is how active, physically and mentally, are people with CFS. The second question is how that activity is measured.

The first question concerns the actual activity levels of people with CFS in comparison to healthy people prior to the intervention. Was the actual level of activity in CFS before the intervention lower than in healthy populations? Or was it only fatigue that was elevated? This being the case, perhaps it was that after the intervention activity levels remained the same, but fatigue was reduced. That would be unlikely, considering that to be diagnosed with CFS a person would have to have severely reduced levels of activity (Fukuda et al., 1994). Furthermore, the research evidence shows that activity is significantly reduced in CFS compared to the healthy people (Black, O'Connor P, & McCully, 2005; Van der Werf, Prins, Vercoulen, Van der Meer, & Bleijenberg, 2000). Particularly, vigorous types of activity are reduced, which is linked to the decreased physiological fitness and to higher CFS symptom severity (Newton et al., 2011). The systematic review by Evering, van Weering, Groothuis-Oudshoorn, and Vollenbroek-Hutten (2011) investigating daily average physical activity levels and patterns also found that physical activity was lower in CFS, compared to the healthy population. On the other hand, the picture of activity may be more complex, as demonstrated by a study that collected data about a wide range of activities in people with CFS (e.g. sleep and rest, household chores, leisure and recreation, work) using self-administered daily activity logs over the course of two days (Jason, Timpo, et al., 2009). The researchers reported that pain-inducing and tiring activities predicted higher levels of fatigue, however, meaningful and pleasant activities were associated with lower levels of fatigue. The limitation of that study was a lack of clarity concerning the exact activities that the CFS group regarded as enjoyable, meaningful, or difficult, leaving the possibility of a large overlap between them.

Jason, King, et al. (1999) suggested that the heterogeneity in CFS populations when it comes to *reporting* symptoms, fatigue and activity may be due to the *experience* of greater

variation, ranges, and fluctuations in fatigue and activity in CFS. The researcher found great daily and weekly fluctuations in the levels of fatigue, activity and symptom severity having conducted several case studies assessing activity levels over a period of two weeks using an actigraph. Jason and colleagues (1999) proposed that the measurement of such fluctuations in levels of fatigue, symptoms and activity might make it easier to identify subgroups within the heterogeneous CFS population, therefore allowing the tailoring of interventions to the specific needs of the patients.

A study using objective (accelerometer) and subjective (daily self-ratings) measures investigated daily physical activity variation in a CFS and a healthy control group for a period of one week (Evering, Tonis, & Vollenbroek-Hutten, 2011). The average daily physical activity in the CFS group started at high intensity in the morning, similar to the controls, but declined more quickly and steeply, so that most of the day was characterized by a low intensity of physical activity. On the other hand, the healthy group operated at a higher intensity for longer, with a more gradual decline in activity through the day. Furthermore, Evering and colleagues (2011) showed that CFS participants were much more aware of the levels and fluctuations of their activity and fatigue levels.

Fulcher and White (2000) showed that activity is reduced in CFS, but the fitness levels of people with CFS are comparable to those of healthy but sedentary people. Moreover, Fulcher and White observed an adverse physiological response to high-intensity activity and significantly slowed down recovery time in CFS. That may be due to reported muscle abnormalities in CFS, impaired muscle metabolism or increased accumulation of lactic acid (Hollingsworth et al., 2008; Jones et al., 2010).

However, the CFS population as has been discussed throughout the thesis is not uniform. Bazelmans, Prins, and Bleijenberg (2006) in their review of cognitive-behavioural interventions distinguished 'passive' and 'active' subgroups of people with CFS who showed different patterns and levels of activity. The 'Passive' subpopulation was characterized by a fear of activity, consequent avoidance, and physiological deconditioning, at which point even minor activity resulted in the increase of symptoms and fatigue. The 'Active' group meanwhile demonstrated a 'boom and bust' cycle of behaviour on the basis of enhanced demands and expectations of their functioning, as described previously (Moss-Morris, 2005; Surawy et al., 1995). This subgroup may exhibit the type of unrealistic beliefs about normal functioning levels described by Fry and Martin (1996a). These patterns were confirmed by another investigation showing that when people with CFS were less active throughout the day with less variation in activity, they experienced less daily fluctuations of fatigue and

pain; on the other hand, when they engaged in more vigorous activity, they demonstrated more fluctuations in activity levels and reported fluctuations in fatigue and pain ratings that matched one another (Meeus et al., 2011).

The two subgroups of CFS, passive and active, therefore would benefit from different types of treatments that would selectively target cognitions, avoidance or fear, and set different plans for the gradual increase in activity (Bazelmans et al., 2006). In order to identify the most appropriate individual patterns of treatment, it is important, firstly, to measure appropriate activities identified as targets for intervention, and secondly, to measure cognitive, affective, and behavioural variables that may be associated with such activities. That leads to the second main question, the one about the methods for measuring activity.

Evering, van Weering, et al. (2011) after completing the systematic review of activity in CFS pointed out the difficulties in assessing the differences between groups due to the lack of uniformity in outcome measures, and the abundant variability between the studies. This variability applied to the measures of activity and health outcomes, the use of objective or subjective measures, and the types of activity that were measured. For example, Moss-Morris et al. (2005) used a measure of heart rate, including the maximum heart rate reached and the predicted heart rate. CBT trials analysed by Wiborg et al. (2010) used an actometer, a motion-sensing device. The PACE trial (White et al., 2011) used a self-report measure of physical functioning, the SF-36 (McHorney et al., 1993; Ware & Sherbourne, 1992), a 6-minute walking ability test, and a Work and Social Adjustment scale, which is not strictly a measure of activity but of disruption of activity (Mundt, Marks, Shear, & Greist, 2002). This indicates that a great variety of activity measures have been employed in CFS research.

With regard to the problem of measuring types of activities, each instrument is limited to measuring one dimension of activity. For example, an actometer is an instrument that strictly measures movement. A heart rate monitoring is a direct physiological measure, but it does not distinguish one activity from another, except perhaps in terms of vigorousness. Walking ability can be a measure of physical movement and fitness, but is unidimensional. Alternatively, self-reports, in spite of problems of subjective measurement, can provide rich information about the types of activities people engage in, or cease to engage in due to illness. Consequently, self-reports could be a good source of activity-related data in people with CFS.

This underscores one important aspect of behavioural interventions, the correspondence between what is being measured and what is being changed in the

intervention. For example, if the treatment aim is that the patient can return to work, then the outcome measure should assess whether people returned to work; if the treatment set out to change the fitness levels, then the outcome should assess the fitness levels pre- and post-treatment.

Graded Exercise Therapy is a relatively straightforward treatment, which specifically addresses physical exertion and exercise, aiming to reverse deconditioning. On the other hand, Cognitive-Behavioural Treatment can be a very rich complex intervention that through its very nature can address a multitude of cognitions, emotions, and behaviours indirectly. Therefore, devising measures of outcome for CBT is a challenge for clinical research, as discussed in evaluations and guidelines for complex interventions addressing changes in behaviors (Craig et al., 2008). Specifically in CFS, measures of activity would be of primary importance considering that reduction in activity is one of its main characteristics (Fukuda et al., 2014). In the light of this, GET and CBT, which aim to reverse deconditioning and return people to premorbid levels of activity, accrued the most evidence of their effectiveness (Smith et al., 2015). Therefore, the current study aimed to explore the components and validity of a newly developed measure of daily activity and lifestyle in a sample of people with CFS, in people with asthma and in a sample of healthy controls.

The large number of existing activity questionnaires, primarily physical activity scales, have been extensively validated and reviewed (Helmerhorst, Brage, Warren, Besson, & Ekelund, 2012). Questionnaires have been developed and used in children, adult, and ageing populations. These measures address several domains of activity: household, occupation, sports/exercise, active living habits, leisure, transportation, walking, and sedentary behaviours or inactivity. The scales measure vigorous, moderate and low activity frequency, duration and/or intensity. A comprehensive list of questionnaire measures and validation studies has been compiled by Applied Research at the National Cancer Institute, US Department of health: http://appliedresearch.cancer.gov/paq/

Two issues become evident upon reviewing the current activity measures. Firstly, they have been primarily developed for and validated in healthy populations. Secondly, they are very diverse in their applications and measured domains. In order to measure more than one dimension of activity it would be needed to include several measures. That would add to the number of self-reports needed to be completed and increase the burden on participants. Adding to the number of measurements may increase the difficulties in conducting research. Particularly, it would be a problem in an area like CFS research where firstly, the population suffers from increased fatigue, mental and physical, and from

problems in concentration and memory, and secondly, there are ongoing difficulties in recruitment and high dropout rates. However, reducing the number of measurements may omit important domains.

The goal of the current study was to combine a number of domains: occupation, exercise, active living habits, leisure, walking, and sedentary behaviours in one measure of daily activity or regular lifestyle. This new self-report measure attempted to explore activities conducted inside and outside the house in relation to lifestyle— that is, activities a person may engage in throughout the day in their regular life. The questionnaire was not aimed specifically at measuring physical activity, which would involve activity primarily involving body movement. It also aimed to measure mental activity (e.g. reading, use of computers, internet, communication devices, talking, listening, writing). Few if any of the existing activity assessments include mental activities such as the use of a computer, phone, email, or reading. These behaviours are generally measured in the context of research on computer and Internet use. The aim was also to make this new questionnaire suitable for measuring activity in a population with chronic illness and reduced mobility such as CFS.

Therefore, the new questionnaire focused on combining several domains of activity and included inside home activities: sedentary, low levels activity, or inactivity types (e.g. staying in bed during the day, watching TV), online activity as part of daily activity (e.g. use of social media), outside of home social and non-social activities (e.g. going for drinks). It also included a measure of walking, due to its importance in physical activity research in general (Kelly et al., 2014) and its emphasis in CFS (White et al., 2011). The scale measured the frequency of performed activities in minutes/hours per day and times per day/week/month.

The second goal of the study was to measure levels of activity in association with cognitions about activity, mood and coping. Avoidant behaviour and fear cognitions, with regard to activity, are two of the components addressed in cognitive-behavioural interventions with CFS. Catastrophic cognitions about pain accompanied decreased exercise capacity and poorer physiological fitness (Nijs et al., 2008). Similarly, catastrophic cognitions about fatigue and fear of movement were linked to lower exercise capacity, if such exercise was a short demanding task (measured through a stair-climbing test), rather than regular daily levels of activity (Nijs et al., 2011). The latter finding underscores the importance of separating different types of activity, not only into low and high intensity but the quality, characteristics, importance, and role of particular activities. For example, walking to work is qualitatively different from taking a walk in the park, though the walking is the common

component. These subtly different types of activities also need to be accounted for, measured, and be a part of the assessment of functioning and outcome.

Exercise and physical activity were found to have a positive effect on mood in general population (Kritz-Silverstein, Barrett-Connor, & Corbeau, 2001), including for those people who reported elevated depressed symptoms (Lane & Lovejoy, 2001). Therefore, the current study investigated the relationship between positive and negative mood, and activity, predicting to find significant relationship between mood and activity in control and asthma groups. On the other hand, levels of activity in the CFS group should be independent of mood, because it is not negative mood that results in activity reduction in CFS, but the illness, symptoms, fear and catastrophising cognitions. Therefore, in the CFS group activity levels should be strongly related to the measure of fear of movement. The Tampa Kinesiophobia Scale (TKS) modified for use with the fatigue population has two subscales measuring fear cognitions based on beliefs about the seriousness of illness and based on beliefs that activity is harmful (Silver et al., 2002). Fear of movement in CFS as measured by TKS was found to be related to objective measures of activity (reduced distance traveled, measured on a stationary bike), but was not related to measures such as symptom severity or fitness (measured by heart rate monitoring) (Silver et al., 2002). Therefore, one would expect that the fear of movement as measured by TKS, and its respective subscales illness and activity beliefs, would be associated with the self-reported activity levels.

In the asthma group, fear cognitions about activity may also play a role in reduced activity. If people with asthma confuse a change in breathing patterns brought on by exercise with the change in lung function due to an impending asthma attack, they may become fearful of physical activity (Emtner et al., 1996). In line with this finding, there is a documented association between greater anxiety and greater inactivity in asthma (Strine, Mokdad, Balluz, Berry, & Gonzalez, 2008). Therefore, it is more likely that in the asthma group reduced activity would be related to greater anxiety and, to a lesser degree, to responses on the activity beliefs subscale of the TKS.

Comparison with the asthma group would show whether there are patterns that are common to people with chronic illness in general, and which patterns may be be unique to CFS. The CFS group, due to the fact that sensations of fatigue are so closely tied to activity, may differ in their perception and cognitions concerning activity from other illness groups. Thus, the study also utilized a measure of perception of activity exploring how people perceive their premorbid, current, and future levels of activity, previously used in research on activity levels in children with CFS (Fry & Martin, 1996a).

Finally, the study used measures of avoidant coping styles of dealing with stress (stress for healthy people, illness for CFS and asthma groups), such as denial and behavioural disengagement, in parallel with the cognitive measure of fear of movement. It would be expected that greater avoidant behaviours would be associated with increased inactivity and reduced activity. However, different patterns would be expected for CFS and Asthma groups. Avoidance in CFS is of a more behavioural nature, such as avoiding activity in order to prevent symptom exacerbation (Bazelmans et al., 2006; Nijs et al., 2013). Therefore, one would expect to observe a relationship between activity and behavioural disengagement in a CFS group. On the other hand, in asthma a repressive coping style, defined as avoidance of the conscious perception of negative feelings (Weinberger, 1995), has been documented and strongly linked to poorer lung function, more symptom severity, negative health outcomes, and greater utilization of health care (Adams, Smith, & Ruffin, 2000; Cooke, Myers, & Derakshan, 2003; Gonzalez-Freire, Vazquez-Rodriguez, Marcos-Velazquez, & de la Cuesta, 2010). Therefore, one would expect to observe associations between activity levels and denial in asthma, in contrast with activity levels and behavioural disengagement in CFS.

In summary, in the current study a newly developed measure of activity was used to investigate physical, mental and social patterns of regular daily activity in CFS, asthma, and healthy control groups. The pattern of associations between reported activity and cognitions about activity, mood and coping styles was explored with the aim of validating the new activity scale.

Specifically, the following hypotheses were tested in the study:

1. In the CFS group, higher symptom frequency and fatigue severity will be associated with reduced activity, in accordance with previous findings (Fulcher & White, 2000; Newton et al., 2011). Increased symptomatology is not expected to be associated with an increase in sedentary behaviours, or inactivity. Higher severity of fatigue and frequency of CFS symptoms will also be related to decreased mental activity in light of the concurrent symptoms of CFS, such as impairments in concentration and memory (Fukuda et al., 1994).

2. In the CFS group, decreased activity will not be associated with negative mood. In contrast, in the asthma and in healthy control groups decreased activity will be associated with increased negative mood.

3. In the CFS group, decreased activity will be related to a heightened fear of movement as measured by TKS. In contrast, in the asthma group decreased activity will be related only to the activity beliefs subscale of TKS (the beliefs that activity is harmful).

4. In the CFS group, more behavioural avoidance, as measured by behavioural disengagement, will be associated with reduction in activity. In the asthma group, decrease in activity will be associated with denial.

Method

Online Study Design

The current study was a survey conducted via the Internet (using Survey Monkey data collection software). The survey consisted of self-report measures of symptoms, functioning, mood, fear cognitions, coping, and activity. The between-subjects factor was group: people with CFS were compared with people with asthma and with healthy controls, all of whom were matched on gender and education. The dependent variables were scores on self-report measures: activity, symptoms, fatigue, functioning, perception of activity, fear of movement, depression, anxiety, positive and negative affect, behavioural disengagement and denial.

In the current chapter, analysis of the component structure of the new measure of daily activity is presented, as is the analysis of the associations between symptoms, fatigue, functioning, mood, fear cognitions and behavioural measures of activity based on the data from a preliminary sample of the online survey. The online survey also included an experimental component, a memory retrieval task. The data from the memory task is presented and discussed in Chapter 6: Memory.

The study has been reviewed by and received ethics clearance through the University of Oxford Central University Research Ethics Committee (CUREC), assigned reference number: MSD/IDREC/C1/2009/111 (Appendix C.2).

Scale Development

A self-report measure of daily activity included 26 items (see Table 1). The measure was designed to assess daily/weekly/monthly patterns of activity: daily living, functioning, active and sedentary behaviours, physical, mental and social types of activity a person may engage in over a period of time (e.g. a monthly behaviour). The 26 items measured the following facets of daily activities:

a) Physical activity (e.g. walking)

b) Mental activity (e.g. reading)

c) Social activity outside of home (e.g. going to a party)

d) Social activity online (e.g. Facebook)

e) Social activity at home (e.g. receiving visitors)

f) Sedentary types of activity (e.g. TV)

g) Activity inside and outside of home (e.g. work, education)

Table 1.

Activity Scale Items

#	Item	Scale of Measurement
1	On average how much time do you spend each day being in bed or lying down on your couch(excluding at night, e.g. between 8am and 11 pm)	minutes/hours per day
2	On average how much time do you spend each day outside of the house	minutes/hours per day
3	How often do you leave the house	times per day/week/month
4	What is the maximum time you spend walking at a stretch without a rest	minutes/hours per day
5	How many hours a day do you work	minutes/hours per day
6	How much time do you spend each day reading	minutes/hours per day
7	How much time do you spend each day watching television	minutes/hours per day
8	How much time do you spend each day playing puzzles/games	minutes/hours per day
9	How much time do you spend each day working on the computer	minutes/hours per day
10	How much time do you spend each day surfing the internet	minutes/hours per day
11	How much time do you spend each day making phone calls	minutes/hours per day
12	How much time do you spend each day sending texts	minutes/hours per day
13	How much time do you spend each day sending emails	minutes/hours per day
14	How much time do you spend each day chatting on the Internet	minutes/hours per day
15	How much time do you spend each day on Facebook	minutes/hours per day
16	How often do you visit other people	times per day/week/month
17	How often do you have visitors	times per day/week/month
18	How often do you go to social gatherings	times per day/week/month
19	How often do you go out for food	times per day/week/month
20	How often do you go out for drinks	times per day/week/month
21	How often do you go out for entertainment (film/theatre/concerts)	times per day/week/month
22	How often do you take part in sport	times per day/week/month
23	How often do you go out to watch sport	times per day/week/month
24	How often do you go out to clubs/parties	times per day/week/month
25	How often do you go to church or other community gatherings	times per day/week/month
26	How often do you go out for educational purposes (classes/lectures)	times per day/week/month

Participants

Data were collected from the preliminary sample of a web-based study consisting of three groups: CFS (*n* = 79), Asthma (*n* = 44), healthy controls (*n* = 132). The recruitment was conducted through contacting UK wide CFS and Asthma support and self-help groups; social media (Facebook); Internet UK-based health forums and discussion boards concerning asthma, CFS, or chronic illness in general; participant recruitment advertisement webpages for universities (Oxford, Warwick, and UCL); and various participants' recruitment web sites (e.g http://www.clinpsy.org.uk/). The inclusion criteria for the study specified a primary diagnosis of CFS, or Asthma, and no other current diagnosis of an acute or chronic physical or psychological disorder. All participants were screened for diagnosed medical/psychiatric

disorders, and excluded if they reported a primary medical and/or psychiatric diagnosis that was not CFS or asthma.

People with CFS were included in the study if they:

1. Reported a primary CFS diagnosis by a qualified medical practitioner (GP, referred specialist). Any person who had received a diagnosis of CFS by their GP or at a specialist clinic in the past unspecified period of time was considered for inclusion into the study.

AND

2. Met the CDC/Fukuda criteria for the presence of current primary unexplained, persistent or relapsing fatigue, which is not relieved by rest and results in significant reduction of activities for the last 6 months (Fukuda et al., 1994).

AND

3. Reported at least four out of 8 concurrent symptoms from the CDC/Fukuda criteria: impairment in short-term memory/concentration, sore throat, tender lymph nodes, muscle pain, multi-joint pain, headache, unrefreshing sleep, post-exertional malaise more than 24 hours. Participants with CFS rated the frequency of 8 symptoms in the past 6 consecutive months, according to the Fukuda/CDC criteria, on a scale from 1 (never experienced) to 5 (experienced all of the time). The range of reported symptom frequency was between 16 (participants reported the required minimum of at least 4 symptoms and rated them as experienced most of the time – score of 4) and 40 out of maximum 40 (all 8 symptoms experienced all of the time with a score of 5 for each symptom). Therefore, all participants with CFS met the CDC/Fukuda criteria and have been experiencing the required minimum of 4 symptoms for most of the time in the past 6 months.

Participants with CFS were excluded if they reported

1. A current acute or chronic primary medical or psychiatric diagnosis that may be the cause of extreme fatigue and would preclude the diagnosis of CFS, for example any diagnosis of the conditions outlined by CDC/Fukuda (1994), Reeves et al (2003; 2005), or NICE (2007) guidelines.

2. A current diagnosis of primary depression, that is depression diagnosed in the past 5 years prior to receiving CFS diagnosis. This is according to the recommendation by Reeves and colleagues (2003, 2005).

Due to reported comorbidity of CFS and depression, the history of depression and anxiety was checked (Mccue et al., 2006). Nine participants with CFS reported episodes of

depression due to CFS, and 4 episodes of anxiety after having received CFS diagnosis, and three participants reported comorbid depression and anxiety. Potential depression and anxiety have also been assessed using Hospital Anxiety and Depression scale (HADS) (Zigmond & Snaith, 1983). Recommended cut-off scores for severity of depression and anxiety for the CFS population are 9-10 points (Morriss & Wearden, 1998). 31 participants with CFS scored above 9 on HADS Depression and 23 scored above 9 on HADS Anxiety. These participants were included in the study because their depression/anxiety did not preclude their diagnosis of CFS.

Participants with Asthma were included in the study if they reported:

1. A primary asthma diagnosis by a qualified medical practitioner (their GP, or referred specialists).

AND

2. Current experience of asthma symptoms.

AND

3. Current use of medication to manage their asthma (preventer/reliever medication, inhaled corticosteroids).

Participants with asthma were excluded if they reported:

1. Another current acute or chronic medical or psychiatric diagnosis.

Participants ranked their current Asthma severity as 1 - Mild, 2 - Moderate or 3 – Severe. They reported the degree in which Asthma interfered with their functioning, measured on a scale from 0 (not at all) to 10 (extremely) (Brooks et al., 1989). Asthma symptoms were assessed by the Asthma Symptom Checklist (ASC), a widely used, well validated and reliable (Cronbach α .84 - .94) measure (Kinsman, Luparello, O'Banion, & Spector, 1973). Participants reported the number of their core symptoms and how frequently they were experienced on a scale from 1 (never) to 5 (always).

Three participants with asthma reported a diagnosis of depression and anxiety in the past, all received after the asthma diagnosis. These participants were included in the study because their depression/anxiety did not preclude their diagnosis of asthma. Potential depression and anxiety have also been assessed using HADS. The recommended cut-off scores for the general population are 8-10 points (Herrmann, 1997; Zigmond & Snaith, 1983). Eleven participants with asthma scored above 8 on HADS Depression and 15

participants scored above 8 on HADS Anxiety. Participants were included because of the absence of psychiatric comorbidity or any history of a psychiatric disorder.

Additional inclusion criteria for all participants specified 18 years of age, and English at the standard of a native speaker. Healthy control participants were excluded if they reported a current acute or chronic medical or psychiatric diagnosis.

Questionnaires

All self-report measures of demographic and illness characteristics and the following questionnaires are presented in Appendix C.4.

Hospital Anxiety and Depression Scale (HADS) consists of 14 items that measure anxiety and depression in populations with non-psychiatric medical conditions, such that the scores are not affected by the physical symptoms a patient experiences as part of their medical condition (Zigmond & Snaith, 1983). The range of scores is 0-21 for each subscale, with higher scores indicating greater severity. The developers of the HADS questionnaire suggest the following classification of cases based on the scores: normal range (0 – 7), mild (8-10), moderate (11-15), severe (16 or higher). For people with CFS, a cut-off score of 9-10 is recommended to distinguish patients with elevated anxiety or depression (Morriss & Wearden, 1998). The scale has good reliability: Anxiety subscale Cronbach's α was 0.87; Depression subscale Cronbach's α was 0.79 (Mccue et al., 2006) and has been validated in different medical settings (Bjelland et al., 2002; Mondolo et al., 2006). In the current sample, Cronbach's α was 0.83 for Depression and 0.83 for Anxiety. The scale was used to assess psychiatric comorbidity in the CFS group.

Positive and Negative Affective Schedule (PANAS) is a 20-item mood measure (Watson et al., 1988) of positive (10 adjectives) and negative (10 adjectives) affect. Participants were asked to read each item and indicate to what extent they were feeling that way right now, that is, at the present moment, using a 5-point scale (1- very slightly or not at all to 5 – extremely). A higher score reflects greater emotion during that moment. The full range of scores for each subscale is 10 – 50. The scale is widely used in different settings to measure mood, and has good validity and Cronbach's α of 0.89 for the Positive Affect (PA) subscale and 0.85 for the Negative Affect (NA) (Crawford & Henry, 2004). In the current sample, the Cronbach's α was 0.84 for PA subscale and 0.83 for the NA subscale. The advantage of PANAS is that it is a good measure of within- and between-individual differences (Rossi & Pourtois, 2012).

The Fatigue Severity Scale (FSS) is a 9-item unidimensional measure for the assessment of the impact that fatigue has on functioning (Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). The scale has previously been validated in patients with multiple sclerosis, patients with systemic lupus erythematosus, and in healthy controls (Krupp et al., 1989). It has been widely used in the assessment of fatigue in chronic illness populations, for example, patients with multiple sclerosis (Mills, Young, Nicholas, Pallant, & Tennant, 2009), hepatitis C (Kleinman et al., 2000), patients with stroke and sleep-wake disorders (Valko, Bassetti, Bloch, Held, & Baumann, 2008), and cancer patients (Stone, Richards, A'Hern, & Hardy, 2000). It is one of the most widely used measures of fatigue in chronic illness and in healthy populations (Valko et al., 2008). The scale has good validity and internal consistency, reporting Cronbach's α in the range of 0.84 - 0.95, and test-retest reliability value of 0.94 (Whitehead, 2009) and is suitable for use in groups with a variety of conditions including CFS (Dittner et al., 2004). In the current sample the Cronbach's α was 0.95. The participants rated the items on a scale from 1 – completely disagree to 7 - completely agree in response to the questions about their fatigue, and its interference with daily functioning, motivation, and activity. For each participant a mean score based on the nine items was calculated. The score of 4 has been suggested as a cut-off point (Armutlu et al., 2007; Kaynak et al., 2006; Valko et al., 2008), and a more conservative score of 5 to identify a severe fatigue impact (Lerdal, Wahl, Rustoen, Hanestad, & Moum, 2005).

The advantage of the scale is its good validity, reliability, brevity, and importantly, its comparability to samples representing other chronic conditions, allowing comparison of fatigue scores of people with CFS, with fatigue scores of people with other chronic illnesses. The disadvantage is that, due to the low use of FSS among people with CFS, comparison with other CFS samples is difficult. The FSS has been used in some small samples of people with CFS (Friedberg & Sohl, 2009a; Neu et al., 2008; Olson, Ambrogetti, & Sutherland, 2003; Packer, Foster, & Brouwer, 1997; Plioplys & Plioplys, 1997), but has not been validated in large samples. Three studies, Friedberg and Sohl (2009), Neu et al. (2008) and Olson et al. (2003) used mean scores (rather than sum scores). For comparison purposes a weighted average was calculated from the above three studies based on the sample numbers, means and standard deviations. The average mean of 6.01 and standard deviation of 0.8 were obtained, allowing the comparison with the sample in this study.

Furthermore, FSS is not specifically a measure of fatigue severity, but rather its interference with functioning (Dittner et al., 2004). It measures fatigue-related severity of functional disability (Taylor, Jason, & Torres, 2000). In contrast, the Chalder Fatigue scale

measures the intensity and severity of fatigue and CFS-related symptoms, since it was developed specifically for CFS population (Chalder et al., 1993), and has been validated in CFS populations (Cella & Chalder, 2010; Morriss, Wearden, & Mullis, 1998). Taylor et al. (2000) compared the Chalder Fatigue scale and the FSS in a sample of healthy and CFS-like groups (CFS-like referred to the community sample who have met the CDC/Fukuda criteria but have not been medically examined to rule out other conditions). The study did not show correlations between the Chalder Fatigue scale and the FSS for the CFS-like sample. That would be expected if the two scales measure different dimensions of fatigue. There was a weak significant correlation for the total sample, including healthy controls. That suggests that both scales might have measured the same construct, but different dimensions of fatigue. Additionally, Taylor and colleagues have shown a number of significant correlations between FSS and CFS symptoms of muscle pain (.24**), post-exertional malaise (.42**) and memory/concentration (.34**), all significant at the level of 0.01. FSS as the measure of fatigue in relation to functioning was chosen for the current study, because it aimed to assess the levels of activity, which would be a measure of functioning, and cognitions about activity. Ideally, both measures should be used to assess fatigue frequency, severity and duration as recommended by Reeves et al (2003, 2005). However, additional measures may increase the burden on participants. Furthermore, the addition of a comparison group with another chronic illness, asthma, also favours the use of FSS for the measure of fatigue in a different population from CFS.

The Physical Functioning subscale from the Medical Outcomes Study - RAND 36 Short-Form Health Survey (SF-36) (Ware & Sherbourne, 1992) was used in the study. The measure of Physical functioning has been demonstrated as a valid measure among CFS populations (Deale et al., 1997; Fulcher & White, 1997), and has been recommended for use in CFS research (Reeves et al., 2005). It consists of 10 items with a reported Cronbach's α is 0.93. In the current sample the Cronbach's α was 0.97. Raw scores on all items are recoded into scores that range from 0 reflecting poorest health and no functioning to a 100, reflecting good health and extremely high functioning.

Perception of Activity questionnaire (Fry & Martin, 1996a) consists of four questions assessing how active an individual was before their illness (PAST), how active they are currently (NOW), how active they 'expect' to be after the illness (EXPECT), and how active they 'would like' to be after the illness (WANT). The items are measured on a visual analogue scale (VAS) ranging from 0 (not at all active) to 100 (extremely). Due to the extended duration of asthma, the questions were adapted for the asthma group by changing before

illness to "6 months ago", and after you get better to '6 months in the future'. The questions were adapted for the Control group by changing the 'before illness' to '6 months ago' and 'after you get better' to '6 months in the future'. The 6 months mark for the control and asthma groups was chosen because the measure of CFS symptoms specifies a 6-month time period. The measure has been applied previously to children and adolescents with CFS (Fry & Martin, 1996a, 1996b). The current sample Cronbach's α was 0.80.

The Tampa Scale of Kinesiophobia – Fatigue (TSK-F) is a 17-item measure of the Fear of Movement/injury adopted for use in people with CFS, where "pain" was substituted by "fatigue" (Silver et al., 2002). The responses are rated on a 4-point scale ranging from 1 – Strongly disagree to 4 – strongly agree. The range of scores is 17 to 68, with higher scores reflecting greater fear of movement. The measure has two subscales: Illness beliefs (beliefs that the illness is serious), and Activity Beliefs (beliefs that activity is harmful). Silver *et al.* reported good validity and Cronbach's α 0.78 for Illness Beliefs, and 0.70 for Activity Beliefs. In the current sample the Cronbach's α was 0.85 for the full scale, 0.84 for the Illness beliefs subscale, and 0.76 for the Activity beliefs subscale. The scale has been used previously in the CFS population (Nijs, Meeus, Heins, et al., 2012; Nijs, Vanherberghen, Duquet, & De Meirleir, 2004).

Coping – Brief COPE (Carver, 1997) is a generic measure of coping behaviours, a well validated 28 item scale adopted from the original coping questionnaire (Carver, Scheier, & Weintraub, 1989). The measure can be applied to the assessment of general and specific stressful situations. In the current study, CFS and asthma groups were asked to assess their coping in relation to their illness. The two subscales, Behavioural Disengagement and Denial were used in the study. Their reported Cronbach's α values were 0.65 for Behavioural Disengagement (2 items) and 0.54 for Denial (2 items). The responses are provided on a 4-point scale ranging from 0 (haven't been doing this at all) to 3 (have been doing this a lot). For the current sample, the Cronbach's α values were 0.68 for Behavioural Engagement and 0.66 for Denial. The behavioural disengagement subscale has been previously used in CFS research (Antoni et al., 1994; Ax, Gregg, & Jones, 2001; Moss-Morris, Petrie, & Weinman, 1996; Ray, Jefferies, & Weir, 1997).

Power Analysis

Principal components analysis - A priori analysis

Calculation of the required sample size was made on the basis of the planned analysis of principal components for the newly designed activity scale. Osborne and Costello

(2004) emphasised the importance of larger subject to item ratios in decreasing the odds of type I error and increasing the odds of obtaining the correct component pattern. The minimum recommended subject to item ratio is 5:1. However, Osborne and Costello noted that as sample size increases the subject to item ratio has less of an impact. However, the practicalities of data collection, dropout rates, missing data, or technical difficulties that may decrease the number of potential participants should be taken into account. Therefore, increasing the ratio, having considered the low likelihood of obtaining a large sample size, would be more suitable in the current study. Thus, the recommended 10:1 ratio of ten participants per item of scale was chosen (Costello & Osborne, 2005; Osborne & Costello, 2004), which would require 260 participants for a 26 item scale.

Equipment

The survey was administered via Survey Monkey software, a web-based platform for data collection. Each participant was able to access the survey through an URL, which took them to the first page of the survey containing the information about the study procedure, ethics, confidentiality (Appendix C.1), and consent form (Appendix C.3).

Procedure

Participants answered screening questions (about their history of medical and psychiatric diagnoses) and filled out the online consent form. The study procedure is presented below (see Appendix C.4 for the list of self-report measures).

1. Information about you (gender, age, education)
2. Information about your health (physical/mental/CFS diagnosis)
3. CFS Checklist (CDC/Fukuda criteria (1994) OR Asthma Checklist
4. Fatigue Severity Scale (presented at the beginning, so that a participant's perception of their fatigue level is not coloured by tiredness from completing the questionnaires)
5. SF36 – Physical Functioning subscale (during the past four weeks)
6. Activity Scale
7. Memory Retrieval Task (The Memory Retrieval Task data is presented in Chapter 6: Memory)
8. Coping scale
9. Perception of Activity
10. Fear of Movement measure - Tampa Kinesiophobia Scale – Fatigue (TSK-F)

11. PANAS – current affect

12. HADS Anxiety/Depression

Data Analysis

Statistical analyses were performed using the Statistical Package for Social Science (SPSS) software version 20.0. Chi-square and univariate ANOVA tests were used to compare the groups on demographic characteristics (gender, education, age), FSS, SF-36 – Physical functioning, TKS-F, Denial and Behavioural Disengagement subscales (COPE), Perception of Activity, PANAS, HADS Depression and Anxiety.

To explore the Activity scale, a Principal Components Analysis was conducted on the 26 items for the entire sample n = 255, using orthogonal and then oblique rotation, to take into account the correlations between items. Kaiser's criterion was applied for the decision how many components to retain in the analysis (Field, 2009, p. 641). Factor loadings above 0.40 were considered based on the recommendations in the literature (Field, 2009; Stevens, 2002).

Principal Component Analysis (PCA) was conducted on the factors that were extracted after the PCA described above, using Orthogonal and Oblique rotation methods. Factors scores were calculated using the Bartlett method because the procedure produces unbiased estimates of the true factor scores (DiStefano, Zhu, & Mindrila, 2009).

Internal consistency was investigated through inter-item correlations, reflected by Cronbach's alpha values. Pearson correlations (2-tailed) were carried out to explore the relationships between the subscales reflecting discovered factors. Convergent and discriminant validity were investigated by exploring Pearson correlations between the activity scale and measures of functioning (e.g. fatigue and physical functioning), perception of activity (PAST, NOW, WANT, EXPECT) cognitions about activity (Fear of Movement measure TKS-F), mood (HADS and PANAS), and coping (Denial and Behavioural Disengagement).

Results

Demographic and Questionnaire Measures

CFS, Asthma and control groups did not differ significantly in gender and educational attainment, in all cases $p > .18$, but differed significantly on Age, $p > .001$. See Tables 2A and 2B for demographic and illness measures, and mean scores on self-reports.

Table 2A.

Demographic and Questionnaire Measures for CFS, Asthma, and Healthy Control Groups

	CFS *(n = 79)*	Asthma *(n = 44)*	Control *(n = 132)*		
	n (%)	*n* (%)	*n* (%)	*χ2*	*p*
Gender (female)	70 (80%)	33 (70%)	106 (80%)	3.43	*ns*
Education (Degree)	35 (44%)	21 (50%)	47 (36%)	3.35	*ns*
Asthma Mild		17 (46%)			
Asthma Moderate		16 (43%)			
Asthma Severe		4 (10%)			
	M (SD)	*M* (SD)	*M* (SD)		
Symptoms duration (years)	11.4 (9.2)				
Time since diagnosis (years)	7.7 (6.9)				
CFS symptom frequency (past 6 months)	30.1 (5.7)				
Asthma severity (1-Mild, 2-Moderate, 3-Severe)		1.7 (0.7)			
Asthma interference (0-10 scale)		3.5 (2.7)			
Asthma Symptom Checklist		77.6 (28.3)			

Table 2B.

Demographic and Questionnaire Measures for CFS, Asthma, and Healthy Control Groups

	CFS *(n = 79)*	Asthma *(n = 44)*	Control *(n = 132)*				
	M (SD)	*M* (SD)	*M* (SD)	*F*	*p*	Pairwise	*p*
Age	37.6 (12.2)	35.5 (15.9)	22.6 (6.1)	60.1	< .001	CFS vs C	< .001
						A vs C	< .001
FSS	6.3 (0.7)	3.6 (1.9)	3.5 (1.3)	128.3	< .001	CFS vs C	< .001
						CFS vs A	< .001
Physical Functioning	39.2 (25.8)	66.7 (35.6)	94.5 (8.9)	5.7	.005	CFS vs C	< .001
						CFS vs A	< .001
						A vs C	< .001
Activity NOW	26.1 (21.3)	45.0 (32.3)	41.9 (30.1)	5.7	.005	CFS vs C	.020
						CFS vs A	.021
Activity PAST	84.9 (19.1)	66.9 (21.5)	42.9 (32.4)	31.4	< .001	CFS vs C	< .001
						CFS vs A	.017
						A vs C	.002
Activity WANT	84.3 (17.5)	83.1 (14.5)	57.3 (33.6)	15.6	< .001	CFS vs C	< .001
						A vs C	< .001
Activity EXPECT	66.2 (25.6)	56.9 (28.4)	47.6 (31.5)	4.8	.010	CFS vs C	.008
FOM Total	41.7 (7.8)	32.1 (10.2)	27.9 (6.1)	72.9	< .001	CFS vs C	< .001
						CFS vs A	< .001
						A vs C	.018
FOM Illness Beliefs	17.9 (4.8)	14.2 (5.4)	11.2 (3.7)	48.7	< .001	CFS vs C	< .001
						CFS vs A	< .001
						A vs C	.003
FOM Activity Beliefs	17.3 (3.7)	12.4 (3.9)	10.8 (2.4)	87.5	< .001	CFS vs C	< .001
						CFS vs A	< .001
COPE Behavioural Disengagement	1.4 (1.6)	0.8 (1.3)	1.0 (1.3)	2.2	*ns*		
COPE Denial	1.1 (1.5)	0.7 (1.3)	0.7 (1.3)	0.9	*ns*		
PANAS Positive	21.9 (8.4)	24.4 (8.9)	25.7 (7.7)	4.5	.012	CFS vs C	.009
PANAS Negative	18.4 (8.9)	14.1 (7.5)	16.5 (6.9)	3.6	.030	CFS vs A	.031
HADS Depression	8.8 (4.5)	5.3 (5.2)	3.8 (2.7)	37.7	< .001	CFS vs C	< .001
						CFS vs A	< .001
HADS Anxiety	8.8 (4.8)	8.1 (4.9)	7.5 (3.8)	1.8	*ns*		

Note. FSS - Fatigue Severity Scale
Physical Functioning subscale of Short-Form Health Survey – SF-36
FOM - Fear of Movement, Tampa Kinesiophobia Scale - Fatigue
PANAS - Positive and Negative Affect Schedule
HADS - Hospital Anxiety and Depression Scale
COPE - Coping Questionnaire
CFS - Chronic Fatigue Syndrome, A - Asthma, C - control
Pairwise comparisons used Bonferroni correction

Principal Components Analysis with Orthogonal Rotation

A Principal Component Analysis (PCA) was conducted on the 26 items of the Activity Scale using Orthogonal rotation (Varimax) using the entire sample, *n* = 255. The Kaiser-Meyer-Olkin measure verified the sampling adequacy for the analysis, KMO = .787 ('good' according to Field, 2009), and all KMO values for individual items were > .60, except Internet Chat variable (.59) which was still above the acceptable limit of .50 (Field, 2009). Bartlett's test of sphericity χ^2 (325) = 2384.444, $p < .001$ indicated that the correlation matrix was significantly different from an identity matrix (where all correlation coefficients are 0), therefore the correlations between items were sufficiently large for PCA.

An initial analysis was run to obtain eigenvalues for each component in the data. Seven components had eigenvalues over Kaiser's criterion of 1 and in combination explained 61.8% of the variance. The scree plot was clear and showed an inflexion at the point of factor 5 that would justify retaining up to 5 factors (including the point of inflexion). The initial Scree plot is presented in *Figure 1.*

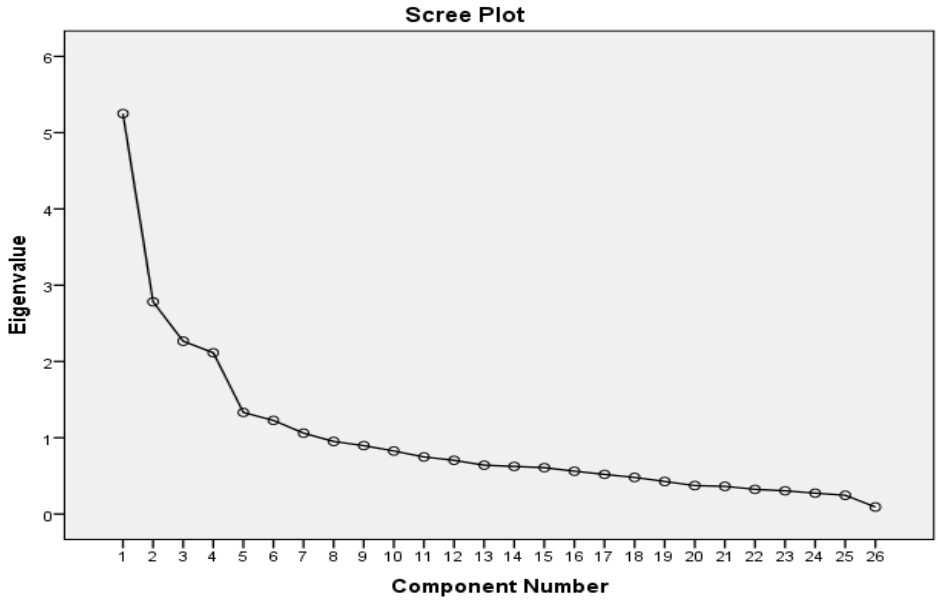


Figure 1. Scree plot for the Principal Components analysis (Orthogonal Rotation), *N* = 255.

Kaiser's criterion can be used based on the following conditions (Field, 2009, p. 641)

1. Less than 30 variables
2. The sample size exceeds 250
3. The average communality after the extraction is above .6

According to the above criterion, 7 components were retained for the final analysis. Table 3 presents the factor loadings after the rotation (Orthogonal Varimax).

Table 3.

