Rumination and reward processing in anorexia nervosa.

Felicity Ann Cowdrey

Lincoln College

This thesis is submitted for the degree of Doctor of Philosophy

Department of Psychiatry

University of Oxford

Trinity Term, 2012

Rumination and reward processing in anorexia nervosa.

Felicity Ann Cowdrey

Lincoln College and the Department of Psychiatry

University of Oxford

Trinity Term 2012

Abstract

Anorexia nervosa (AN) is an eating disorder characterised by severe emaciation due deliberate restriction of food intake and an intense fear of gaining weight. Theoretical accounts of AN have to date focused predominately on cognitive elements of the disorder, yet resulting treatments have been inadequate and outcome for AN remains poor. Understanding the *processes* that maintain the disorder is an important step in developing effective strategies to augment existing treatments. With this in mind, the question arises: what processes drive AN?

Novel frameworks for AN suggest that particular information processing configurations or "modes" may underpin many symptoms of AN, such as preoccupation with control of eating, weight and shape. More specifically, it is proposed that a ruminative mode of processing may function as an avoidance strategy in AN, enabling individuals to neglect salient and rewarding stimuli, such as food, and thus uphold restrictive eating practices. Whilst empirical studies have examined processes such as rumination, avoidance and reward in depression, they have seldom been studied in AN. The aim of this thesis is therefore to understand the role of rumination and reward processes in AN.

Chapter 1 reviews the literature on AN, rumination and reward processing. Chapter 2 presents data demonstrating to what extent the content of rumination in AN differs from rumination in depression and the effect that rumination may have on ED symptoms. The study conducted in Chapter 3 examines whether individuals with AN can be switched out of rumination around meal times and what effect this has on AN psychopathology. Chapter 4 presents neuroimaging data which elucidates the brain regions involved in processing rewarding and aversive food stimuli after recovery from AN. The study reported in Chapter 5 teases apart hedonic (liking) versus motivational (wanting) aspects of food reward in AN. The final study (Chapter 6) provides further evidence using neuroimaging that rumination may be an important process in AN which may override appetitive responses to rewarding stimuli, such as food. The studies reported support the notion that rumination and aberrant reward processing may be involved in the maintenance of AN.

Contents

Declarations

I declare that the work presented in this thesis is my own and has not been submitted for any other degrees in this or in any other university or institute of learning.

Some of the work described in this thesis has previously been published.

Chapter 2

Cowdrey, F. A., & Park, R. J. (2011). Assessing rumination in eating disorders: Principal component analysis of a minimally modified ruminative response scale. *Eating Behaviors*, *12*(4), 321-324.

Cowdrey, F. A., & Park, R. J. (2012). The role of experiential avoidance, rumination and mindfulness in eating disorders. *Eating Behaviors*, *13*(2), 100-105

Chapter 4

Cowdrey, F. A., Park, R. J., Harmer, C. J., & McCabe, C. (2011). Increased neural processing of rewarding and aversive food stimuli in recovered anorexia nervosa. *Biological Psychiatry*, *70*(8), 736-743

Acknowledgements

First and foremost, I would like to thank my primary supervisor Dr. Rebecca Park for her continuous support, encouragement and friendship throughout my time at Oxford. Her clinical insight, novel ideas and academic rigour have been invaluable. Under Rebecca's supervision I have been able to overcome many difficulties, both academically and personally, for which I am very grateful.

I wish to thank my second supervisor, Professor Catherine Harmer, who has offered wonderful guidance and encouragement. I am particularly grateful for all the time that Catherine has spent providing helpful comments on my work. I would like to thank Dr Ciara McCabe for introducing me the fundamentals of designing, conducting and publishing quality neuroimaging research. The combination of her good sense of humour and fierce ambition has made the experience thoroughly enjoyable, productive and rewarding. I have certainly learnt a lot.

There are a number of other colleagues from the Department of Psychiatry I would like to thank. I am truly grateful for the personal support and guidance provided by Professor Zafra Cooper. I would also like to thank Dr Anthony James for being a source of inspiration in my early days and encouraging me to apply for a DPhil. I would like to express my warm appreciation for the OPP and pPOD team members who have made me feel so welcome and provided support, friendship as well as cake!

Results described in this thesis would not have been obtained without a close collaboration with Dr Graham Finlayson (University of Leeds), Dr Nico Filipinni and Professor Steve Smith (FMRIB, Oxford), Dr Anne Stewart and Jill Roberts (Oxford Health NHS Foundation Trust). I feel honored to have worked with these individuals. I also acknowledge the help of BEAT and Cotswold House in participant recruitment. I would like to thank all the participants who gave up their time to help with the studies. The financial support of the Sir Jules Thorn Charitable Trust and Lincoln College is also gratefully acknowledged.

It is a pleasure to thank my friends, both old and new, who supported me through the ups and downs of my DPhil. I am grateful to my psychology/psychiatry friends (particularly Liz, Annabel, Suzie, Kate, Nicola-B and Katie) who gave up their valuable time to be participants, read thesis chapters, provide advice as well as entertainment! My college friends (especially Sarah, Amy, Nicola, Sok, Alice and Ollie) have been fantastic in teaching me how to balance work with play and I am grateful for their support during the happy and hard times. Thank you to Christina, Amie and Terry for making me smile and reminding me that there is life outside of Oxford University!

I am truly grateful for the loving support and tireless encouragement provided by my family- Mum, Dad, Helena and Nan. Thank you particularly to my parents for being my rock, believing in me, and taking such an active interest in all that I have chosen to do.

Felicity Ann Cowdrey
University of Oxford
May 2012

List of Figures

Chapter 5: Liking versus wanting for high and low calorie food in anorexia nervosa

Chapter 6: Resting state functional connectivity in recovered anorexia nervosa: Implications for understanding rumination and reward

Chapter 7: General discussion

List of Tables

Chapter 2: Principle component analysis of a minimally modified Ruminative Response Scale and the association with mindfulness and experiential avoidance

Chapter 3: Rumination and modes of processing around meal times in women with anorexia nervosa

Chapter 4: Neural response to pleasant and aversive food stimuli in recovered anorexia nervosa

Chapter 5: Liking versus wanting for high and low calorie food in anorexia nervosa

Table 5.1 Demographics and questionnaire scores stratified by group

List of Abbreviations

5-HT	Serotonin
AAQ	Acceptance and Action Questionnaire
AN	Anorexia nervosa
BDI	Beck Depression Inventory
BED	Binge eating disorder
BMI	Body mass index
BA	Brodmann area
BN	Bulimia nervosa
BOLD	Blood oxygen level dependent
CAT	Cognitive analytic therapy
CBT	Cognitive behavioural therapy
CIA	Clinical Impairment Assessment
DA	Dopamine
DLPFC	Dorsolateral prefrontal cortex
DMN	Default mode network
DSM-IV	Diagnostic and Statistical Manual (Edition IV)
DSM-5	Diagnostic and Statistical Manual (Edition 5)
ED	Eating disorder
EDE	Eating Disorder Examination
EDNOS	Eating disorder not otherwise specified
EPI	Echo planar imaging
FCPS	Fawcett-Clark Pleasure Capacity Scale
FFMQ	Five Factor Mindfulness Questionnaire
FMRI	Functional magnetic resonance imaging
FSL	FMRIB Software Library
GAD	Generalised Anxiety Disorder Assessment
HC	Healthy control
ICA	Independent component analysis
ICD-10	International Classification of Disease (10th Edition)
ICS	Interacting Cognitive Subsystems

IFG	Inferior frontal gyrus
IPT	Interpersonal psychotherapy
MBCT	Mindfulness-based cognitive therapy
MDD	Major depressive disorder
MELODIC	Multivariate Exploratory Linear Optimized Decomposition into Independent Components
MNI	Montreal Neurological Institute
NART	National Adult Reading Test Revised
NICE	National Institute of Clinical Excellence
OCD	Obsessive compulsive disorder
PANAS	Positive and Negative Affect Scale
PCA	Principal component analysis
PET	Positron emotion tomography
PHQ	Patient Health Questionnaire
RRS	Ruminative Response Scale
RRS-ED	Ruminative Response Scale for Eating Disorders
RSN	Resting state network
RST	Response Style Theory
SCID	Structured Clinical Interview for DSM-IV
SPECT	Single photon emission computed tomography
SPM	Statistical Parametric Mapping
SPSS	Statistical Package for the Social Sciences
VAS	Visual analogue scale
VBM	Voxel-based morphometry
WHO	World Health Organisation

Preface

This thesis investigated the processes underpinning anorexia nervosa (AN), with a specific focus on rumination and reward processing as these have been hypothesised to be central to the maintenance of AN. Using different experimental methods, this thesis investigated how (a) rumination on eating, weight and shape, and (b) reward processing may contribute to the maintenance of AN. The neural mechanisms involved in rumination and reward processing in AN were investigated (Chapters 4 and 6) and were complemented by studies using other methodologies, including a web-based survey (Chapter 2), an exploratory clinical study (Chapter 3) and a controlled behavioural study (Chapter 5). The studies presented used participants at different stages of AN (current, weight-restored, recovered) in addition to healthy volunteers.

Chapter 1

Part I

As part of the literature review the following concepts were defined: AN, rumination and reward. Clinical and psychological features of AN were described and critically evaluated, including diagnostic criteria, comorbidity, cognitive theory and treatment. From this selected literature review, a rationale was provided as to why understanding cognitive, emotional and somatic processes in AN is important in addition to the content of cognition. This rationale was framed within a novel information processing account of AN.

Part II

The possible role of rumination and reward processing in the maintenance of AN was highlighted through a review of the existing literature. A neurobiological framework for understanding symptoms of AN was discussed and parallels were drawn with the information processing account of AN. Neuroimaging studies which support the central tenets of the neurobiological framework for AN were considered.

Chapter 2 (Study 1)

A novel measure of rumination on eating disorder (ED) related themes (Ruminative Response Scale for Eating Disorders) was developed and validated in a female sample with varying levels of eating, weight and shape related concerns in addition to a sample of women who had experience of AN (either currently or in the past). After demonstrating the psychometric properties of the new measure, associations between rumination and related cognitive-affective processes, namely trait mindfulness and experiential avoidance, were examined. As hypothesised, rumination, low trait mindfulness and experiential avoidance were found to be associated with ED symptoms. These results provide preliminary evidence that disorder-specific rumination may play a role in the maintenance of AN.