Summary of the Principal Components Analysis Results for the Activity Scale (N = 255) After the Orthogonal (Varimax) Rotation

		Rotated Factor Loadings						
	Item	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7
1	Visiting	**.80**	.15	.11	-.05	-.05	-.03	.00
2	Drinks Out	**.78**	-.19	.17	.07	.16	.16	-.07
3	Social Gathering	**.75**	-.13	.08	.05	-.07	.14	-.15
4	Having Visitors	**.71**	.23	.06	.04	-.10	-.04	.03
5	Clubbing	**.71**	.04	.06	.12	.19	-.05	-.11
6	Leaving House	**.60**	.15	.31	.06	-.22	-.01	-.01
7	Going out for entertainment	**.60**	.28	.11	-.12	.20	.30	.01
8	Eating Out	**.43**	.32	.10	-.17	.03	.31	.08
9	Watching Sports live	.16	**.87**	-.01	-.01	.23	-.02	.04
10	Education	.27	**.83**	-.03	.05	.21	.04	-.04
11	Community	-.05	**.73**	.20	.01	-.11	.03	-.07
12	Hours of work (per day)	.04	.00	**.69**	-.09	.19	.17	-.03
13	Hours outside the house (per day)	.17	-.28	**.67**	-.10	.31	.06	-.01
14	TV	-.22	-.03	**-.60**	.04	.09	.04	**.47**
15	Doing sport	.25	.15	**.58**	.00	-.28	.03	.19
16	Bed during the day	-.10	-.08	**-.58**	.05	.16	-.09	.36
17	Walking	.14	.19	**.42**	.01	.04	.10	.06
18	Internet Chat	.02	.07	-.04	**.85**	.07	-.02	-.04
19	Facebook	.02	-.09	-.11	**.74**	.16	.05	.37
20	Internet	.11	.13	-.06	**.54**	.03	**.53**	.26
21	Phone	-.01	**.42**	-.06	.09	**.63**	.04	-.02
22	Emailing	-.10	.20	.25	.03	**.60**	.11	.29
23	Texting	.17	-.04	-.03	.38	**.56**	-.05	-.12
24	Reading	.14	.03	.16	.06	-.17	**.78**	-.21
25	Computer	.02	-.05	.28	-.02	.32	**.71**	.19
26	Puzzles/games	-.09	-.05	-.03	.17	-.02	.01	**.82**
	Eigenvalues	5.33	2.91	2.26	2.08	1.30	1.13	1.05
	% of variance	20.49	11.20	8.70	7.99	5.01	4.36	4.04
	α	**.77**	**.66**	**.77**	**.54**	**.52**	**.50**	**.63**

Note: Factor loadings over .40 appear in bold.
Coefficients are sorted by size

The threshold for factor loading cut-offs can be decided based on sample size. According to the Table of Factor Loadings for Practical Significance in relation to sample size (Hair, Tatham, Anderson, & Black, 1998), the threshold for factor loadings cut-off can be set at 0.35, when the sample size is 250. Following recommendations by Stevens (2002), Field (2009) suggested that factor loadings greater than 0.36 should interpreted for a sample size of above 200, and that factor loadings above 0.40 should be interpreted irrespective of sample size. Thus, factor loadings of 0.40 and above were used to place a variable with a given factor (see Table 3).

Principal Components Analysis with Oblique Rotation

According to Field's (2009) recommendation, the above analysis was repeated using oblique rotation. An oblique rotation is preferred to the orthogonal, because the underlying factors may be related if they are measuring the same latent variable. The analysis has replicated the above structure of 7 factors and revealed a number of potential underlying subscales in the Activity scale. The Pattern and Structure Matrices are presented in Table 4 and Table 5, respectively.

Table 4.

Summary of Principal Components Analysis Results for the Activity Scale (N = 255) After the Oblique (Direct Oblimin) Rotation - Pattern Matrix

		Rotated Factor Loadings						
	Item	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7
1	Visiting	**.81**	-.07	-.09	.01	.06	.03	.08
2	Drinks Out	**.79**	.04	.26	.10	-.15	-.03	-.12
3	Social Gathering	**.75**	.03	.19	-.02	.06	-.13	-.12
4	Clubbing	**.72**	.10	.01	.01	-.19	-.08	.09
5	Having Visitors	**.71**	.02	-.18	-.03	.12	.06	.07
6	Leaving House	**.57**	.07	-.11	.22	.26	.00	.05
7	Going out for entertainment	**.56**	-.15	-.22	.01	-.17	.04	-.26
8	Eating Out	.39	-.20	-.27	.00	.01	.10	-.28
9	Internet Chat	-.03	**.85**	-.09	.00	-.04	-.10	.00
10	Facebook	.03	**.72**	.10	-.05	-.08	.34	-.04
11	Watching Sports live	.11	-.03	**-.87**	-.05	-.20	.04	.05
12	Education	.21	.04	**-.82**	-.09	-.19	-.04	-.01
13	Community	-.15	.04	**-.75**	.14	.15	-.09	-.02
14	Hours outside the house (per day)	.12	-.09	.31	**.72**	-.25	.02	.00
15	Hours of work (per day)	-.06	-.07	.02	**.70**	-.12	-.02	-.13
16	TV	-.13	-.02	.03	**-.56**	-.08	**.48**	-.06
17	Doing sport	.18	.03	-.13	**.54**	.38	.19	.03
18	Bed during the day	.01	.00	.08	**-.53**	-.18	.38	.09
19	Walking	.07	.02	-.17	**.41**	.03	.06	-.06
20	Phone	-.05	.05	**-.43**	-.02	**-.61**	-.01	-.02
21	Texting	.16	.35	.04	.04	**-.56**	-.11	.07
22	Emailing	-.14	-.01	-.18	.33	**-.52**	.31	-.06
23	Puzzles/games	-.04	.14	.07	.03	.14	**.82**	.04
24	Reading	.03	.05	.01	.01	.18	-.25	**-.82**
25	Computer	-.06	-.06	.11	.24	-.24	.18	**-.69**
26	Internet	.05	**.50**	-.09	-.11	.05	.22	**-.54**
	Eigenvalues	5.33	2.91	2.26	2.08	1.30	1.13	1.05
	% of variance	20.49	11.20	8.70	7.99	5.01	4.36	4.04
	α	**.77**	**.66**	**.77**	**.54**	**.52**	**.50**	**.63**

Note: Factor loadings over .40 appear in bold.
Coefficients are sorted by size

Table 5.

Summary of Principal Components Analysis Results for the Activity Scale (N = 255) After Oblique (Direct Oblimin) Rotation - Structure Matrix

		Rotated Factor Loadings						
	Item	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7
1	Visiting	**.81**	-.03	-.22	.20	.07	-.06	-.08
2	Drinks Out	**.79**	.09	.10	.28	-.14	-.09	-.26
3	Social Gathering	**.75**	.06	.06	.17	.08	-.20	-.22
4	Having Visitors	**.72**	.05	-.29	.14	.11	-.02	-.07
5	Clubbing	**.71**	.14	-.11	.16	-.18	-.12	-.05
6	Going out for entertainment	**.64**	-.10	-.36	.23	-.18	.02	-.40
7	Leaving House	**.64**	.05	-.21	.35	.25	-.09	-.10
8	Eating Out	**.47**	-.16	-.37	.19	-.01	.08	-.38
9	Internet Chat	.04	**.84**	-.07	-.06	-.12	.02	-.02
10	Facebook	.01	**.78**	.08	-.13	-.20	**.44**	-.08
11	Watching Sports live	.23	-.01	**-.88**	.06	-.23	.09	-.06
12	Education	.34	.06	**-.85**	.05	-.22	.01	-.13
13	Community	.03	-.02	**-.73**	.19	.13	-.06	-.09
14	Hours outside the house (per day)	.23	-.11	.20	**.72**	-.23	-.03	-.16
15	Hours of work (per day)	.13	-.12	-.06	**.72**	-.12	-.05	-.27
16	TV	-.30	.10	.08	**-.61**	-.14	**.54**	.04
17	Bed during the day	-.18	.11	.12	**-.57**	-.21	**.42**	.16
18	Doing sport	.31	-.03	-.20	**.57**	.35	.10	-.13
19	Walking	.20	-.01	-.23	**.45**	.01	.04	-.19
20	Phone	.03	.11	**-.45**	.01	**-.64**	.10	-.10
21	Texting	.18	**.40**	.00	.03	**-.58**	-.03	.00
22	Emailing	-.05	.05	-.24	.31	**-.56**	.38	-.18
23	Puzzles/games	-.12	.22	.05	-.06	.04	**.81**	-.03
24	Reading	.21	.02	-.06	.21	.15	-.19	**-.79**
25	Computer	.08	-.01	.00	.36	-.30	.25	**-.75**
26	Internet	.14	**.55**	-.15	-.03	-.07	.33	**-.57**
	Eigenvalues	5.33	2.91	2.26	2.08	1.30	1.13	1.05
	% of variance	20.49	11.20	8.70	7.99	5.01	4.36	4.04
	α	**.77**	**.66**	**.77**	**.54**	**.52**	**.50**	**.63**

Note: Factor loadings over .40 appear in bold.
Coefficients are sorted by size

The results of both rotations were comparable, except for the Factors 2, 3, and 4 switching places due to change in Eigenvalues (all remaining above 2) and Factors 5, 6, and 7 switching places due to the change in Eigenvalues (all three remaining above 1). The items that clustered on the same factors suggested the structure presented in Table 6.

Table 6.

Results of the Principal Components Analysis for the Activity scale - Final structure

Subscale	Items	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6	Factor 7
Leisure and	Visiting	**.81**	-.03	-.22	.20	.07	-.06	-.08
Recreation	Drinks Out	**.79**	.09	.10	.28	-.14	-.09	-.26
	Social Gathering	**.75**	.06	.06	.17	.08	-.20	-.22
	Having Visitors	**.72**	.05	-.29	.14	.11	-.02	-.07
	Clubbing	**.71**	.14	-.11	.16	-.18	-.12	-.05
	Going out	**.64**	-.10	-.36	.23	-.18	.02	-.40
	Leaving House	**.64**	.05	-.21	.35	.25	-.09	-.10
	Eating Out	**.47**	-.16	-.37	.19	-.01	.08	-.38
	Doing sport	**.31**	-.03	-.20	.57	.35	.10	-.13
Social Activity	Internet Chat	.04	**.84**	-.07	-.06	-.12	.02	-.02
Online	Facebook	.01	**.78**	.08	-.13	-.20	.44	-.08
	Internet	.14	**.55**	-.15	-.03	-.07	.33	-.57
Social Duties	Watching sport	.23	-.01	**-.88**	.06	-.23	.09	-.06
	Education	.34	.06	**-.85**	.05	-.22	.01	-.13
	Community	.03	-.02	**-.73**	.19	.13	-.06	-.09
Work/Daily	Hours outside	.23	-.11	.20	**.72**	-.23	-.03	-.16
	Work hours	.13	-.12	-.06	**.72**	-.12	-.05	-.27
	Walking	.20	-.01	-.23	**.45**	.01	.04	-.19
Communication	Phone	.03	.11	-.45	.01	**-.64**	.10	-.10
	Texting	.18	.40	.00	.03	**-.58**	-.03	.00
	Emailing	-.05	.05	-.24	.31	**-.56**	.38	-.18
Sedentary	TV	-.30	.10	.08	**-.61**	-.14	**.54**	.04
	Bed Day	-.18	.11	.12	**-.57**	-.21	**.42**	.16
	Puzzles/games	-.12	.22	.05	-.06	.04	**.81**	-.03
Mental	Reading	.21	.02	-.06	.21	.15	-.19	**-.79**
	Computer	.08	-.01	.00	.36	-.30	.25	**-.75**
	Eigenvalues	5.33	2.91	2.26	2.08	1.30	1.13	1.05
	% of variance	20.49	11.20	8.70	7.99	5.01	4.36	4.04
	α	**.77**	**.66**	**.77**	**.54**	**.52**	**.50**	**.63**

Principal Components Analysis on the Factor Scores

A Principal Component Analysis (PCA) was conducted on the 7 Factors that were extracted after the PCA (Oblique) described above. The scores were calculated using the Bartlett method, because the procedure produces unbiased estimates of the true factor scores that correlate only with their own factor (DiStefano et al., 2009).

The analysis was conducted with orthogonal rotation (varimax) and then Oblique rotation. The Kaiser-Meyer-Olkin measure verified the sampling adequacy for the analysis, KMO = .569 (mediocre according to Field, 2009), and KMO values for individual items were ≥

.50, above or at the acceptable limit of .50 (Field, 2009). Bartlett's test of sphericity χ^2 (21) = 63.45, $p < .001$, indicated that correlations between items were sufficiently large for PCA.

An initial analysis was run to obtain eigenvalues for each component in the data. Two components had eigenvalues over Kaiser's criterion of 1 and in combination explained 40.1% of the variance. The scree plot showed an inflexion at the point of factor 3 that would justify retaining 2 factors (not including the point of inflexion) (see *Figure 2.*). With the sample of above 200, we can use the scree plot to justify retaining 2 components.

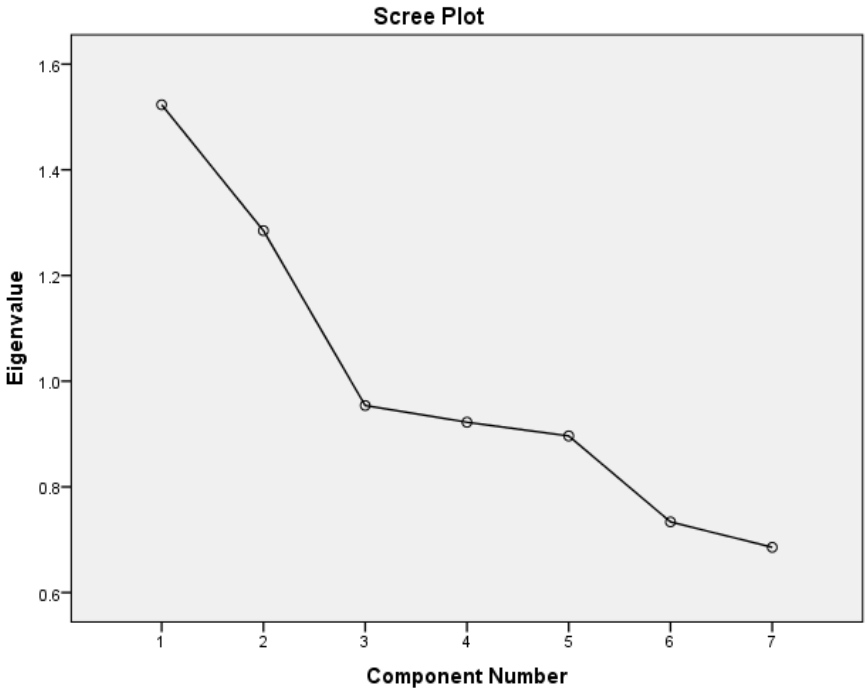


Figure 2. Scree plot for the Principal Components analysis using Factors scores (Bartlett) (Orthogonal Rotation), *N* = 255.

Given the large sample size and the convergence of the scree plot and Kaiser's criterion on 2 components, that was the number of components that were retained in the final analysis. The factors loadings using Oblique rotation are presented in Table 7 - Pattern and Table 8 - Structure Matrix.

Table 7.

Pattern Matrix PCA Results for the Activity Scale (N = 255) on the Factor Scores Calculated Using Bartlett Method

Factor Name	Pattern Matrix Factor Scores	Active Lifestyle Factor 1	Sedentary Lifestyle Factor 2
Leisure and Recreation	BART factor score 1 for analysis 1	**.68**	-.11
Work/Daily Living	BART factor score 4 for analysis 1	**.67**	-.24
Mental Effort	BART factor score 7 for analysis 1	**-.60**	-.21
Social Duties	BART factor score 3 for analysis 1	**-.49**	-.12
Sedentary Behaviour	BART factor score 6 for analysis 1	-.05	**.69**
Online Social Activity	BART factor score 2 for analysis 1	-.02	**.60**
Communication	BART factor score 5 for analysis 1	-.08	**-.58**
	Eigenvalues	1.52	1.29
	% of variance	21.76	40.11
	α	.76	.61

Note: Factor loadings over .40 appear in bold.
Coefficients are sorted by size

Table 8.

Structure Matrix PCA Results for the Activity Scale (N = 255) on the Factor Scores Calculated Using Bartlett Method

Factor Name	Structure Matrix Factor Scores	Active Lifestyle Factor 1	Sedentary Lifestyle Factor 2
Leisure and Recreation	BART factor score 1 for analysis 1	**.68**	-.08
Work/Daily Living	BART factor score 4 for analysis 1	**.66**	-.21
Mental Effort	BART factor score 7 for analysis 1	**-.61**	-.24
Social Duties	BART factor score 3 for analysis 1	**-.49**	-.14
Sedentary Behaviour	BART factor score 6 for analysis 1	-.02	**.68**
Online Social Activity	BART factor score 2 for analysis 1	.00	**.60**
Communication	BART factor score 5 for analysis 1	-.10	**-.58**
	Eigenvalues	1.52	1.29
	% of variance	21.76	40.11
	α	.76	.61

Note: Factor loadings over .40 appear in bold.
Coefficients are sorted by size

Internal Consistency

The full Activity Scale had overall internal consistency of Cronbach's α = .74, rather good (Field, 2009, p. 680). All of Cronbach's α values, taking into account whether items were deleted, were in the range around .70. Therefore, all the items were retained in the scale.

The analysis of internal consistency for each subscale was conducted based on the results of the PCA using Oblique rotation. Table 6 presents the proposed subscale structure based on the interpretation of the factor loadings and Cronbach's α values for each potential subscale. Cronbach's α values were higher for subscales assessing active behaviours in the

range of .60 to .70, and lower .50 - .60 for the subscales assessing more sedentary behaviours, and the use of various communication media; however taking into account the diversity of measured constructs, the values are not unexpected (Kline, 1999 in Field, 2009, p. 675).

The reliabilities for the two subscales (based on the two higher order factors extracted from the PCA on the factor scores) were calculated using the original scores. Tables 7 and 8 present the items selected for higher order subscales on the basis of the PCA analysis and Cronbach's α values of .76 for Active Lifestyle and .61 for Sedentary Lifestyle.

Score Calculation

For each subscale, the sums of participants' scores were calculated based on the structure of subscales described in the tables. The total score was not calculated due to the diverse nature of the items. The scores on higher order subscales (Active Lifestyle and Sedentary Lifestyle) and on lower order subscales (Leisure and Recreation, Online Social Activity, Social Duties, Work/Daily Living, Communication, Sedentary Behaviour, and Mental Effort) were used in the subsequent analyses of the data.

Inter-Correlations between dimensions of Activity Scale

A correlational analysis was conducted on the subscales of activity derived from the PCA, as a check that they are indicating the same construct. The pattern of correlations is presented in Table 9.

Table 9.

Correlations for the Subscales of the Activity Measure

	LeisureRecreation	OnlineSocAct	SocialDuties	WorkDailyLiv	Communication	SedentaryBeh
OnlineSocAct	.057					
SocialDuties	**.307****	.108				
WorkDailyLiv	**.245****	-.062	.032			
Communication	.049	**.268****	**.356****	**.159***		
SedentaryBeh	**-.322****	**.233****	-.083	**-.449****	.087	
MentalEffort	**.193****	**.228****	.048	**.359****	**.222****	**-.176****

Note **. Correlation is significant at the 0.01 level (2-tailed).

Note . Correlation is significant at the 0.05 level (2-tailed).

c. Listwise N=255

There were expected significant associations between Leisure/Recreation and Social duties, Work/Daily living, and Mental effort, all *r* significant at the .01 level (2-tailed). The analysis showed expected significant correlations between online social activity and Communication, Sedentary Behaviour, and Mental Effort, all correlations significant at .01 level (2-tailed). Social Duties subscale was significantly related to Communication $r = .36$, p (2-tailed) < .001; and Work/Daily living was significantly associated with Communication and Mental Effort. The analysis showed significant negative correlations between Sedentary Behaviour and Leisure/Recreation, all significant at below .01 level.

Convergent and Discriminant Validity

For each subscale, including the two subscales based on higher factors, correlations were conducted with measures of fatigue (FSS), physical functioning subscale of SF-36, Perception of Activity (Before, Now, Expect in the Future, Want in the Future), kinesiophobia – fear of movement measure (TSK-F), and mood. For the CFS and Asthma groups, the relationship between symptomatology and activity was investigated.

Activity and CFS symptoms

The correlations between Activity and illness measures for the CFS group, presented in Table 10, revealed no relationship between illness or symptom duration and current activity. More symptoms were associated with reduced work hours and daily functioning, but with more active online resources/internet use, more sedentary behaviours, and in general more sedentary lifestyle. Greater fatigue was similarly associated with reduced work hours and daily functioning, and an increase in sedentary behaviours. Importantly, increased fatigue was related to a decrease in Mental activity and Active Lifestyle.

Table 10.

Correlations between Activity Scale and Illness Measures for CFS Group

CFS	Leisure	Online	Social Duties	Work Daily	Communication	Sedentary Behaviours	Mental	Active Lifestyle	Sedentary Lifestyle
Illness Duration	-.03	-.07	-.06	.08	-.09	-.01	-.03	-.03	-.10
Symptom Duration	-.16	-.06	-.13	.17	.01	.04	-.06	-.14	.00
Symptom Frequency	-.16	**.24***	-.03	**-.25***	.12	**.23***	-.17	-.18	**.24***
Fatigue - (FSS)	-.22	.08	-.21	**-.32****	.01	**.31****	**-.36****	**-.28***	.12

Note: * p < .05, ** p < .01, *** p < .001.

c Listwise N=78

Activity and Asthma symptoms

Correlations between Activity and illness measures for the asthma group (see Table 11), revealed a slightly different pattern. Higher frequency, severity and interference of asthma symptoms were associated with lower Active Lifestyle, specifically, with reduced Leisure and Recreation, Work/Daily functioning and Mental activity. Similar to CFS group, greater symptom frequency was related to more sedentary behaviours. However, more asthma interference was related to lower sedentary behaviours. While that may seem contradictory, it is probably the case that the more active a person is the more likely they would feel that their symptoms interfere with their activities. Similar to the CFS group, there were no significant correlations between activity and duration of asthma. Also comparable to the CFS group, there was a significant association between reduced Work/Daily functioning and increased asthma frequency and interference.

Table 11.

Correlations between Activity Scale and Illness Measures for Asthma Group

Asthma	Leisure	Online	Social Duties	Work Daily	Communication	Sedentary Behaviours	Mental	Active Lifestyle	Sedentary Lifestyle
Illness Duration	-.18	-.03	-.04	.13	.18	-.13	.04	-.15	-.04
Symptom Duration	-.22	.13	-.08	.06	.14	-.05	-.04	-.21	.11
Asthma Severity	**-.32***	-.26	.02	-.12	-.05	.13	**-.30***	**-.32***	-.17
Symptom Frequency (ASC)	**-.36****	.04	-.14	**-.38****	.20	**.46****	**-.38****	**-.41****	.25
Asthma Interference	**-.34***	-.13	.05	**-.39****	.13	**-.35***	**-.35***	**-.37****	.06

Note: * $p < .05$, ** $p < .01$, *** $p < .001$.

c Listwise N=44

Relationships between Activity, Perception of Activity, and Functioning

For the CFS group, the pattern of correlations supported the validity of the Activity measure; higher fatigue was related to reduced active behaviours and increased sedentary behaviours (see Table 12). Similarly, higher physical functioning and higher current activity (Activity NOW) was related to increased active, and reduced sedentary behaviors. Notably, a greater amount of current activity (NOW) was related to more online activity, a relationship unique to the CFS group.

The pattern of correlations for the asthma group in relation to fatigue, physical functioning and activity NOW is similar (see Table 13). In contrast to the CFS group, there was a significant association between EXPECTED future activity and Active Lyfestyles,

including Leisure, Work/Daily and Mental activity. There were no significant relations between any of the subscales of current activity and PAST activity for the asthma group.

The pattern for the Control group was different from both the CFS and asthma groups (see Table 14). There were no significant correlations with fatigue, or perceived activity (past, current or future). Higher physical functioning was related to less engagement with community, which includes activities such as attending community gatherings (e.g. going to church), education (e.g. evening classes) or being spectator at sporting events. It is possible that higher physical functioning would result in more active participation and a more active lifestyle, and in turn in a reduced likelihood of engaging in such events as those described above. However, no significant relationships were detected between physical function and active behaviours and lifestyle.

Activity and Fear of Movement

For the CFS group, higher fear of movement was associated with increased sedentary behaviours (see Table 12). Increased Illness beliefs (the TKS subscale that measures beliefs in the greater seriousness of illness and degree of accompanying disability) were related to more online activity and a greater score on Social Duties subscale (which reflects involvement in community activities or education), a relationship unique to the CFS group. Illness beliefs were also related to increased Sedentary Lifestyle, while Activity beliefs (the TKS subscale the measures beliefs that activity is harmful) were related to decreased Leisure.

The asthma group showed a different pattern (see Table 13.). Higher fear of movement was associated with reduced active behaviours. The illness beliefs subscale showed no significant associations. The activity beliefs subscale was associated with decreased activity, similar to the CFS group.

The Control group showed a similar pattern to the CFS group, with a higher total fear of movement being associated with increased sedentary behaviours (see Table 14). There was a difference between healthy group and the two illness groups with regard to the beliefs that activity is harmful. For CFS and Asthma greater belief that activity is harmful was associated with decreased activity, specifically Leisure and Recreation. For the control group beliefs that activity was harmful were associated with more inactivity, an increase in sedentary lifestyle.

Activity and Coping styles

CFS and Asthma demonstrated different patterns as predicted by the hypothesis that in the CFS group behavioural disengagement (a measure of behavioural avoidance) would be an influencing factor associated with reduction in activity, while in the asthma group denial (cognitive avoidance) would play a role in modulating activity. The CFS group showed that increase in behavioural disengagement was related to higher score on Social Duties (the subscale that reflects engagement with a community, going to church, or education) (see Table 12). There were no significant relationships between denial and any of the activity measures for the CFS group. In contrast, for the asthma group greater denial was related to decreased Work/Daily functioning (see Table 13). For the asthma group, there were no significant correlations with behavioural disengagement and any of the measures. For the control group, greater behavioural disengagement was related to spending more time online, and greater denial was related to more communication (see Table 14).

Activity and Mood

Within the CFS group mood was primarily associated with inactivity: positive affect with a decrease and depressed mood with an increase in sedentary behaviours. Negative affect was correlated with increased online involvement. Higher anxiety was linked to higher score on Social Duties (the subscale that reflects community/church/education involvement) (see Table 12).

Within the asthma group mood was mostly related to activity. Positive affect was associated with more Active Lifestyle. Negative affect, depressed mood and anxiety were associated with decreased Work/Daily activity. Depression, particularly, was associated with lower Mental activity and less Active Lifestyle (see Table 13).

Within the control group, the pattern was closer to the CFS group, with more positive mood being associated with less sedentary beahaviours (see Table 14). In contrast, higher negative affect was related to more active behaviours and more community involvement, but to reduced Work/Daily activity. Similar to the asthma group, depressed mood was related to reduced activity, rather than an increase in sedentary lifestyle.

Table 12.

CFS Group: Correlations between Activity Subscales and Fatigue, Functioning, Activity-Related Beliefs, Mood, and Coping

Measures	Leisure	Online	Social duties	Work Daily	Communication	Sedentary	Mental Effort	Active Lifestyle	Sedentary Lifestyle
FSS	**-.35****	.04	-.24	**-.26***	.02	**.26***	**-.36****	**-.38****	.09
Physical Function	**.60****	.01	**.49****	**.61****	-.06	**-.54****	**.49****	**.69****	-.19
Activity NOW	**.53****	**.24***	.20	**.33****	-.08	**-.36****	**.29***	**.53****	-.11
Activity PAST	.08	-.10	-.18	.19	.02	**-.28***	.11	.07	-.07
Activity WANT	.10	.14	-.04	-.02	.05	-.09	.15	.08	.05
Activity EXPECT	.23	.13	.11	.00	-.09	-.13	.23	.22	-.09
FOM Total	-.14	.21	.21	-.06	.13	**.30****	.07	-.08	**.25****
FOM Illness Beliefs	.02	**.35****	**.30***	-.15	.13	**.28***	.18	.05	**.27***
FOM Activity Beliefs	**-.26***	-.04	-.10	.06	.13	.12	-.11	-.22	.14
HADS Depression	-.14	.20	.12	-.06	-.03	**.29***	-.15	-.11	.10
HADS Anxiety	.22	.17	**.28***	-.03	-.03	.17	.03	.22	.06
PANAS Negative	.09	**.29***	.23	.00	-.08	.02	.08	.11	.00
PANAS Positive	.01	.09	-.18	.17	.00	**-.25***	.21	.02	-.04
Behavioural disengagement	.00	.24	**.31***	.16	.08	.07	-.08	.07	.15
Denial	.22	-.21	.24	-.07	-.08	.12	.04	.21	-.09

Note. ** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Listwise - CFS *n* = 77

Table 13.

Asthma Group: Correlations between Activity Subscales and Fatigue, Functioning, Activity-Related Beliefs, Mood, and Coping

Measures	Leisure	Online	Social duties	Work Daily	Communication	Sedentary	Mental Effort	Active Lifestyle	Sedentary Lifestyle
FSS	**-.43****	-.03	-.10	**-.37***	.16	**.39***	**-.22**	**-.47****	.15
Physical Function	**.48****	.16	.07	**.42****	-.12	**-.35***	**.40****	**.52****	-.03
Activity NOW	**.56****	-.05	.09	**.37***	-.14	**-.49****	.26	**.58****	-.17
Activity PAST	-.23	-.06	.21	-.17	.10	.22	-.09	-.21	.05
Activity WANT	.16	-.15	.15	.25	.13	-.01	.11	.20	-.12
Activity EXPECT	**.42***	.03	.22	**.45****	.01	-.18	**.42****	**.49****	-.05
FOM Total	**-.40****	-.15	-.13	-.13	.08	.21	-.19	**-.41****	-.03
FOM Illness Beliefs	-.25	-.06	-.18	-.18	.06	.12	-.20	-.28	.01
FOM Activity Beliefs	**-.41****	-.20	-.02	-.10	.17	.30	-.19	**-.40****	-.01
HADS Depression	**-.42****	-.09	-.06	**-.48****	-.03	.22	**-.43****	**-.48****	.01
HADS Anxiety	-.20	-.03	-.02	**-.31***	.07	.18	-.25	-.23	.04
PANAS Negative	-.17	.12	-.08	**-.36***	.18	.15	-.22	-.22	.18
PANAS Positive	.30	.15	-.04	.24	.29	-.15	.24	**.31***	.11
Behavioural disengagement	-.18	-.16	.04	-.18	.14	-.03	-.07	-.18	-.12
Denial	-.24	-.08	-.11	**-.39***	.17	.02	-.24	-.29	-.03

Note. ** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Listwise - Asthma *n* = 43

Table 14.

Healthy Control Group: Correlations between Activity Subscales and Fatigue, Functioning, Activity-Related Beliefs, Mood, and Coping

Measures	Leisure	Online	Social duties	Work Daily	Communication	Sedentary	Mental Effort	Active Lifestyle	Sedentary Lifestyle
FSS	-.28	-.08	.15	.20	.12	.16	-.29	-.10	.08
Physical Function	.01	-.11	**-.42****	-.10	-.10	-.10	.00	-.20	-.13
Activity NOW	-.03	-.12	-.09	-.05	.06	.14	.00	-.08	.03
Activity PAST	-.15	-.07	-.14	-.06	.05	.29	.13	-.18	.12
Activity WANT	-.15	-.04	-.25	-.18	.11	.32	.01	-.26	.18
Activity EXPECT	-.16	-.05	-.08	-.10	.15	.28	.07	-.16	.18
FOM Total	.07	.18	.14	.07	.11	.15	-.05	.11	**.21***
FOM Illness Beliefs	-.04	.11	.06	.07	.07	.19	-.04	-.01	.19
FOM Activity Beliefs	-.23	.19	.09	.18	.21	**.41***	.12	-.09	**.38***
HADS Depression	**-.35***	-.06	.30	.17	.27	.27	-.05	-.05	.20
HADS Anxiety	-.19	-.03	-.02	-.22	.09	.10	.07	-.14	.06
PANAS Negative	.08	-.03	**.33***	**-.22***	.08	-.07	-.06	**.22***	-.02
PANAS Positive	.12	-.05	.16	.17	.17	**-.20***	-.04	.17	-.08
Behavioural disengagement	-.03	**.20***	.13	-.14	.02	-.01	.01	.05	.11
Denial	.01	.12	.14	-.05	**.20***	.05	.14	.09	.16

Note. ** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).

Listwise - Control *n* = 111

Discussion

The study investigated the validity of a new self-report measure of activity in order to explore the patterns of active and sedentary behaviours in people with CFS, asthma and in healthy controls. Overall, the new scale and its subscales showed good internal consistency, and a consistent pattern of correlations, suggesting it may be a valid measure of the construct of activity. That validity was confirmed by medium to large correlations between the scores on the activity, physical functioning, and activity perception scales in the CFS and asthma groups. Fittingly, lower scores on the sedentary behaviours subscale were associated with higher physical functioning and perception of current activity in the CFS and Asthma groups. Notably though, there was a distinct lack of significant relationships within the control group. That may suggest that the aim of the study to develop a measure of activity *specifically* for an illness group might have been achieved. It is possible that the chosen list of activities has not been reflective enough of a lifestyle of a person not living with a chronic illness.

In the CFS group, the symptom frequency was associated with more sedentary behaviours and more sedentary lifestyle, reduced work hours and walking ability as reflected by work/daily activity subscale. It was fatigue, specifically, rather than the general CFS

symptomatology, that was associated with reduced activity, physical and mental. That does fit the construct of profound chronic fatigue accompanied by severe reduction in activity. That also fits within the theoretical framework of increased fatigue focus as the core cognitive process underpinning CFS symptom perpetuation (Knoop et al., 2010; Moss-Morris, 2005). This relationship does not quite support the first hypothesis, which predicted that more CFS symptoms would be associated with reduced activity, similar to previous research (Fulcher & White, 2000; Newton et al., 2011). Instead, greater CFS symptomatology was related to increased sedentary behaviours, meaning an increase in *inactivity*. However, the research, showing that activity levels were decreased in CFS populations, specified that it was higher intensity, more vigorous activities that were reduced (Evering, van Weering, et al., 2011; Newton et al., 2011). High-intensity activities were not measured by the current questionnaire. Increased fatigue was associated with reduced mental activity, but there was no relationship between the measure of CFS symptom frequency and mental activity. Considering that impairment in attention and memory is one of the eight accompanying symptoms according to CDC/Fukuda criteria, this finding was unexpected. However, cognitive impairment is only one of the accompanying symptoms and is not required for a diagnosis, whereas elevated fatigue and reduction in activity are required for the diagnosis. As specified above higher fatigue was related to decreased mental activity in CFS group.

In the CFS group higher symptomatology was not related to decreased active behaviours, but in the asthma group it was. Notably in the asthma group, somewhat counter intuitively, greater interference by asthma symptoms was associated with lower score on the subscale measuring sedentary behaviours. That could be possibly, because the more active a person is, the more likely they would be to detect an interference with their activity.

What was also informative was that more asthma symptoms were associated with reduced mental activity, a relationship that was predicted for the CFS group. In contrast, in the CFS group the increased symptomatology was not related to reduced mental activities, which fits the evidence that cognitive deficits are relatively scarce in CFS (Cockshell & Mathias, 2010); but, this does not quite fit with the criteria describing memory and attention impairment as one of the important symptoms of CFS. It was only fatigue, not concurrent CFS symptoms, that was related to decreased mental activity. However, considering that FSS measures fatigue of the interfering type, that relationship would be expected.

Within the CFS group, depressed mood was only associated with more sedentary behaviours (bed rest during the day, TV watching). Accordingly, for CFS group positive mood was associated with less sedentary behaviour. This suggests that involvement in activities

outside of the home, though not necessarily sport or leisure, may bring about a positive mood change; or positive mood may reduce the distress of high fatigue and lower the amount of passive sedentary behaviours. Supporting the second hypothesis that negative mood would be associated with reduced activity only in the asthma group, higher depressed mood was related to decreased activity, and more anxiety was related to reduced work hours and walking in the asthma group. Similarly, in the control group increased depressed and negative mood was related to decreased activity, while positive mood was related to decreased sedentary behaviours.

It has been suggested that some process of fear or anxiety in relation to activity and exertion may play a role not just in the maintenance of CFS symptoms, but also in the absence of successful recovery following treatment, and in the lack of adherence to treatment (Meeus et al., 2011; Nijs, Meeus, Heins, et al., 2012; Nijs et al., 2008). This study purported to investigate the relationship between self-reported activity and fear of movement. For the CFS group, it was predicted that the two facets of fear of movement, beliefs in the seriousness of illness and in the harm of activity, would be associated with reduced activity. Somewhat tangentially of that prediction, a higher score on the illness beliefs subscale of TKS (fear of movement measure) was related to more sedentary behaviours, rather than less active behaviours. In relation to Wiborg et al's (2010; 2011) findings that physical activity levels in CFS may not necessarily increase following treatment, it would be informative to find out whether the levels of inactivity (for example measured sedentary behaviours) would decrease following interventions. Activity and inactivity are two interconnected concepts, but the measurements of each would be different enough, and measuring activity is not always the same as measuring inactivity (Esliger & Tremblay, 2007). This would be a question of measurement for future research, to investigate levels of active and sedentary behaviours, and levels of activity and inactivity. Inactivity measures could be incorporated into the clinical trials as additional measures of outcomes.

Stronger beliefs that activity is harmful, in accordance with the prediction and previous research (Silver et al., 2002), were related to less frequent leisure and recreation activities in CFS group. The picture of the associations described above fits with other evidence from studies of CFS that obtained objective measurements of activity and fitness and demonstrated that catastrophic beliefs about fatigue and pain were related to reduced functioning and capacity for high-level exercise (Nijs et al., 2011; Nijs et al., 2008).

Notably, for the CFS group there was a significant positive correlation between CFS symptom frequency and online activity. That is not surprising considering the positive

association between sedentary behaviours and online activity. However, higher perceived current activity (Activity NOW) was also positively associated with online activity, suggesting that people with CFS may have a wider concept of activity than just physical activity. Stronger beliefs in the seriousness of the illness and higher negative affect were similarly linked to more online activity in CFS group. Taking into account reduced functioning of people severely affected by CFS, the Internet provides a great opportunity for them to remain involved in social activities, discussions, or web-based support groups.

Considering that the CFS sample was recruited from online forums and support groups, it would not be surprising to observe a relationship between higher symptomatology and a proxy measure of utilization of Internet resources. But such a relationship would be expected of both CFS and asthma, and even controls. However, that correlation was unique to the CFS group. What is surprising is that the same type of recruitment for the asthma group did not show the same relationship between elevated symptoms and more online activity. None of the self-report measures in the asthma group were related to online activity. In contrast, in the healthy controls more online activity was associated with more behavioural disengagement strategies, which may be explained by the escapist nature of the Internet.

To summarize the unique pattern of correlations in CFS group: higher online activity was related to more frequent CFS symptoms, perception of higher current activity, stronger beliefs in the seriousness of the illness, and increased negative affect. This is interesting in light of another finding that people with CFS who were members of support groups were more functionally impaired and had poorer prognosis (Sharpe, Hawton, Seagroatt, & Pasvol, 1992). However, the link is tenuous, because the study did not investigate what precisely online activity involved.

The final hypothesis predicted that in the CFS group higher avoidant behavior, as reflected by a coping style of behavioural disengagement, would be associated with reduced activity. The hypothesis was not supported; on the contrary, greater behavioural disengagement was associated with more social duties, which includes involvement in community or pursuing educational opportunities. The concept of behavioural disengagement in this case is very important to consider, because it is not a straightforward measure of avoidant behaviour. In CFS, avoidant behaviours associated with increased symptomatology and negative health outcomes are defined specifically as avoidance of physical activity (Nijs et al., 2013). Behavioural disengagement does not measure avoidance of physical activity. A high score on behavioural disengagement would not mean a high score

on activity avoidance, therefore we may not necessarily obtain a correlation between behavioural disengagement and reduced activity. Behavioural disengagement construct may be tapping into the avoidance of taking active steps in dealing with a problem, or, in the current case, in dealing with the illness perceived as a source of stress. For the CFS group higher score on the Social Duties subscale was also associated with stronger illness beliefs and greater anxiety. Considering, that the social duties subscale measured involvement with a community (for example attending community gatherings, church, sporting events), it is possible that greater anxiety about one's health, greater disability or reduced ability to cope with the illness leads people to seek more social support and comfort from the community, support groups, or church. Notably, community engagement as measured by the Social duties subscale was also related to higher physical functioning. The latter relationship may reflect a positive influence of social support. Alternatively, people who were higher on physical functioning were more likely to engage in education or get involved with their communities. The somewhat contradictory pattern of correlations may also reflect instability of the factor of Social Duties. Furthermore, it may point towards diversity of the subgroups within the sample broadly defined as people with CFS. Next research step would be to stratify a large sample of people with CFS into subgroups (e.g. active versus passive), on the basis of clearly specified criteria, and investigate patterns of correlation within each particular subgroup.

The limitations of this study prevent speculation on the direction of the influence. While the sample was comparatively large due to the advantages of online testing, it is still relatively small for the purposes of path analysis or predictive modeling. The main limitation of this component of the study concerns the Activity scale. The measure did not subdivide activity into intensity levels, and therefore did not allow participants to report low, moderate or high intensity activities. Activity intensity is one of the defining features of activity levels, and one of the main determinants of functioning and health outcomes (Levine, 2005; Manohar, McCrady, Pavlidis, & Levine, 2009). Although the aim of the Activity scale was to measure regular daily functioning, the exercise and sport aspects could have been covered in more detail, as the scale only measured the social aspects of engaging in sports and leisure. Similarly, "daily chores" types of activity should also have been included, because it is likely that CFS symptoms would have had the most interference with these kinds of activities. It would have also allowed a comparison with the study on attentional bias towards activity information in CFS, presented in the previous section of this chapter.

Taking into account technological developments and increasing use of highly portable media, it may be wrong to include online activity into sedentary subscales, in spite of the results of the principal component analysis. People can access the Internet via their phones while moving around, rather than sitting down in front of a computer. Such things as computer use, Internet use, emailing and being on the phone are now not necessarily measures of sedentary types of activity, due to the highly portable nature of media devices.

The Activity scale also did not specify any period of time for activity. Given that CFS diagnostic criteria specify a 6-month period, it might have been more appropriate to limit the time period of self-reported activity to 6 past months, which would allow the patterns of activity, fatigue, and symptoms to be traced over the same time period.

The results highlight the need to study not only the activity and functioning patterns of the CFS population and its subgroups, but also to apply measures of inactivity, for example assessing sedentary behaviours. In an intervention aiming to increase functioning and reduce fatigue in CFS (CBT or GET) it may be informative to include outcome measures of sedentary behaviors or inactivity, such as sleep during the day time or TV watching, or lying down on the couch. Decrease in such passive inactive behaviours may trigger a decrease in fatigue, in negative illness beliefs, fear of movement, or negative mood, and an increase in positive mood. Finally, the advantages of the online methods are underscored in this study, such as easier access to a much larger CFS population. Consequently, a web-based design would allow the identification and testing of subgroups within the greater CFS population.

Chapter 5: Study 4: Interpretation Experiment

Introduction

A cognitive account of Chronic Fatigue Syndrome perpetuation proposes that a negative illness schema may guide cognitive processing, biasing them towards health-threat or illness-related information (Moss-Morris, 2005). Interpretation of ambiguous information is one of those cognitive processes. Fatigue is an ambiguous sensation in itself. It may be interpreted as a natural feeling after exertion. Alternatively, it may be viewed as stemming from emotional state of feeling down and sad. Yet another interpretation of fatigue may be that it is a symptom of a serious underlying illness. The latter interpretation process is part of the cognitive account of CFS (Moss-Morris, 2005), but has been underexplored in research. Moss-Morris and Petrie (2003) conducted the only study to our knowledge that explored interpretation of ambiguous information in CFS using an objective measure.

The ambiguous cues task, used by Moss-Morris and Petrie (2003), is a methodological paradigm designed to measure elaborative, conscious processing and voluntary response (Amir, Beard, & Przeworski, 2005; Hirsch & Mathews, 2000; Vancleef, Peters, & De Jong, 2009). The ambiguous cues task assesses the interpretation process on the basis of word associations generated by the participants. Moss-Morris and Petrie used an auditory presentation of homonyms, words that sound the same but could be interpreted by the listeners in a neutral or health-threatening manner, for example week/weak. The researchers asked CFS and healthy control groups to write down word associations following auditory presentation of an ambiguous word. Comparison of the number of somatic and neutral (unrelated to health and illness) word associations produced by participants showed that the CFS group generated significantly more somatic associations. The study provided evidence for biased interpretation in CFS, and for the manifestation of a negative illness schema, which filters information in a way that reinforces negative illness cognitions. What remains unclear is whether the illness-related meanings of ambiguous words were generated initially when the ambiguity was first encountered, or reinterpreted later at the time of response production.

At a theoretical level Mathews and MacLeod (2005) defined an 'online interpretive process' as interpretation that is made immediately at the first encounter with ambiguity. In contrast, they defined an 'off-line interpretive process', retrospective interpretation, as the making of inferences with regard to past ambiguous events. The meaning of it is that, initially, several alternative interpretations may be generated and then one may be chosen as a response. Self-reports or word association methods may measure the latter off-line

interpretive process, where a meaning may be assigned to events retrospectively. Alternatively, methods such as the lexical decision task can measure response tendencies at the moment when the ambiguous information is first perceived, thus tapping into the process of online interpretation.

Therefore, the current study employed a lexical decision task to measure the online interpretation bias, a spontaneous automatic response to a current ambiguous external stimulus (Hirsch & Mathews, 2000; Vancleef et al., 2009). The task was adapted from a priming task used in studies of anxiety, in order to tap into the subtleties of the interpretation bias (Amir, Beard, & Przeworski, 2005). The method helps avoid experimenter bias, because the response required and measured (latency of lexical decision) is unrelated to the goal of the experiment. A lexical decision task also prevents the confounding effect of response bias, because the alternative meanings of ambiguous words are generated by the researchers.

In the first step of the task, participants were primed with an ambiguous word (week/weak) that could be interpreted either in a neutral non-threatening (time unit) or an illness-related threatening fashion (being frail). They were then presented with a target, a letter string, and asked to identify it as a word or a non-word (stimuli that were generated to look like words and followed the orthographic rules of the language). The meaning of the target could reflect either a threat or a neutral meaning of the ambiguous prime. The third alternative for the target was a meaning completely unrelated to any potential interpretation of the prime; this alternative served as a baseline measure. Priming was judged to have occurred if participants respond more quickly to a word whose meaning fits their own automatically generated interpretation of the ambiguous prime, compared to an unrelated target. Alternatively, if the meaning of the target word was in conflict with their own generated interpretation, it would have slowed down their response, because they first had to discard their own generated meaning in order to process the alternative meaning presented to them. The experiment thus measured whether people with CFS would automatically activate an illness-related meaning of the ambiguous prime, which may interfere with the generation of alternative neutral meanings.

Moss-Morris and Petrie's (2003) study appears to be the only study of interpretation bias in CFS that is measured through an objective cognitive task. However, in research on chronic pain, there are consistent findings of interpretive bias for pain-related information (Pincus & Morley, 2001). In general health research, a study of health- and pain-related anxiety in healthy people provided supporting evidence for an illness-related interpretation

bias in healthy people who have an elevated fear of pain (Vancleef et al., 2009). Vancleef and colleagues found that all participants equally endorsed a health-threatening resolution of ambiguous scenarios over a safe resolution. However, when they compared the group with a low fear of pain to the group with a high fear of pain, it was the latter who responded significantly faster to health-threat resolutions of ambiguity. The researchers proposed that a high level of health-threat would lead to preferential processing, even in a healthy population, as a protective and adaptive response to the potential danger of illness. However, harmful fear cognitions can push that adaptive response towards over-perception and over-monitoring, amplifying the fear and the sensitivity to threat related information; thus, the adaptive process turns into vulnerability.

CFS is also associated with high levels of pain, and that elevated pain is associated with catastrophic beliefs and fear cognitions about movement, injury and fatigue (Nijs, Meeus, Heins, et al., 2012; Nijs et al., 2008). Thus, taking into account how negative cognitions can amplify interpretation bias (Vancleef et al., 2009), one would expect that the negative illness schema in CFS would guide information processing in such a way that a health-threat interpretation of ambiguous stimuli would be favoured over the neutral interpretation (Moss-Morris, 2005).

In summary, the lexical decision task in the current experiment was used to measure the online interpretation bias in CFS and in healthy control groups, and tested the following hypotheses:

a) CFS group will respond faster to word targets that reflect the illness-related meaning of the ambiguous prime, because these targets fit their initial interpretation of the prime, compared to an unrelated meaning baseline. Specifically, the CFS group will obtain higher scores on the Illness Threat bias index compared to the control group.

b) CFS group will have slowed down responses to word targets that reflect the neutral meaning of the ambiguous prime, because these targets do not fit their initial interpretation of the prime, compared to an unrelated meaning baseline. The CFS group will obtain lower scores on the Illness NonThreat bias index compared to the control group.

c) The healthy control group will show the reverse pattern. They will demonstrate speeded up responses to neutral disambiguation and slowed down responses to illness-related disambiguation.

Two control conditions were included in the lexical decision task. The first one included the neutral primes, where ambiguous words could be interpreted in two alternative neutral ways. The second control condition included ambiguous primes for social

threat, words that could be interpreted in a socially-relevant or neutral manner (odd – strange, odd - even). This would assess whether the CFS group may generally favour a threatening disambiguation, or whether it is illness specific. It would be expected that the CFS group would demonstrate interpretation bias only in response to illness primes, compared to the control group, and the priming effect would not generalize to social threat. The prediction was based on the hypothesis that CFS group would have an illness-specific interpretation bias, rather than a general tendency towards catastrophic interpretation. Furthermore, the interpretation bias would also be expected to be independent of depressive or anxious mood, similarly to the attentional bias in CFS found to be independent of depression or anxiety (Hou et al., 2008). Thus, in order to eliminate potential confounds, a number of variables that may influence the dependent variable, the interpretation process, such as depression, anxiety, and rumination were included in the analysis to account for the potential influence of these factors.

Method

Study Design

The data from the lexical decision task, which measured interpretation bias, were gathered as a part of the experimental study described in Chapter 2: Attention and Rumination. The full design and procedure of the study was presented in Chapter 2: Method, Procedure, p. 74 and pp. 85 – 87. The data discussed in the current chapter were obtained from the second computer task.

The second component of the study (presented in Chapter 2), investigating the interpretation bias, also had a quasi-experimental design with one between-subject independent variable: people with a CFS diagnosis were compared to age- and gender- and education-matched healthy controls, the same sample fully described in Chapter 2.

The within-subjects factor for the interpretation task consisted of three types of ambiguous word stimuli (Illness, Social Threat, Neutral). These ambiguous words could be interpreted either in an illness-related manner or in a neutral manner. The main dependent variable was Reaction Times (RTs) from the lexical decision task. RTs were converted into interpretation indices, such as Threat and NonThreat, reflecting responses to either threatening or neutral disambiguation of the ambiguous primes, respectively. Self-report

questionnaires provided the demographic information and measured depression, anxiety, rumination, and social desirability.

The study has been reviewed by and received ethics clearance through the University of Oxford Central University Research Ethics Committee (CUREC), assigned reference number: MSD/IDREC/C1/2007/4 (Appendix A.2).

Participants

Participants who contributed the data presented in the current chapter were the same people who contributed the data to the experiment on attentional bias and rumination described in Chapter 2. The inclusion and exclusion criteria for the participants with CFS and for the healthy controls were described fully in Chapter 2, Method, section on *Participants* p. 75 – 77, including comorbidity assessment and recruitment strategy, p. 75.

Materials

Cognitive State Induction

The cognitive state induction, which participants had undergone at the beginning of the study, was described in Chapter 2, Method, Materials section, p. 77. In the first half of the study the aim was to investigate the relationship between self-focused rumination and attentional bias towards illness-related information. Therefore, the participants have been induced into either a ruminative or a distractive cognitive state. The reasoning behind it was that if in previous research attentional bias was not detected, the illness schema may become salient of one is ruminating on physical state and symptoms, which may bias attention towards the illness-related information. The second half of the study, the focus of this chapter, aimed to investigate the interpretation bias alone. The goal was to check whether the results would replicate the findings by Moss-Morris and Petrie (2003) using a paradigm that assesses earlier stages of the interpretation, which may be independent of the higher-level cognitive processes, such as rumination. Therefore, the procedure was set up in a way that would allow the cognitive state induction to dissipate before the participants engaged in the lexical decision task.

The literature does not specify how long the effect of the cognitive state induction may last (Watkins & Teasdale, 2004). In comparison, the effect of a mood induction was found to last between 25 – 35 minutes (Sinclair et al., 1994). Thus, it was decided that at least 25 minutes should pass between the end of the cognitive state induction and the start of the lexical decision task. Due to practical limitations, such as limited testing time, it was

not possible to have a very long break. Upon starting the second computer task, all participants were past the 30-minute mark, counting from the end of the induction procedure to the beginning of the second computer task, the lexical decision task, which measured interpretation bias.

During the break participants were allowed to leave the testing room and rest for 20 minutes after completing the attention task. For all participants a minimum of 30 minutes would have passed from the end of the cognitive state induction to the start of the interpretation task.

The Lexical Decision Task

The lexical decision methodology was adopted from anxiety research (Hirsch & Mathews, 2000) and modified from a priming task used in a study of anxiety (Amir, Beard, & Przeworski, 2005). The task is a valid measure of cognitive processing for assessing the early stages of interpretation of ambiguous information at the moment of encounter – that is, the spontaneous automatic response to a current external stimulus (Hirsch & Mathews, 2000; Vancleef et al., 2009). Firstly, participants heard a word, the ambiguous prime, that could be interpreted either in a threatening (illness) or non-threatening (neutral) fashion. Then participants were presented with a target, a letter-string on a computer screen, and asked to decide whether it was a word or a non-word. The three types of word target included: a word related to the threat meaning of the ambiguous prime, a word related to the neutral meaning, or a word unrelated to the prime.

Thus, an experimental trial consisted of the auditory presentation of ambiguous prime words (Illness, Social Threat or Neutral) for 1000ms, while a fixation cross was presented on the screen. After the inter-stimulus interval of 1000ms a target stimulus, either a word (related threat, related non-threat, or unrelated meaning) or a non-word, appeared at the centre of the screen. The target remained on screen until the participants responded (or for 2500ms if no response was made). Accordingly, the duration between the start of the presentation of the prime and the appearance of the target was 2000ms. The inter-trial interval lasted 1000ms. *Figure 1* presents a graphic representation of an experimental trial.

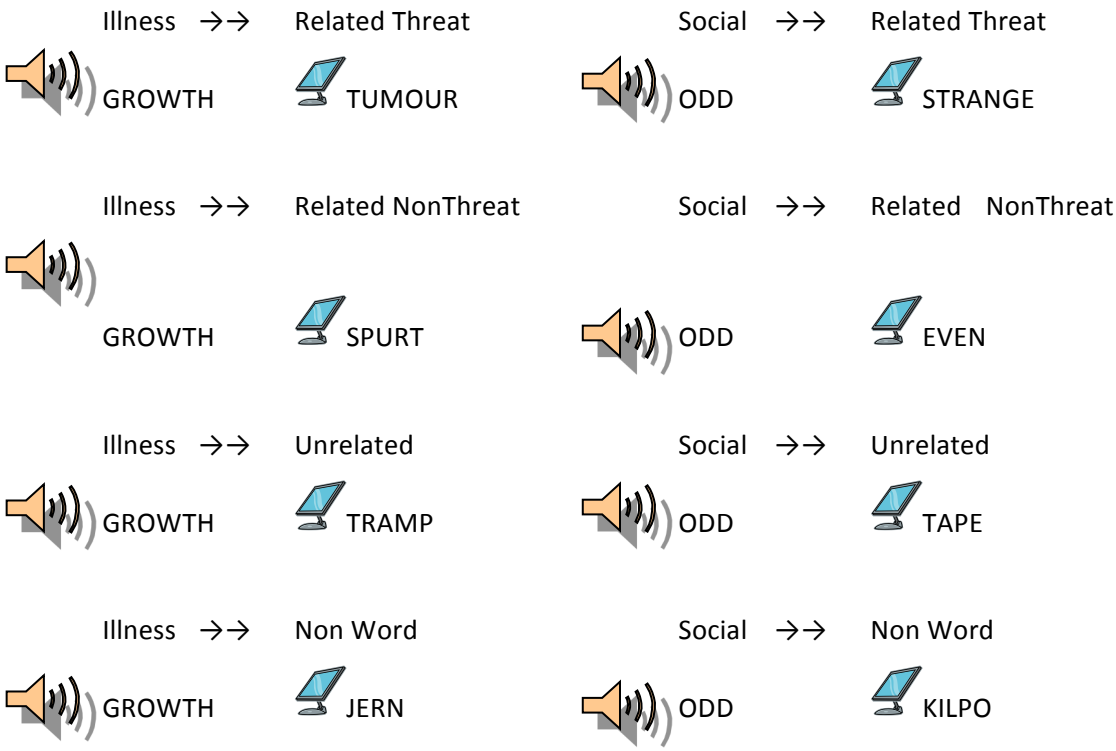


Figure 1. Example of an experimental trial from the lexical decision task, including four types of trials (related threat, related non-threat, unrelated, non-word) for two types of primes, Illness and Social Threat.

Instructions

Participants were instructed to listen to the word coming from the audio speaker, while looking at the fixation cross on the monitor. They were then asked, upon the presentation of the letter string on the screen, to press the **z** key if they thought it was a word or the **m** key if they thought it was a non-word. They were asked to be as fast and as accurate as possible and maintain their attention upon the centre of the screen.

Participants received instructions and completed a practice block, comprised of 18 trials with neutral primes (practice prime words were different from those used in the experimental trials). After the practice, participants had the opportunity to ask questions or rerun the practice. In total, there were 240 experimental trials. Each priming word (60 total, 20 Illness, 20 Social Threat, 20 Neutral) was presented four times, once for each kind of target: related threat, related nonthreat, unrelated, and non-word. The presentation of trials in each block and the order of the experimental blocks were randomized across participants. The task took approximately 6-8 minutes to complete.

Stimuli

The auditory prime stimuli consisted of three types of homophones (words that are pronounced the same way, but have different meanings, neutral or threatening). There were a) 20 Illness ambiguous words, which could be interpreted in either an illness-related or a neutral way (tire – fatigue, tyre – wheel); b) 20 Social Threat ambiguous words, which could be interpreted as threatening or neutral (odd – strange, odd – even); c) 20 Neutral ambiguous words, which could be interpreted in alternate neutral ways (crane – construction, crane – bird).

Some of the Illness words were selected from Moss-Morris and Petrie's (2003) study. The rest of the primes and their threat and non-threat interpretations were adopted from a study on interpretation bias in Irritable Bowel Syndrome (IBS) (Chapman & Martin, 2011b). In the IBS study, 14 independent judges (healthy control volunteers) were asked to write down associations for each word, while 105 homophones were read out to them. The primes were selected on the basis of how many people produced similar associations with a requirement that at least three people out of 14 would produce the same association for each threat and non-threat meaning. The threat and non-threat targets were selected from the list of associations produced by the volunteers. Three researchers, the author of this thesis and two researchers from the above IBS study, have generated the list of unrelated and non-word targets.

All prime words were matched in length, $p > .50$; and frequency of occurrence, $p > .50$, based on the Kucera-Francis written frequency norms (Francis & Kucera, 1967). The three prime types were paired with four target types: related threat, related non-threat, unrelated, and non-word (pseudo-words that looked like words and followed English orthography rules) (see Tables 1 - 3). Prime and target words were also matched on length, $p > .67$; and frequency of occurrence, $p > .81$. That produced 12 experimental trial types.

Table 1.

Illness Ambiguous Prime Words, Their Threat and Non-Threat Interpretations, Lengths and Frequencies for the Lexical Decision Task

Prime Type	Prime	Length	Freq	Threat	Length	Freq	Non Threat	Length	Freq
Illness	Beating	6.0	13.0	punch	5.0	4.0	egg	3.0	4.0
Illness	Break/brake	5.0	13.0	broken	6.0	8.0	car	3.0	13.0
Illness	Cramp	5.0	2.0	leg	3.0	10.0	stuffy	6.0	2.0
Illness	Die/dye	3.0	15.0	death	5.0	15.0	dice	4.0	6.0
Illness	**Exhaust**	6.0	6.0	tired	5.0	2.0	car	3.0	13.0
Illness	Greys/graize	5.0	6.0	scrape	6.0	3.0	cow	3.0	9.0
Illness	Grinding	7.0	10.0	crunch	6.0	4.0	pepper	6.0	3.0
Illness	**Growth**	6.0	11.0	tumour	6.0	2.0	spurt	5.0	2.0
Illness	Heal/heel	4.0	2.0	wound	5.0	12.0	shoe	4.0	11.0
Illness	Pail/pale	4.0	9.0	weak	4.0	11.0	bucket	6.0	4.0
Illness	Pain/pane	4.0	15.0	hurt	4.0	9.0	window	6.0	14.0
Illness	Pound	5.0	9.0	hit	3.0	14.0	money	5.0	14.0
Illness	Strain	6.0	10.0	effort	6.0	14.0	water	5.0	14.0
Illness	Taut/taught	4.0	6.0	tight	5.0	11.0	learnt	6.0	15.0
Illness	Tight	5.0	11.0	pull	4.0	10.0	clothes	7.0	6.0
Illness	Tyre/tire	4.0	8.0	sleep	5.0	10.0	car	3.0	13.0
Illness	**Vein/vane**	4.0	9.0	blood	5.0	14.0	weather	7.0	11.0
Illness	**Weak/week**	4.0	11.0	strong	6.0	14.0	day	3.0	15.0
Illness	Wear	4.0	14.0	out	3.0	15.0	clothes	7.0	6.0
Illness	**Wrench**	6.0	6.0	pull	3.0	13.0	spanner	7.0	9.0
		4.9	**7.6**		**4.8**	**9.8**		**5.0**	**9.2**
		1.0	**4.1**		**1.1**	**4.5**		**1.6**	**4.7**

Note. The words in bold are replicated from Moss-Morris and Petrie (2003).

Table 2.

Social Threat Ambiguous Prime Words, Their Threat and Non-Threat Interpretations, Lengths and Frequencies for the Lexical Decision Task

Prime Type	Prime	Length	Freq	Threat	Length	Freq	Non Threat	Length	Freq
Social Threat	Awkward	7.0	5.0	clumsy	6.0	5.0	difficult	9.0	14.0
Social Threat	Cheek	5.0	7.0	rude	4.0	5.0	face	4.0	14.0
Social Threat	Cross	5.0	13.0	angry	5.0	10.0	jesus	5.0	14.0
Social Threat	Fault	5.0	10.0	blame	5.0	12.0	line	4.0	5.0
Social Threat	Idle/idol	4.0	9.0	lazy	4.0	6.0	pop	3.0	14.0
Social Threat	Left	4.0	15.0	behind	6.0	15.0	right	5.0	14.0
Social Threat	Lie	3.0	14.0	truth	5.0	15.0	down	4.0	14.0
Social Threat	Lone/loan	4.0	6.0	lonely	6.0	8.0	money	5.0	14.0
Social Threat	Mean	4.0	15.0	nasty	5.0	4.0	average	7.0	12.0
Social Threat	Odd	3.0	12.0	strange	7.0	13.0	even	4.0	14.0
Social Threat	Order	5.0	15.0	command	7.0	13.0	sort	4.0	13.0
Social Threat	Present	7.0	15.0	gift	4.0	12.0	TV	2.0	14.0
Social Threat	Reserved	8.0	9.0	quiet	5.0	15.0	saved	5.0	8.0
Social Threat	Retiring	8.0	11.0	shy	3.0	8.0	old	3.0	10.0
Social Threat	Shake	5.0	10.0	scare	5.0	3.0	milk	4.0	12.0
Social Threat	Spoke	5.0	13.0	word	4.0	15.0	wheel	5.0	14.0
Social Threat	Stair/stare	5.0	2.0	look	4.0	15.0	lift	4.0	10.0
Social Threat	Tease/teas	5.0	4.0	flirt	5.0	1.0	coffees	7.0	6.0
Social Threat	Watch	5.0	13.0	see	3.0	15.0	time	4.0	9.0
Social Threat	Leaves	6.0	12.0	goes	4.0	2.0	tree	4.0	9.0
		5.2	**10.5**		**7.2**	**9.6**		**4.6**	**11.7**
		1.4	**3.9**		**1.1**	**5.0**		**1.6**	**3.0**

Table 3.

Neutral Ambiguous Prime Words, Their Threat and Non-Threat Interpretations, Lengths and Frequencies for the Lexical Decision Task

Prime Type	Prime	Length	Freq	Threat	Length	Freq	Non Threat	Length	Freq
Neutral	Counter	7.0	8.0	shop	4.0	13.0	dice	4.0	6.0
Neutral	Court/caught	5.0	13.0	royal	5.0		ball	4.0	12.0
Neutral	Crane	5.0	4.0	bird	4.0	10.0	builder	7.0	4.0
Neutral	Earth	5.0	15.0	soil	4.0	11.0	moon	4.0	12.0
Neutral	Fair	4.0	14.0	just	4.0	15.0	ground	6.0	15.0
Neutral	Flower/flour	6.0	9.0	cake	4.0	8.0	garden	6.0	7.0
Neutral	Lute/loot	4.0	1.0	tune	4.0	6.0	rob	3.0	5.0
Neutral	Match	5.0	12.0	fire	4.0	14.0	game	4.0	10.0
Neutral	Moose/mousse	5.0	2.0	chocolate	9.0	6.0	antlers	7.0	15.0
Neutral	Night/knight	5.0	15.0	day	3.0	15.0	armour	6.0	1.0
Neutral	Notes	5.0	7.0	music	5.0	15.0	message	7.0	13.0
Neutral	Pitch	5.0	9.0	black	5.0	3.0	football	8.0	10.0
Neutral	Right/write	5.0	15.0	pen	3.0	8.0	left	4.0	15.0
Neutral	Ruler	5.0	3.0	measure	7.0	11.0	king	4.0	13.0
Neutral	Sink	4.0	9.0	taps	4.0	7.0	swim	4.0	7.0
Neutral	Sun/son	3.0	14.0	moon	4.0	12.0	daughter	8.0	12.0
Neutral	Tail/tale	4.0	10.0	story	5.0	15.0	animal	6.0	12.0
Neutral	Tap	3.0	9.0	dance	5.0	13.0	bath	4.0	10.0
Neutral	Whole/hole	5.0	6.0	gap	3.0	8.0	all	3.0	15.0
Neutral	Wrung/rung	5.0	5.0	telephone	9.0	4.0	ladder	6.0	10.0
		4.8	**9.0**		**4.8**	**10.2**		**5.3**	**10.2**
		0.9	**4.5**		**1.7**	**3.9**		**1.6**	**4.0**

Data Preparation

The CFS and Control groups did not differ significantly in accuracy rates on the lexical decision task, $p > .33$ (CFS $M = 96.9$ %, $SD = 3.4$, Control $M = 97.6$ %, $SD = 2.2$). The data from the task were filtered by removing RTs for incorrect answers. There were no outliers below 100ms or above 2500ms. Moreover, due to large differences between RTs following non-words and RTs following words, it was decided that data would not be cropped based on standard deviations, in order that potential effects were not masked by removing low scores on words and high scores on non-words; therefore the raw RT data were used (Amir, Foa, & Coles, 1998).

Priming indices were calculated for each ambiguous prime: Illness, Social Threat and Neutral. Illness Threat scores were calculated using the formula $RT_{Unrelated} - RT_{relatedThreat}$ where RTs after targets whose meaning reflected the illness interpretation of the ambiguous Illness prime were subtracted from RTs after targets unrelated to the prime.

The Illness NonThreat index was calculated using the formula $RT_{Unrelated} - RT_{relatedNonThreat.}$ RTs after targets with a neutral meaning in relation to the ambiguous Illness prime were subtracted from RTs after targets that were unrelated to the homophonic prime.

If participants were faster to respond to related meanings than to unrelated, the resulting positive scores would reflect a priming effect. According to the main hypothesis for the CFS group, the difference between related Threat and unrelated would be high positive scores, due to speeded up responses to related threat, compared to unrelated target. In contrast, due to slowed down responses to related Nonthreat (reflecting neutral disambiguation) compared to unrelated targets, the CFS group would obtain negative scores on the Illness NonThreat index. The reverse would be expected for the healthy control group; they would demonstrate higher positive scores on the Illness NonThreat index and negative scores on the Illness Threat index.

Analogous calculations were performed for the Social Threat ambiguous prime to obtain Social Threat index and Social NonThreat index. The effect was not expected to generalize to Social Threat primes, where no significant differences between CFS and control groups were predicted.

The same formula was used to calculate the Neutral Index. In this case the two indices (equivalent to Threat and NonThreat indices above) reflected the responses to two alternative neutral meanings of the Neutral ambiguous prime (see Table 3 for the list of alternative neutral meanings for the Neutral prime words).

Questionnaires

All self-report measures utilized in the study and their psychometric properties were described fully in Chapter 2, Method, *Questionnaires,* pp. 82 – 84. The self-report measures used in the analysis of this interpretation task included the Hospital Anxiety and Depression Scale (HADS), the Social Desirability Scale (SDS), and the Ruminative Responses Scale (RRS).

The social desirability measure was included in the analysis, because previous research showed that social desirability differences may affect cognitive biases, and the scale can be used to check for a potential response bias (Eysenck & Derakshan, 1997).

Depression and anxiety may exert an influence on the interpretation process, as it does with attention (Amir, Beard, & Bower, 2005; Gotlib & Joormann, 2010), and therefore HADS scores were used as covariates in the statistical analysis of the interpretation bias scores.

The Ruminative Responses Scale was included in the analysis to account for the potential effect of rumination on interpretation process, and included as a covariate.

Visual Analogue Scales (VAS) measured current mood: Happy, Sad, Anxious, Angry, Calm, to check for the dissipation of the effect of the cognitive state induction.

Power analysis

In order to determine the appropriate sample size for the interpretation bias study the effect sizes were calculated for previously reported studies, using G*Power, version 3.1.3 (Faul et al., 2009; Faul et al., 2007). The effect size detected in Moss-Morris and Petrie (2003) study was estimated d = 1.07 for t-tests, and f = 0.54 for ANOVA tests, both exceeding d = .80 and f = .40, signifying large effect sizes according to Cohen's convention (Cohen, 1992).

In order that the Lexical Decision task can detect the critical interaction of Group (CFS; Control) x Prime Type (Illness; Social Threat; Neutral) x Target Type (non-word; unrelated; related nonthreat; related threat) a total sample size of 48 participants would be needed to detect a large effect size and 96 for a medium effect size. For matched pairs t-tests total sample size needed was calculated as 16 participants to obtain large effect and 34 for the medium. For the independent samples t - tests 42 participants would be needed to detect large effect above Cohen's d = .80, and 108 participants to detect a medium effect, Cohen's d = .50 medium (Cohen, 1988, p. 355).

Equipment

The lexical decision computer task was run on a desktop computer (CTX Model: PR711T, CTX Ultra Screen Monitor, 17 inch screen) and a Toshiba Satellite A100 laptop (15.4 inch screen). The presentation of the task and data collection was conducted using E-Prime software version 1.1 (SP3) (1.1.4.4). Participants sat in a comfortable position in front of the computer screen. The distance between the participant and the screen was approximately 50cm. Previous research suggests that any variation in distance between the participant and computer screen has no significant influence on the effect (Owens et al., 2004).

Procedure

For clarity the study procedure is replicated here from Chapter 2, pp. 131 - 133. The procedure relevant to this chapter starts from Step seven. Participants were tested alone in a single session lasting approximately one hour. Sessions took place at the Department of Experimental Psychology in a standard testing room specifically set up for experimental purposes, and alternatively in Wolfson College, Oxford in a room designated for study purposes. The college was chosen as a location with convenient parking, which allowed

access for people with restricted mobility. Each room was quiet with minimal distraction for participants and fit the requirements for testing.

The study procedure was outlined and explained by the investigator in addition to participants reading an information sheet (Appendix A.1) about the study. All questions were addressed before obtaining the written informed consent prior to commencing the study (Appendix A.3).

The steps of the procedure are presented below in order:

1. Information and consent
2. Participants filled out a VAS mood measure (Time1)
3. Participants underwent induction into the cognitive state to which they were allocated: Rumination or Distraction.
4. Participants filled out a VAS mood measure (Time2)
5. Participants completed an attentional task: Exogenous Cueing task
6. Participants filled out a VAS mood measure (Time3)

7. Participants took a 20-minute break to relax and rest in order to allow the effects of the cognitive state induction to dissipate before continuing to the next stage of the study.
8. Participants filled out a VAS mood measure (Time4)
9. Participants completed an interpretation task: Lexical decision task
10. Participants completed questionnaire measures in the following order:
    - Demographic questions: age, gender, education
    - Social desirability questionnaire (SDS)
    - Ruminative responses scale (RRS)
    - Depression/Anxiety questionnaire (HADS)
    - Health questions
    - CDC/Fukuda (1994) CFS diagnostic criteria

10. Participants filled out a VAS mood measure (Time5) to check for lasting effects of negative mood for ethical reasons.
11. Participants were fully debriefed, their questions were answered, and they received their payment for the study (5 pounds).

Statistical analysis

Statistical analyses were performed using Statistical Package for Social Science (SPSS) software version 17.0. Chi-square and univariate ANOVA tests were used to compare the groups on demographic characteristics (gender, education, age), HADS Depression and Anxiety, and RRS Depressive, Brooding, and Reflecting subscales, and Social Desirability.

To check that the effect of induction had dissipated, VAS mood scores at Time 4 (after the break in the experimental session before starting Lexical decision task assessing interpretation bias) were analysed by conducting a 2 x 2 x 2 x 5 ANOVA where Group 2 (CFS, Control) and Induction 2 (Rumination, Distraction) were the between-subjects independent variables. Time 2 (Pre-Induction, Post-Break) and Mood 5 (Sad, Anxious, Angry, HappyREV, CalmREV) were within-subjects repeated measures. Independent samples *t*-tests were used to compare VAS mood scores between Distraction and Rumination conditions for CFS and control groups.

An analysis of raw Reaction Time (RT) data from the lexical decision task was conducted to investigate a potential interaction effect between group, prime type, and target type, and to check the validity of the experimental procedure. Reaction times were entered into a 2 x 3 x 4 factorial ANOVA. Group 2 (CFS, Control) was the between-subjects independent variable. Prime 3 (Illness, Social Threat, Neutral) and Target 4 (Related Threat, Related Non-Threat, Unrelated, Non-word) were within-subjects independent variables. Post-hoc pairwise comparisons (Bonferroni method was implemented to adjust for multiple comparisons) were used to clarify any significant results. HADS Depression and Anxiety and demographic variables (age, education) were entered as covariates into the above 2 x 3 x 4 ANOVA to check for the effect of those variables, particularly due to the significant difference on HADS Depression between CFS and control groups.

To investigate the relationship between interpretation bias and the number of reported CFS symptoms, a 3 x 3 x 4 ANOVA was conducted. The between-subjects independent variable was Group 3 (CFS Low number of symptoms; CFS High number of symptoms; Control). Prime 3 (Illness, Social Threat, Neutral) and Target 4 (Related Threat, Related Non-Threat, Unrelated, Non-word) were the within-subjects independent variables. HADS and demographic variables (age, education) were entered as covariates into the above 3 x 3 x 4 ANOVA to check if underlying potential differences, particularly depression, may underpin the results.

Priming indices from the lexical decision task were entered into a 2 x 3 x 2 ANOVA with Group 2 (CFS, Control) as between-subjects independent variable and Prime 3 (Illness,

Social Threat, Neutral) and Priming Index 2 (Threat, NonThreat) as within-subjects independent variable. HADS, age and education were also entered as covariates into the above 2 x 3 x 2 ANOVA.

Independent samples *t*-tests were used to compare CFS and control group scores on Illness Threat and Illness NonThreat indices, testing the main experimental hypothesis. In order to explore the magnitude of the priming effect within each group one sample *t*-tests were conducted to compare each mean against 0, where 0 signifies that priming effect has not occurred (Gotlib, McLachlan, & Katz, 1988). Paired samples *t*-tests were used to compare Illness and Social threat priming indices to the baseline of Neutral priming index separately for each group (CFS, Control).

Pearson correlations were carried out to explore the relationships between interpretation bias indices and the self-reported number of CFS symptoms, the duration of the illness and symptoms, and levels of Depression and Anxiety within the CFS group.

Results

Demographic and Questionnaire Measures

For clarity, the table of the demographic and questionnaire measures is reproduced here from Chapter 2 (see Table 4, p. 90). CFS and control groups did not differ significantly in age, gender, or education, in all cases $p > .05$. The CFS group scored significantly higher on HADS Depression, compared to the control group $F(1,62) = 8.49$, $p = .005$, $\eta_p^2 = .120$. All other comparisons of questionnaire scores were non-significant, all $p > .05$.

Table 4.

Demographic and Questionnaire Measures for CFS and Healthy Control Groups

	CFS *(n = 33)*	Control *(n = 33)*		
	***n* (%)**	***n* (%)**	*χ2*	*p*
Gender (female)	22 (67%)	17 (52%)	1.57	*ns*
Education (Degree)	26 (78%)	31 (93 %)	3.21	*ns*
	***M* (SD)**	***M* (SD)**	*F*	*p*
CFS symptoms duration (years)	9.7 (11.9)	–		
Time since diagnosis (years)	7.6 (6.7)	–		
Number of CFS symptoms	4.8 (1.9)	–		
Current treatment	10 (30%)			
Treatment: medication	7 (21%)			
Treatment: pacing	2 (6%)			
Treatment: CBT	1 (3%)			
Age	38.1 (16.1)	32.3 (9.2)	3.34	*ns*
Social Desirability Scale	15.3 (5.3)	16.4 (5.5)	0.33	*ns*
HADS Depression	6.1 (3.5)	3.3 (2.5)	13.40	.001
HADS Anxiety	8.3 (3.6)	8.1 (3.2)	0.04	*ns*
RRS Depressive	26.9 (6.2)	26.6 (6.1)	0.03	*ns*
RRS Reflective	11.0 (3.4)	11.7 (3.5)	0.52	*ns*
RRS Brooding	10.4 (2.7)	10.2 (2.7)	0.06	*ns*

Note: HADS - Hospital Anxiety and Depression Scale;
RRS - Ruminative Responses Scale.
Treatment medication included: antivirals, antidepressants, antibiotics, painkillers
Number of CFS symptoms is out of 8 additional symptoms in the CDC/Fukuda criteria

Manipulation Check

To check that by the time the participants started the lexical decision task the effects of cognitive state induction had dissipated, VAS mood scores were compared between Time 1 (Pre-induction) and Time 4 (After the break, prior to completing the Lexical decision task). The ANOVA of mood scores demonstrated no significant main effects of Group, Induction, or Time, all $p > .29$. Importantly, the 2 (Group) x 2 (Induction) x 2 (Time) x 5 (Mood) ANOVA did not reveal significant interactions with group, induction type, or time, for all cases $p > .14$.

Independent samples *t*-tests comparing mood scores measured at Time 4 between participants in the rumination and the participants in the distraction conditions did not reveal significant differences neither for CFS, $p > .15$, nor for the control group, $p > .17$.

Lexical Decision Task: Interpretation Bias

Raw Data Analysis

The 2 (Group: CFS, Control) x 3 (Prime: Illness, Social Threat, Neutral) x 4 (Target: Related Threat, Related Non-Threat, Unrelated, Non-word) ANOVA with prime and target types as repeated measures did not reveal a significant group difference or any interactions with the group factor, $p > .05$ for all (See *Figure 2*).

A significant main effect of prime $F(2, 128) = 7.69$, $p < .001$, $\eta_p^2 = .107$ showed that all participants responded significantly slower to Illness primes (M = 777.48ms, SD = 171.15), than to Neutral (M = 747.02ms, SD = 156.03) $p = .002$ (Bonferroni), and slower to Social Threat primes (M = 767.72ms, SD = 165.79) than to Neutral $p = .020$. Responses to Illness and Social Threat primes did not differ significantly, $p > .60$.

There was also the expected main effect of target type $F(3, 192) = 73.43$, $p < .001$, $\eta_p^2 = .534$ (Related Threat M = 711.71ms, SD = 164.89; Related Non-Threat M = 723.80ms, SD = 155.37; Unrelated M = 748.02ms, SD = 153.65; Non-word M = 872.76ms, SD = 206.29) showing that RTs to non-words were significantly slower than all other target types, all $p < .001$, supporting the validity of the experimental premise. RTs to unrelated targets were significantly slower than to related threat ($p = .001$). There were no significant differences between unrelated and related non-threat ($p = .146$) or related non-threat and related threat ($p > .90$). Thus the hypothesis that, unlike controls, the CFS group would show faster responses on Illness related threat trials was not supported.

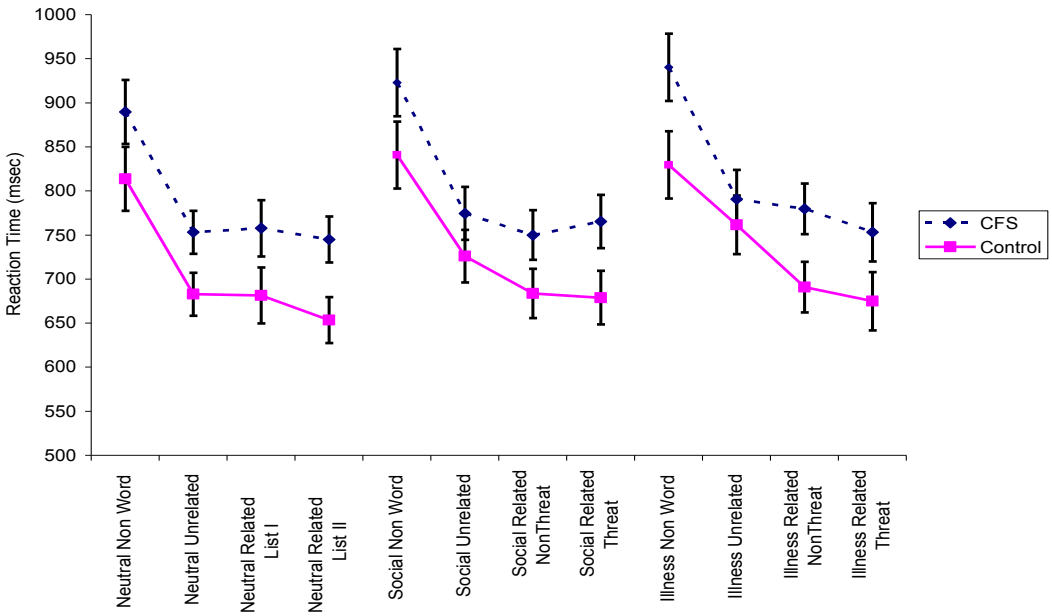


Figure 2. Lexical Decision Task: Mean RTs (msec) and standard errors for CFS and control groups for four different types of target (non-word, unrelated, related non-threat, related threat) following Neutral, Social Threat and Illness ambiguous prime**.**

In order to control for the potential effect of demographic variables on participants' RTs in the lexical decision task, age and education were entered as covariates in the above 2 x 3 x 4 ANOVA, which produced comparable results. Similarly, the ANCOVAs including the HADS measures of depression and anxiety, Social desirability scale, or Ruminative Responses scale, showed no significant effect of group factor, or critical interactions with group, all $p > .05$.

Relationship between Interpretation Bias and CFS Symptom Measure

The CFS group was split into two groups with low and high numbers of self-reported symptoms. Those who reported below 5 symptoms were allocated to the Low symptom group (n = 19) while those who reported 5 symptoms and above (out of total 8) were allocated to the High group (n = 14). The 3 x 3 x 4 factorial design ANOVA with Group 3 (CFS Low; CFS High; Control) as between-subjects measure and Prime and Target types as repeated measures demonstrated significant difference between groups $F(2, 63) = 3.57$, $p = .030$, $\eta_p^2 = .10$, but no significant interactions with group factor $F \leq 1$, $p > .10$.

Scheffé's post-hoc tests showed that the CFS subgroup with a low number of symptoms (M = 845.60ms, SD = 158.71) was significantly slower than the Control group (M = 726.37ms, SD = 132.84), $p = .037$. The CFS subgroup with a high number of symptoms (M =

749.19ms, *SD* = 190.12) did not differ significantly in RTs from the control group (p = .893) or from the CFS subgroup with a low number of symptoms (p = .210). Additional ANCOVAs with depression, anxiety, age and education, social desirability, and ruminative responses as covariates revealed comparable results; in particular, group*prime*target interaction of interest remained non-significant, $p > .90$.

Interpretation Bias Priming Indices

A 2 x 3 x 2 ANOVA with Group 2 (CFS, Control) as between-subjects measure and Prime 3 (Illness, Social Threat, Neutral) and Priming Index (Threat, NonThreat) as repeated measures did not show significant main effects of group, prime, or priming effect, all $p > .06$, and no significant interactions with group factor, all $p > .73$ (See Table 5 for means and standard deviations and *Figure 3* for graphical representation of participants scores on priming indices). Addition of age, depression, anxiety, and social desirability scores as covariates demonstrated comparable non-significant results all $F \leq 1$, $p > .50$.

The analysis was repeated with the Symptom number group factor; a 3 Group (CFS Low; CFS High; Control) x 3 Prime (Illness, Social Threat, Neutral) x 2 Priming Effect (Threat, NonThreat) ANOVA showed no significant effects or interactions, all $p > .05$. Analogous ANCOVAs with age, education, depression and anxiety, and social desirability as covariates did not show significant main effects or interactions all $F \leq 1$, $p > 10$.

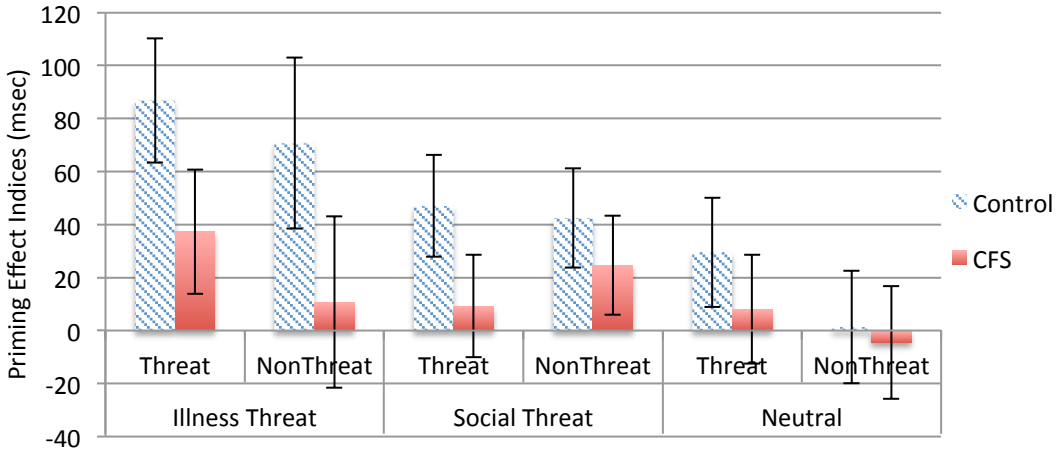


Figure 3. Means and standard errors for Threat and NonThreat indices for three different ambiguous primes (Illness, Social Threat, Neutral) for CFS and Controls.

Note. Threat and NonThreat meanings for Neutral primes were both related to alternative neutral meanings of the prime.

Table 5.

Priming Indices and Raw Reaction Times Means and Standard Deviations for the Lexical Decision Task

	Illness		Social Threat		Neutral	
	CFS	Control	CFS	Control	CFS	Control
Priming Indices	***M* (SD)**	***M* (SD)**	***M* (SD)**	***M* (SD)**	***M* (SD)**	***M* (SD)**
Threat	37.30 (134.68)	86.77 (104.46)	9.24 (110.78)	47.07 (123.13)	8.03 (118.15)	29.48 (78.97)
NonThreat	10.72 (185.46	70.73 (104.93)	24.69 (107.47)	42.43 (129.53)	-4.55 (121.89)	1.34 (150.70)
Raw RTs						
NonWord	940.23 (234.97)	829.36 (203.41)	922.85 (241.09)	840.81 (193.45)	889.62 (228.19)	813.71 (185.12)
Unrelated	790.47 (214.77)	761.45 (163.77)	774.56 (179.20)	725.96 (164.49)	753.00 (158.46)	682.71 (117.68)
NonThreat	779.75 (197.00)	690.72 (124.05)	749.87 (189.76)	683.53 (125.45)	757.55 (176.53)	681.37 (189.17)
Threat	753.17 (236.60)	674.68 (128.35)	765.31 (202.67)	678.89 (140.40)	744.97 (176.85)	653.23 (116.50)

Note. For the Neutral ambiguous prime threat and non threat related interpretations are neutral

The result of the independent samples *t*-test comparing the CFS and control groups on Illness Threat index was not significant, $p > .10$. Thus, the hypothesis that the CFS group would score significantly higher than the control group on Illness Threat index, demonstrating the interpretation bias favouring illness-related disambiguation, was not supported.

Similarly, no group differences were observed on the Illness NonThreat index, $p > .11$ Therefore, the hypothesis that the CFS group would score significantly lower on the Illness NonThreat index compared to controls was also not supported.

One sample *t*-tests were used to investigate the difference in priming indices for each group against 0, where 0 represented an absence of any difference between RTs to related and RTs to unrelated targets, suggesting that no priming effect occurred. There were no significant differences from 0 for the CFS group on any of the priming indices, all $p > .10$, indicating that the CFS group was not primed by any of the ambiguous words.

In contrast, the control group showed significant difference from 0 for Illness Threat score $t(32) = 4.77$, $p < .001$, Illness NonThreat $t(32) = 3.87$, $p = .001$, Social Threat $t(32) = 2.19$, $p = .035$, Neutral Threat $t(32) = 2.14$, $p = .040$. (For group means and standard deviations see Table 5.) The results suggested that priming speeded up the reaction times of the control group, regardless of the type of prime (see *Figure 3*).

Within the CFS group, paired samples *t*-tests that compared Illness and Social Threat priming indices against the baseline of Neutral priming index did not reveal any significant

differences for the CFS group, all $p > .30$, again indicating that no priming effect occurred for the CFS group (see Table 5 and *Figure 4*).

The control group had significantly higher Illness Threat scores than Neutral index baseline scores $t(32) = 2.54$, $p = .016$, $M_{diff} = 57.29$, 95% *CI* M_{diff} [11.29, 103.29], or alternative neutral threat scores $t(32) = 2.71$, $p = .013$, $M_{diff} = 85.43$, 95% *CI* M_{diff} [21.13, 149.73]. That means that the control group responded significantly faster to both threatening and nonthreatening targets following an Illness prime, compared to their responses to a neutral prime (see Table 5 and *Figure 4*). For the Social Threat prime, paired samples *t*-tests did not demonstrated significant differences compared to the Neutral prime baseline, both $p > .17$ (See Table 5 for means and standard deviations).