Chapter 3 (Study 2)

The results from the study reported in Chapter 2 led to the question of whether the mode of processing (i.e., rumination) could be manipulated in individuals with AN and what effect manipulating the mode of processing may have on the meal time experience. Therefore a quasi-experimental study, in which participants with AN employed different training exercises (rumination induction, mindful breathing and distraction) prior to a meal time, was conducted (Chapter 3). Participants completed pre-post measures and it was found that a rumination exercise increased analytical self-focus compared to a mindful breathing exercise. The effect of mindful breathing on present-moment awareness was not significantly different to the distraction exercise and there were no differences in feelings of fatness or meal time management after using any of the exercises. A qualitative analysis was also conducted to examine the participants' experience of using the different exercises around meal times. The results highlighted the difficulties experienced around meal times generally and how interrupting rumination and enhancing a more accepting stance in individuals with current symptoms of AN may be experienced as aversive.

Chapter 4 (Study 3)

From the study reported in Chapter 3, it was apparent that eating in AN elicits a range of aversive cognitions, emotions and behaviours. This suggested that food stimuli, which is highly valued and generally experienced as rewarding by those without AN, may be processed aberrantly in those with the disorder. As the studies reported in Chapters 2 and 3 were limited by their reliance on self-report, a neuroimaging study was conducted in Chapter 4 to index objectively the neural response to food stimuli in AN. The study employed a previously validated functional magnetic resonance imaging (FMRI) paradigm involving the sight and taste of pleasant chocolate and aversive mouldy strawberry (Chapter 4). To avoid the confound of starvation, individuals recovered from AN were recruited. The behavioural and neural responses to the food stimuli in the recovered AN participants were compared to healthy control

(HC) participants. Despite no significant differences in subjective ratings of liking or wanting for the stimuli between the groups, individuals recovered from AN showed an increased neural response to both the pleasant chocolate and aversive strawberry conditions in brain regions mediating reward and aversion processing respectively. The data therefore suggested that even after recovery from AN, differences can be detected at the neural level when presented with food stimuli compared to those never ill.

Chapter 5 (Study 4)

One question raised from Chapter 4, was what underlies the discrepancy between the objective neural measures and subjective ratings of food stimuli in women recovered from AN. A behavioural study which aimed to further explore the components of reward was therefore conducted (Chapter 5). A computer task which has been designed and validated previously to measure the processes of liking (hedonic impact) and wanting (incentive salience) for food at both and implicit and explicit level was employed. For the study reported in Chapter 5, the task was modified to include high and low calorie foods. Women at different stages of AN illness (current AN, weight-restored AN, recovered AN) in addition to HC participants were recruited. The results showed that whilst there were no between-group differences in hedonic liking for food, both those currently diagnosed with AN and those weight-restored wanted to consume high calorie foods significantly less, and low calorie foods significantly more than either HC or recovered participants. This study therefore supported the notion that the aberrant response to food that characterises AN may be driven by motivational rather than hedonic processes and supports contemporary maintenance frameworks of AN. This chapter therefore raised the question of whether higher-level cognitive processes, such as rumination, mediate the association between the objective physiological response and the subsequent conscious evaluation of food stimuli.

Chapter 6 (Study 5)

The aim of Chapter 6 was to draw the themes of rumination and reward together using a brain imaging approach called resting state functional connectivity. This approach has been used to identify neural circuits which are thought to correspond to critical brain functions such as cognitive control and self-referential processing. Thus resting state functional connectivity has the potential to identify functional circuits that may be linked to rumination and reward processing in AN (and the potential interaction between them). Using the recovered AN and HC participants detailed in Chapter 4, increased resting state functional connectivity between the default mode network and the precuneus and the dorsolateral prefrontal cortex/inferior frontal gyrus was found in the recovered AN participants compared to the HC participants. As the default mode network is thought to drive self-referential processing, it was suggested that this finding may represent the increased self-focused rumination and increased cognitive control in relation to eating and the body exhibited in AN.

Chapter 7

A summary of the research findings was provided in Chapter 7. Based on findings from the studies reported in Chapters 2-6, it was argued that increased cognitive processing in the form of rumination on eating, weight and shape may function to inhibit appetitive responses to rewarding stimuli, for example consuming energy-dense, palatable foods. It was therefore proposed that rumination and reward processing may have a critical role in the maintenance of AN. Strengths and limitations of the research were considered. Clinical implications and future directions for research were discussed.

1 Rumination and reward processing in anorexia nervosa

1.1 Overview of Part I: Anorexia nervosa theory, treatment and processes

This chapter presents a brief review of the literature relating to anorexia nervosa (AN), rumination and reward processing. The literature review is divided into two parts. In Part I, working definitions are provided of AN, rumination and reward. Existing cognitive theories and psychological treatments for AN are then described. From this selective literature review, a rationale is provided as to why examining specific processes in AN may be imperative for understanding the disorder. Part I therefore provides a backdrop for an evaluation of the extant literature on rumination and reward processing in AN (which is reported in Part II of the literature review).