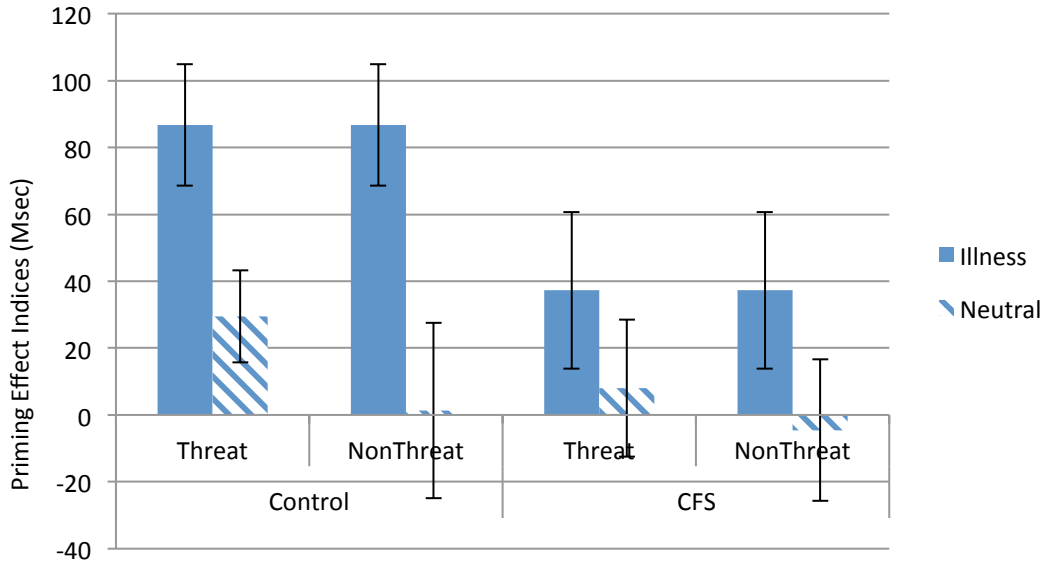


Figure 4. Means and standard errors for the comparison of Illness prime threat index compared with the Neutral prime threat and Nonthreat indices for CFS and Control groups.

Note. In this graph Neutral Threat and Neutral NonThreat refer to the two alternative neutral meanings of the Neutral prime.

Relationship between Interpretation bias indices and individual measures

Bivariate correlations analysis was conducted on the CFS group only ($n = 31$) due to the missing data from 2 participants following the listwise exclusion of the missing data. There were no significant relationships between illness measures: Number of symptoms, Illness duration (since the diagnosis), and Symptom duration. There were also no significant relationships between any of the priming indices; all r in the range of -.24 and .17, all $p > .10$. Similarly, no significant correlations were observed between HADS depression and anxiety

and interpretation bias indices; all r in the range of -0.19 and 0.19, all $p > .20$. Social desirability, similarly, was not related significantly to any of interpretation bias indices, r in the range of -.06 to .24, all $p > .17$. Among the Ruminative responses subscales, only Brooding was significantly negatively associated with Illness NonThreat index, r (31) = .37, p = .036, suggesting that, if participants with CFS were less likely to engage in ruminative brooding, they were more likely to interpret ambiguous Illness prime in a neutral manner. Within the control group (n = 33), none of the correlations between interpretation indices and HADS, Social desirability or Ruminative Responses subscales were significant, all $p > .28$.

Discussion

The experiment investigated the online interpretive bias in people with CFS by measuring an automatic response to ambiguous words that could be interpreted in either a neutral or illness-related way. The results of the lexical decision task did not show significant differences between the CFS and control groups in their response to ambiguous prime words. Thus, the main hypothesis, that the CFS group would favour an illness-related interpretation of the ambiguity by responding faster to target words, which expressed the illness threat meaning of the ambiguous Illness prime, was not supported. All participants showed similar reaction times to different lexical targets, taking the longest time to make a lexical decision following the non-word, demonstrating the validity of the experimental procedure. The responses to both threat and non-threat disambiguation were close in speed signifying an absence of preferential processing of threatening information by all participants.

Contrary to the hypothesis, the only significant results that emerged concerned the healthy control group. It was healthy participants rather than those with CFS who showed a stronger priming effect overall. More specifically, the healthy control group showed a greater priming effect following an ambiguous Illness prime (a word that could be interpreted in a health-threat way or in a neutral way) than following a neutral prime (a word that had two neutral meanings). This result is consistent with other research that demonstrated presence of interpretation bias in healthy people, given a high enough severity of health-threat stimuli (Vancleef et al., 2009). However, the control group did not show preference for either illness-related or neutral disambiguation of the illness prime, indicating the absence of interpretation bias. That priming effect did not generalise to Social

Threat primes for the control group, where there were no significant differences between the Social Threat index and the Neutral index baseline.

The patterns of response for the CFS and control groups showed potential for significant difference only in the speed of the information processing; this is consistent with previous research (Cockshell & Mathias, 2010; Michiels & Cluydts, 2001; Scheffers, Johnson, Grafman, Dale, & Straus, 1992). Considering that in general it was the control participants who showed stronger priming effects across all primes and responded faster to all related meanings, threat or non threat, that may be further evidence for slower processing speed in CFS. When the comparisons were made between the CFS subgroups with lower and higher numbers of symptoms and the control group, the low symptom CFS subgroup was significantly slower than controls, whereas the high symptom number CFS subgroup was not. The possible explanation for this counterintuitive finding may be that the group who reported more symptoms has a more volatile pattern of behavior, with high activity followed by high exhaustion, conceptualized as a boom and bust cycle (Bazelmans et al., 2006; Moss-Morris, 2005; Surawy et al., 1995). So, while they were able to perform as well as controls for the duration of the task, they might have experienced a spike in symptoms later (Dickson et al., 2009). On the other hand, people with a low number of CFS symptoms might have attempted to pace themselves, resulting in a more stable and consistent pattern of behaviour, but in a slower speed of processing. This subgroup, perhaps, may correspond to a CFS group identified as implementing 'passive' and avoidant coping strategies (Bazelmans et al., 2006).

The lack of an interpretation bias being found within a patient group is inconsistent with the research in chronic pain (Edwards & Pearce, 1994; Pincus et al., 1994; Pincus et al., 1996). Most importantly, it is not in keeping with Moss-Morris and Petrie's (2003) study that demonstrated that participants with CFS were more likely to interpret ambiguous information in an illness-related way, compared to the controls. The difference in the results may be due to differences in methodologies, which might respond to different components of the interpretation process or different aspects of the illness schema.

In the method employed by Moss-Morris and Petrie (2003) that tapped into the off-line interpretive processes, it is possible that all the meanings (threat and non-threat) were activated and the participant had to make a choice which one to write down (Amir, Beard, & Przeworski, 2005). Therefore, the CFS group might have demonstrated an elaborative later-stage response bias rather than the kind of automatic online interpretation bias (Vancleef et al., 2009) that would be measured by the lexical decision task in the current study.

The current procedure might have avoided the confounding effects of response bias and demand effects, because the alternative meanings of the ambiguous words were generated by the researchers. However, a potential criticism of the lexical decision method may be that it is not sensitive enough to tap into a negative illness schema, which guides a more elaborative higher level cognitive process.

The current task was designed to investigate the on-line process, the automatic interpretation of ambiguity at the moment of the first (Vancleef et al., 2009). The results suggest an absence of interpretation bias during the automatic generation of meaning in CFS participants. In contrast, Moss-Morris and Petrie (2003) demonstrated evidence for an interpretation bias at a later, elaborative level of processing and response production. If cognitive impairments in CFS mainly affect the response stage, involving selection and execution (Scheffers et al., 1992), then it does follow that the preferential processing of one type of information over another may appear during that later stage, once the negative illness schema is activated and accessed (Hirsch & Mathews, 2000). Thus, a more plausible explanation of the inconsistency between the findings of this study and existing research is due to differing use of illness schema at the two stages of interpretation. In the ambiguous cues task, used by Moss-Morris and Petrie (2003), participants were asked to write down the first word that came into their mind after hearing the ambiguous word. This was likely to involve a higher order stage of interpretation, where participants had to actively generate a schema to produce a response. In the case of people with CFS, compared to controls, this would more frequently be an illness-related schema, resulting in the production of an illness-related response.

The lack of an interpretation bias in the current study compared to that of Moss-Morris and Petrie's study does not appear to be down to the two studies assessing different types of illness schema. There is a limited pool of ambiguous English words with a meaning related to illness, and most of these words in both studies were not specific to CFS, but were more general illness words. There does not appear to be any obvious systematic differences in the words used in the two studies, but in both studies the illness interpretations of the ambiguous words were generally considerably less threatening than for example words used in the investigation of attentional bias towards health threat (Hou et al., 2008). In this study the strongest illness interpretations of the ambiguous primes were death, tumour, and blood, while other thirteen words were along the lines of effort, weak, broken, tight. Meanwhile, Hou and colleagues (2008) used words like cancer, coffin, coronary, hospitalised.

The interpretation of the null results is one of the potential limitations of the current study. The results can be interpreted as null results, demonstrating the absence of the phenomenon of interest; however that is in contrast with the previous findings (Moss-Morris & Petrie, 2003). Alternative interpretations include the possibility that the study lacked the statistical power to detect an effect. Thus a post hoc power analysis was conducted on the current sample.

With the total sample size of 66 and alpha set at .01, the power to detect the critical within/between interaction of prime type and target type with the group factor in the lexical decision task was equal to .96. Thus, the study had an estimated 96% chance of detecting Moss-Morris and Petrie's (2003) large effect size at the significance level of p = .01. Additionally, the study had a 75% (Power .7583) chance to detect a medium effect size. Taking into account the expectation of a large size effect, and a large difference between the means that was previously demonstrated with small sample sizes, the post hoc power analysis shows that the null results obtained in the current study are unlikely to be due to the lack of statistical power.

Regardless of the power analysis, the relatively small sample size is one of the main limitations, even though it is comparable to the three studies that have used cognitive tasks to assess information-processing biases in CFS: the study by Moss-Morris and Petrie (2003), and the two studies by Hou et al (2008, 2014) on attentional bias. The increase of power by adding more participants may reveal significant interactions with the group factor in the analyses of raw and bias scores. However, this does not seem likely, since examination of F values, which are all close to 1, and of graphs, showing similar response patterns, does not suggest any underlying differences between groups.

Alternatively, the two studies might access two qualitatively different populations. Moss-Morris and Petrie (2003) recruited from a medical practice that specialized in the treatment of CFS. The current study has recruited from the community. The limitations in the generalizability of this sample has been discussed in Chapter 2, Discussion with regard to the attentional bias and rumination (pp. 102 - 104). As a community sample, this group of people with CFS might not have been representative of a clinical sample who may suffer from higher severity fatigue, and experience more symptoms. Due to the lack of specific assessment of the severity of fatigue, and of the severity and frequency of additional symptoms, this group with CFS cannot be compared to those in other studies.

Another limitation that needs to be considered is the potential effect of the cognitive state induction during this part of the study procedure. The literature does not

specify the duration of the effect following a cognitive state induction (Watkins & Teasdale, 2004). Even though in the current study, participants took a break and there was a minimum of 30 minutes for the induction effect to dissipate, it may have had a lasting effect. However, mood measured at the time before participants started the lexical decision task was similar to their mood state before the induction. In spite of that, there still may have been an effect on the lexical decision task that has not been accounted for. Besides, it would be expected that induced rumination would amplify the interpretation bias, according to the evidence from healthy populations that rumination is significantly associated with interpretation bias (Mor, Hertel, Ngo, Shachar, & Redak, 2014). Accordingly, the correlational analysis within the CFS group showed that less ruminative brooding was associated with greater likelihood to endorse a neutral meaning of the ambiguous illness prime. However, Mor and colleagues (2014) also found the same relationship between interpretation bias and reflection, which is supposed to characterize adaptive non-judgmental contemplation (Treynor et al., 2003). It would be informative for the future research to take a closer look at the effect of cognitive state on the interpretation bias in CFS, taking into consideration the complexity of the rumination construct. A future study may separate the constructive ruminative processes (reflective) associated with adaptive planning and health-promoting behaviours and the unconstructive (brooding) processes associated with physical health difficulties (Watkins, 2008). Inducing brooding and reflective states would make for a more informative comparison than rumination against distraction.

In summary, it appears that the most likely account is that in CFS the illness schema acts on the later elaborative stage of the interpretation of ambiguous information rather than at the initial automatic stages. This may occur as late as explicit response production, and would account for the different findings in the current study and the Moss-Morris and Petrie (2003) study. One of the ways to measure cognitive processing at its different stages, from the earlier preconscious to the voluntary production of the response, is to explore the time course of the schema activation and change by varying the stimulus onset time and the duration of the stimulus presentation.

Moreover, for the next research step, the choice of stimuli needs careful consideration, in terms of the division between mildly and severely threatening words. Additionally, to increase ecological validity the words need to be put in a context, as the ambiguity of real life situations cannot be expressed by one word alone. The use of sentences or vignettes would be more appropriate to study the interpretation of ambiguity. Similarly, linguistic stimuli may not be the most suitable type of information in a study of

chronic illness condition. Non-verbal stimuli, for example pictures of facial expressions reflecting various emotions or sensations, can be used. Images of various body poses and stances, which may be expressing reactions to pain or fatigue, would be better suited for the investigation of the interpretive bias in CFS.

Chapter 6: Study 5: Memory Survey

Introduction

Memory research in CFS is focused predominantly on processing deficits, such as impairments in working memory and in the long-term storage and retrieval (Cockshell & Mathias, 2010). Research on preferential or enhanced memories for particular types of information, for example somatic, health-threat and illness-related stimuli, is scarce. However, a number of recent findings may indicate a selective process in the formation and retrieval of memories for fatigue in CFS.

Friedberg and Sohl (2008) asked people with CFS to provide momentary ratings of their fatigue (participants recorded the level of their fatigue six times a day for a week) and a retrospective global rating of fatigue at the end of the week. The results showed that the retrospective global fatigue rating was significantly higher than the average of the momentary fatigue ratings. Sohl and Friedberg (2008) found that more widely fluctuating fatigue levels in CFS were associated with less accurate recall. A similar pattern was observed in chronic pain studies for the memory of pain (Stone, Broderick, Shiffman, & Schwartz, 2004). The above evidence is also in parallel with the findings concerning the perception of activity and exertion. People with CFS underestimate their activity levels and overestimate their fatigue (Fry & Martin, 1996a, 1996b) and report higher levels of exertion, compared to non-CFS groups, including a healthy control group, after the same amount of activity and exercise (Cook et al., 2003; Fulcher & White, 2000). The findings point towards possible distortions in memory processing of fatigue, pain, and activity in CFS.

The reviewed evidence fits the concept of symptom amplification, an alteration in the perception of a somatic sensation leading to the experience of increased intensity of that sensation (Barsky & Borus, 1999; Barsky et al., 1988). This symptom amplification endures over time and may affect the immediate (at the moment of experience) and the global (retrospective) symptom perception. Thus, fatigue and pain may be viewed as constant and stable characteristics of one's life, in line with the concept of negative schema proposed by Beck (1967). Within the negative illness schema, fatigue, pain, and exertion sensations may command attentional focus, leading to an amplification of these sensations, which would guide the interpretation of fatigue and pain as symptoms of a serious illness (Moss-Morris, 2005). The negative illness schema in CFS would similarly guide memory processing. Somatic, illness-related, and potentially health-threatening events would be preferentially processed, encoded and recalled, because of the amplified attention towards somatic

sensations and the dominant style of interpreting them as health-threatening and as symptoms of a serious illness (Moss-Morris, 2005).

Research on the features of memory processing, enhanced memory for illness-related and health-threat information, and autobiographical memory in CFS is limited, in spite of the chronicity of the illness and associated memory deficits. This limitation needs to be addressed, considering that memory impairment is one of the eight accompanying CFS symptoms (Fukuda et al., 1994) reported to be one of the most disabling symptoms (Jason, King, et al., 1999; Jason, Richman, et al., 1999). Additionally, CFS can be a chronic, potentially life-long, condition with widely fluctuating levels of symptoms and functioning, (Fuentes et al., 2001; Sohl & Friedberg, 2008; Stone et al., 1994; Wood et al., 1992), thus investigating the features of autobiographical memory may be informative.

Autobiographical memory is defined as the recollection of previous events in relation to one's personal sense of self, as an aid to future problem-solving and goal attainment (Conway & Pleydell-Pearce, 2000). Thus, looking into the characteristics of autobiographical memory in CFS may elucidate additional facets of cognitive processing that may contribute to symptom exacerbation and perpetuation. Furthermore, CBT, GET and Mindfulness interventions for CFS can be further tailored to reflect the needs of people with CFS, by targeting maladaptive features of memory processing.

One such maladaptive feature is overgeneral memory (OGM), frequently observed in depression and Post Traumatic Stress Disorder (PTSD) (Kleim & Ehlers, 2008; Raes et al., 2006; Sumner, 2012; Sumner, Griffith, & Mineka, 2010). OGM refers to a style of autobiographical recall where the content lacks specific concrete details of particular events (I went for a walk in Hyde Park), and instead reflects categories of similar events (I used to go for walks) or refers to an extended period of time (when I was on vacation last summer). OGM is associated with greater vulnerability to developing depression, increased risk of reoccurring depressive episodes, and delayed recovery from depression (Sumner, 2012; Sumner et al., 2010; Williams et al., 2007).

As a potentially life-long condition with unclear prognosis, CFS may exert a physical and mental toll on the sufferers, hence the documented association between CFS and depression (Arpin-Cribbie & Cribbie, 2007; Faulkner & Smith, 2008; Sohl & Friedberg, 2008), and the elevated risk of developing secondary depression in CFS (Janssens et al., 2015) fitting with the general pattern of comorbidity of depression and chronic physical illness (Qin et al., 2014; Shahar et al., 2014). However, in spite of the high risk of depression, research on OGM in the area of chronic illness is scarce. OGM has been observed in chronic pain (Liu et

al., 2014) and in anorexia nervosa (Nandrino, Doba, Lesne, Christophe, & Pezard, 2006), and is associated with elevated depression in people who are currently hospitalised (Sampson, Kinderman, Watts, & Sembi, 2003). Therefore, one would also expect to observe OGM in CFS, taking into account elevated depressive mood and the observed comorbidity between CFS and depression.

Theory and empirical evidence also link OGM with avoidant coping strategies (Geraerts, Dritschel, Kreplin, Miyagawa, & Waddington, 2012; Hermans, Defranc, Raes, Williams, & Eelen, 2005; Williams et al., 2007). In depression and PTSD, OGM is hypothesized to inhibit emotional distress in relation to past traumatic events through the mechanism of functional avoidance (Williams et al., 2007). In other words, people can reduce negative affect by avoiding the processing of distressing details of past events. Moreover, that process can generalize to also include positive events (Dalgleish et al., 2003; Iqbal, Birchwood, Hemsley, Jackson, & Morris, 2004; Van Vreeswijk & De Wilde, 2004).

Avoidance is a widespread coping strategy in CFS (Nijs et al., 2013). Therefore, one would expect to observe in CFS the same association between overgeneral memory and avoidant coping styles, such as denial and behavioural disengagement. However, avoidance in CFS is of a more behavioural nature than it is in depression. In CFS, it primarily involves avoidance of activity, in order to prevent the post-activity increase in fatigue and pain, termed 'post-exertional malaise' in the CFS symptomology (Bazelmans et al., 2006; Nijs et al., 2013). There is little evidence for cognitive-level avoidance in CFS (Brown, Brown, & Jason, 2010; Nater et al., 2006), and people with CFS are more likely to demonstrate a high anxious-defensive rather than a repressive avoidant coping style (Creswell & Chalder, 2001). Fear and catastrophic beliefs, rather than avoidant cognitions, accompany the behavioural avoidance and predict decreased functioning in CFS (Nijs et al., 2011; Nijs et al., 2008). Therefore, it would be expected to observe the association between over-general memories and behavioural disengagement in CFS, fitting within the mechanism of functional avoidance. On the other hand, a more catastrophic cognition, such as fear of movement, would be associated with less general illness-related memories, for example memories of fatigue, pain, or exertion.

Importantly, cognitive theories of symptom perpetuation in CFS implicate heightened focus on somatic sensations rather than cognitive avoidance or repression of illness-related information (Moss-Morris, 2005). Increased attentional focus on somatic symptoms, such as fatigue and pain, leads to increased perceived severity of these symptoms following exertion, resulting in a reduction of activity (Knoop et al., 2010). Theories and evidence from

treatment trials converge on the preferential processing of somatic sensations as a potential maintaining factor in CFS (Knoop et al., 2010; Wiborg et al., 2011). In line with the cognitive theories of CFS is the concept of the sensitization of the central nervous system (CNS), a potential causal factor of CFS; this CNS sensitization may also be maintained by a cognitive process, such as attentional vigilance (Nijs, Meeus, Van Oosterwijck, et al., 2012).

Consequently, in contrast to OGM, there is the phenomenon of specific memory, the recollection of the past that is filled with concrete details of singular events. Sohl and Friedberg (2008) showed that high intensity fatigue in CFS led to more accurate reporting and to greater agreement between ratings of fatigue within the moment as it is experienced and ratings of fatigue that are delayed. It means that intense fatigue resulted in the formation of more concrete and accurate memories. Therefore, people with CFS may be more prone to retrieving specific memories of somatic sensations, such as fatigue and pain, rather than overgeneral memories.

Furthermore, Cockshell and Mathias (2010) found evidence of impaired working memory in CFS, which is relevant to the theory of memory retrieval proposed by Conway and Pleydell-Pearce (2000). According to Conway and Pleydell-Pearce model, specific memories are retrieved spontaneously and rapidly through a direct sensory-perceptual process in response to an internal or external cue. In contrast, general categorical memories are retrieved via a more elaborate top-down search sifting through concepts and categories of representations of events. The direct sensory-perceptual process of retrieving specific memories is less demanding on cognitive resources than searching through many higher level representations (Conway & Pleydell-Pearce, 2000). People with CFS may prefer the direct, low-demanding, quick retrieval, because they would attempt to conserve cognitive resources. Retrieving general memories may be more difficult for people with CFS as it may require sustained effort.

Deary (2008) proposed that in CFS, where there is an established “precarious balance” between energy and activity, the threat to health could be perceived in the events that may disrupt that fragile balance and lead to symptom exacerbation. For example, increased physical activity may disturb such balance and increase symptom severity. Therefore, physical activity may be perceived as a health-threatening and illness-relevant event. Evidence shows that people can retrieve specific memories of events that involve direct encounters with a source of their fears or distress (Golden, Dalgleish, & Mackintosh, 2007; Wenzel, Jackson, Brendle, & Pinna, 2003). People also tend to retrieve specific illness-

relevant memories if they are in a state of ruminative analytical self-focus (Sansom-Daly, Bryant, Cohn, & Wakefield, 2014).

Therefore, one would expect to observe increased memory specificity in CFS based on the following reasons. Direct retrieval (leading to specific memories) would be the preferred strategy in people with CFS because of difficulties in sustaining mental effort and impaired working memory (Cockshell & Mathias, 2010). Memories of elevated activity, fatigue, and pain would be more likely to be specific because of the increased attentional focus (Knoop et al., 2010), accompanied by the CNS sensitization (Nijs et al., 2012). Activity would be more likely to be recalled in a specific manner by a CFS group, because of its potential health-threatening and distressing nature (Deary, 2008) and high illness relevance (Nijs et al., 2013). These more specific memories would be more likely to be associated with catastrophic cognitions, such as fear movement (Nijs et al., 2011; Nijs et al., 2008).

Overgeneral or overly specific autobiographical memories may be recalled from two points of view: first person point of view, referred to as field perspective; and third person point of view, called the observer perspective (Nigro & Neisser, 1983; Robinson & Swanson, 1993). Field perspective is associated with more accurate and detailed recall of physical and psychological states (Bagri & Jones, 2009; McIsaac & Eich, 2002), and higher emotionality of memories (Kuyken & Howell, 2006). Thus, field perspective is focused more on the internal state as opposed to external environment. Therefore, it would follow that specific memories, being self-focused and detailed, would be more likely to be viewed from the field perspective. In the current study, participants were asked to recall unusually high instances of pain, fatigue, activity or happiness, events that are deeply psychological and physical. Therefore, one would expect that greater specificity of such memories would be associated with field perspective. Consequently, if people with CFS demonstrate overly specific memories then these memories would be recalled from the field perspective. This hypothesis is based on the evidence that high intensity fatigue is more accurately recalled in CFS (Sohl and Friedberg, 2008), in addition to the amplified attention towards somatic information (Knoop et al., 2010; Moss-Morris, 2005), and oversensitisation of CNS (Nijs, Meeus, Van Oosterwijck, et al., 2012).

Unlike field perspective which is more self-focused, an observer perspective was found to be associated with memories for space and action, focused on appearance, locations, and peripheral information (McIsaac & Eich, 2002). Thus, observer perspective is more externally oriented. McIsaac and Eich (2004) reported that recollection from the observer perspective had an objective 'flat affect' character, and elicited less anxiety and

negative emotion, while field perspective was recalled with greater emotional involvement. Observer perspective is associated with a reduction in the emotional intensity of memories (Berntsen & Rubin, 2006; Robinson & Swanson, 1993; Sekiguchi & Nonaka, 2014; Vella & Moulds, 2014). Consequently, when remembering high levels of physical or emotional threat people were more likely to use the observer perspective (Nigro & Neisser, 1983). The reduced emotionality of the observer perspective likens it to the mechanism of overgeneral memories (functional avoidance), which exerts its protective effect by reducing the emotional distress (Sumner, 2012). Accordingly, observer perspective has been found in memories of people with depression (Kuyken & Howell, 2006) and in people with PTSD when recalling past traumatic events, who regarded the observer perspective as offering protection from the emotional distress of the trauma (McIsaac & Eich, 2004). In spite of its protective quality, McIsaac and Eich found that adopting the observer perspective did not result in better outcomes, and proposed that such perspective may underpin impaired emotional processing and fear-avoidant behavioural tendencies. This is similar to the OGM effect and its mechanism of functional avoidance (Williams et al., 2007). Therefore, both OGM and the observer perspective can be maladaptive long-term. Consequently, one would expect that over-general memories in CFS would be associated with observer perspective.

Like CFS, asthma is a chronic, often life-long, illness leading to reduced activity (Avallone & McLeish, 2013), and elevated fatigue (Small & Lamb, 1999) and pain (Taniguchi, Kanbara, Hoshino, & Izumi, 2009). Since there is no cure for asthma, the current treatment strategies emphasise control and management of symptoms (British Thoracic Society, 2014; GINA, 2015). Therefore, the features of autobiographical memory with regard to physical activity, pain, or fatigue may also be relevant to understanding how people choose to manage their asthma, and may be targeted in interventions to achieve better symptom management and control, and to prevent psychological distress.

In asthma, repressive coping (avoidance of the conscious perception of negative feelings (Weinberger, 1995)) can be a barrier to successful symptom control and management. Repressive coping is common in asthma and is associated with poorer lung function, greater symptom severity, negative health outcomes, and increased health-care utilization (Adams et al., 2000; Cooke et al., 2003; Gonzalez-Freire et al., 2010). As reviewed above avoidant coping style is associated with over-general memory (Geraerts et al., 2012; Hermans et al., 2005). Importantly, asthma also has a high comorbidity with depression (Trojan et al., 2014), where OGM is prevalent (Sumner et al., 2010; Williams et al., 2007).

Similar to avoidance, depression is also associated with poorer symptom control in asthma (Lavoie et al., 2006).

Therefore, people with asthma may be susceptible to developing an overgeneral memory style, which would impede good symptom management due to increased avoidance. Therefore, one would expect to observe OGM in asthma with regard to activity, fatigue and pain, which would also generalize to happy memories, and would be associated with repressive cognitive style, such as denial. This is in contrast to the prediction for the CFS group, where over-general memory is expected to be associated with more behavioural type of avoidance, as measured by the construct of behavioural disengagement.

Thus, the current study aimed to investigate whether CFS group would demonstrate a unique cognitive style, independent of depression comorbidity so prevalent in physical illness. Alternatively, CFS group may demonstrate a cognitive style comparable to that of people with depression. This would be because of the effect that depression may exert on the cognitive processing in people with chronic illness, as would be shown by the asthma group's increased tendency to retrieve over-general memories.

Understanding the features of autobiographical memories of health-related and illness-related events in CFS may shed light on the mechanisms behind the discrepancy between real time fatigue ratings and the amplified retrospective recall of fatigue (Friedberg & Sohl, 2008); or the discrepancies between perceived exertion and objective performance on physical tasks (Blackwood, MacHale, Power, Goodwin, & Lawrie, 1998; Cook et al., 2003; Fry & Martin, 1996a, 1996b). So far there has not been an examination of the way different types of illness-relevant events are recalled by people with CFS. Investigation is needed into the mechanisms of recall of activity, fatigue and pain. Furthermore, the contents of such memories may also be a rich source of information. Therefore, the current study performed a thematic analysis of the participants' memories to explore in depth the kind of information people recall in relation to illness-relevant events. The current study looked to identify dominant themes and patterns in recollection of unusual physical activity, fatigue, pain, and happiness.

The current study investigated four types of autobiographical memory: physical activity, fatigue, pain, and happiness. For the CFS group, two contrasting hypotheses were proposed:

1. If the CFS group has a similar cognitive processing style to people with depression, then they will recall over-general autobiographical memories of activity, fatigue, and pain. The effect is expected to generalise to positively valenced memories, such as the memories

of happy moments, echoing the findings in depression research. Additionally, OGM will be associated with increased avoidant behaviours, such as behavioural disengagement.

2. If, in contrast, CFS is underpinned by CNS sensitization, amplified attention towards somatic symptoms, catastrophic fear cognitions, and preservation of cognitive resources, then the CFS group will demonstrate over-specific memories of activity, fatigue and pain, compared to the healthy control group and the asthma group, because activity, fatigue and pain will be regarded as distressing, illness-relevant, and health-threatening. Specific memories will be associated with increased fear of movement in the CFS group.

The following hypothesis was tested regarding the asthma group: due to the elevated comorbidity between depression and asthma, participants with asthma will recall more over-general autobiographical memories of the four types of events: activity, fatigue, pain, and happiness, compared to the healthy control group. The overgeneral memories will be associated with increased denial.

With regard to the interaction of over-general/specific memories and memory perspective, the following hypotheses were tested:

The CFS group will rate specific memories of activity, fatigue, and pain higher on field perspective, compared to asthma and control groups.

The CFS group will rate over-general memories of activity, fatigue, and pain higher on observer perspective, compared to asthma and control groups.

Method

Online Study Design

The study was a survey conducted via the Internet (using Survey Monkey data collection software). The measures included an autobiographical memory task and self-report questionnaires. Chapter 4B described the analysis of the component structure of a newly developed self-report measure of activity. The analysis was conducted on the data from a preliminary sample where groups were significantly different in age. In the current chapter, the analysis is presented based on the data from age-, gender-, and education-matched groups.

The component of the study presented in this chapter had a quasi-experimental design with one between-subjects independent variable, group: people with a CFS diagnosis were compared to age-, gender- and education-matched people with asthma and with

healthy controls. Within-subjects factor for a memory task included four types of stimuli (Activity, Pain, Fatigue, Happy), these were word cues to prompt memory recall.

The main dependent variable from the memory task was the categorical variable of memory classification (Specific, General Categorical, General Extended). The other two dependent variables of interest were memory perspective ratings: field (first person point of view) and observer (third person point of view).

The other dependent variables included scores on self-report measures of symptoms, functioning, coping strategies, perception of activity, activity, fear of movement, depression, anxiety, and positive and negative affect.

The study has been reviewed by and received ethics clearance through the University of Oxford Central University Research Ethics Committee (CUREC), assigned reference number: MSD/IDREC/C1/2009/111 (Appendix C.2).

Participants

The total number of people who started the survey was 607. After the primary diagnosis screening and consent procedure, 103 CFS, 78 Asthma, and 176 Control participants went on to participate in the study. Due to the significant difference in age in the preliminary sample described in Chapter 4B (pp. 185 – 187) recruited for the online study, participants below the age of 20 were excluded from the current analysis in order to obtain a better match on age, gender and education between groups. Participants with missing data were also excluded from the current analysis. The final sample consisted of 87 people with CFS, 56 people with asthma, and 60 healthy control participants. Their demographic characteristics and questionnaire scores are presented in Table 1.

Recruitment was conducted by contacting UK wide CFS and Asthma support and self-help groups; social media (Facebook); Internet UK-based health forums and discussion boards concerning asthma, CFS, or chronic illness; participant recruitment advertisement webpages for universities (Oxford, Warwick, and UCL); and various participants' recruitment web sites (for example http://www.clinpsy.org.uk/). The inclusion criteria for the study specified a primary diagnosis of CFS or Asthma, or no current medical or psychological disorder diagnosis, 18 years of age and fluent English. All participants were screened and excluded if they reported a primary diagnosis that was not CFS or asthma.

People with CFS were included in the study if they:

1. Reported a primary CFS diagnosis by a qualified medical practitioner (GP, referred specialist). Any person who had received a diagnosis of CFS by their GP or at a specialist clinic in the past unspecified period of time was considered for inclusion into the study.

AND

2. Met the CDC/Fukuda (1994) criteria for the presence of current primary unexplained, persistent or relapsing fatigue, which was not relieved by rest and resulted in significant reduction of activities for the last 6 months (Fukuda et al., 1994).

AND

3. Reported at least four symptoms from the eight outlined by the CDC/Fukuda criteria: impairment in short-term memory/concentration, sore throat, tender lymph nodes, muscle pain, multi-joint pain, headache, unrefreshing sleep, post-exertional malaise more than 24 hours. For the diagnosis of CFS based on CDC/Fukuda criteria the required minimum number of concurrent symptoms is four symptoms experienced in the past 6 months.

Participants with CFS rated the frequency of their symptoms in the past 6 consecutive months on a scale from 1 (never experienced) to 5 (experienced all of the time). The range of reported symptom frequency was between 24 (which is above the minimum score of 16, when at least 4 symptoms were experienced most of the time – score of 4) and 40 out of maximum 40 (all 8 symptoms experienced all of the time – score of 5). Therefore, all participants with CFS in the final sample met the CDC/Fukuda criteria and had been experiencing frequent symptoms in the past 6 months.

Participants with CFS were excluded if they reported:

1. Another acute or chronic primary medical or psychiatric diagnosis that may be the cause of extreme fatigue and would preclude the diagnosis of CFS, for example any diagnosis of the conditions outlined by CDC/Fukuda (1994), Reeves et al. (2003, 2005), or NICE (2007) guidelines.

2. A current diagnosis of primary depression, if depression was diagnosed prior to receiving CFS diagnosis in the past 5 years, according to the recommendation by Reeves and colleagues (2003, 2005).

Due to reported comorbidity of CFS and depression, the history of depression and anxiety was checked. Nine participants with CFS reported episodes of depression following CFS, four participants reported episodes of anxiety after having received CFS diagnosis, and three participants reported comorbid depression and anxiety. These participants were

included into the study because their depression/anxiety did not preclude their CFS diagnosis.

Depression and anxiety were also assessed using the Hospital Anxiety and Depression Scale, and the severity was judged based on the recommended cut-off scores for CFS population above 9-10 points (Morriss & Wearden, 1998). 31 CFS participants scored 10 and above on HADS Depression, and 32 scored 10 and above on Anxiety. These participants were included in the analysis, because either they did not report a diagnosis of depression/anxiety or their psychological state was due to the effects of having CFS.

Participants with asthma were included in the study if they reported:

1. Primary asthma diagnosis by the qualified medical practitioner (their GP, or referred specialists).

AND

2. Current experience of asthma symptoms.

AND

3. Current use of medication to manage their asthma (e.g. preventer/reliever medication, inhaled corticosteroids).

Participants with asthma were excluded if they reported another current acute or chronic medical or psychiatric diagnosis.

Participants ranked their current Asthma severity as 1 - Mild, 2 - Moderate or 3 – Severe. They reported the degree that Asthma interfered with their daily functioning on a scale from 0 (not at all) to 10 (extremely) (Brooks et al., 1989). Asthma symptoms were assessed by the Asthma Symptom Checklist (ASC), a widely used, well validated and reliable (Cronbach α .84 - .94) measure (Kinsman et al., 1973). Participants reported the frequency of their symptoms on a scale from 1 (never) to 5 (always). Total ASC scores were obtained in addition to scores on five subscales: Panic-Fear, Irritability, Fatigue, Hyperventilation-Hypocapnia, Bronchoconstriction (Brooks et al., 1989).

Seven participants with asthma reported a diagnosis of depression and three of anxiety in the past, all received after the asthma diagnosis due to effects of the illness. These participants were included into the study because their depression/anxiety did not preclude their diagnosis of asthma. Potential depression and anxiety have also been assessed using HADS, based on the recommended cut-off scores for general population, 8-10 points (Herrmann, 1997; Zigmond & Snaith, 1983). Fourteen participants with asthma scored 8 and above on HADS Depression, and 35 participants scored 8 and above on HADS Anxiety.

Participants were included because reported history of depression and anxiety was due to effects of having chronic illness.

Additional inclusion criteria for all participants specified 18 years of age, and English at the standard of a native speaker. Healthy control participants were excluded if they reported current acute or chronic medical or psychiatric diagnosis.

Materials

Memory Retrieval Task

The memory retrieval task was a retrospective measure of autobiographical memory modified from the task employed in assessing memory perspective (Martin & Jones, 2012) and from the Autobiographical Memory Task (Williams & Broadbent, 1986). Participants were asked to remember four different specific events:

Please, remember a 'particular occasion' when
1) You felt happier than usual
2) You felt physical pain
3) You were very tired
4) You were more physically active than usual

Participants were given the opportunity to provide a short title for the event (consisting of one or two words) and to describe the memory, recording how long ago the event occurred. The recency of the event was coded as the categorical variable: 1 - events occurring within the last year; 2 – occurring between 1 and 5 years ago; 3 – occurring over 5 years ago. All participants were presented with the same order of recalled events, due to limitations of the online testing software.

Memory Classification

Each description was coded by the current investigator as Specific, General Category, or General Extended (see Appendix C.6 for examples of memory coding). Specific memory referred to an event lasting no longer than one day, with a mention of date, location, and/or name (example: 'I ran a 7 mile race for charity last Sunday').

General Category referred to a series of similar or regularly occurring events (e.g. Happy - birth of my children; Pain – back pain if I overdo things; Fatigue - when revising for exams; Activity - when going to the gym).

General Extended referred to an extended unspecified period of time, and would involve a mention of a time period (e.g. Happy - when I was on holiday; Pain – chronic back pain last year; Fatigue – the time I was taking care of a disabled relative; Activity - swimming in Spain during a holiday).

Memory classification was based on the criteria used in previous research on OGM (Williams et al., 2007; Williams & Broadbent, 1986). Reliability of the memory classification was checked by two independent judges, who were blind to the experimental purpose and participants' group membership. Inter-rater reliability was good for all memory types, Judge 1: Happy memories *K* = .92, Pain *K* = .92, Fatigue *K* = .91, and Activity *K* = .94; Judge 2: Happy memories *K* = .82, Pain *K* = .92, Fatigue *K* = .89, and Activity *K* = .91.

Memory Attributes

Participants recorded how long ago the recalled event occurred. The recency of the event was coded as categorical variable: events occurring within the last year; 1 – 5 years ago; and over 5 years ago. Participants rated each memory on vividness between 1 – not vivid at all and 7 – as vivid as if it were happening right now. Participants also rated the frequency of their memories (that is, how often they thought about the memory) on a 5-point scale ranging from 1 (1-5 times) to 5 (101 or more times).

Memory Perspective

Participants were asked to rate on a scale from 1 (not at all) to 7 (completely) to what extent they experienced a particular memory as if viewed 'through their own eyes' or 'by an outside observer'. All participants received instructions that included the following explanation of the memory perspective:

1. Field perspective - remembering the event as though seeing it THROUGH YOUR OWN EYES again, as when you experienced it originally.
2. Observer perspective – remembering the event as being viewed by an OUTSIDE OBSERVER (for example, a bird's eye view), seeing yourself in the situation.

Additional explanation specified that it is possible for participants to remember events from only one or the other of those views. Alternatively, it is possible to switch between the views while remembering the event.

Questionnaires

All self-report measures of demographic and illness characteristics and the following questionnaires are presented in Appendix C.4. Self-report measures used in the current study were described in Chapter 4B, Method, pp. 188 – 191 and included:

Fatigue Severity Scale (FSS)

Medical Outcomes Study - RAND 36 Short-Form Health Survey (SF-36)

Tampa Scale of Kinesiophobia – Fatigue (TSK-F)

Brief COPE: Behavioural disengagement and Denial subscales

Perception of Activity measure

Positive and Negative Affective Schedule (PANAS)

Hospital Anxiety and Depression Scale (HADS)

Activity scale

Activity scale scores, by summation, were calculated for each subscale, derived from the principal components analysis, described in Chapter 4B. Additional scores were calculated for the higher level subscales based on the two higher-level factors derived from the PCA on factor scores: Active lifestyle, Sedentary lifestyle.

Subscales included:

1) Leisure and Recreation - 8 items included: Visiting others, Drinking out, Attending social gatherings, Receiving visitors, Clubbing, Going out for entertainment (e.g. film, theatre), Eating out, Doing sports, Leaving house.

2) Online activity – 3 items included: Chatting on the Internet, Online activity, Facebook.

3) Social duties – 3 items included: Attending sporting events as spectator, Attending community gatherings (e.g. church), Education.

4) Work/Daily activity – 3 items included: Time spent out of the house, Walking, Work hours.

5) Communication – 3 items included: Phoning, texting, emailing.

6) Sedentary behaviour – 3 items included: TV, Puzzles/Games, Bed rest during the day.

7) Mental effort – 2 items included: Reading, Working on the computer.

Higher-level subscales:

1) Active lifestyle – subscales included: Leisure and Recreation, Social duties, Work/Daily, Mental effort.

2) Sedentary lifestyle – subscales included: Online social activity and Sedentary behaviour.

Power Analysis

Calculation of the required sample size was made on the basis of the planned statistical tests: ANOVAs for group means' comparisons, multiple regressions to test associations between variables. All calculations were performed using G*Power, version 3.1.3 (Faul et al., 2009; Faul et al., 2007).

Required total sample size for one-way ANOVAs was 159 with parameters: power .80, significance .05, medium effect size of Cohen's f = .25. Alternatively, 228 participants are needed if significance level is set at .01. Additionally a total of 128 (64 per group) would be needed for a *t*-test to detect a medium effect size Cohen's d = .50.

To calculate the sample size needed for each group for regression analysis, the parameters were set in the following way: linear multiple regression random model, 2-tailed tests, power at .80, significance .05, medium effect size $\rho^2 = 0.13$ as per Cohen's convention. Varying the number of predictors between 2 and 10, the sample sizes required 84 and 140 respectively. For the linear multiple regression, fixed model, R^2 deviation from 0, the sample size required based on the number of predictors was 68 participants for 2 predictors and 118 for 10 predictors in order to detect a medium effect size of $f^2 = .15$.

Taking into account the practicalities of recruitment from populations such as people with CFS, the requirement to match the groups on gender, education, and age, and the unknown value of expected effect sizes, the aim was to recruit 80 participants per group to satisfy the requirements for statistical power.

Equipment

The survey was administered via Survey Monkey software, a web-based platform for data collection. Each participant was able to access the survey through an URL, which took them to the first page of the survey containing the information about the study procedure, ethics, confidentiality (Appendix C.1), and consent form (Appendix C.3).

Procedure

Participants answered screening questions (about their history of medical and psychiatric diagnoses) and filled out the online consent form. The study procedure is presented below (see Appendix C.4 for the list of self-report measures). The same procedure is also described in Chapter 4B, p. 192.

1. Information about you (gender, age, education)

2. Information about your health (reporting of the a diagnosis of CFS, asthma, physical or mental health disorder)

3. CFS diagnostic criteria based on CDC/Fukuda criteria 1994 OR Asthma Checklist

4. Fatigue Severity Scale (at the beginning, so that their perception of their fatigue level is not coloured by tiredness from having completed all the questionnaires)

5. General Health Questionnaire - SF36 – Physical Functioning subscale (during the past four weeks)

6. Activity Scale

7. Memory Retrieval Task (including Memory frequency/vividness, and Memory perception)

8. Coping Scale

9. Perception of Activity

10. Tampa Kinesiophobia Scale – Fatigue (TSK-F)

11. PANAS – current affect

12. HADS Anxiety/Depression

Thematic Analysis

The methodology for thematic analysis was adopted from a qualitative study by Picariello et al. (2015) conducted on people with CFS, for better methodological comparability across studies. The current thematic analysis, similar to Picariello and colleagues, was based on the principles of Braun and Clarke (2006), who described an inductive method of looking at the data without a "pre-existing coding frame", a data-driven atheoretical approach not based on existing theories or experimental question and purpose. Such an approach would capture details of the memory descriptions that would reflect the richness of the data. For example, if a researcher was interested in descriptions of unusual physical activity, then, using an inductive approach, the researcher would read and re-read the data for any themes related to aspects of physical activity. Then, the researcher would code diversely without paying attention to the themes that previous research on the topic might have identified.