1.2 Definitions

Anorexia nervosa is defined according to the International Classification of Disease (ICD-10) (World Health Organisation, 1992) or the Diagnostic and Statistical Manual for Mental Disorders (DSM-IV) criteria (American Psychiatric Association, 1994) as described in Section 1.3.

Rumination has been broadly defined as: “A class of conscious thoughts that revolve around an instrumental theme and recur in the absence of immediate environmental demand or cueing” (Martin & Tesser, 1996) (p.7). For the purpose of this thesis, rumination in AN is defined as: Recurring thoughts that focus one’s attention on eating, weight and shape and their control.

Rewards are objects or events that are advantageous or essential for survival and thus organisms will work to maximize their exposure to them (Schultz, Dayan, & Montague, 1997). Rewards can be parsed into essential primary rewards (for example, food and sex) and desirable secondary rewards (for example, money). This thesis will focus mainly on primary rewards and in particular the processing of food stimuli by individuals with AN.

1.3 Classification and diagnosis of EDs

The current versions of the DSM-IV (American Psychiatric Association, 1994) and the ICD-10 (World Health Organisation, 1992) recognises two specific EDs in adults: AN, bulimia nervosa (BN) as well as a residual category of eating disorder not otherwise specified (EDNOS) which includes binge-eating and sub threshold cases of AN and BN. Disturbance in eating behaviour and over evaluation of shape, weight and their control are common to all three categories. However, the distinguishing feature of AN from the other EDs is the active maintenance of a body weight that is below a minimally normal level given the age and height (for example, a body mass index [BMI] less than or equal to [≤] 17.5kg/m^2 according to the ICD-10, or ≤ 18.5kg/m^2 according to the World Health Organisation [WHO]).

1.3.1 DSM-IV diagnostic criteria for AN

A. Refusal to maintain body weight at or above a minimally normal weight for age and height (for example, weight loss leading to maintenance of body weight less than 85% of that expected; or failure to make expected weight-gain during period of growth, leading to body weight less than 85% of that expected).
B. Intense fear of gaining weight or becoming fat, even though underweight.
C. Disturbance in the way in which one’s body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or denial of the seriousness of the currently low body weight.

D. In postmenarcheal females, amenorrhea, i.e., the absence of at least three consecutive menstrual cycles (a woman is considered to have amenorrhea if her periods only occur following hormone administration).

A distinction is made between two types of AN: restricting type and binge-eating/purging type. The distinction is made based on the presence or absence of binge-eating and/or purging behaviour (i.e., self-induced vomiting or the misuse of laxatives, diuretics or enemas).

1.3.1.1 Problems with the diagnostic criteria for EDs

The diagnostic criteria for EDs have received much criticism, mainly because there is a mismatch between the clinical reality of individuals who present at services with EDs and the criteria used to diagnose. Whilst a full evaluation of the diagnostic criteria for EDs is beyond the scope of this thesis, a brief appraisal is required as diagnostic issues have implications for ED research as well as clinical practice.

ED classification

The majority of patients who present with an ED for assessment and/or treatment do not meet the full criteria for AN or BN and are therefore diagnosed with EDNOS, the supposedly residual diagnosis (Fairburn & Bohn, 2005). They will have some of the core features of AN and BN but will differ in terms of the constellation of symptoms present and the frequency or severity of symptoms. For example, Fairburn and Cooper (2011) applied the DSM-IV criteria to 167 consecutive adult cases with an

ED (with a BMI > 15.0) and found that 52.7% of cases met criteria for EDNOS. This is problematic because the overall aim of the DSM is to provide guidelines to enable accurate diagnosis, inform treatment decisions and predict treatment outcomes.

Secondly, the classification system does not take account of the temporal instability of EDs. For example, a recent study has shown that 35% of patients with AN will experience diagnostic cross over to BN (Eddy et al., 2008). In addition, patients will go through sub threshold periods during the course of their illness. For example, an individual with AN who regains weight and thus has a BMI above 17.5kg/m^2 will no longer meet the criteria for AN but rather EDNOS, despite still displaying other core symptoms of AN. Lastly, the classification system is not able to account for migration within AN. A study has shown that over a 8-12 year follow up period, approximately 62% of cases crossed over from restricting AN to the binge-eating/purging type of AN (Eddy et al., 2002).

1.3.2 DSM-5

With an overall aim of expanding the scientific basis for psychiatric diagnosis and classification, work on a revised DSM commenced in 1999 and the approved DSM-5 manual is expected for publication in May 2013. In terms of the ED category, the most fundamental change that has been proposed is the recognition of binge-eating disorder (BED) as a third specific ED. The inclusion of this category in the DSM-5 aims to reduce the number of individuals who are diagnosed with EDNOS.

Similarly, in an attempt to reduce the number of individuals diagnosed with EDNOS, Criterion A of the AN criteria has been substantially rephrased and rather than having the arbitrary guideline of 85% for minimal healthy body weight, it focuses more on a "significantly low body weight". This aims to enable inter-individual variation to be considered. However, concern has been expressed about the lack of clear guidance regarding what constitutes a "significantly low weight" and exactly how clinicians will determine whether an individual has fallen below his/her minimally normal weight (for example, Hebebrand & Bulik, 2011).