Each memory description was explored word by word, to detect common descriptors that reflect a recurrent theme or pattern. Based on those descriptors, memories were

grouped together to distinguish minor and major themes. For reliability, two researchers, the experimenter and an independent judge (unaware of the experimental purposes), separately looked through the memory descriptions with participants' group membership masked. Identified subthemes and main themes were discussed in order to reach a consensus. After the identification of major themes, three groups were compared on the number of memories within particular themes to identify if some themes were more prevalent within different groups.

Thematic Analysis Procedure

The following steps were taken to explore the content of the memory descriptions given by participants for four memory types (Activity, Fatigue, Pain, Happy)

Step 1: Each memory description was read and brief notes were made, which included notable words, expressions, and main descriptors.

Memory Description	Memory Title	Type of event	Notes	Subthemes	Theme
Activity					
Had personal training and group training session in one day	Workout	training	personal, group, session, training	Regular exercise	Exercise
Whilst on an activity day, quad biking and climbing	quad biking	biking, climbing	activity day, quad biking, climbing	Physical challenge	Exercise
Cycle race in late September 1982	Herts League 50 mile Road Race	cycling	race, cycle, 50 mile	sporting competition	Exercise
Fatigue					
day before leaving for Loughborough; had read a lot of articles	thursday evening	reading	read a lot, day before	work or study, mental effort	Study
Pain					
When I had glandular fever and had an intensely bad sore throat with acute tonsillitis so that I couldn't even swallow	Sore throat	tonsilitis, sore throat	sore throat, tonsilitis, intensely bad, glandular fever	symptoms, illness	Illness
Happy					
Visited Highclere castle with my daughter	Coach trip	trip, visit	trip, daughter (family)	family fun, trip out	Fun event

Step 2: The notes were studied and common descriptors were identified, in order to distinguish potential subthemes.

Step 3: Memories with common descriptors in the notes were grouped together to identify common subthemes

Memory Description	Memory Title	Type of event	Notes	Subthemes
Entering a race with my work	Blenheim run	running, race	race, run	sporting competition
Weekend long gymnastics display competition.	Gymfest.	gymnastics	competition, gymnastics, long	sporting competition
When I was training for a swimming titles	swimming	swimming	training, swimming, title	sporting competition

Step 4: Descriptions of these subthemes were generated.

Step 5: Common subthemes were grouped together to distinguish larger themes.

Step 6: The subthemes and larger themes were reviewed to ascertain if they could be linked into larger patterns, or if the major themes could be subcategorized.

Step 7: The descriptions of memories and their common descriptors were reviewed again in relation to the generated subthemes and themes. The coding manual can be found in Appendix C.7

Theme	Code	Subtheme	Description	Example	Exclusions	Excluded Example
Exercise	1.3	Sporting competition	Mention of sporting competition, training for competition, competitive sports	Weekend long gymnastics display competition.	Excluding regular exercise, non competitive training for health, fitness purposes	I was at home and had drunk some coffee at around 10pm. Since I'm trying to stay healthy and usually do not work-out, I had the good intention to do at least some sun salutations each day. Because of the coffee I didn't feel sleepy at all and ended up practicing yoga for almost a complete hour

Activity memories – emotional impact

Taking into account the prevalence of overgeneral memory in depression (Williams et al., 2007), the emotional valence of activity memories was checked. Depression research showed that overgeneral memories were produced regardless of the cue valence, in response to negative and positive stimuli (Kleim & Ehlers, 2008). Activity memories were coded as Positive, Negative and Neutral by two coders, the experimenter and an independent judge (blind to experimental purposes). Coding was conducted with group membership masked. The inter-rater agreement was K = .91.

Activity memories were coded as

1. Positive if they included positive emotional descriptors, such as free, energetic, happy, fun (e.g. “When I was training for a swimming titles. Vibrant, full of life, happy”).

2. Neutral, a description without any emotional content, reflection, or observation (e.g. “Had personal training and group training session in one day”).
3. Negative, if recollections had potential negative connotations, stress, pressure (e.g. “When I joined the Health club and was obsessed with losing weight”).

Data Analysis

Statistical analyses were performed using the Statistical Package for Social Science (SPSS) software version 20.0; and the web-based statistical computation software *VassarStats: Website for Statistical Computation* (Lowry, n.d.). Chi-square and univariate ANOVA tests were used to compare the groups on demographic characteristics (gender, education, age), FSS, SF-36 – Physical functioning, Activity scale, Fear of Movement (TKS-F), Denial and Behavioural Disengagement subscales (COPE), Perception of Activity, PANAS, and HADS. Pairwise comparisons with Bonferroni correction for multiple comparisons were used to clarify significant group differences.

Log-linear analysis of the frequencies of all categories of recall was conducted on a 3-way contingency table of Memory Type (Happy, Pain, Fatigue, Activity) by Memory Classification (Specific, Categorical, Extended) by Group (CFS, Asthma, Control). To clarify significant interactions separately for each Memory Type (Happy, Pain, Fatigue, Activity), the frequency analysis was performed using Pearson chi square tests to compare the number of specific, general categorical, and extended memories between the three Groups (CFS, Asthma, Healthy Control).

Properties of memory, such as recency, vividness, and recall frequency were explored through ANOVA procedures, comparing group means on the ratings of recency, vividness, and frequency of recall for each memory type. Multinomial logistic regression was conducted to investigate the association between the predictor variables: group (CFS, Asthma, Control), memory frequency and age, and the outcome variable: Memory Classification (Specific, General Categorical, General Extended). Univariate ANOVAs were used to investigate the associations between the generality of Activity memories and self-report measures of symptoms, function, activity, mood and coping styles.

Univariate ANOVAS were used to compare groups (CFS, Asthma, Control) on field and observer ratings of each memory type (Happy, Pain, Fatigue, Activity). To investigate the interaction between memory classification and memory perspective, a series of 2-way independent measures ANOVAS were conducted with Group (CFS, Asthma, Control) and Memory Classification (Specific, General) as between factors. The General categorical and

General extended memories were collapsed into one category (General memories) to reduce the number of comparisons. Field and observer memory perspectives were two dependent variables. Independent samples *t*-tests were used to clarify significant interactions, comparing CFS, asthma and control groups on field and observer ratings of the four memory types. The Bonferroni method of correction was used to account for the likelihood of Type I error and adjust the significance value for multiple comparisons; the value of 0.05 was divided by the number of tests performed on the data set to adjust the significance value. Chi-square test was used to analyse the relationship between the group factor and emotional valence of the activity memories, and similarly, between the group factor and the frequency of particular themes identified by the thematic analysis of memory content.

Results

Demographic and Questionnaire Measures

Groups did not differ significantly in age, gender, educational attainment, in all cases $p > .05$. See Tables 1A and 1B for demographic, illness, and self-report measures.

Table 1A.

Demographic and Questionnaire Measures for CFS, Asthma, and Healthy Control Groups

	CFS *(n = 87)*	Asthma *(n = 56)*	Control *(n = 60)*		
	n (%)	*n* (%)	*n* (%)	*χ2*	*p*
Gender (female)	70 (80%)	33 (70%)	106 (80%)	2.77	*ns*
Education (Degree)	27 (31%)	14 (25%)	21 (35%)	7.25	*ns*
Asthma Mild		22 (40%)			
Asthma Moderate		24 (47%)			
Asthma Severe		6 (10%)			
	M (SD)	*M* (SD)	*M* (SD)		
Symptoms duration (years)	10.8 (8.8)	24.6 (13.1)			
Time since diagnosis (years)	7.6 (7.1)	22.9 (13.5)			
CFS symptom frequency (past 6 months)	29.9 (5.6)				
Asthma severity (1-Mild, 2-Moderate, 3-Severe)		1.7 (0.7)			
Asthma interference (0-10 scale)		3.8 (2.9)			
Asthma Symptom Checklist		82.1 (28.1)			
ASC Panic-Fear		16.2 (7.1)			
ASC Irritability		13.9 (5.9)			
ASC Fatigue		16.1 (7.3)			
ASC Hyperventilation - Hypocapnia		12.2 (4.7)			
ASC Bronchoconstriction		23.7 (7.6)			

Table 1B.

Demographic and Questionnaire Measures for CFS, Asthma, and Healthy Control Groups

	CFS *(n = 87)*	Asthma *(n = 56)*	Control *(n = 60)*				
	M (SD)	*M* (SD)	*M* (SD)	*F*	*p*	Pairwise comparisons	*p*
Age	36.9 (11.6)	36.3 (15.8)	31.8 (11.9)	2.9	*ns*		
FSS	6.2 (0.9)	3.8 (1.9)	3.2 (1.2)	112.9	< .001	CFS vs C	< .001
						CFS vs A	< .001
						A vs C	.031
Physical Functioning	39.3 (26.2)	68.5 (33.3)	94.2 (10.1)	86.5	< .001	CFS vs C	< .001
						CFS vs A	< .001
						A vs C	< .001
Activity NOW	26.5 (21.5)	46.2 (29.4)	52.2 (24.1)	6.7	.002	CFS vs C	.008
						CFS vs A	.011
Activity PAST	86.3 (17.8)	64.2 (26.8)	56.3 (22.4)	24.3	< .001	CFS vs C	< .001
						CFS vs A	< .001
Activity WANT	85.2 (16.2)	85.3 (15.1)	72.6 (19.3)	7.6	< .001	CFS vs C	< .001
						A vs C	.013
Activity EXPECT	66.6 (22.1)	62.3 (27.2)	64.8 (19.7)	2.6	*ns*		
FOM Total	41.7 (8.1)	31.9 (9.6)	28.1 (7.1)	54.5	< .001	CFS vs C	< .001
						CFS vs A	< .001
						A vs C	.040
FOM Illness Beliefs	17.9 (4.8)	14.2 (5.4)	11.7 (3.8)	33.8	< .001	CFS vs C	< .001
						CFS vs A	< .001
						A vs C	.009
FOM Activity Beliefs	17.3 (3.7)	12.3 (4.2)	10.9 (3.1)	63.8	< .001	CFS vs C	< .001
						CFS vs A	< .001
COPE Behavioural Disengagement	1.3 (1.5)	0.9 (1.2)	0.9 (1.2)	2.1	*ns*		
COPE Denial	0.9 (1.4)	0.5 (1.1)	0.9 (1.2)	2.5	*ns*		
PANAS Positive	22.6 (7.9)	25.1 (8.9)	26.1 (8.4)	3.5	.031	CFS vs C	.038
PANAS Negative	17.9 (8.8)	14.3 (6.2)	15.4 (6.5)	4.3	.015	CFS vs A	.017
HADS Depression	8.3 (4.1)	5.7 (4.6)	3.4 (3.3)	21.3	< .001	CFS vs C	< .001
						CFS vs A	< .001
HADS Anxiety	8.9 (4.7)	9.1 (4.6)	6.4 (3.9)	7.4	< .001	CFS vs C	.003
						A vs C	.003

Note. FSS - Fatigue Severity Scale
Physical Functioning subscale of Short-Form Health Survey – SF-36
FOM - Fear of Movement, Tampa Kinesiophobia Scale - Fatigue
PANAS - Positive and Negative Affect Schedule
HADS - Hospital Anxiety and Depression Scale
COPE - Coping Questionnaire
CFS - Chronic Fatigue Syndrome, A - Asthma, C - control

Measure of Activity

Between-group comparisons of the subscales of the Activity self-report measure are presented in Table 2. Due to differences between groups on Depression and Anxiety, and due to non-significant but numerical difference in age, HADS and Age were entered as covariates. The CFS group scored significantly lower on work/daily activity, sedentary behaviours, mental effort, and overall Active lifestyle.

Table 2.

Group Means and Mean Comparisons for CFS, Asthma, and Healthy Control Groups on Activity Scale

	CFS	Asthma	Control		ANOVA		Pairwise
Measure	*n* = 87	*n* = 56	*n* = 60	*F*	*p*	Groups	*p*
	M (SD)	*M* (SD)	*M* (SD)				
Leisure and Recreation	37.9 (43.5)	64.2 (58.2)	70.5 (59.5)	2.30	*ns*		
Online activity	3.1 (3.8)	3.8 (8.4)	3.5 (3.2)	.42	*ns*		
Social Duties	3.3 (6.7)	4.8 (7.4)	15.7 (69.7)	2.01	*ns*		
Work/Daily	8.9 (6.4)	12.8 (7.2)	16.4 (5.4)	10.70	< .001	CFS - C CFS - A	< .001 .028
Communication	2.5 (12.8)	1.3 (1.7)	1.8 (2.5)	.41	*ns*		
Sedentary Behaviours	7.1 (4.4)	4.8 (4.4)	3.4 (3.1)	4.70	.010	CFS - C	.009
Mental Effort	4.2 (3.4)	5.8 (3.8)	7.5 (4.2)	5.40	.005	CFS - C	.004
Active Lifestyle	54.9 (51.4)	87.2 (64.8)	110.4 (118.8)	3.40	.035	CFS - C	.035
Sedentary Lifestyle	12.6 (14.4)	9.7 (10.6)	8.7 (6.2)	.81	*ns*		

Note. CFS - Chronic Fatigue Syndrome group
A - Asthma group, C - Healthy Control group
Pairwise comparisons between groups, Bonferroni correction
The ANOVA included Age, HADS Depression and Anxiety as Covariates

General and Specific Memories

The log-linear analysis revealed a significant 3-way interaction, $G^2(28) = 84.22$, $p < .0001$, between Memory Type (Activity, Fatigue, Pain, Happy), Memory Classification (Specific, General Categorical, General Extended) and Group (CFS, Asthma, Control) and a 2-way interaction between Memory Type and Memory Classification, $G^2(6) = 61.76$, $p < .0001$.

Chi-square analysis of each Memory Type showed significant association between memory classification (Specific, General Categorical, General Extended) and group (CFS, Asthma, Control) for Activity memories χ^2 (4, N = 200) = 12.47, $p = .014$. Investigation of the standardised residuals indicated that CFS and Asthma participants were more likely to recall

specific memories in contrast to the Control participants who were more likely to recall general memories of Activity (Standardised residual 2.4) (see Table 3 and *Figure 1*). Calculated Effect sizes were Cohen's *d* = .52, and *r* = .25, indicating a medium effect size.

Further decompositions revealed that the CFS group differed from healthy controls, $\chi^2(2) = 8.40$, p =.015, Cramer's V = 0.247, as did the Asthma group, $\chi^2(2) = 9.37$, p =.009, Cramer's V = 0.285, but that the CFS group and the Asthma group did not differ significantly from each other, $\chi^2(2) = 0.68$, $p > .70$; both the CFS and Asthma groups recalled proportionately more specific Activity memories than did the healthy controls.

There were no significant associations between Group and Memory Classification for Happy, Pain, or Fatiguing events, all three $p > .24$. See Table 3 for numbers of specific and general memories for each group.

Table 3.

Number and Percentage of Specific and General Memories for Each Memory Type and Group

		CFS		Asthma		Control	
Memory classification	Memory type	*n* = 87		*n* = 56		*n* = 60	
Specific		N	%	N	%	N	%
	Happy event	72	82.8	44	78.6	43	72.9
	Pain event	48	55.8	31	55.4	38	64.4
	Fatigue event	38	43.7	27	48.2	24	40.7
	Activity event	40	45.9	30	53.6	18	30.5
	Std. Res. for Activity	0.3		1.1		-1.5	
General Categorical							
	Happy event	8	9.2	5	8.9	5	8.5
	Pain event	15	17.4	14	25.0	14	23.7
	Fatigue event	32	36.8	18	32.1	25	42.4
	Activity event	21	24.7	12	21.4	28	47.5
	Std. Res. for Activity	-1.0		-1.2		2.4	
General Extended							
	Happy event	7	8.0	7	12.5	12	18.6
	Pain event	23	26.7	11	19.6	7	11.9
	Fatigue event	17	19.5	11	19.6	10	16.9
	Activity event	25	29.4	14	25.0	13	22.0
	Std. Res. for Activity	0.6		-0.1		-0.6	

Note. Standardised residuals values from chi-square analysis on memories of Activity

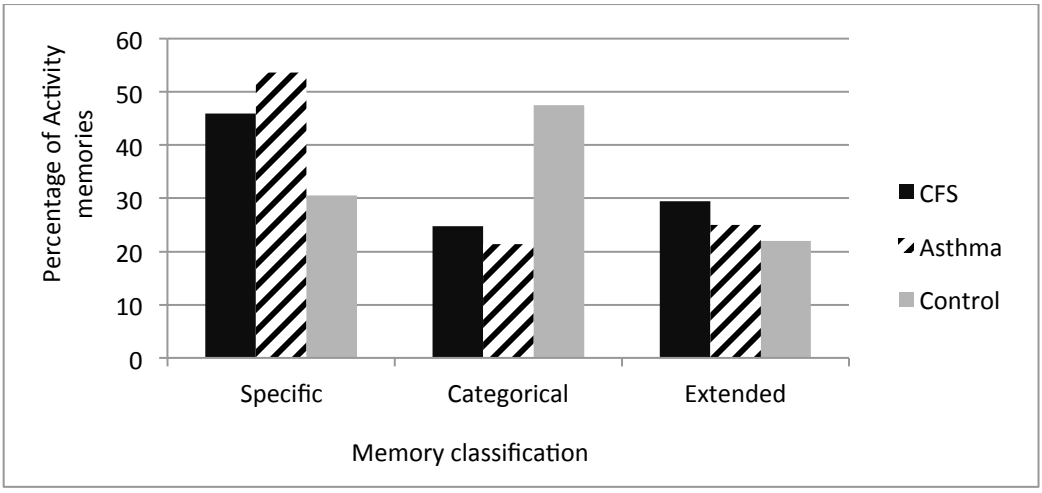


Figure 1. The percentage of Specific, General Categorical, and General Extended memories of Physical Activity for each group (CFS, Asthma, Healthy Control).

Memory properties

Recency of memories (how long ago the recalled event has occurred) did not differ significantly between groups, for all ANOVA tests for each memory type $p > .10$. Therefore, group differences in recall of general and specific Activity memories were unlikely to be due to the CFS and Asthma groups remembering more recent events, or the Control group remembering more distant past. Vividness ratings for each memory type also were not significantly different between groups, in all cases $p > .05$.

Memory frequency ratings (how often one thinks about the event) were not significantly different between groups for Happy, Pain or Fatigue memories, all three $p > .28$. A significant difference between the three groups in terms of the frequency of recall of Activity memories F (2, 199) = 5.12, p = .007 showed that the CFS group thought about Activity memories significantly more often M = 2.44 (which corresponds to between 10 and 20 times since the event happened) (SD = 1.40) than Controls M = 1.83 (corresponding to less than 6 times since the event occurred) (SD = 0.93), planned comparison (Bonferroni correction) p = .011. The Asthma group M = 2.43 (SD = 1.19) also thought about Activity memory more often than the healthy controls, planned comparison (Bonferroni correction) p = .028.

Therefore, group differences in general versus specific recall of Activity memories could be due to the tendency of CFS and Asthma groups to think about recalled activity events more frequently. To investigate the potential effect of recall frequency on the generality of Activity memories, a multinomial logistic regression was conducted, where

group membership (CFS, Asthma, Control) was the categorical predictor, Activity memory frequency the continuous covariate, and memory classification (Specific, General Categorical, General Extended) was the categorical outcome variable. Age was added as a covariate, due to its potential effect on memory recall. The backward stepwise method was used for variable entry, and the main effects of the three variables (Group, Frequency, and Age) and their interactions were investigated.

At step 1, the interaction Group*Frequency*Age, and all interactions involving Age were removed due to the non-significance of the likelihood ratio, all chi square $p > .15$. The final model explained a significant amount of variability χ^2 (6) = 22.57, p = .001, R^2 = .11 (cox & Snell), and .12 (Nagelkerke). The model also showed a good fit for the data, Pearson χ^2 (392) = 398.78, p = .396, Deviance χ^2 (392) = 407.23, p = .287, demonstrating non-significant difference between the observed data and the data predicted by the model.

The parameter estimates presented in Table 4 showed that the group membership had a significant effect on whether a person would recall a specific or general memory. The odds of a healthy control participant recalling a general activity memory rather than a specific memory were significantly higher than for the CFS group b = 1.46, Wald χ^2 (1) = 9.8, p = .002. The odds ratio of 4.32, 95% CI [1.73 – 10.79] indicated that a healthy control participant had a 4.32 times greater chance of producing a general memory than a participant with CFS or asthma. The odds of producing categorical versus specific memories were not significantly different between CFS and asthma groups, $p > .47$. The odds of producing an extended versus specific memory were not significantly different for any of the groups, all $p > .10$. Frequency of recalled memories was a significant predictor only of extended memories (which meant that people thought more often about their extended memories, for example holidays), b = .47, Wald χ^2 (1) = 9.94, p = .002. Multinomial logistic regression analysis for the other Memory Types (Fatigue, Pain, Happy) revealed no significant effects of frequency, age or group on memory generality, all $p > 0.30$.

Table 4.

Multinomial Logistic Regression for Activity Memories

Activity Memory Classification	*B* (SE)	95% CI for Odds Ratio Lower	Odds Ratio	Upper
Categorical				
Intercept	-1.33 (.49) **			
Frequency	.18 (.15)	0.89	1.19	1.60
Group = 0	1.46 (.47)**	1.73	4.32	10.79
Group = 1	.31 (.44)	0.58	1.36	3.22
Extended				
Intercept	-1.95 (.51) **			
Frequency	.47 (15) **	1.19	1.59	2.13
Group = 0	.75 (.51)	0.78	2.11	5.71
Group = 1	.32 (.43)	0.59	1.37	3.16

Note: * p < .05, ** p < .01, *** p < .001.

Note: The reference category is Specific Memories

The relationship between Activity memory specificity and self-report measures

Univariate ANOVAs were used to investigate a relationship between self-report measures and memory specificity. General Categorical and General Extended memories were collapsed into one category of General memories, in order to have a similar number of participants in the two groups. The analysis was conducted separately for each group.

For the CFS group, Activity memory specificity was significantly associated with the Behavioural disengagement, F (1, 83) = 7.28, p = .008. Participants with CFS who recalled specific memories were less likely to use behavioural disengagement as a coping strategy M = 0.79 (SD = 1.3) than those who recalled general Activity memories M = 1.71 (SD = 1.60).

The associations between memory specificity and CFS symptom frequency, fatigue and physical functioning were non-significant, all p > .34. Similarly, there were no significant associations between Activity memory specificity and activity measures, all p > .05, or between Activity memory specificity and fear of movement measure, p > .05; or between Activity memory specificity and mood measures (HADS and PANAS), all p > .20.

The same analysis within Asthma group demonstrated that Activity memory specificity had a significant effect on the coping style of Denial, F (1, 54) = 5.26, p = .026, where participants with asthma who recalled specific memories were less likely to use denial as a strategy for coping with stress, M = 0.20 (SD = 0.55), than those who recalled general Activity memories, M = 0.81 (SD = 1.33). The results of other comparisons were non-significant, all p > .05.

None of the comparisons of the scores' on self-report measures between people who recalled general and people who recalled specific memories within the healthy control group reached statistical significance, all $p > .05$.

Memory Generality and Perspective

Univariate ANOVAS compared groups (CFS, Asthma, Control) on field and observer ratings of each memory type (Fatigue, Pain, Activity, Happy). The groups did not differ significantly on field ratings of any of the memory types, all $p > .05$; or on observer ratings of any of the memory types, all $p > .50$. It means all participants viewed their memories in a similar way be it through field or observer perspective.

Memory Generality and Field Perspective

Two-way ANOVAs with group (CFS, Asthma, Control) and memory classification (Specific, General) as between measures, and field perspective as dependent variable, did not show any main effects or interactions for Fatigue, Pain, or Happy memories; in all cases, $p > .20$.

The analysis showed a significant group by memory classification interaction for Activity memories F (2, 194) = 4.31, p = .015, η^2 = .042, but no significant main effects of group or memory classification $p > .40$. The significant interaction indicated that group ratings on field perspective differed within Specific or General Activity memory categories (see *Figure 2*).

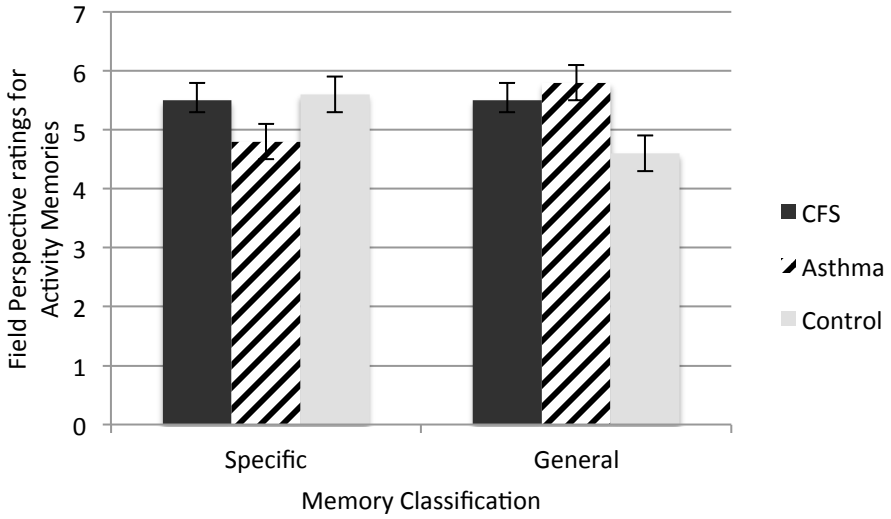


Figure 2. Field perspective ratings for specific and general Activity memories for three groups (CFS, Asthma, Healthy Control).

The hypothesis that the CFS group would rate specific activity memories higher on field perspective was not supported; three independent *t*-tests (CFS vs control, CFS vs Asthma, and Asthma vs control) did not show any significant differences, all $p > .10$.

The CFS group rated general Activity memories significantly higher on field perspective than the control group, $t(85) = 2.33$, $p = .022$. The Asthma group also rated general Activity memories significantly higher on field perspective than the control group, $t(65) = 2.84$, $p = .006$. CFS and Asthma groups did not differ on field ratings of general memories, $p > .40$. Applied Bonferroni correction for multiple comparisons (0.05/3) indicated that *p* value should fall below .016. The results of the comparison between the asthma and control groups meet that requirement with *p* at .006. This suggests the chance of type I error for the comparison of CFS and control groups may be too high.

Memory Generality and Observer Perspective

Two-way ANOVAs with group (CFS, Asthma, Control) and memory classification (Specific, General) as between measures, and observer perspective as dependent variable did not show any main effects or interactions for Pain or Happy memories, all $p > .20$.

Fatigue memories and Observer Perspective

The analysis showed a significant group by memory classification interaction $F(2, 194) = 3.33$, $p = .038$, $\eta^2 = .033$ for Fatigue memories, but no significant main effects of group or memory classification, $p > .23$. The significant interaction indicated that group ratings on observer perspective differed within Specific or General Fatigue memory (see *Figure 3*).

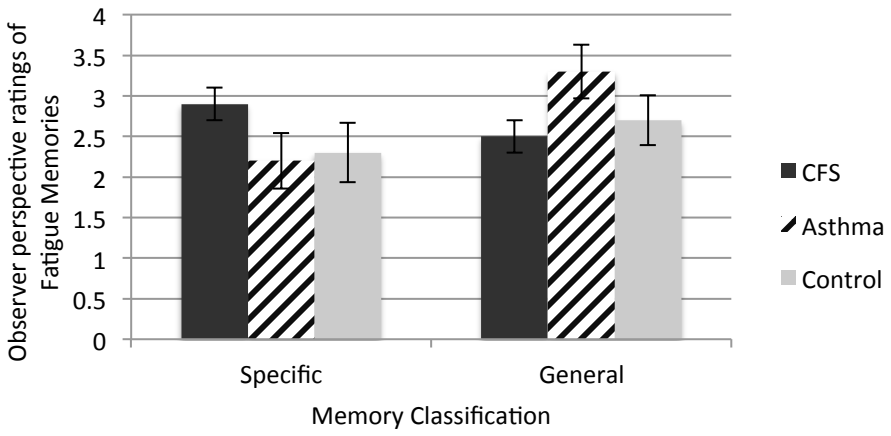


Figure 3. Observer perspective ratings for specific and general Fatigue memories for three groups (CFS, Asthma, control).

Planned comparisons (CFS vs Control; CFS vs Asthma) showed that the CFS group, *M* = 2.97 (*SD* = 1.92), did not differ from the control group *M* = 2.33 (*SD* = 1.20) or Asthma group *M* = 2.22 (*SD* = 1.71) in observer ratings of specific fatigue memories, for both $p > .10$.

The hypothesis that the CFS group would rate general fatigue memories higher on observer perspective was not supported. Independent samples *t*-tests did not show significant differences between CFS *M* = 2.49 (*SD* = 1.86) and control *M* = 2.74 (*SD* = 1.70) groups or between CFS and asthma *M* = 3.28 (*SD* = 1.98) groups, both $p > .05$.

Paired samples *t*-tests showed that within Asthma group general Fatigue memories *M* = 3.28 (*SD* = 1.98) were rated significantly higher on observer ratings than specific *M* = 2.22 (*SD* = 1.71), $t(54) = 2.12$, $p = .039$. Observer ratings of general and specific Fatigue memories were not significantly different for the CFS or control groups, $p > .20$.

Activity memories and Observer Perspective

The analysis of the effect of group and memory classification on the observer perspective ratings of Activity memories showed a significant group by memory classification interaction, $F(2, 194) = 3.56$, $p = .030$, $\eta^2 = .035$, but no significant main effects of either group or classification, $p > .60$ (see *Figure 4*).

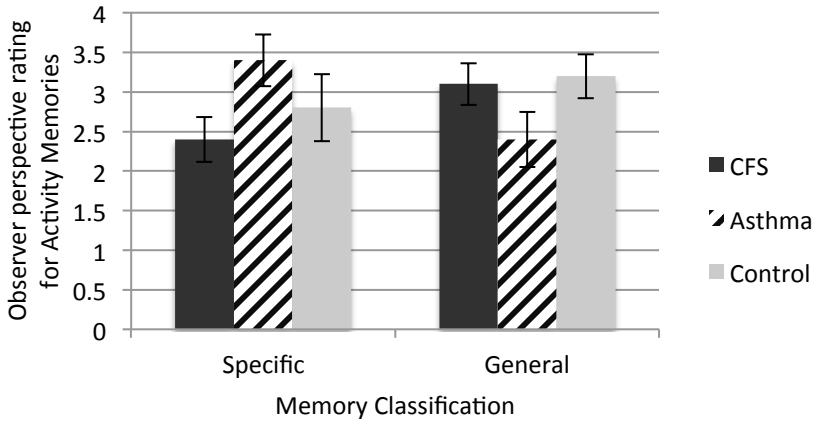


Figure 4. Observer perspective ratings for specific and general Activity memories for three groups (CFS, Asthma, control).

Independent samples *t*-tests demonstrated that the CFS and control groups did not differ in observer perspective ratings of specific Activity memories, $p > .43$. However, the CFS group rated specific Activity memories significantly lower on observer perspective than the asthma group, $t(67) = 2.31$, $p = .024$.

The hypothesis that the CFS group would rate general Activity memories higher on observer perspective was not supported. Independent samples *t*-tests did not reveal significant differences between CFS and healthy controls, CFS and asthma groups, or between the asthma group and healthy controls, all $p > .06$. Group means and standard deviations for field and observer perspective of specific and general Activity memories are presented in Table 5.

Table 5.

Field and Observer Perspective Ratings for CFS, Asthma, and Control Groups for General and Specific Activity Memories.

		CFS *M* (SD)	Asthma *M* (SD)	Control *M* (SD)
Field	Specific	5.5 (6.8)	4.8 (1.8)	5.6 (1.5)
	General	5.5 (1.6)	5.8 (1.6)	4.6 (1.6)
Observer	Specific	2.4 (1.5)	3.4 (1.9)	2.8 (1.9)
	General	3.1 (1.9)	2.5 (1.9)	3.3 (1.6)

Activity memories – emotional impact

Chi-square results did not show a statistically significant difference in emotional valence of Activity memories among the three groups, CFS, Asthma, and healthy controls, $p > .15$ (see Table 6).

Table 6.

Results of Chi-square Test and Descriptive Statistics for Emotional Valence of Activity Memories by Group

	Group		
Activity Memories	CFS	Asthma	Control
	n (%)	n (%)	n (%)
Positive	38 (44)	14 (25)	24 (40)
Neutral	39 (45)	34 (61)	31 (53)
Negative	9 (11)	8 (14)	4 (7)

Note. $\chi^2 = 6.51$, df = 4. Numbers in parentheses indicate column percentages.
*p < .05, ** p < .01

Within each group, the analysis of the relationship between the emotional valence of Activity memories and specificity of Activity memories also did not show significant associations, for all three groups $p > .10$. Therefore, for CFS, Asthma and control groups, positive memories were not more likely to be specific than neutral or negative memories.

Thematic Analysis

Activity memories

Investigation of the content of physical Activity memories produced six main themes:

1. Exercise – the theme concerns some type of prolonged or regular strenuous physical activity. Participants described their memories of being physically active, in relation to fitness, sport, training, or structured exercise. Descriptions of activities included adjectives such as strenuous, vigorous, intense, energetic. It was the most prevalent theme for all participants, 95 (47%) of all participants described being unusually physically active in relation to exercise. Frequency comparison between groups suggested that exercise memories were significantly more prevalent in the healthy control group 43 (45%) than for CFS group 28 (30%) or for the asthma group 24 (25%) χ^2 (199) = 38.77, $p < .001$. Additional observation suggested that for healthy participants these exercise memories were primarily classified as general 29 (49%), while for CFS and Asthma the majority of exercise-related memories were classified as specific 11 (40%) and 14 (60%), respectively.

"One time, I was having a good spell, so I decided I was going to bike 40 miles on a sandy trail. It actually went well". (CFS, Female, 22)

The examples of memories include primarily CFS group. The rest of the examples of memories from the asthma and control groups are presented in the Appendix C.8.

The major Exercise theme included 4 subthemes:

1) Physical challenge: Mention of an event that involved a bout of vigorous physical activity

"Center Parcs High Ropes Course" (CFS, Female, 30)

2) Regular exercise - Mention of a type of exercise done on a more regular basis (e.g. running, cycling, swimming, gym).

"Going cycling with my dad. Cycled 6 miles." (CFS, Female, 42)

3) Sport and/or sporting competition – Mention of sporting competition, training for competition, or involvement in competitive sports.

"Cycle race in late September 1982. Herts League 50 mile Road Race" (CFS, Male, 50)

4) Games/Recreation – mention of recreational activity, one time or regular game.
"My birthday again, played football with my cousins and brother and pretty much screwed my body up doing so". (CFS, Male, 24)

2. Walking – this theme was so prevalent that it was excluded from the exercise-related theme and put into its own category. It was the second most prevalent theme, with 32 (16%) of the participants describing memories in relation to walking, CFS 14 (44%), Asthma 11 (34%), Control 7 (22%). The theme included memories that mention walking or walking-related activities, e.g. hiking.

"Walking to the post office" (CFS, Female, 46)

This theme included subthemes, such as intense walking (e.g. hiking), more relaxed walking (e.g. on holiday, a stroll in the park), and chores-related walking (e.g. walking to the post office).

1) Higher intensity walking – included a mention of prolonged rigorous high intensity walking.
"Day before yesterday… Long walk, 2 hours" (CFS, Female, 33)

2) Holiday/Relaxed - mention of relaxation, holiday time.
"I went for a walk near where I live… I was able to walk further than I expected and felt really uplifted… I did not think too much about whether it would be something I could repeat, or whether I would pay the price for doing it… In fact I didn't just enjoy it, I felt serene and elated, if that makes sense?" (CFS, Female, 60)
Full memory description can be found in Appendix C.8

3) Chores-related - mention of walking in order to complete chores.
"Walking to the post office" (CFS, Female, 46)

3. Chores – the memories within this pattern fell into the theme reflecting daily grind type of activities, e.g. shopping, tidying, gardening, housework. Activities distinguished between inside home, housework activities, and outside activities (e.g. shopping, gardening). Twenty seven (14%) of all participants described memories within this theme, CFS 9 (33%), Asthma 13 (48%), Control 5 (19%).

"Walking around the shops at Trafford Center" (CFS, Female, 40)

Two subthemes also emerged within Chores theme:

1) Moving - included memories of moving houses, flats, offices.

"1998, when i moved flat and changed jobs" (CFS, Female, 41)

2) Daily grind - included inside home, housework type of activities, and external (e.g. shopping, gardening) types of activities.

"After a new move… doing my garden" (CFS, Female, 52)

4. Fun – this theme included pleasant memories of activities with friends and families (e.g. celebrations, parties). These memories were more prevalent in CFS 21 (77%) than in Asthma 4 (15%) and Control 2 (7%) groups. Crosschecking with memory classification showed that in the CFS group these memories were mainly classified as specific 18 (88%).

"Bowling for my daughter's birthday" (CFS, Female, 35)

5. Work – this theme included memories of work, employment, or a job. That kind of work happened outside of home and was not related to doing chores outside the house. Nine (4.5%) of the participants recalled memories that fit that theme: CFS 7 (78%) and Asthma 2 (22%).

"working a Friday a while back. catch up." (CFS, Female, 31)

6. **Health-related** – this theme included memories regarding health (e.g. illness, symptoms, hospital, rehabilitation). Nine (4.5%) participants from CFS and Asthma groups recalled memories that fit this pattern, and none of the healthy control participants.

"After starting treatment for orthostatic hypotension, I was feeling ambitious and wanted to see if it had impacted my exertional thresholds. I walked about 4 blocks with my mother and it was still too much." (CFS, Female, 34).

Fatigue memories

Investigation of the content of Fatigue memories produced 11 main themes:

1. **Travel** – this theme included any mention of travel (e.g. flying, driving, trips). It was the most prevalent theme in fatigue memories. In total, 40 participants (20%) of the sample described increased fatigue post-travel.

"Coming back from holiday this summer. travelling back" (CFS, Male, 34)

2. **Study** – this theme reflected any description of school, university, or studying. It was the second most prevalent theme, mentioned by 34 (17%) of participants. The theme was significantly more prevalent among the asthma 15 (27%) and healthy control 12 (20%) groups, as compared to the CFS group 7 (8%), χ^2 (201) = 65.34, $p < .001$.
"After having handed in my masters dissertation" (CFS, Female, 26)

3. **Profound fatigue** – this theme reflected comments about fatigue not related to specific events, and included descriptions such as "all the time", "every day", "constant". It was the third most prevalent theme, observed primarily in the CFS group 24 (83%). 30% of all fatigue memories within the CFS group were classified as Profound. This theme was not unique to the CFS group, but only 2 healthy control participants and 3 people from the asthma group made comments that were classified as such.

"All the time. Exhaustion from health problems" (CFS, Female, 27)

4. **Work** – this theme reflected work, work-stress, employment, job-related fatigue memories. 22 participants (11%) overall recalled work-related fatigue. It was slightly more predominant among healthy control group 10 (17%), than in CFS 6 (7%) and Asthma 6 (11%) groups.

"Being exhausted at work and unable to excel in my job." (CFS, Male, 44)

5. **Post-pleasant event activity** – this theme reflected memories of being tired after a celebratory, pleasant event.

"Yesterday - post holiday. My Birthday" (CFS, Female, 42)

6. **Illness** – these memories recalled fatigue due to illness, specifically mentioning illness, injury, or trauma.

"When I had a gastro bug and had been being ill in the bathroom for hours and missed out on sleep." (CFS, Female, 30)

7. **Sleep** – this theme reflected memories regarding sleepiness, sleep problems, insomnia, sleeplessness. Only one control participant recalled such a memory, in contrast to 5 (6%) from the CFS group, and 5 (9%) people from the asthma group.

"Was exhausted from a tough day but only managed to sleep 3 hours that night, so the next day I was even more tired and couldn't drive. Not enough sleep!" (CFS, Female, 21).

8. **Chores** - this theme included mentions of fatigue in relation to housework, shopping, or anything related to daily types of activities outside of work/school. Asthma participants did not recall any fatigue memories with this theme.

"Shopping, boring, necessary, noisy" (CFS, Female, 50)

9. **Care** – these memories described an event or a period of time of being a carer. This theme was specific to CFS 2 (2%) and Asthma 5 (9%) groups.

"When I was looking after my disabled brother" (CFS, Female, 22)

10. **Exercise** – the theme reflected memories of fatigue in relation to exercise, and post-exercise fatigue. Four from the control group, 2 from the CFS group and one person from the asthma group recalled post-exercise fatigue.

"the doctor advised me to go to the gym, which I did, then came home and passed out with fatigue" (CFS, Female, 35)

11. **Post - Negative event** – these memories described a negative event, primarily emotional event, which was not an illness, injury, or trauma, that led to increased fatigue. Only four (5%) people from CFS group and one person (2%) from the asthma group recalled memories classified into this theme.

"When wife gave up on me" (CFS, Male, 53)

Pain Memories

Investigation of the content of pain memories produced 8 main themes:

1. **Injury** – memories of pain experienced post-injury. This was the most prevalent theme among the entire sample 90 people (45% of the sample). It was most prevalent among the control group 42 (71% of the group), compared to the CFS group 16 (18% of the group) and Asthma group 32 (57% of the group). Frequency comparison suggested a significant group difference, χ^2 (202) = 69.79, $p < .001$.

"I twisted my knee. I remember it hurting so much I couldn't cross the room without agony." (CFS, Female, 30)

2. **Illness** – memories of experiencing pain in relation to specific illness. It was the second most prevalent theme in the sample with 35 (17%) people recalling pain memories due to illness. It was more prevalent in the CFS group 23 (26% of the group), than in the Asthma group 8 (14% of the group) and the Controls 4 (7% of the group).

"When I had glandular fever and had an intensely bad sore throat with acute tonsillitis so that I couldn't even swallow" (CFS, Female, 26)

3. **Chronic pain** – these memories included mentions of back pain, headache, period pain, or repetitive experience of pain in general.

"Now. all the time, suffer". (CFS, Female, 30)

4. **Post event** – these memories reflected experiencing pain after an event that was outside of medical/illness-related or injury context. This theme included memories of pain after such events like a family dinner, or going out, or making a trip. Importantly, these memories were mostly specific to the CFS group where 18 (21%) people recalled memories with this theme, compared to none from the control and only three (5%) from the asthma group.

"Walking around the city all day long" (CFS, Female, 21)

5. **Operation** – this theme reflected memories that involved pain post surgery, operation, or medical interventions.

"Taking part in a 3 week Function Restoration Course at the Nuffield + Visiting Dentist" (CFS, Female, 58)

6. **Birth** – a number of memories were in relation to giving birth, therefore that was kept as a separate theme, which was expressed among all groups, 9 people overall (5% of the sample).

"Giving birth" (CFS, Female, 49)

7. **Exercise** – this theme reflected pain experienced after rigorous exercise and strenuous activity. Only four memories reported by people from the control group (7% of the group) were classified into this theme, and none from CFS or asthma groups.

"Last night circuit training" (Healthy, Female, 32)

Happy memories

Investigation of the content of Happy memories produced five main themes.

1. **Pleasant event** – this theme included memories of joyful, fun, pleasant activity with friends, family or alone. This was the most prevalent theme for all participants 77 (38%) of the sample, spread equally across the groups, CFS 27 (31%), Asthma 24 (42%), and Control 26 (44% of the group).

"Having a picnic with friends on gap year" (CFS, Female, 21)

2. **Celebration** – this theme included memories of being happy after celebratory events (e.g. birthdays, weddings). It was the second most prevalent theme, CFS 35 (40%), Asthma 16 (30%) and Control 17 (30%).

"Watching my son being page boy at my friend's wedding and seeing her look so beautiful and happy." (CFS, Female, 29)

3. **Achievement** – this theme reflected happy memories of achieving a goal, a turning point, or a finishing something (e.g. graduation, getting a new job). This was the third most prevalent happy memory, CFS 17 (20%), Asthma 8 (15%), Control 10 (17%).

"When I was promoted to a director" (CFS, Female, 48)

4. **Relationships** – in this theme were included memories that reflected romantic and relationships-related events, with 17 (8%) people from the total sample recalling memories reflecting this theme.

"When I first starting going out with my boyfriend" (CFS, Female, 23)

5. **Symptom free** – this theme was specific to CFS, 4 people with CFS (5% of the CFS group) reflected on memories of joy at being able to do something while feeling free of symptoms.

"Sisters of mercy gig and symptoms generally low" (CFS, Male, 42)

Discussion

The study investigated the features of autobiographical memories among people with CFS in comparison to asthma and healthy control groups. Two contrasting hypotheses were tested regarding autobiographical memory retrieval by the CFS group. One hypothesis

predicted that the CFS group, compared to healthy controls, would retrieve overgeneral memories when asked to recall unusually high activity, fatigue, pain or happiness. The hypothesis was based on the observed comorbidity of depression and CFS (Janssens et al., 2015) and the prevalence of overgeneral memories in populations with depression (Williams et al., 2007). In spite of the elevated depressed mood observed in the CFS group in the current study, that hypothesis was not supported.