The term "refusal" has been replaced with "restriction of energy intake" in Criteria A of the DSM-5. This is important as to date it is uncertain whether active or passive mechanisms lead to AN (Hebebrand & Bulik, 2011). The proposed addition of "persistent behaviour to avoid weight gain" to the "intense fear of gaining weight or becoming fat" for Criterion B recognises that fear of gaining weight or becoming fat is more transitory than stable and is often only present at certain periods of the illness (Becker, Thomas, & Pike, 2009). The last point of note is the omission of the controversial amenorrhea criterion (Criterion D). Together, it is therefore hoped that the DSM-5 will be a useful, easy to apply and replicable criteria for diagnosing AN in clinical and research practice.

1.4 Comorbidity

AN has high rates of comorbidity with other psychiatric disorders, particularly depression and anxiety (Godard et al., 2007; Kaye et al., 2004). Estimates are hugely variable, but a meta-analysis has reported that the lifetime prevalence of major depressive disorder (MDD) is between 9.5% and 64.7% in restricting type AN and between 50% and 71.3% in the binge-eating/purging type (Godart et al., 2007). Importantly, it has been shown that those diagnosed with both AN and MDD have a worse outcome (Mischoulon et al., 2011), including an increased rate of suicide (Franko et al., 2004). However, disentangling the effects of malnourishment on mood versus co-occurring AN and MDD is challenging as it is known that malnourishment is associated with symptoms typically seen in MDD (as described by Kalm & Semba, 2005). Studies investigating the comorbidity between AN and MDD often neglect the role of malnourishment on mood and so it is possible that estimates of comorbidity are inflated (Godart et al., 2007). That said, a study by Wagner, Barbarich-Marsteller and colleagues (2006) demonstrated that even after recovery from AN, individuals still have elevated depression symptom scores. The fact that depression symptoms persist in some individuals after recovery from AN suggests that depressed mood may be a trait factor rather than a by-product of malnourishment (Wagner, Barbarich-Marsteller et al., 2006).

There is now evidence to suggest that anxiety disorders, or at least an anxious temperament, may predate the onset of AN and persist after recovery (Kaye et al., 2004; Klump et al., 2004; Wagner, Barbarich-Marsteller et al., 2006). A range of other Axis I and Axis II disorders may also coexist with AN, for example substance-abuse/dependence (Root et al., 2010) and bipolar disorder (Fornaro et al., 2010). Comorbid conditions, particularly anxiety and depression, present AN researchers and clinicians with the challenge of trying to parcel out effects due to AN psychopathology versus effects due to co-occurring symptoms.

1.5 Theoretical models for AN

Early clinical observations and anecdotal reports of AN highlighted the role of complex cognitive processes in the onset and maintenance of AN (for example, Bruch, 1978; Crisp & Fransella, 1972). For example, Hilde Bruch stated:

> …on the one hand they declare they do not see how thin they are, and deny the existence of even severe emaciation, but at the same time they take extraordinary pride in it and consider it their supreme achievement (Bruch, 1978, p.7).

Accounts from Bruch (1978) and others which emphasised the cognitive aspects of the disorder paved the way for the development of cognitive theories of AN. The next section will review the main cognitive theories for AN.

Garner and Bemis (1982): A cognitive behavioural approach to AN

Despite earlier accounts of AN, it was Garner and Bemis (1982) who provided the first cognitive-behavioural approach to AN. Garner and Bemis' (1982) theory started from the premise that common to all individuals with AN is the cognition "I must become thin". According to this account, the origins of such dysfunctional cognitions are traced back to adolescence where premorbid personality characteristics can be identified such as introversion, asceticism and an eagerness to please others. The authors proposed that an episode of AN is precipitated by a period of self-isolation combined with feelings of helplessness and loss of control which may be exacerbated by a change in the external or internal environment in addition to societal and familial attitudes that value control over one's weight. These factors foster the notion in vulnerable individuals that losing weight and controlling one's figure will ease the turmoil being experienced mentally.

In the early stages of illness, it is suggested that weight loss is experienced as rewarding as it facilitates feelings of being in control and may be positively reinforced by family members and peers (Garner & Bemis, 1982). Over time, it is proposed that eating elicits high levels of anxiety and individuals develop a strong avoidance reaction to food. The effects of starvation, including depressed mood, anxiety, poor concentration and rigid thinking, results in the individual becoming even more socially withdrawn and therefore less likely to experience situations that may alter their beliefs. Based on this, Garner and Bemis (1982) acknowledge that any therapeutic work needs to challenge the dysfunctional beliefs about the importance of thinness in inferring personal value and self-worth.

Fairburn, Shafran and Cooper (1999): A cognitive behavioural theory of AN

Fairburn and colleagues propose that central to the maintenance of AN is the need to control eating (Fairburn, Shafran, & Cooper, 1999). The pathological need for control over eating did not feature specifically in the theory proposed by Garner and Bemis (1982). However, in an early functional account of AN by Slade (1982), the need to control eating in the context of perceived failure is detailed as a maintenance factor for AN. In their cognitive theory, Fairburn and colleagues aim to integrate the over evaluation of shape and weight from Garner and Bemis' (1982) theory with the need for control from the functional account of AN by Slade (1982).