The alternative hypothesis, predicting that CFS group would recall specific memories of fatigue, pain and activity was partially supported. The results showed that the CFS group, compared to the healthy controls, retrieved more specific Activity memories, thus supporting the alternative hypothesis. The latter predicted increased memory specificity in CFS group on the basis of a number of theoretical approaches and empirical findings. It was argued that people with CFS would prefer to utilise a direct retrieval strategy, preserving their cognitive resources. Enhanced processing of illness-relevant and health-threat information, such as amplified attentional focus on symptoms (Knoop et al., 2010), accompanied by the CNS sensitization (Nijs et al., 2012) would also lead to increased memory specificity for events that are potentially health-threatening (Deary, 2008), and illness-relevant (Nijs et al., 2013).

Increased specificity of activity memories in the CFS group may be due to over-processing of activity-related information, an enhanced processing of health-threat and illness-relevant information. Thus, the finding fits within cognitive theories of CFS. These theories propose that increased attention towards somatic and health-threat information, and enhanced cognitive processing of somatic, symptom- and illness-related information maintains CFS symptom perpetuation (Fry & Martin, 1996a, 1996b; Knoop et al., 2010; Moss-Morris, 2005). Increased activity memory specificity is also in line with the finding by Sohl and Friedberg (2008) that highly intense fatigue resulted in formation of more representative and accurate memories of tiredness, and with the evidence that people with CFS are more highly aware of activity patterns and resulting fatigue levels (Evering, Tonis, et al., 2011; Evering, van Weering, et al., 2011). If activity is regarded as a health-threat to the established and vigilantly maintained energy balance (Deary, 2008), then it may be accompanied by enhanced processing and increased monitoring of activity and energy levels in order to prevent symptom exacerbation. Then specificity of activity memories would be one facet of that over-monitoring process. That fits with the previous findings demonstrating that people retrieve specific memories of events that involve direct encounters with a source of their fears or distress (Golden et al., 2007; Wenzel et al., 2003).

Similarly, the proposed oversensitivity of the central nervous system in CFS may underpin the attentional focus on physical activity and consequent sensations, making sensory-perceptual features more salient. The evidence of specific activity memories in CFS fits with the Conway and Pleydell-Pierce (2000) model, which proposes that direct retrieval, an involuntary, automatic, spontaneous and rapid process, would lead to more specific recollection. As an automatic and direct process, it may conserve cognitive resources, and therefore would result in more specific memories in CFS. The need to preserve cognitive resources would prompt people with CFS to utilise the direct retrieval method of the memory system, tapping into sensory-perceptual experience and resulting in specific memories (Conway & Pleydell-Pearce, 2000).

Fittingly, Hou and colleagues (2014) demonstrated that attentional bias for health-threat in CFS may be underpinned by reduced executive control. Thus, in the CFS group, specific memories may reflect reduced executive capacity and cognitive resources, therefore exacerbating attentional bias towards activity, exertion, and somatic symptoms. That would amplify sensations of fatigue, and its higher intensity would be reflected in more detailed and accurate memories (Sohl & Friedberg, 2008).

Furthermore, high self-relevance of activity memories may also result in their over-specificity, as suggested by Sumner (2011) and Golden et al. (2007) who demonstrated that memory specificity increased together with self-relevance of memory cues. Activity events may be more self-relevant to the CFS group than to healthy controls, because their sense of self and their perception of their illness status may be linked to their concept of activity.

The hypothesis predicting overgeneral memory recall in the asthma group was not supported. The asthma group also demonstrated specific memories of activity. That also may be explained by the greater self-relevance of activity cues in the asthma group. In asthma, physical activity may induce an anxious state, because it may bring on breathlessness, wheezing, and potentially an asthma attack. For example, people with asthma may confuse change in breathing patterns brought on by exercise with the change in lung function due to an impending asthma attack, and may become fearful of physical activity (Emtner et al., 1996). Consequently, there is evidence of the association between greater anxiety and reduced activity in asthma (Strine et al., 2008). Thus, physical activity may have direct relevance and may be highly salient to people with asthma, which would lead to more specific activity memories. It is similarly fitting with the evidence of the increased specificity of memories that involve a source of fear or distress (Golden et al., 2007; Wenzel et al., 2003). Over-specificity of activity memories could be confounded by

memory recency or vividness; however, the groups did not differ on either memory property. Similarly, the frequency of memory recall had no effect on memory specificity.

There was no evidence of group differences in the retrieval of fatigue, pain, or happy memories. Increased levels of fatigue and decreased functioning in CFS (Fuentes et al., 2001; Jason, Timpo, et al., 2009; Sohl & Friedberg, 2008) may explain the lack of memory specificity. If fatigue and pain are perceived as constant and pervasive sensations, even in spite of their self-relevance, they may be recalled in a more general manner. Importantly, although fatigue and pain are highly relevant to CFS, they are not unique to CFS, and they are frequently experienced by the general healthy population (Kocalevent, Hinz, Brähler, & Klapp, 2011; Macfarlane, Beasley, Smith, Jones, & Macfarlane, 2015). Therefore, fatigue and pain may be equally self-relevant to CFS, asthma and healthy people. As a result, there may not be any differences between these populations, in whether these sensations are recalled in general or specific manner.

The lack of group differences in the retrieval of happy memories between CFS, asthma and healthy controls suggests that the CFS and asthma groups process autobiographical memories differently from people with depression, who consistently show overgeneral memories in response to all cues regardless of valence (Sumner et al., 2010). This observation is especially surprising when one bears in mind the elevated risk of depression, higher depressed mood and negative affect found in CFS; in CFS, then, depressed mood does not appear to be underpinned by the kind of negative schema hypothesised to be present in depression (Gotlib & Joormann, 2010).

On the basis of the theory that functional avoidance is one of the mechanisms of OGM (Williams et al., 2007) and considering the evidence for the behavioural avoidance of activity in CFS (Nijs et al., 2013), the hypothesis was tested that behavioural disengagement in CFS and denial in asthma would be associated with overgeneral memories. Accordingly, the CFS group (but not asthma or control) showed a relationship between increased behavioural disengagement and overgeneral activity memories. In contrast, in the asthma group overgeneral memories were associated with a greater likelihood of using denial as a coping strategy.

In summary, neither the CFS nor the asthma group showed the typical pattern found in depression, of overgeneral autobiographical memory in response to both positive and negative cues, despite having elevated levels of depression. Instead, both the CFS and asthma groups showed more specific autobiographical memories of physical activity, compared to healthy controls. No differences were found between the CFS, asthma and

healthy controls in memory generality/specificity for fatigue, pain, and happy autobiographical memories.

Overall, no group differences were detected in the adoption of field or observer perspectives for any of the memory types. The main hypothesis of the interaction between memory generality and perspective predicted that the CFS group would demonstrate the pattern of viewing specific fatigue, pain, and activity memories from the field perspective, and general fatigue, pain, and activity memories from the observer perspective, compared to the control and asthma groups. The hypothesis with regard to fatigue and pain memories was not supported.

Regarding activity memories, the opposite pattern was detected, with the CFS and Asthma groups rating *general* activity memories higher on field perspective, compared to the control group. Previous research showed that events recalled from the observer perspective were more likely to be high in threat and low in emotional engagement with the memory (Nigro & Neisser, 1983). However, in the current study an investigation of the emotional valence of activity memories showed that they were primarily positive and neutral for all three groups, indicating that activity memories were not regarded as highly threatening by the CFS participants. The positive or neutral emotional valence may explain why general activity memories were viewed from the field perspective by CFS and Asthma groups, in accordance with the evidence suggesting that positive memories would be more likely to be viewed from the field observer perspective (D'argembeau, Comblain, & Van Der Linden, 2003).

The rating of general memories higher on field perspective is once again a pattern that differs from people with depression, who tend towards observer perspective, which is associated with greater cognitive and behavioural avoidance and greater negative evaluation of self (Kuyken & Moulds, 2009). Nigro and Neisser (1983) showed that the majority of healthy people recall memories from the field perspective, with only a minority, approximately one-third, of events being recalled from the observer perspective. In the CFS and asthma groups, the tendency to view activity memories from the field perspective extends to overgeneral memories. Another explanation for field view of general memories may be that for the CFS and asthma groups even general activity memories may be more emotionally impactful and richer in feeling and content, as field perspective memories tend to be (Berntsen & Rubin, 2006; Siedlecki, 2015). Looking deeper into the content of memories demonstrated why even general activity memories would be more likely to be viewed from field perspective by CFS and asthma groups.

Exercise was the most frequently recalled activity memory for all participants, but it was significantly more common for the control group and less so for the CFS and asthma groups. Notably, the exercise memories for the control group were more likely to be general, while for the people with CFS and asthma, they were more likely to be specific. Activity memories were primarily pleasant memories, which may explain why CFS and asthma groups rated them higher on field perspective. While exercise was the predominant theme for the healthy controls, for the CFS group and to less extent for the asthma group activity memories were much more varied in content, encompassing primarily physical activity (e.g. sport, exercise, walking), general pleasant events (e.g. family events, social outings), activities that were work-, chores- and, particularly, health-related. Only CFS and asthma groups recalled activity memories that mentioned health, illness, symptoms, hospital, or some sort of physical rehabilitation. This suggests that the CFS and asthma groups have a varied concept of what activity is, while the control group had a more one-dimensional concept. This may explain why activity memories were more specific and rated higher on field perspective, even while there is a high degree of activity fear and avoidance in CFS (Nijs et al., 2013), which was reflected in the fact that the CFS group scored highest on fear of movement.

With regard to activity memories, the general positive slant and the multidimensionality of activity may explain its higher rating on field perspective by the CFS group, regardless of the degree of specificity. That multidimensionality of the concept of activity in the CFS group may be what makes it more self-relevant and linked to sense of self. Activity may be something people with CFS see as profoundly present in all aspects of their daily functioning. That may explain the predominance of specific activity memories in CFS group. In contrast, healthy people interpret activity mainly as exercise and unusual exertion, so their sense of self is much less likely to be tied to the concept of activity.

Fatigue memories showed a similar pattern, with a greater variation of memory themes in the CFS group, and to a lesser degree in the asthma group, than among the controls. Travel was the most prominent theme, but travel in the control group was described more along the lines of long-haul flights, while for the CFS participants it also included driving and walking places. Study and work themes were more common for the healthy and asthma groups, compared to the CFS group. Profound type of fatigue was a theme that emerged specifically in the memories of the CFS group. Those memories were less likely to be specific, and instead reflected the intensity and magnitude of fatigue sensation, and focus on fatigue in all areas of life, not just with regard to activity or exercise.

Informatively, there were very few mentions of exercise-related fatigue by the CFS group. It would be expected that more memories of exercise and physical exertion-related fatigue would have been present in the CFS group, in accordance with the evidence from people with CFS who regard exercise-based treatments as ineffective in reducing fatigue or, indeed, as downright harmful (Action for ME, 2008; ME Association 2010). Similarly, theories, suggesting that fear of movement and exercise avoidance play main roles in CFS symptom exacerbation and maintenance, would predict a higher number of memories of exercise-related fatigue among people with CFS (Nijs et al., 2013). It appears, however, that fatigue, like activity, while being more of a one-dimensional concept for healthy participants, is a much more varied and global one for the CFS group. The latter regarded fatigue as a consequence of different activities in all areas of life. Also, only people in the CFS group, and just one person from the asthma group, mentioned experiencing fatigue after negative events, that were not related to injuries, illnesses, or physical traumas. That indicates that the healthy group may regard feelings after negative events as less physical and more emotional, less fatigue and more sadness and depression. It would be informative to know if healthy people would describe memories of negative events using emotional terms, in contrast to people with CFS who would describe them in terms of feelings of fatigue. The suggestion that the CFS group experiences the sensation of fatigue after a negative event, rather than a depressed mood, would fit with the evidence that people with CFS interpret a wide range of sensations as fatigue and illness symptoms (Moss-Morris & Chalder, 2003; Moss-Morris & Petrie, 2001).

For pain memories, a theme that emerged mainly for the CFS group included pain that was experienced after regular, non-outstanding events, including pleasant events (e.g. a birthday party), and, particularly, after events that included walking or regular daily functioning. That fits with the concept of post-exertional malaise which is regarded as one of the core symptoms of CFS across the range of CFS case definitions and diagnostic criteria.

Similarly to fatigue memories, there was a general lack of memories for pain after exercise or after more rigorous types of activity and exertion in the CFS group. The most dominant themes for all participants were accidental injury and illness. In the CFS group, the illness in question was primarily CFS or an infection/virus, preceding their CFS diagnosis. Childbirth emerged as a theme among female participants, and was the only pain memory that had a positive connotation.

Happy memories were fairly uniform for all three groups, and included celebrations of momentous occasions and achievements (e.g. graduations), or a variety of pleasant happy

events (e.g. holidays). Unique to the CFS group was a theme of being symptom-free and being able to engage in pleasant activities, or simply experiencing no symptom interference with daily functioning. That fits together with the general pattern observed in the CFS group, who showed the highest fatigue, and lowest physical functioning and activity.

The current study examined the process of cued memory retrieval, but the process of encoding of fatigue, pain and activity memories in CFS remains unexplored. It would be important to investigate earlier memory processes, specifically, the encoding of somatic sensations and illness-related experiences. It may be informative to investigate what kind of memory perspective is present at the encoding stage, and whether the perspective changes at retrieval stage. It may be informative to investigate how memory specificity may be affected by what kind of perspective is adopted at the encoding stage. Memory perspective can be manipulated by asking people to use field or observer perspective at the encoding stage and then measure the number of general or specific memories recalled. Other types of memories should also be explored, beyond fatigue, pain or activity. Specificity of the cues can also be manipulations, for example the more general word "symptoms" may be used as a memory cue or a more specific "post-exertional malaise". The emotional valence of cues can be similarly manipulated to explore the effect on the emotional valence of recalled memories. Furthermore, it would be informative to investigate closer the relations between memory specificity and specific illness cognitions and cognitive and behavioural coping strategies specific to illness rather than the ones employed in coping with general stress.

In terms of limitations, the quasi-experimental design and self-report measures do not allow for conclusions about directions of influence or the causal role of memory specificity in CFS. The memory task in the current study differs from the classical version of the Autobiographical Memory task, which is timed when utilised in laboratory conditions. The online survey software did not provide the opportunity to limit the time participants could spend on one question. Neither did it allow randomisation. All participants were presented with the same order of memory cues: happy, pain, fatigue, and finally activity. Therefore, specificity of activity memories might have been primed by the recollection of happy, fatigue, and pain memories; albeit, that would have been the same process for everyone, not just for the CFS and asthma groups. Most importantly, the representativeness of the sample needs to be considered. While the scores on fatigue and physical function were comparable to other CFS groups in the literature (Friedberg & Sohl, 2009b; Reeves et al., 2005; White et al., 2011), participants in the current study did not undergo medical tests to rule out other possible explanations of fatigue, and therefore their CFS diagnosis might be

questioned. That is one of the disadvantages of any web-based studies that rely on self-report measures.

Further investigation of the memory specificity effect may have implications for such interventions where restructuring of the current perception of activity and increased engagement in activity may be achieved by exploring memories of past activity experiences. Treatments such as Cognitive Behavioural Therapy and Graded Exercise for CFS attempt to change the perception of activity and gradually increase the activity level to battle physiological deconditioning in order for a patient either to return to the premorbid, or achieve a desired level of functioning. The contrast between, on the one hand, the amount of activity one perceives oneself as currently performing and, on the other, the detailed memory of being active in the past, may sensitise people with CFS to that discrepancy in previous and current activity levels. The perception of such discrepancy may lead to distress and prompt the desire to return as quickly as possible to previous activity levels. This may be why those people with more specific memories within the CFS group were less likely to engage in behavioural avoidance. The prevalence of this comparison process may also underpin the "all or nothing" cycle of behaviour found in the CFS population, where bursts of intense activity are followed by severe fatigue (Bazelmans et al., 2006; Moss-Morris, 2005). Therapists could explore the effect of comparing past activity with current activity and whether such comparisons might cause distress, increase the amount of more extreme activity, or interfere with adherence to an exercise regime. If any of these effects are found, clinicians may focus on reducing this tendency to engage in a comparison process.

Chapter 7: Final Discussion

The primary aim of this thesis was to test the hypothesis that people with CFS demonstrate enhanced cognitive processing of illness-related information. This cognitive bias results in an over-perception of symptoms, which contributes to CFS symptom perpetuation (Knoop et al., 2010; Moss-Morris, 2005). The empirical studies focused on three cognitive processes: attention, interpretation, and memory. These were measured using objective experimental tasks, such as exogenous cueing and visual probe, lexical decision, and cued recall, respectively. Two cognitive stages were investigated: preconscious automatic and conscious strategic processing of illness-related, health-threat, and activity information. This final chapter discusses the strength of evidence for the enhanced processing of illness-related information in CFS. The clinical implications of the studies presented in this thesis are discussed in terms of how distortions in cognitive processes and symptom monitoring may be addressed in CFS treatment.

Attention

Experiments investigating attention tested the hypothesis that a negative illness schema in CFS amplifies attentional focus on symptoms, which manifests as attentional bias towards health-threat (Knoop et al., 2010; Moss-Morris, 2005). The early preconscious attentional hypervigilance towards illness-related information was not evident in a group of people with CFS, compared to a healthy control group. Similarly, there was no evidence for preconscious attentional bias towards health-threat under the influence of self-focused rumination in a CFS group, compared to people with CFS in a state of distraction and to healthy controls.

The second attention experiment provided mixed results and was difficult to interpret due to the methodological limitations of the study (specifically, small sample size). Attention was measured under a low and high cognitive load, using an exogenous cueing and a visual probe task, respectively. Additionally, the experiment explored the effect of neutral or depressive mood on attention. An attentional bias towards health-threat was not conclusively shown in the CFS group, as compared to healthy controls and to a group with asthma. The experiment, however, raised a question with regard to the role of attentional avoidance in CFS.

The issue is that there may be two alternative interpretations of the results from the exogenous cueing task in the second experiment on attention. One interpretation may be that the CFS group might have demonstrated attentional avoidance of health-threat. The problem with this interpretation is that the asthma and healthy control groups showed a similar avoidant cognitive strategy. It may be that under low cognitive load, people, regardless of their heath state, tend towards avoidance of health-threatening stimuli.

An alternative interpretation may be that the CFS group demonstrated a healthy attentional pattern, an inhibition of return response, previously observed in exogenous cueing tasks (Lupianez et al., 2006; Posner et al., 1985). The inhibition of return occurs when attention is prevented from returning to a place that has already been attended to in order to move on to a novel stimulus. The occurrence of the inhibition effect in the CFS group may suggest that this aspect of attention is not impaired in CFS. It may also explain why the results are not in line with the evidence for attentional bias in CFS demonstrated by Hou et al. (2008, 2014). In the 2014 study Hou and colleagues found attentional bias only in those people with CFS who had attentional deficits, such as impaired attentional control.

The results from the visual probe task, the high cognitive load condition, partially replicated the Hou et al. (2008) experiment. The CFS group showed an attentional bias towards health-threat, but only in comparison to the asthma group who demonstrated avoidance, and not if compared to the healthy control group. Furthermore, the bias only emerged in neutral mood and was diminished in depressive mood. Hou and colleagues (2008, 2014) found that attentional bias in CFS was independent of the effect of mood, such as anxiety or depression. Therefore, it was expected that in CFS attentional bias would be a pervasive cognitive style, not modulated by their mood state.

The results suggested that higher task difficulty, and consequent increased cognitive load, may activate the illness schema and the attentional bias may emerge. Taking into consideration the finding that impaired attentional control is associated with attentional bias in CFS (Hou et al., 2014), it may be likely that under a high cognitive load attentional control is compromised, negative illness schema may be activated, and the attentional bias towards health-threat becomes evident.

Methodological paradigms

The two experiments on attention were the first to utilise the exogenous cueing task to measure attentional bias in CFS. The lack of evidence for attentional bias was not in line with current cognitive theories that propose increased focus on fatigue as the core cognitive

process behind symptom perpetuation (Knoop et al., 2010; Moss-Morris, 2005) or the evidence from another attentional bias experiment (Hou et al., 2008). The difference in experimental results, however, may be due to different methodologies employed, such as the visual probe task used by Hou and colleagues. A more recent experiment by Hou et al (2014) identified the conditions for attentional bias in CFS, which emerges when attentional control is impaired. Therefore, it is possible that even if the people with CFS who were tested in this thesis had an impairment in attentional control, it may not have become evident, because the exogenous cueing task was too simple, the stimulus presentation time was too short, and competition for cognitive resources was lacking. The findings indicated an absence of attentional bias under the light cognitive load at preconscious and strategic processing levels.

There were also difficulties in the interpretation of results from the exogenous cueing. The task may not be sensitive enough to the early movement of attention due to natural rapidity of responses on valid trials, making it difficult to differentiate between very quick reactions to threat versus similarly quick reactions to non-threat (Fox et al., 2001; Mogg et al., 2008). Finally, the negative illness schema hypothesised to drive the attentional bias may not be activated at such an early cognitive stage, or in the absence of competition for cognitive resources. Finally, the stimuli may not be relevant or threatening enough to tap into a negative illness schema.

Another methodological aspect in need of consideration is the visual probe task. Recent findings suggest that the visual probe paradigm may lack reliability and consistency of measurements, with participants producing different patterns of response on different occasions (Schmukle, 2005; Staugaard, 2009). This has implications for future research if the differences in findings between different studies have more to do with unreliability and inaccuracy of the chosen methods of measurement, as opposed to the presence or absence of attentional bias, or to our ability to tap into an illness schema, or to the recruitment of different populations under the umbrella of CFS.

Rumination, Mood, and CFS Symptoms

One of the research aims of the first attentional experiment was to investigate the relationship between ruminative self-focus, mood, and attentional bias. The hypothesis was based on cognitive theories proposing that excessive rumination on the current physical and psychological state may amplify selective attention to somatic symptoms in CFS (Brosschot, 2002; Deary et al., 2007). There was no evidence that rumination had an amplifying effect on

attentional bias. However, there was evidence of self-focused rumination intensifying negative mood in people with CFS. In contrast, being in a state of distraction led to a significant decrease in negative mood in CFS. The above evidence might point to an idiosyncratic process of emotion regulation in CFS, also supported by fMRI data showing reduced activity in people with CFS within the networks concerned with emotional regulation and inhibition (Caseras et al., 2008).

The results in this thesis hinted at a complex interaction between the direction of cognitive focus (towards self or away from self), negative mood and symptom reporting in CFS. There was a positive correlation between negative mood and the number of symptoms reported for those participants with CFS who were under the effect of self-focused rumination. This is in line with findings of the positive relationship between negative mood and symptom reporting in healthy populations (Howren & Suls, 2011). A combination of ruminative self-focus and negative mood may amplify subjective perception of symptoms and lead to an increased reporting of symptoms.

Participants with CFS whose thoughts were directed away from somatic information experienced less emotional distress, and their symptom reporting was not associated with increased negative mood. Thus, distraction can be a temporary protective technique, which has been documented as effective in the short-term, although not long-term (Mullen & Suls, 1982). The effectiveness of distraction as a coping technique in chronic conditions may be compromised by the influence of catastrophic and fear-related cognitions and lead to an increase in suffering (Johnson, 2005). However, attentional distraction can be effective for short periods of time, and specifically during a bout of exercise (Deforche & De Bourdeaudhuij, 2015; Hutchinson, Karageorghis, & Jones, 2014; Jones, Karageorghis, & Ekkekakis, 2014), which can be utilised in exercise-based treatments of CFS.

Activity, Avoidance and Fear of Movement

Another aspect of attention investigated in this thesis was the processing of activity-related information. It was proposed that activity-related information may be perceived as health-threatening, similarly to the illness-related information, because it is relevant to somatic sensations, body monitoring and the CFS symptom of post-exertional malaise. Therefore, in the framework of the negative illness schema, people with CFS may be similarly biased towards activity-related information as towards illness stimuli. The hypothesis was based on Deary's (2008) theory that illness representations in CFS may reflect events that are perceived as dangerous to the established physiological, affective,

cognitive, and behavioural balance. Anything that threatens the balance may be perceived as a health-threat. Thus, if people with CFS believe that activity leads to symptom exacerbation, they may consequently perceive activity as health-threatening.

The results from the exogenous cueing task did not support the hypothesis, as demonstrated by the lack of significant differences in responses by the CFS, asthma, and healthy control groups. All participants demonstrated an inhibition of return response with regard to activity stimuli, similarly to their response towards health-threat stimuli. This response either suggests a healthy adaptive attentional pattern in CFS, or avoidant tendencies. Informatively, the visual probe task results indicated a greater likelihood of attentional avoidance of activity in CFS group, compared to asthma and control groups. Thus, avoidance manifested itself in the more difficult task under the higher cognitive load, fitting with the evidence of higher cognitive load impairing information processing (Capuron et al., 2006; Cockshell & Mathias, 2010; Glass, 2006; Majer et al., 2008). This cognitive avoidance is also in parallel with the behavioural process of avoidance of activity and exercise in CFS, underpinned by a fear of exacerbating fatigue and pain (Bazelmans et al., 2006; Nijs et al., 2013).

The finding of attentional avoidance does not fit within the proposed hypothesis of enhanced processing of health-threat information in CFS. It is also contradictory to another significant finding to emerge from the experiment. On the exogenous cueing task in the CFS group attention was more likely to be captured by activity images when in depressive mood, unlike the asthma or control groups.

There are a number of methodological limitations that might have led to contradictory results. Small sample size was the main limitation. Intra-individual and inter-individual variability, demonstrated by the large standard deviations, could have compromised the results. Furthermore, Bonferroni correction applied to multiple comparisons indicated that there was a high likelihood of committing type I error, therefore the findings might have been spurious.

The conflicting results are not, however, quite as irreconcilable with each other and with the cognitive theories of CFS perpetuation and empirical evidence. Hou and colleagues (2014) demonstrated that attentional bias emerged when attentional control was impaired in a group of people with CFS. Putting the results into the context of the Hou et al. (2014) study, it might have been that the influence of pictorial stimuli and depressive mood compromised attentional control and the attentional bias emerged in the low cognitive load task. Similarly, the deficit in attentional control might have led to attentional avoidance

emerging in the high load cognitive task, independent of mood state or stimulus type (words or pictures of activity). Moreover, exogenous cueing task is meant to be a measure of the earlier reflexive attention, while the visual probe task can tap into the later elaborative attentional stage (Fox et al., 2001). Thus, the results in the current thesis may indicate that the early attentional bias towards threat may turn into avoidance of threat at a later processing stage. That would fit with the hypervigilance-avoidance cognitive pattern that may underpin the fear of movement cognitions and behavioural avoidance pattern in CFS (Nijs et al., 2013). Furthermore, the findings point towards the next step in the attentional research in CFS. Future studies should investigate in more detail the attentional control impairment and its interaction with attentional processing of various types of information (e.g. physical activity, mental activity, CFS specific threat, general health-threat), while varying stimulus duration in order to track the changes in processing over the time course of attention.

The study, described in this thesis, that investigated attentional patterns towards activity-related information in CFS was the first to do so, thus comparison across studies is premature. The results indicated that increased cognitive load may lead to cognitive avoidance of activity-related information in CFS, in parallel to the behavioural avoidance. On the other hand, depressed mood and activity images may lead to increased attentional engagement with activity-related information.

The study raised the question whether physical activity stimuli should be considered pleasant or unpleasant, and if the avoidance may be due to a perceived unpleasantness. It was hypothesised that activity information would be perceived as threatening and dangerous to the established health-illness balance (Deary, 2008). Thus, a suggestion for future research would be to include deeper consideration of activity stimuli, not only whether they are linguistic or pictorial, but also the emotional impact, valence, and perceived threat value.

Previous empirical evidence pointed towards increased attentional focus on fatigue as a main symptom-perpetuating factor, and a reduction in attentional focus leading to a reduction in fatigue (Knoop et al., 2010; Moss-Morris, 2005; Moss-Morris et al., 2005; Wiborg et al., 2011; Wiborg et al., 2010). This thesis provides initial evidence that activity-related stimuli may be more likely to result in cognitive avoidance, which may underpin the behavioural avoidance.

Bazelmans and colleagues (2006) identified two subtypes within the CFS population: an *active* and a *passive* group, who differed in their approach to activity. The *passive* group's

coping was characterized by avoidance, while the *active* group's coping featured the 'boom and bust' activity cycle. Both coping styles were earlier identified and implicated in the perpetuation of CFS symptoms (Moss-Morris, 2005; Surawy et al., 1995). This underscores the importance of two goals in research: the development of a sensitive and multidimensional measure of activity, and the understanding of the nature of fear cognitions in relation to activity.

The online study of activity and memory introduced a new scale to assess activity patterns in CFS. The scale aimed to measure different dimensions of activity (e.g. exercise, leisure, work, mental effort, social functioning) and dimensions of inactivity. Importantly, the scale aimed to measure sedentary behaviours (e.g. staying in bed during the day, watching TV), as representative of a construct of inactivity.

In the CFS group, fatigue was associated with reduced activity, while more CFS symptoms were associated with increased inactivity (more sedentary lifestyle). An important finding was that negative mood was also related to increased sedentary behaviours but not to decreased activity, unlike in the asthma group where negative mood was associated with reduced activity similar to the pattern in the healthy control group. Fear of movement in the CFS group was similarly related to an increased sedentary lifestyle rather than to a decrease in active lifestyle. Wiborg and colleagues (2010; 2011) demonstrated that after CFS treatment, the actual amount of physical activity did not increase, and the reduction in symptoms was due to a reduced focus on fatigue. It is possible that while activity did not increase, inactivity or sedentary behaviour decreased instead. Therefore, an assessment of inactivity could be added to the outcome measures of intervention trials for CFS, assessing both active and sedentary behaviours.

Stronger beliefs that activity was harmful were associated with a decrease in leisure and recreation, which represented pleasant and fun activities. Thus, believing that activity is harmful may lead a person to stop engaging in pleasant activities. Though we cannot predict what the consequences of that may be on the basis of the results of this study, they are unlikely to be positive. Accordingly, Jason and colleagues (2009) found that pain-inducing and tiring activities predicted higher fatigue, but meaningful and pleasant activities were associated with decreased fatigue. This may have clinical implications, such as that if an exercise-based treatment utilizes pleasant activities as part of its plan to increase activity, people would be more likely to adhere to treatment, less likely to drop out, less likely to perceive it as harmful, and more likely to regard it as beneficial.

A noteworthy finding was a pattern of positive correlations between online activity and more frequent CFS symptoms, stronger beliefs in the seriousness of the illness, and negative affect. Parallel to that was a somewhat paradoxical pattern of correlations between greater community-related activity (e.g. attending community gatherings) and higher physical functioning, but also between greater community-related activity and stronger beliefs in the seriousness of the illness, greater anxiety, and increased behavioural disengagement. That pattern of associations observed in the CFS group, more online activity and more community involvement being associated with stronger illness beliefs, anxiety and negative affect, and greater symptomatology fits with the previous observation that people with CFS who are members of support groups may be more functionally impaired and have poorer prognosis (Sharpe et al., 1992). However, since the nature of the online activity or community involvement was not investigated, it could not be confirmed to what degree people in this CFS sample engaged with various support groups (online or in real life).

The scale showed a satisfactory convergent validity and internal consistency. However, an exploration of the patterns of correlation separately for CFS, asthma, and control groups showed a lack of any significant relationships between the new scale and other measures of activity and physical functioning in the healthy group. Thus, the measure may be more suitable for measuring activity in people with a chronic condition. The chosen activities might not have been relevant to healthy people, or their current physical functioning was independent of how active or sedentary their lifestyle was.

Interpretation

The negative illness schema that may be developed by people with CFS is hypothesised to alter the information processing (Moss-Morris, 2005). This alteration would include catastrophic interpretation of ambiguous information. Somatic sensations, like fatigue or pain, can be inherently ambiguous. They may be signs of a physiological need (hunger or thirst), of psychological state (anxiety, apprehension, fear), of physical state (exhaustion), or of an illness of varying degrees of seriousness. Interpretation bias in CFS can be defined as a catastrophic and illness-focused interpretation of these ambiguous somatic sensations (Moss-Morris, 2005). This biased interpretation is one of the facets of enhanced processing of illness-related information.

The interpretation experiment did not provide the evidence to support the hypothesis that there is an interpretation bias in CFS. The study measured an online interpretive process, which is an interpretation made in the first moment of encounter with

ambiguous information, at an earlier automatic processing stage (Hirsch & Mathews, 2000). The CFS group did not show an enhanced response to an illness interpretation of ambiguous information over a neutral disambiguation. Thus, the evidence indicated that at the automatic stage of meaning generation, the interpretation bias in CFS does not manifest. In contrast Moss-Morris and Petrie (2003) showed evidence of interpretation bias at the later elaborative stages of response production. If cognitive impairments in CFS mainly affect the response stage, selection and execution (Scheffers et al., 1992), then it follows that the preferential processing of one type of information over another may appear in that later stage in people with CFS, once the negative illness schema is activated and accessed (Hirsch & Mathews, 2000). Thus, it seems that the more plausible explanation of the inconsistent findings is that they are due to participants' use of illness schema being different at the two stages.

Informatively, the results of the experiment indicated that the priming effect has not occurred in the CFS group, because participants with CFS were not affected by ambiguous words carrying potentially health-threatening or socially threatening meaning. In contrast, the healthy participants showed a significant priming effect by the ambiguous words carrying potentially health-threatening implications. This susceptibility to a potential health-threat shown by the healthy group is in line with previous findings that when a potential threat is high in severity or self-relevant, healthy people may also demonstrate an interpretation bias (Vancleef et al., 2009).

However, why wasn't the CFS group primed by the ambiguous words like the healthy group? Healthy people may draw clear distinctions between the potentially illness-related ambiguous information and any other potential ambiguous threat. Illness threat would be more novel to them, hence they would be susceptible to being primed by a potentially health-threatening word. In contrast, CFS is a profound and pervasive illness with multiple different symptoms, thus a potentially illness-related ambiguous prime has lost its novelty for the CFS group, making them less sensitive to the potential threat expressed in a linguistic stimulus. This lack of priming effect is somewhat comparable to people with depression, who demonstrate a general flat cognitive-affective approach to different types of information with no preferential processing (Gotlib et al., 1988).

Based on the results of the experiment described in this thesis and another experimental study of interpretation bias in CFS (Moss-Morris & Petrie, 2003) a likely account is that in CFS the illness schema acts on the later elaborative stage of the interpretation of ambiguous stimuli rather than at the initial automatic stages.

Memory

The final study in this thesis investigated the properties of autobiographical memory for illness-related information in CFS. The aim was to determine whether memory would also show enhanced processing of illness and activity information in CFS. Evidence of biased memory processing would provide further support for the presence of negative illness schema in CFS that guides the attentional focus, interpretation, and memory towards health-threat (Knoop et al., 2010; Moss-Morris, 2005; Surawy et al., 1995).

The main finding that emerged was that the CFS group showed a greater specificity of activity memories compared to the healthy control group, who demonstrated more general memories of activity. Informatively, the asthma group also showed increased specificity of activity memories, indicating that particular cognitive processing may be common to people with a chronic illness. The specificity of memories in CFS and asthma did not generalise to fatigue, pain or happy memories. Greater specificity of activity memories may be one of the facets of enhanced processing of somatic information. It is in line with cognitive theories that enhanced processing of somatic information may underpin exacerbation and perpetuation of CFS symptoms (Fry & Martin, 1996a, 1996b; Knoop et al., 2010; Moss-Morris, 2005) and with the evidence of higher awareness of activity patterns and fatigue levels in people with CFS (Evering, Tonis, et al., 2011; Evering, van Weering, et al., 2011). The memory specificity in CFS also points to a difference in cognitive processing between CFS and depression, because the CFS group did not show a pattern of over-general recollection that is typical in depression. However, it's important to note that avoidant coping strategies were associated with over-general memories in the CFS group, as predicted by the theory that functional avoidance is one of the mechanisms maintaining over-general memory style (Williams et al., 2007).

Another key finding was that the CFS group had a greater tendency to view activity, specifically general activity memories, from a field perspective, compared to healthy controls. Rating of general memories higher on a field perspective is a pattern that also differs from people with depression, who tend towards an observer perspective. The latter is associated with greater cognitive and behavioural avoidance and negative evaluation of self (Kuyken & Moulds, 2009). An increased tendency to view activity memories, regardless of whether they are general or specific, through a field perspective does fit into the theories of enhanced somatic focus in CFS (Moss-Morris, 2005), potential health-threatening nature of activity (Deary, 2008) and higher awareness of activity patterns in CFS (Evering, Tonis, et al., 2011; Evering, van Weering, et al., 2011).

Exploration of the emotional valence of activity memories cast doubt on the idea that activity might have been viewed as health-threatening by people with CFS. Activity memories for the CFS group, similar to the asthma and healthy control groups, were primarily positive and neutral. However, investigation of the themes expressed in recalled activity memories showed the concept of activity may be more multidimensional in CFS in contrast to healthy controls. This may explain why, in spite of the theories proposing a high degree of activity fear and avoidance in CFS (Nijs et al., 2013) and the fact that the CFS group scored the highest on fear of movement, the activity memories were more specific, and why general activity memories were rated higher on field perspective.

Thematic analysis of activity memories presented a complex and multidimensional view of activity by people with CFS, which included exercise of various intensities, walking (daily and for exercise purposes), chores, pleasure, work, and health-related exercise (physiotherapy, rehabilitation). In contrast, the healthy group viewed the concept of activity as primarily exercise related. The multidimensionality of activity concept for the CFS group may be what makes it more self-relevant and linked to sense of self, if it is something they see as profoundly present in their everyday lives. In contrast, healthy people seemed to view activity simply in terms of exercise or unusual exertion, so their sense of self is much less likely to be tied to the concept of activity.

Similarly to activity, the thematic analysis of fatigue memories indicated that for people with CFS, fatigue was a complex phenomenon, varied and global, and was viewed as a consequence of different activities in all areas of life. There was a sense of profoundness of fatigue in the CFS group, unlike the healthy controls who viewed it as more of a one-dimensional concept. The healthy group was also more likely to describe fatigue in emotional terms rather than physical. It would be informative in future research to explore if healthy people, compared to people with CFS, would describe fatigue more in terms of depressed mood or negative affect. The CFS group experiencing fatigue after a negative event were more likely to label it as fatigue and a symptom of an illness, rather than that of depressed mood, fitting the evidence that people with CFS interpret a wide range of sensations as fatigue and regard it to be of physical origin (Moss-Morris & Chalder, 2003; Moss-Morris & Petrie, 2001).

Thesis Limitations

Heterogeneity within the CFS population and great intra-individual variability of symptoms and functioning, pathophysiology, prognosis and treatments (Jason, Kin, Taylor, &

Kennedy, 2000; Jason, Richman, et al., 1999) make it difficult to compare the findings in this thesis with other studies. Hence, generalizability of the experimental results is limited. The lack of agreement on CFS case definitions and diagnostic criteria increases the chance of different studies investigating diverse populations under the umbrella of CFS. The decision was made for the purposes of this thesis to use the CDC/Fukuda (1994) criteria for reasons outlined in Chapter 1. These were that the CDC/Fukuda case definition is currently the most validated and widely used in research and clinical settings, which allows comparisons across studies (Brurberg et al., 2014). Additionally, White and colleagues (2011) proposed that the results of the application of different criteria may be generalizable across subgroups under the broadest CFS criteria as long as extreme fatigue remains the main symptom.

All the studies in this thesis relied on the report of a diagnosis made by a medical practitioner, with regard to both CFS and Asthma groups. For the CFS group laboratory tests to rule out other potential explanations for extreme fatigue or to attempt to stratify the sample were not conducted. Similarly, for the asthma group, the diagnosis was not confirmed by physiological assessment of the current severity, duration, and frequency of the symptoms. There was no data on how well asthma was managed and controlled in the samples in this thesis, thus severely limiting its generalizability, and the validity of conclusions with regard to the asthma group. Asthma population is, similarly to the CFS, very diverse. Based on the results from a small group of people with asthma, whose diagnosis or current symptomatology were not confirmed by the established and well-validated physiological tests, it is premature to make any generalizations or conclusions with regard to the role of the cognitive processing biases in asthma symptomatology.

Concerning the CFS group, the existence of distinct subgroups under the umbrella of CFS is one of the explanations for the differences in the results reported in the studies in this thesis and in the wider CFS literature. The absence of cognitive bias towards health-threat in the early stages of information processing may be due to current studies accessing a different subgroup within a wider CFS population. Recruitment from a community rather than specialist clinics might have resulted in a more diverse group. Large variability within the group might have obscured the results. However, Hou and colleagues (2008) also recruited from the community (a CFS/ME support group, similar to the recruitment strategy in this thesis), but obtained firm evidence of attentional bias and a large effect size.

The investigation of attentional bias towards health-threat and activity presented in Chapters 3 and 4 particularly suffered from the severe limitation of a small sample size. The problem has been discussed in detail in Chapter 3, pp. 146 – 148. Taking into consideration

the complexity of the experimental design, the small sample size severely limited the analysis and the ability to draw firm conclusions from the results.

CFS research in general suffers from the problem of small sample sizes. One reason may be the nature of CFS, which limits people's ability to participate in research if they are severely affected. The problem of accessing highly disabled and most severely affected CFS groups persists in research. The issue of access is particularly central for laboratory-based experimental studies, because they demand extended effort from people with CFS, such as traveling to a location and engaging in cognitive tasks that demand concentration for long periods of time. It is most likely that the experimental studies described in this thesis did not include severely affected people with CFS due to their low functioning and limited mobility. The online study might have addressed this problem, because it did not place high demands on people in terms of time and effort. However, the issue with a web-based data collection is the reduced control over the participant selection and inability to verify the diagnosis. In this thesis the same issue affects the experimental studies, because of the lack of laboratory tests and physiological measures for CFS.

The problem of the small sample size has been addressed in the final study on autobiographical memory by using an online method of data collection. The advantage of an online study was wider access to people with CFS, with an added advantage of potentially involving people with severe CFS. Comparing the largest CFS sample in this thesis to the samples from other studies in terms of fatigue and functioning paints the following picture. One of the limitations of the online study included using the Fatigue Severity Scale (FSS), a measure of fatigue that is widely used in healthy and illness populations but less so in CFS research. Previous research suggested a cut-off point of 4 (Armutlu et al., 2007; Kaynak et al., 2006; Valko et al., 2008) and even more conservatively the score of 5 to identify severe fatigue impact (Lerdal et al., 2005). The online study CFS sample had a mean score of 6.2, compared to asthma (3.8), and healthy control (3.2) groups. The CFS group's score was above both recommended cut-off points. The weighted average across studies that have used FSS produced the score of 6.01, which is comparable to our online sample.

The assessment of physical functioning was done via a well-established (Deale et al., 1997; Fulcher & White, 1997) and recommended for CFS research (Reeves et al., 2005) subscale of a health survey SF-36 measure (Ware & Sherbourne, 1992). The score of 39.9 in the online sample is comparable to other studies, which showed a range of scores from 25 to 57 (Friedberg & Sohl, 2009b; Fulcher & White, 1997; Olson et al., 2003; Reeves et al., 2005; White et al., 2011). The score of 39.9 is well below the proposed cut-off score of 70

(Reeves et al., 2005) and very close to the range of scores for the four treatment groups in the PACE trial at baseline: adaptive pacing 37.2, CBT group 39.2, GET 36.7, and specialist care 39.2 (White et al., 2011). While the CFS group, recruited for the online study, is comparable to other CFS groups in the literature in terms of reduced functioning, it is premature to claim that web-based methods allow access to more severely affected populations.

With regard to measurements used, another limitation of this thesis involves the methodological paradigms. The difference in the findings from the visual probe and the exogenous cueing tasks, between the studies in this thesis and other studies, may be due to tasks tapping into different facets of cognitive processing. However, it may also be due to unreliability of measures, as discussed earlier in this chapter (Schmukle, 2005; Staugaard, 2009). Within the methodology issue the question of stimuli used to tap into hypothesised illness schema also needs consideration. The findings in this thesis showed that more symptom-related stimuli were not associated with biased processing in CFS. In contrast, more generic and severe health-threat appears to produce more consistent results within this thesis and in other studies (Hou et al., 2008; Hou et al., 2014; Moss-Morris & Petrie, 2003).

In summary, it is possible that the CFS groups who participated in the studies described in this thesis were less representative of a CFS population, and might have represented a population with elevated chronic fatigue, rather than a diagnosable illness. The small sample sizes in the experimental studies severely limited the ability to draw firm conclusions. It is vital to consider the methods of recruitment for studies of CFS and address the issues of small samples and lack of access to severely affected populations. The PACE trial provides a good example of how some of these limitations may be addressed. The main advantage is the collaboration between basic science research and clinical research, which allows for both the provision of treatment and the study of the range of physical and psychological factors that play a role in CFS perpetuation. Other advantages include use of different case definitions and diagnostic criteria, selection of multidimensional and validated assessment methods, detailed analysis of treatment components which can then be investigated further in science research, and long-term follow up (Chalder et al., 2015; Sharpe et al., 2015; White et al., 2013).

Clinical implications

A heated debate is currently taking place with regard to the treatment for CFS, particularly the role of exercise and "positive thinking" (Lancet, 2011; Spencer, 2015, October 28; Stratton, 2015, October 28). The fact, that in the media Graded Exercise Therapy (GET) and Cognitive-Behavioural Therapy (CBT) are reduced to "take exercise" and "positive thinking", respectively, reflects major misconceptions about the role of psychology and of the nature of psychological treatments. Controversy aside, GET and CBT are the two treatments with the weight of evidence behind them (Larun et al., 2015; Malouff et al., 2008; Price et al., 2008; Smith et al., 2015). Therefore, the clinical implications are discussed primarily in the context of GET and CBT.

The experiment on attention towards activity raised the question of whether activity stimuli viewed by people with CFS were aversive and fearful, or positive and pleasant. As activity can be regarded as enjoyable or painful in CFS (Jason, Timpo, et al., 2009), the activity stimuli may be perceived as threatening or pleasant. Similarly, the findings of possible attentional avoidance of activity information among people with CFS may have clinical relevance for GET. Activity perception can be measured using cognitive tasks. An attentional task could then be utilised to train an increased attentional focus on pleasant and meaningful activity, while decreasing the focus on unpleasant and aversive activities. This attentional modification may help reduce fear and distress in relation to activity, modify perception of exertion, decrease focus on fatigue, and consequently help reduce fatigue and increase activity in CFS (Jason, Timpo, et al., 2009; Wiborg et al., 2011; Wiborg et al., 2010).
A measure of attentional processing, helping identify attentional bias towards health-threat or avoidance of activity, can aid in identifying subgroups of people with CFS who would benefit from different treatment approaches. Cognitive avoidance of activity can be reduced prior to engaging in Graded Exercise Therapy, which may help with reducing dropout rates. Enhanced processing of activity can be modified by the Cognitive-Behavioural treatment prior to GET. Similarly, providing Mindfulness-based cognitive therapy, which may reduce catastrophic or avoidant cognitions about activity, prior to initiating GET may also be effective. Alternatively, mindfulness strategies can be used in between bouts of exercise to keep control of the cognitive processing of activity, fatigue, pain, symptom-related and health-threat information, to prevent avoidance or catastrophising. On the other hand, the dearth of consistent findings with regard to cognitive biases at the early stages of attention and interpretation suggests that the use of Cognitive Bias Modification techniques to redirect or decrease attentional focus in CFS (Hertel & Mathews, 2011) may be premature.

The finding that self-focused rumination leads to an increase in negative mood, and that distraction leads to a decrease in negative mood, may have implications for the use of Mindfulness in the treatment of CFS. Mindfulness involves attending to current sensations, thoughts, and emotions in a non-judgmental experiential fashion and without attempts at change or avoidance (Segal, Teasdale, & Williams, 2004). Recent studies report reductions in fatigue, impairment, depression, catastrophic thinking and all-or-nothing behaviours in CFS following Mindfulness training (Rimes & Wingrove, 2013; Surawy et al., 2005). People with CFS who have ruminative tendencies may benefit from strategies that would reduce rumination and consequent emotional distress, which may help them to re-evaluate their current symptoms. Mindfulness would serve to turn the process of brooding, depressive or analytical rumination into more reflective and experiential thinking, described as more adaptive type of thinking (Watkins & Teasdale, 2004).

Continuing on to the memory specificity, even though the CFS group showed enhanced memory specificity, there was a group who did recall over-general memories, which were associated with avoidant coping such as behavioural disengagement. Raes and colleagues (2009) developed a Memory Specificity Training (MEST) protocol for depression treatment, which could be adapted for CFS. MEST aims to increase memory specificity through systematic practice of memory retrieval in response to neutral and emotional cue words, starting with positive cues and gradually introducing negative cues. Thus, for those CFS patients who do have over-general activity memories, it may be helpful to train to form more specific activity memories using a modified version of the MEST procedure. Furthermore, this kind of training could be easily incorporated into larger behavioural interventions, and adapted for delivery via the Internet.

Alternatively, if increased activity memory specificity in CFS group is one of the facets of over-processing of illness-related information and enhanced processing of health-threat, then that may be relevant for CBT and GET interventions. Thematic analysis of activity memories indicated that activity was perceived as a complex multidimensional construct for people with CFS that may be tightly linked to the sense of self. The concept of fatigue, similarly, appeared to have achieved the status of global, stable and profound characteristic that encompasses all their activities. That finding was in line with the view that people with CFS have an enhanced focus on fatigue and view fatigue as a consequence of underlying unspecified serious illness (Moss-Morris, 2005; Moss-Morris & Chalder, 2003; Petrie et al., 1995). This may also be exploited in CBT/GET and Mindfulness interventions, by

reducing the profound, complex, and global view of activity and fatigue to more specific, less catastrophic and more situational concepts.

Finally, one of the goals of this thesis was to explore if the cognitive tasks may be used as diagnostic tools in clinical practice. Based on the results of the experimental studies, this may be premature, especially given the potential unreliability of attentional tasks (Schmukle, 2005; Staugaard, 2009). Similarly, it would be premature to argue for the use of the new activity scale. However, the new scale and the investigation of activity memory themes indicated firstly that activity is a multidimensional construct for people with CFS, and secondly, that it is important to measure different components of activity. The construct of inactivity may be of particular use to clinical trials, and specifically to Graded Exercise Therapy, where it may be used as one of the outcome measures. It is important not only to increase activity in CFS, but to decrease inactivity, as represented by sedentary behaviours. At the end of the day the two goals of CFS interventions are to reduce fatigue and increase functioning to help people return to their desired levels of activity.

Conclusion

The primary aim of this thesis was to test whether there was an enhanced processing of illness-related information in CFS, as reflected in biased attentional, interpretive and memory processes. The evidence considered together did not refute the existence of the biased processing of illness information and the existence of a maladaptive illness schema (Deary et al., 2007; Knoop et al., 2010; Moss-Morris, 2005; Surawy et al., 1995). The evidence showed that self-focused rumination led to emotional distress. The early attentional and interpretation processes appeared to be unbiased. There was tentative evidence pointing towards cognitive avoidance of activity-related information at a later processing stage under a high cognitive load. This would be important to explore in future research to understand the interaction between cognitive and behavioural avoidance and fear cognitions. High specificity of activity memories and preference for field perspective in people with CFS may be one of the facets of enhanced processing of illness-related information. The multidimensionality of activity and fatigue concepts conveyed in memories of people with CFS also fit with the notion of enhanced processing of illness information leading to the perception of fatigue as profound and global.

The findings in this thesis, considered together with the wider literature, point at a cognitive and behavioural intra- and inter-individual variability within the CFS population, which underpins the differences in symptoms, outcomes, and treatment responses. In order

for us to understand what CFS is and how to treat it, a research approach is needed that aims to understand the nature of the psycho-somatic link in CFS, rather than focusing on somatic or cognitive aspects alone. This research can only be conducted in a collaborative manner between biologically and psychologically inclined branches of science in order to counter the mind/body dualism that plagues CFS research, treatment and public perception.

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Appendices

Appendix A.1
Study 1: Attention and Rumination for Chapters 2 and 5

Information Sheet

Iana Alexeeva
Dept. of Experimental Psychology
University of Oxford
South Parks Road
Oxford OX1 3UD
TEL: [redacted]
EMAIL: iana.alexeeva@wolfson.ox.ac.uk

Cognitive factors and Chronic Fatigue Syndrome
Participant information sheet

Thank you for expressing interest in taking part in this study. Before deciding whether to take part, please read the information about the study below. If you have any questions please ask us. Take as long as you want to make your decision.

If you take part in this study, one of the researchers will arrange to meet you for about an hour in the Department of Experimental Psychology, University of Oxford, South Parks Road. This could be whenever is convenient for you. During this hour, you will be asked to fill in some questionnaires, and perform two simple tasks on a computer. We would like to find out whether people with chronic fatigue syndrome perform these tasks differently from people without. Although the study involves some medical questions, no member of the team is medically trained.

Questionnaires
The questionnaires will ask some questions to find out about your health and personality. There will be a small number of questions on your medical history and current mood. Please be aware that any information you give will be treated with strict confidentiality, unless in the rare circumstance that you or someone else is at risk of serious harm. In this circumstance, only information directly relating to the emergency will be disclosed.

Computer task
The computer task is not difficult. It involves pressing buttons when dots appear on a screen. Sometimes words will appear before these dots. This task is not designed as a test, and there are no wrong answers. The task takes about 6 minutes.

Computer Task # 2
This task involves listening to a list of words and pressing buttons when another word or a non-word appears on a computer screen. The task takes approximately 6 minutes.

Inclusion criteria
People with a history of medical disorders other than chronic fatigue syndrome cannot take part in this study. You need to have normal, or corrected to normal vision, and be able to press buttons quickly with your hands in order to take part in the computer task. Finally, your English must be at the level of a native speaker.

Written consent
You will be asked to give written consent before completing the study. You can still withdraw from the experiment at any time without giving any explanation for this, by telling the researcher that you wish to do this.

Storage of data
Questionnaires and the results of the computer task will be kept anonymous by using numbers to identify them. All data will be kept in a locked room, which only the researchers can access. If any results of these experiments are published or reported, it will not be possible to identify you from the reports.

Financial compensation
Everyone who takes part in the study will receive £5 to compensate them for their time. We will also cover your travelling and parking expenses.

Further information
For further information please contact Iana Alexeeva, by telephone on 07726 634551, or email, iana.alexeeva@wolfson.ox.ac.uk

This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. Maintenance of confidentiality of information is subject to normal legal requirements.

Ms. Iana Alexeeva and Prof. Maryanne Martin
Dept. of Experimental Psychology, University of Oxford

Appendix A.2
Study 1: Attention and Rumination
Ethical Approval

University of Oxford
Medical Sciences Office
John Radcliffe Hospital, Headington, Oxford OX3 9DU

From Carol Green

CONFIDENTIAL
Ms Iana Alexeeva
Department of Experimental Psychology
South Parks Road

Ref.
MSD/IDREC/C1/2007/
4

26 March 2007

Dear Ms Alexeeva,

CUREC checklist

I am writing to acknowledge receipt of your CUREC/1 form for your project 'Cognitive and Personality Factors in Chronic Fatigue Syndrome' which, on the basis of the information you have provided, has now been approved by the Medical Sciences IDREC.

The reference number for this project is MSD/IDREC/C1/2007/4 and may I remind you that your project may be reviewed at some stage during an annual audit of projects.

Amendments

Should you at some stage alter some of the techniques or procedures then you should first undertake a checklist (CUREC/1) to see whether these changes alter the ethics of the research. If these remain the same then the committee will require notification of the changes to lodge with the project. If they do not remain the same then you may need to complete a CUREC/2 form and undergo further scrutiny by the committee.

Please do not hesitate to contact me if you have any queries about this.

Yours sincerely,

Carol Green

Carol Green (Miss)

Tel: 01865-221689 Fax: 01865-750750
Direct Line: 01865-221620 E-Mail: carol.green@medsci.ox.ac.uk

Appendix A.3
Study 1: Attention and Rumination
Consent Form

Cognitive Factors and Chronic Fatigue Syndrome
Consent form

Thank you for volunteering to take part in this study. Please read the information below and tick the boxes if you agree with the statements.

We are trying to find out how people with chronic fatigue syndrome think about fatigue.

Name:_____(block capitals)

I have read the participant information sheet ☐
I have had the opportunity to ask questions about the study. ☐
My questions about the study have been answered ☐
I understand that:

- I can withdraw from the study at any point without penalty by telling the researchers of this decision ☐
- Only the researchers named above will have access to the data I provide. ☐
- My personal details will be stored separately from the data I provide, and will be kept in a secure location. ☐

I am aware that all personal information will be treated with full confidentiality, except in the rare circumstance that you or somebody else if at risk of serious harm. (In this case only information necessary to an emergency will be revealed.) ☐
I agree to take part in this study. ☐

Signed: …… Date:……..

Signed:……(researcher) Date:…….

If you have any questions please contact Iana Alexeeva, on [redacted] or at iana.alexeeva@wolfson.ox.ac.uk.

Thank-you!

Appendix A.4
Study 1: Attention and Rumination
Questionnaires

Information about you

Are you … Male ☐ Female ☐

What is today's date? _____ (dd/mm/yyyy)

What is your date of birth? _____ (dd/mm/yyyy)

What is the highest level of educational qualification you have received?

GCSE ☐
A level ☐
Degree ☐
Higher/ postgraduate degree ☐
NVQ or vocational qualification ☐
No formal qualifications ☐
Other (please state) _____

Information about your health

Have you been diagnosed with any medical disorder? Yes ☐ No ☐

If yes, please state what you were diagnosed with (please write below)?

Have you been diagnosed with a mental health disorder? Yes ☐ No ☐

If yes, please state what you were diagnosed with and approximately when?

Have you ever been diagnosed with Chronic Fatigue Syndrome? Yes ☐ No ☐

If yes, when were you first diagnosed?

_____

If yes, when did you first start experiencing symptoms?

_____

Are you still experiencing symptoms? Yes ☐ No ☐

If so, what treatment are you currently receiving (please write below)?

Q. CFS diagnostic criteria (Fukuda et al. 1994)

Questions about your Chronic Fatigue

Please tick the appropriate boxes

1. In the last 6 months, did you *often*, have unexplained, persistent or relapsing chronic fatigue?

☐ Yes ☐ No or rarely → skip to the end

2. Is the fatigue reduced by rest?

☐ Yes ☐ No or rarely

3. Does the fatigue result in a reduction of your activities (occupational, educational, social or personal)?

☐ Yes ☐ No or rarely

4. Have you had any of the following symptoms, persistent or recurring, during the past 6 months (*tick all that apply*)

☐ Impairment in short-term memory and/or concentration
☐ Sore throat
☐ Tender cervical or axillary lymph nodes
☐ Muscle pain
☐ Multi-joint pain without swelling or redness
☐ Headaches of a new type, pattern or severity
☐ Unrefreshing sleep
☐ Post-exertional malaise lasting more than 24 hours

Q. Hospital Anxiety and Depression Scale – HADS (Zigmond & Snaith, 1983)

Please tick the box next to one response for each statement. Try not to think too hard about your answer- just put down the first thing that comes to mind.

I feel tense or 'wound up':
- Most of the time ☐
- A lot of the time ☐
- From time to time, occasionally ☐
- Not at all ☐

I feel as if I am slowed down:
- Nearly all the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

I still enjoy the things I used to enjoy:
- Definitely as much ☐
- Not quite so much ☐
- Only a little ☐
- Hardly at all ☐

I get a sort of frightened feeling like 'butterflies' in the stomach:
- Not at all ☐
- Occasionally ☐
- Quite Often ☐
- Very Often ☐

I get a sort of frightened feeling as if something awful is about to happen:
- Very definitely and quite badly ☐
- Yes, but not too badly ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

I have lost interest in my appearance:
- Definitely ☐
- I don't take as much care as I should ☐
- I may not take quite as much care ☐
- I take just as much care as ever ☐

I can laugh and see the funny side of things:
- As much as I always could ☐
- Not quite so much now ☐
- Definitely not so much now ☐
- Not at all ☐

I feel restless as I have to be on the move:
- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

Worrying thoughts go through my mind:
- A great deal of the time ☐
- A lot of the time ☐
- From time to time, but not too often ☐
- Only occasionally ☐

I look forward with enjoyment to things:
- As much as I ever did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

I feel cheerful:
- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

I get sudden feelings of panic:
- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

I can sit at ease and feel relaxed:
- Definitely ☐
- Usually ☐
- Not Often ☐
- Not at all ☐

I can enjoy a good book or radio or TV program:
- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

Q. Social Desirability Scale – SDS (Crowne & Marlowe, 1960)

Personal Reaction Inventory

Listed below are a number of statements concerning personal attitudes and traits. Read each item and decide whether the statement is true or false for you.

	True	False
1. Before voting I thoroughly investigate the qualifications of all the candidates.	☐	☐
2. I never hesitate to go out of my way to help someone in trouble.	☐	☐
3. It is sometimes hard for me to go on with my work, if I am not encouraged.	☐	☐
4. I have never intensely disliked anyone.	☐	☐
5. On occasion I have had doubts about my ability to succeed in life.	☐	☐
6. I sometimes feel resentful when I don't get my way.	☐	☐
7. I am always careful about my manner of dress.	☐	☐
8. My table manners at home are as good as when I eat out in a restaurant.	☐	☐
9. If I could get into a movie without paying and be sure I was not seen, I would probably do it.	☐	☐
10. On a few occasions, I have given up doing something because I thought too little of my ability.	☐	☐
11. I like to gossip at times.	☐	☐
12. There have been times when I felt like rebelling against people in authority even though I knew they were right.	☐	☐
13. No matter who I'm talking to, I'm always a good listener.	☐	☐
14. I can remember "playing sick" to get out of something.	☐	☐
15. There have been occasions when I took advantage of someone.	☐	☐
16. I'm always willing to admit it when I make a mistake.	☐	☐
17. I always try to practice what I preach.	☐	☐
18. I don't find it particularly difficult to get along with loud-mouthed, obnoxious people.	☐	☐
19. I sometimes try to get even rather than forgive and forget.	☐	☐
20. When I don't know something I don't at all mind admitting it.	☐	☐
21. I am always courteous, even to people who are disagreeable.	☐	☐
22. At times I have really insisted on having things my own way.	☐	☐
23. There have been occasions when I felt like smashing things.	☐	☐

	True	False
24. I would never think of letting someone else be punished for my wrongdoings.	☐	☐
25. I never resent being asked to return a favour.	☐	☐
26. I have never been irked when people expressed ideas very different from my own.	☐	☐
27. I never make a long trip without checking the safety of my car.	☐	☐
28. There have been times when I was quite jealous of the good fortune of others.	☐	☐
29. I have almost never felt the urge to tell someone off.	☐	☐
30. I am sometimes irritated by people who ask favours of me.	☐	☐
31. I have never felt that I was punished without cause.	☐	☐
32. I sometimes think when people have a misfortune they only got what they deserved.	☐	☐
33. I have never deliberately said something that hurt someone's feelings.	☐	☐

Q. Ruminative Responses Scale – RRS (Nolen-Hoeksema et al., 1993)

Responses to Situations

People think and do many different things when they feel sad, blue, or depressed.
Please read each of the items below and indicate whether you Never, Sometimes, Often, or Always think or do each one when you feel sad, down, or depressed. Circle the right number.
Please indicate what you *generally* do, **not** what you *think* you should do.

	Never	Sometimes	Often	Always
1. I think about how alone I feel.	1	2	3	4
2. I think "I won't be able to do my job if I don't snap out of this".	1	2	3	4
3. I think about my feelings of fatigue and achiness.	1	2	3	4
4. I think about how hard it is to concentrate.	1	2	3	4
5. I think "What am I doing to deserve this?"	1	2	3	4
6. I think about how passive and unmotivated I feel.	1	2	3	4
7. I analyse recent events to try to understand why I am depressed.	1	2	3	4
8. I think about how I don't seem to feel anything anymore.	1	2	3	4
9. I think "Why can't I get going?"	1	2	3	4
10. I think "Why do I always react this way?"	1	2	3	4
11. I go away by myself and think about why I feel this way.	1	2	3	4
12. I write down what I am thinking and analyse it.	1	2	3	4
13. I think about a recent situation, wishing it had gone better.	1	2	3	4
14. I think "I won't be able to concentrate if I keep feeling this way."	1	2	3	4
15. I think "Why do I have problems other people don't have?"	1	2	3	4
16. I think "Why can't I handle things better?"	1	2	3	4
17. I think about how sad I feel.	1	2	3	4
18. I think about all my shortcomings, failings, faults, and mistakes.	1	2	3	4
19. I think about how I don't feel up to doing anything.	1	2	3	4
20. I analyse my personality to try to understand why I am depressed.	1	2	3	4
21. I go somewhere alone to think about my feelings.	1	2	3	4
22. I think about how angry I am with myself.	1	2	3	4

Q. Visual Analogue Scale

How are you feeling?

Please place a cross on the line to show how much of the emotion you are feeling at the moment?

Not at all Happy — Extremely Happy

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100

Not at all Sad — Extremely Sad

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100

Not at all Anxious — Extremely Anxious

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100

Not at all Calm — Extremely Calm

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100

Not at all Angry — Extremely Angry

0-----10-----20-----30-----40-----50-----60-----70-----80-----90-----100

Appendix A.5
Study 1: Attention and Rumination
Induction Procedure for Chapter 2

Rumination Induction (Nolen-Hoeksema et al., 1993; Watkins & Teasdale, 2001).

For the next few minutes, try your best to focus your attention on each of the ideas on the following pages.
Read each item slowly and silently to yourself. As you read the items, use your imagination and concentration to focus your mind on each of the ideas. Spend a few moments visualising and concentrating on each item.

Please continue until the experimenter returns.

Think about: the physical sensations you feel in your body

Think about: your character and who you strive to be

Think about: the degree of clarity in your thinking right now

Think about: why you react the way you do

Think about: the way you feel inside

Think about: the possible consequences of your current mental state

Think about: how similar or different you are relative to other people

Think about: what it would be like if your present feelings lasted

Think about: why things turn out the way they do

Think about: trying to understand your feelings

Think about: how awake or tired you feel now

Think about: the amount of tension in your muscles

Think about: whether you are fulfilled

Think about: your physical appearance

Think about: whether you feel stressed right now

Think about: the long-term goals you have set

Think about: the amount of certainty you feel

Think about: your present feelings of fatigue or energy

Think about: possible explanations for your physical sensations

Think about: how hopeful or hopeless you are feeling

Think about: the level of motivation you feel right now

Think about: the degree of helplessness you feel

Think about: the degree of calmness or restlessness you feel

Think about: the possible consequences of the way you feel

Think about: what your feelings might mean

Think about: how sad or happy you are feeling

Think about: the expectations your family has for you

Think about: why your body feels this way

Think about: why you get this way sometimes

Think about: how passive or active you feel

Think about: what people notice about your personality

Think about: how optimistic or pessimistic you feel about the future

Think about: how weak or strong your body feels right now

Think about: the degree of relaxation or agitation you feel

Think about: the kind of person you think you should be

Think about: the degree of control you feel right now

Think about: what would happen if your current physical state lasted

Think about: sitting down and analysing your personality

Think about: why you turned out this way

Think about: the things that are most important in your life

Think about: how quick or slow your thinking is right now

Think about: the degree of decisiveness you feel

Think about: trying to understand who you are

Think about: how you feel about your friendships

Think about: whether you have accomplished a lot so far

Distraction Induction

For the next few minutes, try your best to focus your attention on each of the ideas on the following pages.
Read each item slowly and silently to yourself. As you read the items, use your imagination and concentration to focus your mind on each of the ideas. Spend a few moments visualising and concentrating on each item.

Please continue until the experimenter returns.

Think about: and imagine a boat slowly crossing the Atlantic

Think about: the layout of a typical classroom

Think about: the shape of a large black umbrella

Think about: the movement of an electric fan on a warm day

Think about: raindrops sliding down a window pane

Think about: a double-decker bus driving down a street

Think about: and picture a full moon on a clear night

Think about: clouds forming in the sky

Think about: the layout of the local shopping centre

Think about: and imagine a plane flying overhead

Think about: fire darting round a log in a fire-place

Think about: and concentrate on the expression on the face of the *Mona Lisa*

Think about: the car park at a large supermarket

Think about: two birds sitting on a tree branch

Think about: the shadow of a stop sign

Think about: the layout of the local post office

Think about: the structure of a high-rise office building

Think about: and picture the Eiffel Tower

Think about: and imagine a lorryload of apples

Think about: the pattern on an Oriental rug

Think about: the 'man in the moon'

Think about: the shape of the continent of Africa

Think about: a band playing outside

Think about: a group of polar bears fishing in a stream

Think about: the shape of Sydney Opera House

Think about: the shape of Great Britain

Think about: the way Stonehenge looks at sunset

Think about: the outline of the Houses of Parliament

Think about: a train stopped at a station

Think about: a lone cactus in the desert

Think about: the shape of the country Italy

Think about: a row of shampoo bottles on display

Think about: a petrol station on a major road

Think about: the fuzz on the shell of a coconut

Think about: the queens' head on a stamp

Think about: a band playing the National Anthem

Think about: the shape of a cello

Think about: the birthmark on Gorbachev's head

Think about: the shape of the United States of America

Think about: the baggage claim area at the airport

Think about: the size of the Statue of Liberty

Think about: the shape of a cricket bat

Think about: a freshly painted door

Think about: the shiny surface of a trumpet

Think about: a kettle coming to the boil

Appendix B.1

Study 2: Attention and Mood for Chapters 3 and 4

Information Sheet

Iana Alexeeva
Dept. of Experimental Psychology
University of Oxford
South Parks Road
Oxford OX1 3UD
TEL: [redacted]
EMAIL: iana.alexeeva@psy.ox.ac.uk

Psychological factors in Chronic Illness
Participant information sheet

Thank you for expressing an interest in taking part in this study. Before deciding whether to take part, please read the information about the study below. If you have any questions or concerns, please contact us by emailing iana.alexeeva@psy.ox.ac.uk. Take as long as you like to make your decision.

Our research group is interested in kinds of role which particular thoughts, emotions, and behaviours play in the maintenance of symptoms of chronic health conditions. We are investigating whether some particular patterns of thinking and behaving influence how people cope with their disorder. The end goal of our research is to be able to provide an effective psychosocial support for people who suffer from chronic health problems with a focus on self-management and self-reliance.

If you take part in this study, one of the researchers will arrange to meet you for approximately 1 hour at the Department of Experimental Psychology or at another convenient suitable location. During this hour, you will be asked to read some statements, fill in a few questionnaires, and perform two simple tasks on a computer. Although the study involves some medical questions, no member of the team is medically trained. There are no known risks involved in this study.

Any information you give will be treated with strict confidentiality, unless in the rare circumstance that you or someone else is at risk of serious harm. In this circumstance, only information directly relating to the emergency will be disclosed.

If you have a concern about any aspect of this project, please contact the researcher concerned (iana.alexeeva@psy.ox.ac.uk) who will do her best to answer your query. If you remain unhappy and wish to make a formal complaint, please contact the Research Ethics Committee at the University of Oxford (ethics@medsci.ox.ac.uk; Medical Sciences Inter-Divisional Research Ethics Committee, Medical Sciences Divisional Office, Level 3 John Radcliffe Hospital, Oxford, OX3 9DU, UK).

Questionnaires
The questionnaires will ask some questions to find out about your health, thoughts, emotions and personality. There will be a small number of questions on your medical history and current mood.

Mood Procedure
In order to assess how your mood may affect your thinking we will ask you to focus on some neutral or sad thoughts and images. You will be asked to bring to mind some sad or neutral thoughts while reading a list of statements and listening to music for a few minutes. The statements describe the kinds of thoughts and feelings people may have when they are in a sad mood or neutral mood. This procedure is called "mood induction" and would be under your own control the whole time.

Computer task #1
The computer task is not difficult. It involves pressing buttons when dots appear on a screen. Sometimes words or images will appear before these dots. This task is not designed as a test, and there are no wrong answers. The task takes about 13 minutes.

Computer Task # 2
This task involves pressing buttons when arrows appear on a screen. Sometimes words or images will appear before these arrows. This task is not designed as a test, and there are no wrong answers. The task takes about 13 minutes.

Inclusion criteria
People with no current medical diagnosis.
OR People whose current primary diagnosis is Asthma
OR People whose current primary diagnosis is Chronic Fatigue Syndrome or M.E.
You need to have normal, or corrected to normal vision, and be able to press buttons quickly with your hands in order to take part in the computer task.
Your English must be at the level of a native speaker.

Written consent
After an initial screening questionnaire to discover if you are in an eligible group, you will be asked to fill in a consent form indicating that you agree to take part in the study. You can ask any questions about the study before you decide to participate by emailing Iana Alexeeva iana.alexeeva@psy.ox.ac.uk. You will be free to quit the study at any point if you wish to do so. There will be no follow up if you decide to quit the study, and you do not need to tell us why.

Storage of data
Any responses you give which can be used to identify you will be anonymised or stored separately from the rest of your answers. Online data will be stored securely and only accessible to the researchers, and any hard copies of your responses will be anonymised and kept in a locked room only accessible by the researchers. If any results of these experiments are published or reported, it will not be possible to identify you from the reports.

The University of Oxford is committed to the dissemination of its research for the benefit of society and the economy and, in support of this commitment, has established an online archive of research materials. This archive includes digital copies of student theses successfully submitted as part of a University of Oxford postgraduate degree programme.

Holding the archive online gives easy access for researchers to the full text of freely available theses, thereby increasing the likely impact and use of that research.

If you agree to participate in this project, the research will be written up as a thesis. On successful submission of the thesis, it will deposited both in print and online in the University archives, to facilitate its use in future research. The thesis will be published with open access. All the information contained in the thesis will be completely anonymised, and it will not be possible to identify you from the information contained in the thesis.

Further information
For further information please contact Iana Alexeeva by email, iana.alexeeva@psy.ox.ac.uk, or phone 01865 271108

Ethics
This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. Maintenance of confidentiality of information is subject to normal legal requirements.

Ms. Iana Alexeeva (MSc, DPhil Candidate) and Prof. Maryanne Martin (MA, DPhil)
Dept. of Experimental Psychology, University of Oxford

Appendix B.2
Study 2: Attention and Mood
Ethical Approval

University of Oxford
Medical Sciences Office
John Radcliffe Hospital, Headington, Oxford OX3 9DU

From Carol Green

CONFIDENTIAL
Ms Iana Alexeeva
c/o Professor Maryanne Martin
Department of Experimental Psychology
South Parks Road

Ref.
MSD/IDREC/C1/2009/42

26 May 2009

Dear Ms Alexeeva,

CUREC checklist

I am writing to acknowledge receipt of your CUREC/1 form for your project: 'Attentional bias in Chronic Fatigue Syndrome'.
On the basis of the information you have provided this has now been approved by the Medical Sciences IDREC **subject to:**

(a) Receipt of a hard copy of your application signed by your head of department; and
(b) Your agreeing to follow protocol MSD/IDREC/2005/P1.1

The reference number for this project is MSD/IDREC/C1/2009/42 and may I remind you that your project may be reviewed at some stage during an annual audit of projects.

Amendments
Should you at some stage alter some of the techniques or procedures then you should first undertake a checklist (CUREC/1) to see whether these changes alter the ethics of the research. If these remain the same then the committee will require notification of the changes to lodge with the project. If they do not remain the same then you may need to complete a CUREC/2 form and undergo further scrutiny by the committee.
Please do not hesitate to contact me if you have any queries about this.

Yours sincerely,
Carol Green (Miss)
Secretary to the
MSD IDREC

Appendix B.3
Study 2: Attention and Mood
Consent Form

Iana Alexeeva
Dept. of Experimental Psychology
University of Oxford
South Parks Road
Oxford OX1 3UD
TEL: 01865 271108
EMAIL: iana.alexeeva@psy.ox.ac.uk

Psychological Factors in Chronic Illness
Consent form

Thank you for volunteering to take part in this study. Please read the information below and tick the boxes if you agree with the statements.

Name:_____(block capitals)

- I have read the participant information sheet ☐
- I have had the opportunity to ask questions about the study. ☐
- My questions about the study have been answered ☐
- I understand that:
  - I can withdraw from the study at any point without penalty by telling the researchers of this decision ☐
  - Only the researchers named above will have access to the data I provide, which includes personal details. ☐
  - My personal details will be stored separately from the data I provide, and will be kept in a secure location. ☐
  - Anonymised data may be deposited in an archive and made available to other researchers.
- I am aware that all personal information will be treated with full confidentiality, except in the rare circumstance that you or somebody else if at risk of serious harm. (In this case only information necessary to an emergency will be revealed.) ☐
- I agree to take part in this study. ☐

Signed: …… Date:……..

Signed:……(researcher) Date:…….

If you have any questions please contact Iana Alexeeva, on 01865 271417 or at iana.alexeeva@psy.ox.ac.uk.

Thank-you!

Appendix B.4
Study 2: Attention and Mood
Questionnaires

Information about you

Are you
Male ___
Female ___

What is today's date? _____ dd/mm/yyyy

What is your date of birth? _____ dd/mm/yyyy

What is the highest level of educational qualifications you have received?

GCSE	☐	NVQ or vocational qualification	☐
A level	☐	No formal qualifications	☐
Degree	☐	Other (please state)	
Higher/ postgraduate degree	☐		_____

Information about your health

Have you been diagnosed with any medical disorder? (please circle the answer) Yes No

If yes, please state what you were diagnosed with and when (please write below)?

Have you been diagnosed with a mental health disorder? Yes No

If yes, please state what you were diagnosed with and when?

Have you ever been diagnosed with Chronic Fatigue Syndrome? Yes No

If yes, when were you first diagnosed? Day/Month/Year

_____

If yes, when did you first start experiencing symptoms? Day/Month/Year

_____

Are you still experiencing symptoms? Yes No

Are you receiving any treatment? Yes No

If yes, please state what kind of treatment you are receiving

Q. CFS diagnostic criteria (Fukuda et al. 1994)

Questions about your Chronic Fatigue

Please tick the appropriate boxes

2. In the last 6 or more consecutive months, did you *often*, have unexplained, persistent or relapsing chronic fatigue?

☐ Yes ☐ No or rarely → skip to the end

2. Is your fatigue the result of on-going exertion?

☐ Yes ☐ No

2. Is your fatigue reduced by rest?

☐ Yes ☐ No or rarely

3. Does the fatigue result in a reduction of your activities (occupational, educational, social or personal)?

☐ Yes ☐ No or rarely

4. During the past 6 or more consecutive months how often did you have any of the following symptoms? *Circle the appropriate number*

	Never	Rarely	Occasionally	Most of the Time	All of the Time
Impairment in short-term memory and/or concentration	0	1	2	3	4
Sore throat	0	1	2	3	4
Tender lymph nodes on the sides or the front of your neck	0	1	2	3	4
Muscle pain	0	1	2	3	4
Multi-joint pain without swelling or redness	0	1	2	3	4
Headaches of a new type, new pattern, or new severity	0	1	2	3	4
Unrefreshing sleep	0	1	2	3	4
Exhaustion lasting more that 24 hours after taking exercise	0	1	2	3	4

Q. Information about Asthma

Information about your health

Have you been diagnosed with asthma? (please circle the answer) Yes No

If yes, please state when you were diagnosed (Day/Month/Year). If you cannot remember the date, please, state your best estimate.

If yes, when did you first start experiencing symptoms? Day/Month/Year

_____

Are you still experiencing symptoms? Yes No

Are you receiving any treatment? Yes No
If yes, please state what kind of treatment you are receiving

---

---

a) Please, rate the severity of your asthma

None Severe

0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

b) To what degree does asthma interfere with your daily activity

Not at all Extremely

0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

Q. Positive and Negative Affect Scale – PANAS (Watson et al., 1988)

PANAS
Positive and Negative Affect Scales

This scale consists of a number of words that describe different feelings and emotions. Read each item and then mark the appropriate answer in the space next to that word. Indicate to what extent you feel this way right now, that is, at the present moment. Use the following scale to record your answers.

1	2	3	4	5
Very slightly Or not at all	a little	moderately	quite a bit	extremely

_ interested
_ distressed
_ excited
_ upset
_ strong
_ guilty
_ scared
_ hostile
_ enthusiastic
_ proud
_ irritable
_ alert
_ ashamed
_ inspired
_ nervous
_ determined
_ attentive
_ jittery
_ active
_ afraid

Q. Brief Fatigue Inventory - BFI (Mendoza et al., 1999).

Throughout our lives, most of us have times when we feel very tired of fatigued.
Have you felt unusually tired or fatigued in the last week? Yes ____ No ____

1. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your fatigue right NOW.

No As bad as
Fatigue you can imagine
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

2. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your USUAL level of fatigue during the past 24 hours.

No As bad as
Fatigue you can imagine
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

3. Please rate your fatigue (weariness, tiredness) by circling the one number that best describes your WORST level of fatigue during the past 24 hours.

No As bad as
Fatigue you can imagine
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

4. Circle the one number that describes how, during the past 24 hours, fatigue has interfered with your:

A. General activity

Does not interfere Completely interferes
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

B. Mood
Does not interfere Completely interferes
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

C. Walking ability
Does not interfere Completely interferes
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

D. Normal work (include both work outside the home and daily chores)
Does not interfere Completely interferes
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

E. Relations with other people
Does not interfere Completely interferes
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

F. Enjoyment of life
Does not interfere Completely interferes
0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------10

Q. Hospital Anxiety and Depression Scale – HADS (Zigmond & Snaith, 1983)

Please tick the box next to one response for each statement. Try not to think too hard about your answer- just put down the first thing that comes to mind.

I feel tense or 'wound up':
- Most of the time ☐
- A lot of the time ☐
- From time to time, occasionally ☐
- Not at all ☐

I feel as if I am slowed down:
- Nearly all the time ☐
- Very often ☐
- Sometimes ☐
- Not at all ☐

I still enjoy the things I used to enjoy:
- Definitely as much ☐
- Not quite so much ☐
- Only a little ☐
- Hardly at all ☐

I get a sort of frightened feeling like 'butterflies' in the stomach:
- Not at all ☐
- Occasionally ☐
- Quite Often ☐
- Very Often ☐

I get a sort of frightened feeling as if something awful is about to happen:
- Very definitely and quite badly ☐
- Yes, but not too badly ☐
- A little, but it doesn't worry me ☐
- Not at all ☐

I have lost interest in my appearance:
- Definitely ☐
- I don't take as much care as I should ☐
- I may not take quite as much care ☐
- I take just as much care as ever ☐

I can laugh and see the funny side of things:
- As much as I always could ☐
- Not quite so much now ☐
- Definitely not so much now ☐
- Not at all ☐

I feel restless as I have to be on the move:
- Very much indeed ☐
- Quite a lot ☐
- Not very much ☐
- Not at all ☐

Worrying thoughts go through my mind:
- A great deal of the time ☐
- A lot of the time ☐
- From time to time, but not too often ☐
- Only occasionally ☐

I look forward with enjoyment to things:
- As much as I ever did ☐
- Rather less than I used to ☐
- Definitely less than I used to ☐
- Hardly at all ☐

I feel cheerful:
- Not at all ☐
- Not often ☐
- Sometimes ☐
- Most of the time ☐

I get sudden feelings of panic:
- Very often indeed ☐
- Quite often ☐
- Not very often ☐
- Not at all ☐

I can sit at ease and feel relaxed:
- Definitely ☐
- Usually ☐
- Not Often ☐
- Not at all ☐

I can enjoy a good book or radio or TV program:
- Often ☐
- Sometimes ☐
- Not often ☐
- Very seldom ☐

Appendix B.5
Study 2: Attention and Mood
Mood Induction Procedure for Chapters 3 and 4

For the next few minutes, try your best to focus your attention on each of the ideas on the following pages. Read each item slowly and out loud. As you read the items, use your imagination and concentration to focus your mind on each of the ideas. Spend a few moments visualising and concentrating on each item. Please continue until the experimenter returns.

Depressive (Negative) Mood Statements

1. Today is neither better nor worse than any other day.
2. I feel rather sluggish now.
3. Every now and then I feel so tired and gloomy that I'd rather just sit than do anything.
4. Sometimes I wonder whether school is all that worthwhile.
5. I can remember times when everybody but me seemed full of energy.
6. Too often I have found myself staring listlessly into the distance, my mind a blank, when I definitely should have been working.
7. It has occurred to me more than once that study is basically useless, because you forget almost everything you learn anyway.
8. People annoy me; I wish I could be by myself.
9. I've had important decisions to make in the past, and I've sometimes made the wrong ones.
10. I do feel somewhat discouraged and drowsy - maybe I'll need a nap when I get home.
11. Perhaps university takes more time, effort, and money than it's worth.
12. I just don't seem to be able to get going as fast as I used to.
13. I couldn't remember things well right now if I had to.
14. Just a little bit of effort tires me out.
15. I've had daydreams in which my mistakes kept occurring to me - sometimes I wish I could start over again.
16. I'm ashamed that I've caused my parents needless worry.
17. I feel terribly tired and indifferent to things today.
18. Just to stand up would take a big effort.
19. I'm getting tired out. I can feel my body getting exhausted and heavy.
20. I'm beginning to feel sleepy. My thoughts are drifting.
21. At times I've been so tired and discouraged that I went to sleep rather than face important problems.
22. My life is so tiresome - the same old thing day after day depresses me.
23. There have been days when I felt weak and confused and everything went miserably wrong.
24. I can't make up my mind; it's so hard to make simple decisions.
25. I want to go to sleep - I feel like just closing my eyes and going to sleep right here.
26. I'm not very alert; I feel listless and vaguely sad.
27. I've doubted that I'm a worthwhile person.
28. I feel worn out. My health may not be as good as it's supposed to be.
29. It often seems that no matter how hard I try, things still go wrong.
30. I've noticed that no one seems to really understand or care when I complain or feel unhappy.
31. I'm uncertain about my future.
32. I'm discouraged and unhappy about myself.

33. I've lain awake at night worrying so long that I hated myself.
34. Things are worse now than when I was younger.
35. The way I feel now, the future looks boring and hopeless.
36. My parents never really tried to understand me.
37. Some very important decisions are almost impossible for me to make.
38. I feel tired and depressed; I don't feel like working on the things I know I must get done.
39. I feel horribly guilty about how I've treated my parents at times.
40. I have the feeling that I just can't reach people.
41. Things are easier and better for other people than for me. I feel like there's no use in trying again.
42. Often people make me very upset. I don't like to be around them.
43. It takes too much effort to convince people of anything. There's no point in trying.
44. I fail in communicating with people about my problems.
45. It's so discouraging the way people don't really listen to me.
46. I've felt so lonesome before, that I could have cried.
47. Sometimes I've wished I could die.
48. My thoughts are so slow and downcast. I don't want to think or talk.
49. I just don't care about anything. Life just isn't any fun
50. Life seems too much for me - my efforts are wasted.
51. I'm so tired.
52. I don't concentrate or move. I just want to forget about everything.
53. I have too many bad things in my life.
54. Everything seems utterly futile and empty.
55. I feel dizzy and faint. I need to put my head down and not move.
56. I don't want to do anything.
57. All of my unhappiness of my past life is taking possession of me.
58. I want to go to sleep and never wake up.

Neutral Mood Induction

For the next few minutes, try your best to focus your attention on each of the ideas on the following pages. Read each item slowly and out loud. As you read the items, use your imagination and concentration to focus your mind on each of the ideas. Spend a few moments visualising and concentrating on each item. Please continue until the experimenter returns.

Neutral Statements

1. Oklahoma city is the largest city in the world in area, with 631.166 square miles.
2. Japan was elected to the United Nations almost fourteen years after Pearl Harbor.
3. At the end appears a section entitled “Bibliography notes.”
4. We have two kinds of nouns denoting physical things: individual and mass nouns.
5. This book or any part thereof must not be reproduced in any form.
6. Agricultural products comprised seventy per cent of the income.
7. Saturn is sometimes in conjunction, beyond the sun from the earth, and is not visible.
8. Some streets were still said to be listed under their old names.
9. The system is supervised by its board of regents.
10. There is a large rose-growing center near Tyler, Texas.
11. Many states supply milk for grammar school children.
12. It is God’s will that the fittest survive.
13. The typography, paper, and bind were of the highest quality.
14. The machine dominated county posts for as long as anyone could remember.

15. The desk was old, and scratched into its surface was a profusion of dates, initials, and pleading messages.
16. The Orient Express travels between Paris and Istanbul.
17. When the Banyan bent down under its own weight, its branches began to take root.
18. There isn't a scientific explanation for every U.F.O. sighting.
19. The Hope diamond was shipped from South Africa to London through the regular mail service.
20. The review is concerned with the first three volumes.
21. The ship was ancient, and would soon be retired from the fleet.
22. Slang is a constantly changing part of the language
23. There is a small article in the local newspaper which indicates acceptance of the kidnappers' terms.
24. There are some forms in which no oath is required.
25. Entramatics find mates for the lonely.
26. 99.1% of Alaska is owned by the federal government.
27. Two men dressed as repairmen will appear shortly after the van pulls up.
28. The wood was discolored as if it had been held in a fire.
29. A light was noticed in the dark outside, and it moved eerily towards the house.
30. Painting in a few other non-European countries is treated in a separate volume.
31. A recent study revealed that one half of all university students were unable to find summer jobs.
32. Provoked arousal and orientation are accompanied by steeper negative shifts.
33. The names on the Christmas mailing list are alphabetically ordered.
34. Significantly, these changes occur during the full moon.
35. West Samoa gained its independence in 1965.
36. The magazine's report was slanted, as usual.
37. The map would prove useless as a beginning guide.
38. The speaker outlined a plan whereby the current deficits could be eliminated.
39. Black and white pictures are arranged in ten sections.
40. The voices come only at night, and whisper words, terrible words.
41. The papers had been front-paging it for days.
42. The notice made it clear that coffee breaks were being limited.
43. No man worked harder than he.
44. Potter wrote numerous satires on social cynicism.
45. Boeing's main plant in Seattle employs 35,000 people.
46. The doorkeeper was dressed in red.
47. During the next ten years, the group participated in politics.
48. The organization depended on the people for support.
49. In 1965, Elizabeth made the first state visit by a British monarch to Germany in 56 years.
50. It was their sixth consecutive best seller.
51. It all fitted in with the officer's story.
52. The merges did not change the company's policy.
53. The mansion was rented by the delegation.
54. Ninety occupations were listed as eligible for the grads in business.
55. Utah is the beehive state.
56. Changes were made in transport of lumber after the border incident.
57. The Chinese language has many dialects, including Cantonese, Mandarin, and Wu.
58. Things were booming once again in the little gold rush town of Angel.
59. At low tide the hulk of the old ship could be seen.
60. A free sample will be given to each person who enters the store.