Fairburn, Shafran and Cooper's (1999) account suggests that against a personality profile of low self-esteem, a personal sense of ineffectiveness and perfectionism, a general need for self-control becomes focused on eating. Dietary control becomes reinforced over time by the rewarding sense of self-control it provides. The symptoms associated with restriction (weight loss, altered hunger and satiety, impaired concentration, hypothermia) are interpreted as a personal success. Excessive concern about shape and weight, promoted by a Western society that values thinness, results in behaviours which exacerbate the disorder. For example, hypervigilent monitoring of body shape and weight results in increased anxiety and self-focused attention. Finally, individuals find themselves having to restrict more and more to obtain their perfectionistic standard of weight loss. Individuals will often start engaging in additional weight loss behaviours such as self-induced vomiting and excessive exercise. This once again facilitates the feeling of being in control.

Based on this model, Fairburn, Shafran and Cooper (1999) propose that lasting recovery from AN will involved a focused treatment strategy that targets both the over evaluation of shape and weight and the use of dietary restriction to achieve a sense of control, as well as the pathological need for control in general (Fairburn, Shafran & Cooper 1999).

Fairburn, Cooper and Shafran (2003): A transdiagnostic theory

In recognition of the overlap in psychological processes which maintain EDs and the migration which is observed between ED diagnoses, Fairburn, Cooper and Shafran (2003) published a transdiagnostic theory of maintenance which aims to conceptualise all EDs. In essence, the transdiagnostic theory proposes that central to all EDs is the over evaluation of eating, weight and shape and their control. In addition, Fairburn, Cooper and Shafran (2003) propose that in a subset of individuals with EDs, one or more of four additional maintaining processes interact with the core cognitive disturbance. The additional mechanisms include clinical perfectionism, mood intolerance, interpersonal difficulties and unconditional low self-esteem. From this model, the authors propose a transdiagnostic therapy which is suitable for all outpatients with an ED (Fairburn, 2008). Importantly, the ED diagnosis is not relevant in determining the content of therapy, rather content is dictated by the presence of specific clinical features and maintaining processes.

Wolff and Serpell (1998): A cognitive model of AN

Unlike the account of Garner and Bemis (1982) and Fairburn and colleagues (1999, 2003), this model does not emphasize the role of weight and shape factors in the maintenance of AN. This account focuses on the role of organised cognitive structures (or unconditional schemata) in the onset and maintenance of the disorder (Wolff & Serpell, 1998). These schemata are extreme and characterised by dichotomous states (for example, “If I am not special, I am worthless”) and individuals shift between the diametrically opposed positions. It is proposed that a critical event activates the dysfunctional schemata and an individual begins to engage in weight loss strategies which facilitate feelings of specialness and control. According to this account, contributing factors to the maintenance of AN include: positive reinforcement from others due to weight loss, physiological changes associated with starvation, and rumination about food which functions to suppress aversive emotions. It is also proposed that metacognitions in the form of pro-anorexic beliefs enhance the resistance to change (for example, “AN makes me feel in control and safe”) (Wolff & Serpell, 1998).

Whilst this account highlights some novel and potentially important maintaining factors, such as pro-anorexic thoughts and rumination, unfortunately few empirical studies have been conducted to test the account. That said, a recent cognitive-interpersonal maintenance account for AN by Schmidt and Treasure (2006) does draw on the work of Wolff and Serpell (1998) by emphasising the importance of pro-anorexic beliefs in the maintenance of AN. Thus, indirectly, some of the maintaining factors proposed by Wolff and Serpell (1998) may be examined in future research.

1.6 Translating theory into treatment

Despite a range of cognitive behavioural theories, there remains no effective evidence-based psychological or pharmacological treatment for AN (Fairburn, 2005; Flament, Bissada, & Spettigue, 2011). The National Institute for Health and Clinical Excellence (NICE) guidelines recommend that most people with AN should be managed on an outpatient basis and receive at least 6 months of psychological therapy such as cognitive behavioural therapy (CBT), interpersonal psychotherapy (IPT), cognitive analytic therapy (CAT) or focal psychodynamic therapy.

Despite the recommendations from NICE, for adults with AN no one psychological intervention has proven efficacy, let alone effectiveness, over another and outcome from the treatment trials remains poor (Fairburn & Harrison, 2003). As an illustrative point, McIntosh and colleagues (2005) randomized 50 broadly defined (BMI < 19) AN participants to either CBT, IPT or non-specific supportive clinical management (SSCM). Contrary to the author's hypothesis, using an intention-to-treat analysis, they found that SSCM was superior to specialised psychotherapies at post treatment with 75% having a good outcome (versus 33% for CBT and 15% for IPT) (McIntosh et al., 2005). A recent publication reports on the long term (5 years) outcome of these three treatments (Carter et al., 2011) which is especially important considering the high rate of relapse in AN (Carter, Blackmoore, Sutandar-Pinnock, & Woodside, 2004). At follow-up the authors report that there were no significant differences between the three conditions on any of the outcome measures with 49% of the 43 women reaching criteria for good outcome (Carter et al., 2011). Therefore, whilst SSCM seemed to have rapid effects, women in this group tended to deteriorate over the follow-up period, unlike in the other two psychological treatments. That aside, with over half the women having a poor outcome, this trial emphasises the need to continue treatment development in order to improve outcome from AN.

The lack of well controlled treatment trials for AN reflects the challenges inherent in conducting research in this field. Recruitment is difficult as AN is a relatively rare disorder with prevalence rates in adolescent females being reported as 0.3% (Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011) and 0.9% among adult women (Hudson, Hiripi, Pope, & Kessler, 2007) . In addition, many individuals with AN remain highly ambivalent about treatment and so engaging participants in therapy is challenging and this may explain in part the high attrition rates reported in existing treatment trials. Also, the samples are often heterogeneous particularly in relation to ED severity, comorbid conditions and medication status. It is therefore difficult to compare across studies.

Interim summary

There is no evidence-based treatment for AN and outcome remains poor. AN is therefore associated with high levels of morbidity and elevated mortality (Arcelus, Mitchell, Wales, & Nielsen, 2011; Steinhausen, 2009). Since existing psychological treatments for AN have been largely derived from cognitive theories, it suggests that such theories may not capture the full range of phenomena experienced by those with AN despite having relevant clinical and conceptual foundations. Specifically, it has been argued that current cognitive theories focus too heavily on the content of cognition, ignoring details of underlying cognitive, affective and somatic processes and the interactions between such processes (Park, Dunn, & Barard, 2011). Parallels can be drawn with the theoretical literature on depression where Beck's cognitive theory of depression (Beck, 1972) has been augmented by an information processing framework. The Interacting Cognitive Subsystem (ICS) account of depression, which will be described in more detail in Section 1.7, considers the interactions between cognitive, affective and somatic processes thus enabling conflicting aspects of psychological experience in depression to be modelled (Teasdale, 1999; Teasdale & Barnard, 1993). This approach may be particularly relevant in AN which like depression is also thought to be characterised by conflicting cognitive, emotional, and somatic processes. The next section will review a novel information processing account of AN which considers all three domains (cognition, emotion and somatic processes) and the interaction between them in AN.

1.7 Park, Dunn and Barnard (2011, 2012): Interacting cognitive subsystems in AN

This is a maintenance account of AN which is derived from the ICS framework and thus closely related to the ICS for depression (Teasdale, 1999; Teasdale & Barnard, 1993). ICS is a metatheoretical framework which describes the mind in terms of interactions between different cognitive subsystems and this framework has been applied to a number of psychopathological conditions. Within the ICS for depression, three mutually exclusive configurations or "modes" of processing emotional information corresponding to different qualities of subjective experience can be identified: "mindless emoting", "conceptualising doing" and "mindful experiencing"(or "being" mode) (Teasdale and Barnard, 1993). Only mindful experiencing is hypothesised to facilitate effective emotional processing, whereas the conceptualising doing mode is dominated by ruminative, discrepancy-based processing which hinders effective emotion processing and maintains depressive states (Teasdale, 1999) (see Figure 1.1). As shown by recent treatment trials involving mindfulness-based cognitive therapy (MBCT), shifting the mode in which information is processed to mindful experiencing may be a valuable strategy in psychological disorders that are characterised by rumination (Kuyken et al., 2008; Teasdale et al., 2000).

Figure 1.1 A schematic representation of the "Being" and "Doing" modes of processing

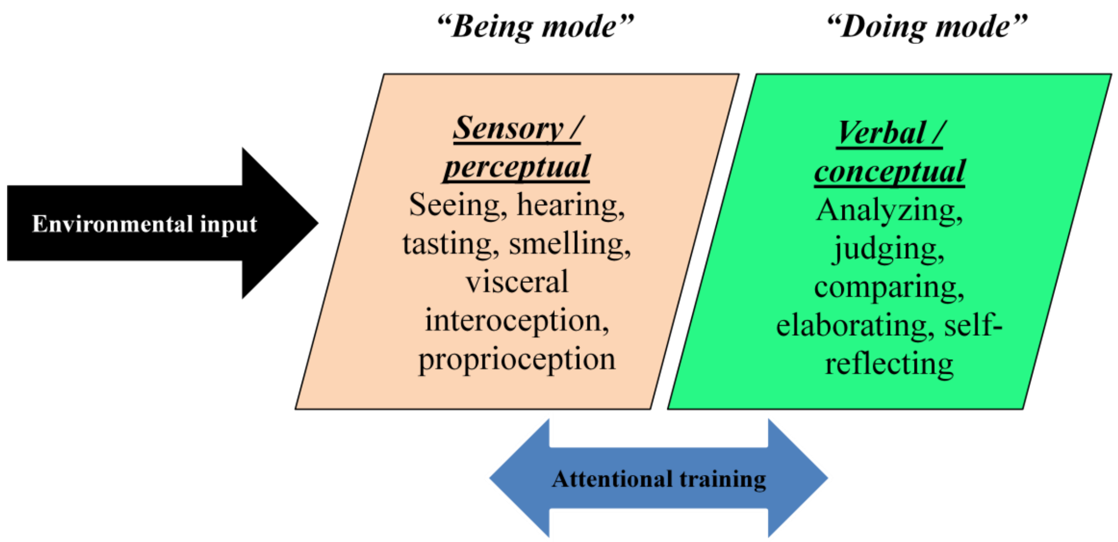


Figure 1.1
Two modes of processing are thought to make up mental experience. Attentional training (for example, MBCT) enables individuals to recognise the different modes of processing and shift attention between the modes. Figure 1.1 is adapted from "Mindfulness and psychological process" by J.M.G. Williams, 2010, *Emotion, 10* (1), p.2.