Appendix B.6
Study 2: Attention and Mood
Picture Stimuli for Chapter 3

B.6.1
16 Heath – Threat images used in the Exogenous Cueing Task
16 Health-Threat and Neutral Pairs used in the Visual Probe Task

1. Cancer



2. Casualty



3. Coffin



4. Collapse



5. Coronary




6. Corpse




7. Diseased




8. Dying




9. Fatal




10. Funeral



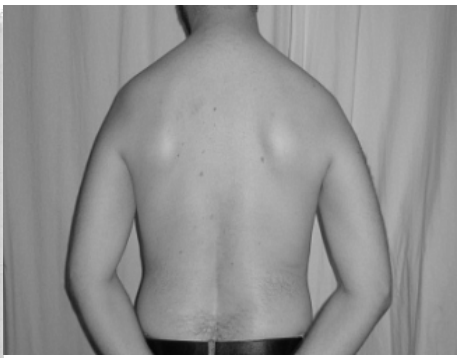

11. Hospitalised




12. Illness




13. Infectious

14. Operation




15. Paralysed




16. Spasm




B.6.2

16 Activity images used in the Exogenous Cueing Task in Chapter 4
16 Activity and Neutral Pairs used in the Visual Probe Task in Chapter 4

1. Bicycles



2. Cleaning



3. Dusting



4. Gardening



5. Gym




6. Hurrying




7. Ironing




8. Jogging




9. Lifting




10. Mopping




11. Skipping




12. Sweeping




13. Swimmer




14. Vacuuming




15. Washing




16. Wiping



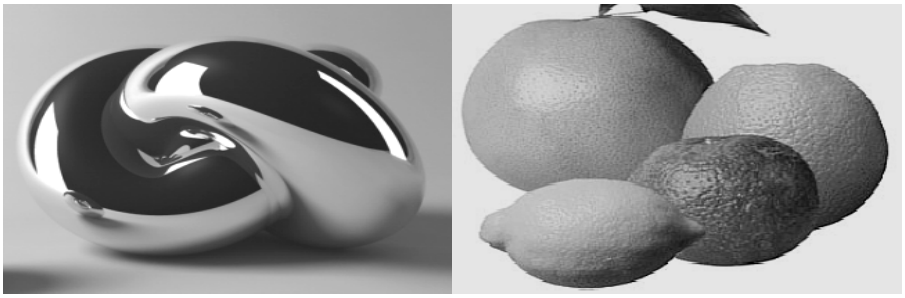

B.6.3

16 Neutral images used in the Exogenous Cueing Task
16 Neutral - Neutral Pairs used in the Dot-Probe Task
Words in Bold are the images not matching the neutral words in either EC or DP tasks, chosen to match the complexity and the content.

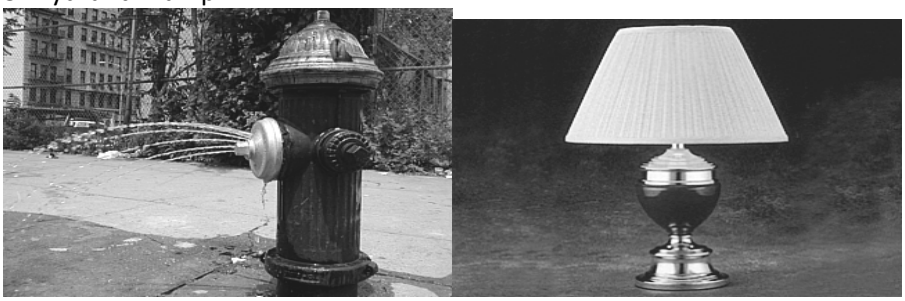
1. Coniferous - Barley



2. Chrome - Citrus



3. Hydrant - Lamp



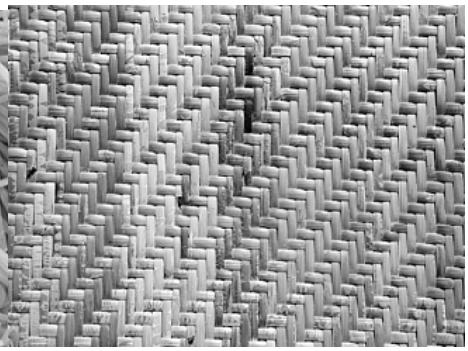
4. Flowery - Clearing



5. Farmyard - Shed



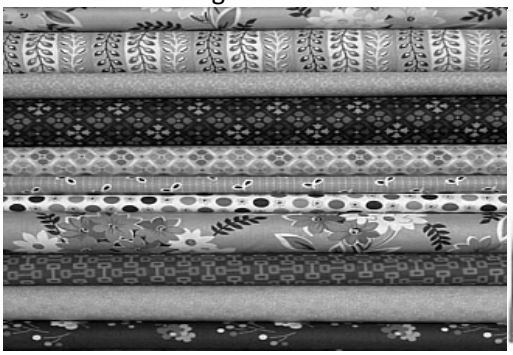

6. Spaghetti - Woven

7. Ribbon - Whistle



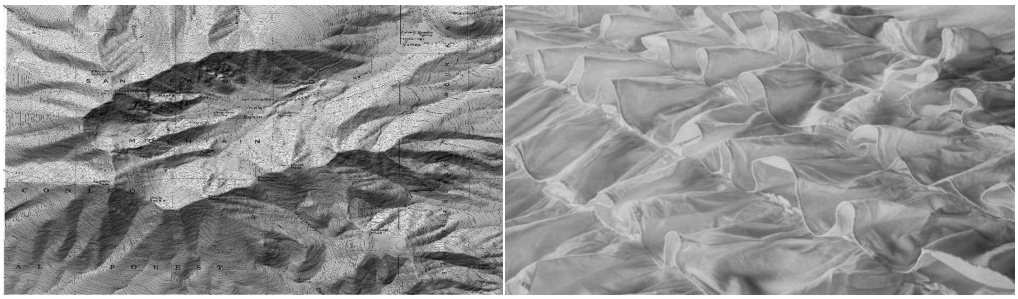

8. Fabric - Markings




9. Gleaming - Touching



10. Terrain – Ruffles



11. Sprinkler - Livestock



12. Moccasins - Envelope





13. Tractors - Farmyard




14. Dwelling - Manor




15. Architecture - Cottage




16. Quadrangle **-** Insulation




Appendix C.1
Study 3: Online Survey for Chapter 4B and Chapter 6

Information Sheet

Iana Alexeeva
Dept. of Experimental Psychology
University of Oxford
South Parks Road
Oxford OX1 3UD
EMAIL: iana.alexeeva@wolfson.ox.ac.uk

Chronic Illness: Psychological Factors
Information for Participants

Thank you for expressing an interest in taking part in this study.
Before deciding whether to take part, please, read the information about the study below. If you have any questions or concerns, please contact us by emailing iana.alexeeva@psy.ox.ac.uk. Take as long as you want to make your decision.

Our research group is interested in how people monitor their health and illness, how they cope with psychological side effects of having a chronic illness, and how certain thoughts, emotions, and behaviours may affect the severity and duration of distress that results from battling conditions like Myalgic Encephalomyelitis (M.E.) /Chronic Fatigue Syndrome (CFS), or Asthma. We are investigating whether some particular thought and behavioural patterns influence how people choose to cope with their illness and its treatment.

Survey Content
If you decide to take part in this study, we will ask you to provide some demographic information (education, age, gender). You will be asked to fill out questionnaires about your health, activity, thoughts, and emotions. The study will take about 30 - 40 minutes. However, you can leave the survey to rest and come back an hour or a day later. You can click exit survey, but do not close the browser window. When you come back to the survey it should take you back to where you stopped.

There will be a brief screening questionnaire before the main study. If you are excluded from the study for any reason your data will be deleted. Also, some of the questions will be about your health. However, no member of the research team is medically trained, so we are unable to give medical advice.

Inclusion Criteria
People with no current medical or mental health diagnosis.
People with a diagnosis of Chronic Fatigue Syndrome/ M.E.
People with Asthma diagnosis

Exclusion criteria
You need good English to take part in the study. People who have a current PRIMARY

diagnosis other than M.E./Chronic Fatigue Syndrome or asthma should not take part in this study.

Confidentiality
Any information you give will be treated with strict confidentiality, unless in the rare circumstance that you or someone else is at risk of serious harm. In this circumstance, only information directly relating to the emergency will be disclosed. Any responses you give which can be used to identify you will be anonymised or stored separately from the rest of your answers. Online data will be stored securely and only accessible to the researchers, and any hard copies of your responses will be anonymised and kept in a locked room only accessible by the researchers. If any results of these experiments are published or reported, it will not be possible to identify you from the reports.

Informed Consent
After the screening questionnaire, you will be asked to fill in a consent form indicating that you agree to take part in the study. You are still free to quit the study at any point if you wish to do so, by exiting the survey. There will be no follow up if you decide to quit the study, and you do not need to tell us why.

Ethical approval
This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. Maintenance of confidentiality of information is subject to normal legal requirements.

Further information
If you have any questions about the study, please contact Iana Alexeeva at iana.alexeeva@psy.ox.ac.uk.

Researchers:
Iana Alexeeva (STUDY CONTACT)
Address: Department of Experimental Psychology, South Parks Road, University of Oxford OX1 3UD UK
Email: iana.alexeeva@psy.ox.ac.uk

Prof. Maryanne Martin
Address: Department of Experimental Psychology, South Parks Road, University of Oxford OX1 3UD UK

Appendix C.2
Study 3: Online Survey
Ethical Approval

University of Oxford
Medical Sciences Office
John Radcliffe Hospital, Headington, Oxford OX3 9DU

From Carol Green

CONFIDENTIAL
Ms Iana Alexeeva
c/o Professor Maryanne Martin
Department of Experimental Psychology
South Parks Road

Ref.
MSD/IDREC/C1/2009/111

26 November 2009

Dear Ms Alexeeva,

CUREC checklist

I am writing to acknowledge receipt of your CUREC/1 form for your project: 'Psychological Factors in Chronic Illness.

On the basis of the information you have provided this has now been approved by the Medical Sciences IDREC **subject to:**

(a) Receipt of a hard copy of your application signed by your head of department; and
(b) Your agreeing to follow the BPS guidelines for online research

The reference number for this project is MSD/IDREC/C1/2009/111 and may I remind you that your project may be reviewed at some stage during an annual audit of projects.

Amendments

Should you at some stage alter some of the techniques or procedures then you should first undertake a checklist (CUREC/1) to see whether these changes alter the ethics of the research. If these remain the same then the committee will require notification of the changes to lodge with the project. If they do not remain the same then you may need to complete a CUREC/2 form and undergo further scrutiny by the committee.

Please do not hesitate to contact me if you have any queries about this.

Yours sincerely,
Carol Green (Miss)
Secretary to the
MSD IDREC

Appendix C.3
Study 3: Online Survey
Consent Form

Consent form

Thank you for volunteering to take part in this study. Please read the information below and tick the boxes if you agree with the statements.

We are trying to find out how people with chronic illness think and feel about their condition and how they choose to cope with it.

Name:_____(block capitals)

I have read the participant information sheet	☐
I have had the opportunity to ask questions about the study.	☐
My questions about the study have been answered	☐
I understand that:	
• I can withdraw from the study at any point without penalty by telling the researchers of this decision	☐
• Only the researchers named above will have access to the data I provide.	☐
• My personal details will be stored separately from the data I provide, and will be kept in a secure location.	☐
I am aware that all personal information will be treated with full confidentiality, except in the rare circumstance that you or somebody else if at risk of serious harm. (In this case only information necessary to an emergency will be revealed.)	
I agree to take part in this study.	☐

If you have any questions please contact Iana Alexeeva, on 01865 271108 or at iana.alexeeva@psy.ox.ac.uk.

Thank-you!

Appendix C.4
Study 3: Online Survey for Chapters 4B and 6
Questionnaires

Q. Information about you

Demographic Information

***1. Date of birth**

DD MM YYYY

Date / /

***2. Today's Date**

DD MM YYYY

Date / /

***3. Are you...?**

- ○ Male
- ○ Female

***4. What is the highest level of educational qualification you have received?**

- ☐ GCSE
- ☐ A level
- ☐ Degree
- ☐ Higher/ postgraduate degree
- ☐ NVQ or vocational qualification
- ☐ No formal qualifications

Other (please specify)

Q. Information about your health (CFS)

CFS information

***1. If yes, please state when were you first diagnosed? Please state day, month and year DD/MM/YYYY. If you cannot remember the exact date please enter your best estimate.**

Date DD / MM / YYYY

***2. Is this the exact date?**

- ◯ Yes
- ◯ No

***3. When did you first start experiencing symptoms of CFS?**
If you cannot remember the exact date, please, enter your best estimate.

Date DD / MM / YYYY

***4. Is this the exact date?**

- ◯ Yes
- ◯ No

***5. If yes, are you still experiencing symptoms?**

- ◯ Yes
- ◯ No
- ◯ Other

Other (please specify)

***6. If so, are you receiving any treatment?**

- ◯ Yes
- ◯ No
- ◯ Other

Other (please specify)

***7. What kind of treatment are you receiving?**

Q. CFS diagnostic criteria (Fukuda et al. 1994)

Questions about Fatigue

***1. In the last 6 or more consecutive months, did you OFTEN, have unexplained, persistent or relapsing chronic fatigue?**

- ◯ Yes
- ◯ No or rarely

***2. Is your fatigue the result of ongoing exertion?**

- ◯ Yes
- ◯ No

***3. Is your fatigue reduced by rest?**

- ◯ Yes
- ◯ No or rarely

***4. Does the fatigue result in a reduction of your activities (occupational, educational, social or personal)?**

- ◯ Yes
- ◯ No or rarely

***5. During the past 6 or more consecutive months how often did you have any of the following symptoms?**

	Never	Rarely	Occasionally	Most of the time	All of the time
Impairment in short term memory and/or concentration	◯	◯	◯	◯	◯
Sore throat	◯	◯	◯	◯	◯
Tender lymph nodes on the sides or the front of your neck	◯	◯	◯	◯	◯
Muscle pain	◯	◯	◯	◯	◯
Multi-joint pain without swelling or redness	◯	◯	◯	◯	◯
Headaches of a new type, new pattern, or new severity	◯	◯	◯	◯	◯
Unrefreshing sleep	◯	◯	◯	◯	◯
Exhaustion lasting more than 24 hours after taking exercise	◯	◯	◯	◯	◯

Q. Information about your health (Asthma)

Asthma

There are some things we need to check before you take part in the study. Please answer the following questions. All responses will be treated in the strictest confidence.

***1. Have you ever been diagnosed with Asthma?**

- ◯ Yes
- ◯ No

Other (please specify)

***2. If yes, please state when were you first diagnosed? If you cannot remember the exact date please enter your best estimate.**

Date DD / MM / YYYY

***3. Is this the exact date?**

- ◯ Yes
- ◯ No

***4. When did you first start experiencing symptoms of asthma?**
If you cannot remember the exact date, please, enter your best estimate.

Date DD / MM / YYYY

***5. Is this the exact date?**

- ◯ Yes
- ◯ No

***6. If yes, are you still experiencing symptoms?**

- ◯ Yes
- ◯ No

***7. If so, are you receiving any treatment?**

- ◯ Yes
- ◯ No

If yes, please state what kind of treatment you are receiving?

***8. Please, rate the severity of your asthma**

◯ Mild ◯ Moderate ◯ Severe

Other (please specify)

***9. To what degree does asthma interfere with your daily activities**

◯ 0 no interference ◯ 1 ◯ 2 ◯ 3 ◯ 4 ◯ 5 ◯ 6 ◯ 7 ◯ 8 ◯ 9 ◯ 10 greatly interferes

Q. Asthma Symptoms Checklist – ASC (Kinsman et al., 1973)

On a scale of 1 to 5, please, rate how frequently you experience each one of the listed symptoms within the past year.

1 never 2 rarely 3 sometimes 4 most of the time 5 Always

1. Cramps ___
2. Numbness ___
3. Mucous congestion ___
4. Cranky ___
5. Irritable___
6. Hard to breath___
7. Headache___
8. Edgy___
9. Frightened ___
10. Uncomfortable___
11. Short of breath___
12. Chest Congestion ___
13. Afraid of being left alone___
14. Afraid of dying___
15. Frustrated with things___
16. Dizzy___
17. Worn out___
18. Panicky___
19. Weak___
20. Pins and needles___
21. Wheezing___
22. Worried about attack___
23. Tingling in spots___
24. Chest tightening___
25. Tired___
26. Scared___
27. Nervous___
28. Fatigued___
29. Helpless__
30. Chest filling up___
31. Short tempered___
32. Worried___
33. Chest pain___
34. Exhausted___
35. Coughing___
36. No energy___

Q. Fatigue Severity Scale – FSS (Krupp et al., 1989)

FSS

Please read each statement carefully and tick a number from 1 to 7, depending on how appropriate you feel the statement applies to you OVER THE PAST WEEK.
1 indicates that the statement is not appropriate at all
7 indicates complete agreement.

***1. During the past week I have found that:**

	1 completely disagree	2	3	4	5	6	7 completely agree
1. My motivation is lower when I am fatigued.	○	○	○	○	○	○	○
2. Exercise brings on my fatigue.	○	○	○	○	○	○	○
3. I am easily fatigued.	○	○	○	○	○	○	○
4. Fatigue interferes with my physical functioning.	○	○	○	○	○	○	○
5. Fatigue causes frequent problems for me.	○	○	○	○	○	○	○
6. My fatigue prevents sustained physical functioning.	○	○	○	○	○	○	○
7. Fatigue interferes with carrying out certain duties and responsibilities.	○	○	○	○	○	○	○
8. Fatigue is among my three most disabling symptoms.	○	○	○	○	○	○	○
9. Fatigue interferes with my work, family, or social life.	○	○	○	○	○	○	○

Q. Medical Outcomes Study - RAND 36 Short-Form Health Survey – SF-36: The SF-36 (Ware & Sherbourne, 1992);

Physical Functioning subscale of Physical Health

***3. The following items are about activities you might do during a typical day. Does your health NOW limit you in these activities? If so, how much?**

	1 Yes, limited a lot	2 Yes, limited a little	3 No, not limited at all
1. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.	○	○	○
2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.	○	○	○
3. Lifting or carrying groceries.	○	○	○
4. Climbing SEVERAL flights of stairs.	○	○	○
5. Climbing ONE flight of stairs.	○	○	○
6. Bending, kneeling, or stooping.	○	○	○
7. Walking more than a mile.	○	○	○
8. Walking several blocks.	○	○	○
9. Walking ONE block.	○	○	○
10. Bathing or dressing yourself.	○	○	○

Q. Activity Scale

Physical Activity

***1. On average how much time do you spend each day being in bed or lying down on your couch (excluding at night. e.g. between 8 am and 11pm)?**

Minutes

Hours

***2. On average how much time do you spend in bed at night? (e.g. between 11pm and 8am)**

Minutes

Hours

***3. On average how much time do you spend each day outside of the house?**

Minutes

Hours

***4. How often do you leave the house?**

Per day?

Per week?

***5. What is the maximum time you spend walking at a stretch without a rest?**

Minutes

Hours

***6. Do you use a wheelchair?**

◯ Yes

◯ No

***7. Do you use a walking stick?**

◯ Yes

◯ No

Work

***1. What sort of work do you do?**

- [ ] Paid work
- [ ] Volunteering work
- [ ] Student
- [ ] Unemployed
- [ ] On long term sick leave
- [ ] Home-maker
- [ ] Other

Other (please specify)

***2. Do you work**

- [ ] Part Time
- [ ] Full Time
- [ ] Casual

***3. How many hours a day do you work?**

***4. What type of work do you do? Please describe:**

Mental Activity

How much time do you spend each day:

***1. Reading?**

Minutes

Hours

***2. Watching television?**

Minutes

Hours

***3. Doing puzzles?**

Minutes

Hours

***4. Working on the computer?**

Minutes

Hours

***5. Surfing the internet?**

Minutes

Hours

Social Activity

How much time do you spend each day:

***1. Making phone calls?**

Minutes

Hours

***2. Sending text messages?**

Minutes

Hours

***3. Sending emails?**

Minutes

Hours

***4. Chatting on the Internet?**

Minutes

Hours

***5. On Facebook?**

Minutes

Hours

Social Activity 2

How often do you

***1. Visit other people?**

Per day	
Per week	
Per month	

***2. Have visitors?**

Per day	
Per week	
Per month	

***3. Go to social gatherings?**

Per day	
Per week	
Per month	

Social Activity 3

How often do you:

***1. Go out for lunch/dinner?**

Per week

Per month

***2. Go out for drinks?**

Per week

Per month

***3. Go out for entertainment (e.g. film/theatre/concerts)**

Per week

Per month

***4. Take part in sport?**

Per week

Per month

***5. Go out to watch sport?**

Per week

Per month

***6. Go out to parties/clubs?**

Per week

Per month

***7. Go to church or other community gatherings (e.g. book club)?**

Per week

Per month

***8. Go out for educational purposes (e.g. evening classes)?**

Per week

Per month

Q. Coping – Brief Cope (Carver, 1997; Carver et al., 1989)

Brief COPE

These items deal with ways you've been coping with the stress in your life since you found out you were going to have to have this operation. There are many ways to try to deal with problems. These items ask what you've been doing to cope with this one. Obviously, different people deal with things in different ways, but I'm interested in how you've tried to deal with it. Each item says something about a particular way of coping. I want to know to what extent you've been doing what the item says. How much or how frequently. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Use these response choices. Try to rate each item separately in your mind from the others. Make your answers as true FOR YOU as you can.

1 = I haven't been doing this at all
2 = I've been doing this a little bit
3 = I've been doing this a medium amount
4 = I've been doing this a lot

1. I've been turning to work or other activities to take my mind off things.
2. I've been concentrating my efforts on doing something about the situation I'm in.
3. I've been saying to myself "this isn't real.".
4. I've been using alcohol or other drugs to make myself feel better.
5. I've been getting emotional support from others.
6. I've been giving up trying to deal with it.
7. I've been taking action to try to make the situation better.
8. I've been refusing to believe that it has happened.
9. I've been saying things to let my unpleasant feelings escape.
10. I've been getting help and advice from other people.
11. I've been using alcohol or other drugs to help me get through it.
12. I've been trying to see it in a different light, to make it seem more positive.
13. I've been criticizing myself.
14. I've been trying to come up with a strategy about what to do.
15. I've been getting comfort and understanding from someone.
16. I've been giving up the attempt to cope.
17. I've been looking for something good in what is happening.
18. I've been making jokes about it.
19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping.
20. I've been accepting the reality of the fact that it has happened.
21. I've been expressing my negative feelings.
22. I've been trying to find comfort in my religion or spiritual beliefs.
23. I've been trying to get advice or help from other people about what to do.
24. I've been learning to live with it.
25. I've been thinking hard about what steps to take.
26. I've been blaming myself for things that happened.
27. I've been praying or meditating.
28. I've been making fun of the situation.

Q. Perception of Activity (Fry and Martin, 1996a)

Perception of activity

1. Please place a cross on the line to show how active you were before your illness

Not at all Extremely

0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

2. Please place a cross on the line to show how active you are currently

Not at all Extremely

0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

3. Please place a cross on the line to show how active you expect to be when you get better

Not at all Extremely

0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

4. Please place a cross on the line to show how active you would like to be when you get better

Not at all Extremely

0-------10-------20-------30-------40-------50-------60-------70-------80-------90-------100

Q. Tampa Scale of Kinesiophobia – Fatigue (TSK-F) (Silver et al., 2002)

The statements below describe responses to exercise and activity. Please *circle the number* which best represents how strongly you think the statement is true.

	Strongly Disagree			Strongly Agree
1. I am afraid that I might make my symptoms worse if I exercise.	1	2	3	4
2. If I were to try to overcome my fatigue it would increase.	1	2	3	4
3. My body is telling me I have something dangerously wrong.	1	2	3	4
4. My fatigue would probably be relieved if I were to exercise	1	2	3	4
5. People are not taking my medical condition seriously enough.	1	2	3	4
6. My illness has put my body at risk for the rest of my life.	1	2	3	4
7. Fatigue always means I have harmed my body.	1	2	3	4
8. Just because something increases my fatigue, it does not mean it is dangerous.	1	2	3	4
9. I am afraid that I might make my symptoms worse accidentally	1	2	3	4
10. Simply being careful that I do not make any unnecessaty movements is the safest thing I can do to prevent my fatigue from worsening.	1	2	3	4
11. I would not have this much fatigue if there was not something potentially dangerous going on in my body.	1	2	3	4
12. Although I am fatigued, I would be better off if I were physically active.	1	2	3	4
13. Fatigue lets me know when to stop exercising so that I do not harm myself.	1	2	3	4
14. It is really not safe for a person with a condition like mine to be physically active.	1	2	3	4
15. I cannot do all the things normal people do because it's too easy for me to get tired.	1	2	3	4
16. Even though something makes me fatigued, I do not think it is actually harming me.	1	2	3	4
17. No one should have to exercise when he/she is fatigued.	1	2	3	4

Q. Positive and Negative Affective Scale – PANAS (See p. 376)

Q. Hospital Anxiety and Depression Scale – HADS (See p. 378)

Appendix C.5
Study 3: Online Survey
Memory Task for Chapter 6

Memory Retrieval Task (Martin & Jones, 2012)

Memory Retrieval

In this section, you will be asked to remember four different specific events in your life, and to answer some questions about each memory.

When you remember a specific event from your life, you can do so in two ways. You can remember the event as though it is being viewed by AN OUTSIDE OBSERVER (for example, a bird's eye view), seeing yourself in the situation.

Or alternatively you can remember the event as though seeing it THROUGH YOUR OWN EYES again, as when you experienced it originally.

For some events, it may be that you remember them from only one or other of these views. For other events, it may be that you remember them from both views, switching between the views while you think about the event.

The four events to be remembered are as follows.

Memory Scales Happiness

***1. Please remember a particular occasion on which you felt happier than usual**

***2. Write a word or two as a title for the event:**

***3. How long ago was this event (approximately)?**

***4. How vivid is your memory of the event?**

1 not vivid at all	2	3	4	5	6	7 As vivid as if it were happening now

***5. To what extent do you experience the memory as if viewed by AN OUTSIDE OBSERVER?**

1 Not at all	2	3	4	5	6	7 Completely

***6. To what extent do you experience the memory as if viewed THROUGH YOUR OWN EYES?**

1 Not at all	2	3	4	5	6	7 Completely

***7. How often have you thought about this event, since it happened?**

1 1-5 times	2 6-10 times	3 11-20 times	4 21-100 times	5 101 or more times

Memory Scales Pain

***1. Please remember a particular occasion on which you felt physical pain**

***2. Write a word or two as a title for the event:**

***3. How long ago was this event (approximately)?**

***4. How vivid is your memory of the event?**

1 not vivid at all	2	3	4	5	6	7 As vivid as if it were happening now

***5. To what extent do you experience the memory as if viewed by AN OUTSIDE OBSERVER?**

1 Not at all	2	3	4	5	6	7 Completely

***6. To what extent do you experience the memory as if viewed THROUGH YOUR OWN EYES?**

1 Not at all	2	3	4	5	6	7 Completely

***7. How often have you thought about this event, since it happened?**

1 1-5 times	2 6-10 times	3 11-20 times	4 21-100 times	5 101 or more times

Memory Scales Fatigue

***1. Please remember a particular occasion on which you were very tired**

***2. Write a word or two as a title for the event:**

***3. How long ago was this event (approximately)?**

***4. How vivid is your memory of the event?**

1 not vivid at all	2	3	4	5	6	7 As vivid as if it were happening now

***5. To what extent do you experience the memory as if viewed by AN OUTSIDE OBSERVER?**

1 Not at all	2	3	4	5	6	7 Completely

***6. To what extent do you experience the memory as if viewed THROUGH YOUR OWN EYES?**

1 Not at all	2	3	4	5	6	7 Completely

***7. How often have you thought about this event, since it happened?**

1 1-5 times	2 6-10 times	3 11-20 times	4 21-100 times	5 101 or more times

Memory Scales Active

***1. Please remember a particular occasion on which you were more physically active than usual**

***2. Write a word or two as a title for the event:**

***3. How long ago was this event (approximately)?**

***4. How vivid is your memory of the event?**

1 not vivid at all	2	3	4	5	6	7 As vivid as if it were happening now

***5. To what extent do you experience the memory as if viewed by AN OUTSIDE OBSERVER?**

1 Not at all	2	3	4	5	6	7 Completely

***6. To what extent do you experience the memory as if viewed THROUGH YOUR OWN EYES?**

1 Not at all	2	3	4	5	6	7 Completely

***7. How often have you thought about this event, since it happened?**

1 1-5 times	2 6-10 times	3 11-20 times	4 21-100 times	5 101 or more times

Appendix C.6
Study 3: Online Survey
Memory Coding for Chapter 6

Code type	Memory Type	Code	Explanation of Code	Example of Memory
Generality	Happy	1	*Specific*: A particular event lasting no longer than one day/24 hours, AND/OR if it involves a mention of specific date, day and time, location, name	Watching my son being page boy at my friends wedding and seeing her look so beautiful and happy."
		2	*General Category*: Category of similar events, several occurrences of similar events, events regularly occurring	When I first starting going out with my boyfriend
		3	*General Extended*: an event extended over an unspecified period of time	A trip to Barcelona with my daughters
	Pain	1		Wednesday last. Playing sport and slammed into the wall with my knee
		2		birth of 3 children
		3		Being ill with swine flu
	Fatigue	1		When I had a gastro bug and had been being ill in the bathroom for hours and missed out on sleep."
		2		Most of time, tiredness
		3		travelling from France to Sweden. long trip
	Activity	1		One time, I was having a good spell, so I decided I was going to bike 40 miles on a sandy trail. It actually went well
		2		When I moved to this home and had loads to do
		3		Hiking trip in northern Wales, which involved hiking for most of the day every day for about five days."
Emotionality	Activity	1	*Positive:* Language used that portrays a positive attitude/emotion AND/OR events recalled that have positive connotations	having a busy day at work, but being happy and dancing with patients, taking them for walks etc
		2	*Neutral:* No language used to describe emotion/attitude AND/OR events that are neither positive or negative	Walking to the post office
		3	*Negative:* Language is used that portrays a negative attitude/emotion AND/OR events recalled that have negative connotations	My birthday again, played football with my cousins and brother and pretty much screwed my body up doing so

Appendix C.7
Thematic Analysis Coding Manual for Chapter 6

Type	Theme	Subtheme	Code	Description	Example	Exemptions	Excluded Example
Activity	Exercise	Physical Challenge	1.1	Mention of an event that involves vigorous unusual physical activity	I went mountain trekking in the Himalaya, covering several miles a day, every day, for two weeks. The last day of the journey was particularly arduous as we had a lot of ground to cover to reach the pick-up point, and little water	Walking, hiking-related activities	Hiking trip in northern Wales, which involved hiking for most of the day every day for about five days.
		Regular Exercise	1.2	Mention of a type of exercise done on a more regular basis, running, cycling, swimming, gym	first starting at the gym		
		Sport/Competition	1.3	Mention of sporting competition, training for competition, competitive sports	Running a half marathon		
		Games/Recreation	1.4	mention of recreational activity, one time or regular game.	Went golfing with friends and family despite health		
	Walking	High Intensity	2.1	mention of prolonged rigorous high intensity walking	Hiking in the mountains in Wales.	Unusual, rigourous activities, which overlap with Physical challenge	I went mountain trekking in the Himalaya, covering several miles a day, every day, for two weeks. The last day of the journey was particularly arduous as we had a lot of ground to cover to reach the pick-up point, and little water
		Holiday/Relaxation	2.2	mention of relaxation, holiday time	My husband and I went out for a walk on one of the Saturdays in November. We first drove from where we live to Cotswold and parked our car close to a pub there. Before we went, my husband had looked online and found a nice public footpath there. It was a beautiful and sunny day, although it was quite windy. We took some photos and chatted as we walk. I remember walking pass a manor house that was located below a hill with lots of trees and sheeps around it. It was amazing. It took us about 3 hours to walk back to our car. We went to the pub, had some drinks and lunch, and did some shopping in the town.		
		Chores related	2.3	mention of walking in order to complete chores.	Walking to the post office		
	Chores	Moving	3.1	mentions moving houses, flats, offices, et cet...	When we were moving house		
		Daily grind	3.2	mentions housework type of activities, and external – shopping, gardening types of activities.	10 min gardening	Mentions walking	Walking to the post office
	Fun	na	4	mentions pleasant memories of activities with friends, families. It included birthday celebrations, parties, going out...	Mum's birthday trip		
	Work	na	5	mentions work, employment, job place related memories of activities that happened outside of home, not related to doing chores outside the house.	The first day of filming - on my feet and very busy for about 10 hours		
	Health-relate	na	6	mentions health, illness, symptoms, hospital, rehabilitation, et cet...	physio at hospital		
Fatigue	Travel		1	mention of travel, flying, driving, trips.	Falling asleep on the train when riding to visit hometown		
	Study		2	description of school, university, studying.	after performing an interview for my dissertation at uni - listening and talking to someone for over an hour		
	Profound		3	comments about fatigue that do not have specific events or time line, and would include descriptions such as "all the time", "every day", "constant".	I'm tired almost every day. Nothing stands out for this question.		
	Work		4	mentions work, work-stress, employment, job related fatigue memories.	Following a night shift at work		
	Post-pleasant event		5	mentions being tired after a celebratory, pleasant event.	New Year's Day		
	Illness		6	mentions fatigue due to illness, specifically mentioning illness, injury, trauma.	Asthma recovery		
	Sleep		7	comments regarding sleepiness, sleep problems, insomnia, sleeplessness.	Was exhausted from a tough day but only managed to sleep 3 hours that night, so the next day I was even more tired and couldn't drive.		
	Chores		8	mentions of house work, shopping activities, anything related to daily types of activities outside of work/school.	Struggle over Xmas period, more commitments than I could do.		
	Care		9	mentions event or a period of time of being a carer.	Molly's first year. Feeling so tired I could drop her. child care		
	Exercise		10	mentions exercise, and post-exercise fatigue.	After a yoga class. Exhaustion		
	Post-negative event		11	mentions negative event that led to increased fatigue, which was not an illness, injury, or trauma	Best mates Funeral		
Pain	Injury		1	memories of pain experienced post-injury.	Falling on a slippery pavement when walking the dog late one evening		
	Illness		2	mentions experiencing pain in relation to illness, specific or otherwise	every day since getting this illness		
	Chronic		3	mention of back pain, head ache, period pain, in general repetitive experience of pain.	tore ankle ligaments, chronic severe	Excluded due to mention of illness	every day since getting this illness
	Post-event		4	these memories reflected experiencing pain after an event that would be outside of medical/illness-related or injury context.	When I went to the theatre, Trapezius pain at the theatre		
	Operation		5	memories that involved pain post surgery, operation, medical interventions.	When I had a hysterectomy	child birth memories	
	Child birth		6	memories were in relation to giving birth	Child birth		
	Exercise		7	this theme reflects pain experienced after rigorous exercise and strenuous activity.	Muscle ache after a run	If mention of injury	Exercising and suffering shin splints
Happy	Pleasant event		1	memories of joyful, fun, pleasant activity with friends, family or alone.	Ice skating with Helena		
	Celebration		2	memories of events specifically in celebration of something, e.g. birthdays, weddings.	Went to church to celebrate Christmas Day		
	Achievement		3	memories of achieving a goal, a turning point, or a finishing something, e.g. graduation, getting a new job.	Getting my first paid academic post and completing all the paperwork that allowed me to go and take up the job.	mentions celebration of someone else's achivement	Daughter's Graduation
	Relationship		4	memories that reflected romantic and relationships-related events	When my boyfriend told me he had bought an engagement ring		
	Symptom-free		5	mentions joy at being able to do something while feeling free of symptoms.	When I was feeling very healthy for the first time in five years and was able to go horse riding for a couple of hours; when I got home, I was still feeling quite well.		

Appendix C.8
Thematic Analysis Results for Chapter 6
Examples of memories described by participants

Activity Memories

Main Themes

1. Exercise

"One day at 6th form I had a string of free periods so decided to go to the gym and do as much as I could in an attempt to raise my fitness. I stayed for several hours and did quite an intense workout. My friend joined me in the middle for an hour but she had classes." (Asthma, Female, 20).
"Swimming more than usual in one go" (Healthy control, Female, 23)

Exercise Subthemes
1) Physical challenge
"I completed the Tour du Mt Blanc, a 120km trek around in the French Alps" (Asthma, Male, 22).
"I went mountain trekking in the Himalaya, covering several miles a day, every day, for two weeks. The last day of the journey was particularly arduous as we had a lot of ground to cover to reach the pick-up point, and little water" (Healthy, Male, 29)

2) Regular exercise
"Cycled to hospital Thursday afternoon, then went for a run Friday morning" (Asthma, Female, 22).
"Jogging" (Healthy, Female, 23)

3) Sport and/or sporting competition
"London 10k … Charity run." (Asthma, Female, 27)
"Weekend long gymnastics display competition". (Healthy, Male, 27)

4) Games/Recreation
"Playing touch (American) football with college friends" (Asthma, Female, 30)
"Played badminton". (Healthy, Female, 23)

2. Walking
"Going round an exhibition. RA outing" (Asthma, Female, 60)
"Walking holiday in Lakes" (Healthy, Female, 34)

Walking Subthemes
1) Higher intensity walking
"Family trip, spent nearly the entire day walking without a good rest." (Asthma, Male, 20).
"Hiking trip in northern Wales, which involved hiking for most of the day every day for about five days." (Healthy, Male, 24).

2) Holiday/Relaxed
"I went for a walk near where I live. It was lovely weather and the surroundings were beautiful - fields, trees, horses, sheep, views of the downs, and a lake and the sea. I was able to walk further than I expected and felt really uplifted. It was exhilarating to be able to do something I hadn't been able to do for a very long time. I did not think too much about whether it would be something I could repeat, or whether I would pay the price for doing it. Even if I did suffer for it, it seemed worthwhile at the time and I decided to just enjoy it for what it was. In fact I didn't just enjoy it, I felt serene and elated, if that makes sense?" (CFS, Female, 60)

"My husband and I went out for a walk on one of the Saturdays in November. We first drove from where we live to Cotswold and parked our car close to a pub there. Before we went, my husband had looked online and found a nice public footpath there. It was a beautiful and sunny day, although it was quite windy. We took some photos and chatted as we walked. I remember walking pasts a manor house that was located below a hill with lots of trees and sheeps around it. It was amazing. It took us about 3 hours to walk back to our car. We went to the pub, had some drinks and lunch, and did some shopping in the town." (Asthma, Female, 34)

"Walking around Menorca" (Healthy, Female, 28)

3) Chores-related
"Walking to DVD shop" (Asthma, Female, 40)
"Visiting college then internet service provider's local office and then their head office. multi destination visits" (Healthy, Male, 27)

3. Chores
"Lying Turf in back yard" (Asthma, Male, 69)
"Tidying parent's house up" (Healthy, Female, 24)

Chores subthemes
1) Moving
"When I moved to this home and had loads to do" (Asthma, Female, 70)
"Carrying boxes of books and clearing out an office…" (Healthy, Female, 39)

2) Daily grind
"Shopping trip to Witney" (Asthma, Female, 34)
"A usual day when I did far more work inside and outside the house for no obvious reason." (Healthy, Female, 29)

4. Fun
"Performing arts summer school. all day rehearsals for 3 weeks" (Asthma, Female, 20)
"Fieldtrip" (Healthy, Female, 60)

5. Work
"When I was able to work" (Asthma, Male, 52)
"having a busy day at work, but being happy and dancing with patients, taking them for walks etc" (Healthy, Female, 23)

*6. **Health-related***
"physio at hospital" (CFS, Male, 42)
"This past week. Had energy. (CFS, Female, 50)
"Sitting up for a lot longer when my friend came to visit and holding her baby." (CFS Female, 30).
"coming out of hospital last time. Parolled." (Asthma, Female, 36).

Fatigue memories

*1. **Travel***
"Jet lag, returning from holiday" (Asthma, Male, 34)
"Travelling from France to Sweden. long trip" (Healthy, Female, 33).

*2. **Study related***
"At the end of my first term at uni" (Asthma, Female, 31)
"Pulling 3 all-nighters in a row at University undergrad." (Healthy, Male, 25)

*3. **Profound fatigue***
"Yesterday, very tired" (Healthy, Female, 28)
"Very tired" (Healthy, Female, 60)
"Can't remember a specific time. unspecific tiredness" (Asthma, Female, 67)

Typical memories in CFS group included:
"I'm tired almost every day. Nothing stands out for this question." (CFS, Female, 47)
"Most of the time, tiredness" (CFS, Female, 53)
"Yesterday was particularly bad. I found it very hard to do anything at all and even very simple tasks were very hard to do and felt a great chore. I hoped that doing something would make this abate but that wasn't the case and it was a very real struggle to do any of the things I needed to do and that included things like, dressing, washing, feeding my cats." (CFS, Female, 60).

*4. **Work***
"post night shift" (Asthma, Female, 31)
"completing order for a customer, one time delivery" (Healthy, Male, 27)

*5. **Post-pleasant event activity***
"With friends in South Africa. Coffee Bay Bar". (Asthma, Male, 24)
"May day morning: returning to my room after having breakfast and deciding to stay up and not go back to bed and killing time on the internet until I felt more awake." (Healthy, Female, 23)

*6. **Illness***
"Swine Flu" (Asthma, Female, 26)
"Last year when I was ill" (Healthy, Female, 34).

*7. **Sleep***
"Suffered panic attacks and did not sleep in case I choked" (Asthma, Female, 72).
"Yesterday. Dozing off" (Healthy, Male, 35)

8. ***Chores***
"I came home after work, the husband was entertaining himself and friends and I had to clean up the house, wash the dishes, feed, bathe and put the toddler to bed, while husband socialised." (Healthy, Female, 33)

9. ***Care***
"When looking after my dad with terminal cancer" (Asthma, Female, 52)

10. ***Exercise***
"After I had cycled from Oxford to Cambridge" (Asthma, Female, 22)
"After a yoga class." (Healthy, Female, 24)

11. ***Post - Negative event***
"Abortion" (Asthma, Female, 22)

Pain Memories

1. ***Injury***
"Wednesday last. Playing sport and slammed into the wall with my knee" (Asthma, Female, 28)
"I cut my finger (minorly) when peeling a potato." (Healthy, Female, 22)

2. ***Illness***
"When I possibly had mumps and my face swelled up." (Asthma, Female, 22)
"Being ill with swine flu" (Healthy, Female, 34)

3. ***Chronic pain***
"Pain in hips" (Asthma, Female, 25)
"I had terrible period pain for several years" (Healthy, Female, 48)

4. ***Post event***
Typical examples included:
"Walking around the city all day long" (CFS, Female, 21)
"The day after my birthday, I pushed myself too hard the day before and all my muscles were aching, this lasted for at least 3 months." (CFS, Male, 24)
"when I walked round town" (CFS, Female, 40)
"getting any one of my piercings done - as a memory they all exist together" (Asthma, Female, 31)
"Trying to get groceries on my own" (Asthma, Female, 42)
"Friday at the Rehab Gym" (Asthma, Female, 26)

5. ***Operation***
"Had bone surgery on my foot" (Asthma, Female, 28)
"When I had appendicitis and had surgery to remove the appendix. The recovery was very painful." (Healthy, Female, 39)

6. ***Birth***
"Birth of 3 children" (Asthma, Female, 69)
"Baby being born" (Healthy, Female, 33)

7. ***Exercise***
"Muscle ache after a run" (Healthy, Female, 22)

Happy memories

1. ***Pleasant event***
"Going to the theatre" (Asthma, Female, 60)
"Seeing my young nephew" (Healthy, Female, 24)

2. ***Celebration***
"Daughter's birth" (Asthma, Male, 34)
"When I got married (civil ceremony)" (Healthy, Female, 34)

3. ***Achievement***
"The day I finished my university prelims" (Asthma, Male, 21)
"I was offered a very good job in my area of study having been doing a low-paid, unchallenging job for 15 months" (Healthy, Male, 28)

4. ***Relationships***
"Recommencing a relationship with my partner" (Asthma, Female, 22)
"Fun date" (Healthy, Male, 35)

5. ***Symptom free***
"It happens often, several times a week, when I am not fatigued" (CFS, Male, 37)
"Going out after a better than usual day; few CFS symptoms. It is after finals, I have little work and few responsibilities; no need to conserve energy for the really important things, (study, revision, exams, classes)…" (CFS, Female, 22)