Park, Dunn and Barnard (2011, 2012) have applied core principles from the ICS for depression to explain the complex interaction between cognitions, emotions and somatic processes in AN. As with the ICS framework for depression, Park and colleagues (2011) propose that there are two mutually reinforcing modes of processing information which are adopted by individuals with AN and these function to maintain the disorder but the content of these modes is specific to AN. The conceptualising “doing AN” mode is characterised by ruminative focus on eating, weight and shape and this is proposed to enable individuals with AN to avoid emotions and bodily experiences that are associated with the starvation state (Park et al., 2011). According to the ICS account, this state is initially experienced as rewarding as it provides a sense of control, agency and safety (Park et al., 2011). Parallels can be drawn here with the cognitive models outlined in Section 1.5 which emphasised the rewarding sense of control restriction and subsequent weight loss provides. It is proposed by Park et al. (2011) that the switch from the over controlled doing AN mode to a “mindless emoting” mode is triggered by any perceived lapses in control (for example, eating more than a set calorie limit, sensory feedback from clothing) (see Figure 1.2). The mindless emoting mode is characterised by overwhelming and aversive experiences of bodily sensations and emotional beliefs which are avoided whilst in doing AN mode. It is therefore proposed that individuals with AN strive to reinstate the controlled cognitive and behavioural routines (for example, restricted eating and exercise) to facilitate transition back into the secure and initially rewarding doing AN mode.

Figure 1.2 Modes of processing which have been proposed to maintain AN

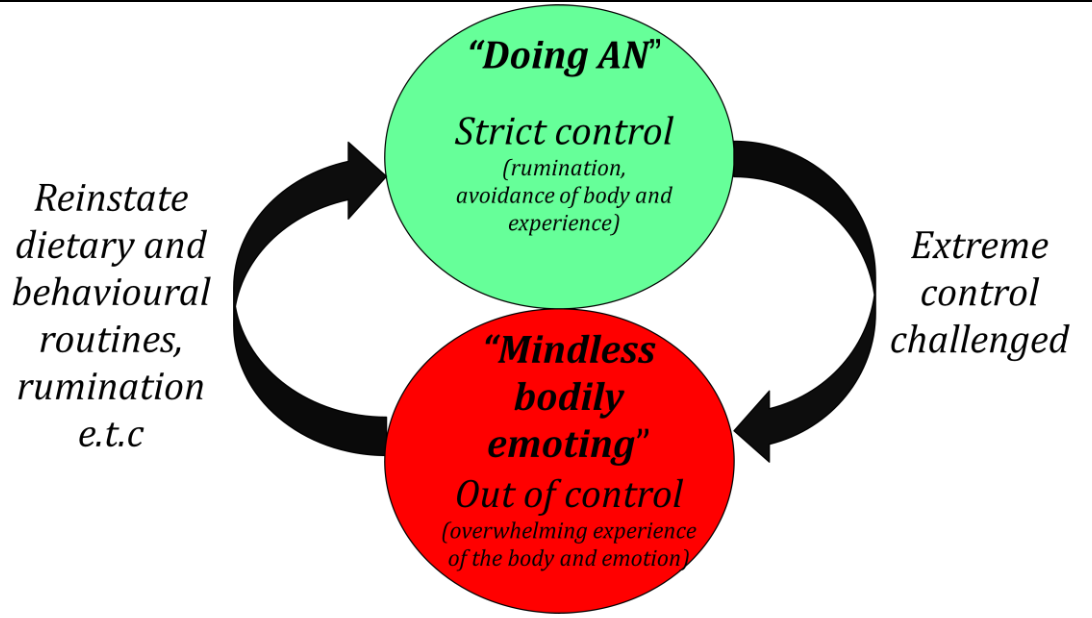


Figure 1.2
The ICS account applied to AN suggests that two mutually reinforcing modes of processing perpetuate AN psychopathology.

Over time, it is proposed that the different modes of processing become mutually reinforcing and the disorder becomes more resistant to change (Park et al., 2011). Park, Dunn and Barnard (2011) suggest that the relative amount of time spent in each of the modes of processing may relate to the different AN diagnoses (i.e., restriction versus binge-eating/purging type) and also the fluidity of diagnoses across the ED category within the same individuals.

A specific hypothesis generated from this process account is that ED psychopathology can be attenuated by interrupting the doing AN mode and enhancing a mindful experiencing or "being embodied" mode of self-focus (see Figure 1.3). The ICS account predicts that this shift would be characterised by a reduction in rumination and experiential avoidance and an increase in mindful awareness and non-judgemental attention to bodily states (Park, Dunn, & Barnard, 2012).Thus salient sensory and emotional cues that were previously avoided would be attended to directly and incorporated into more healthy self-representations which in turn may reduce ruminative processing.

Figure 1.3 "Being embodied" as a recovery mode of processing for AN

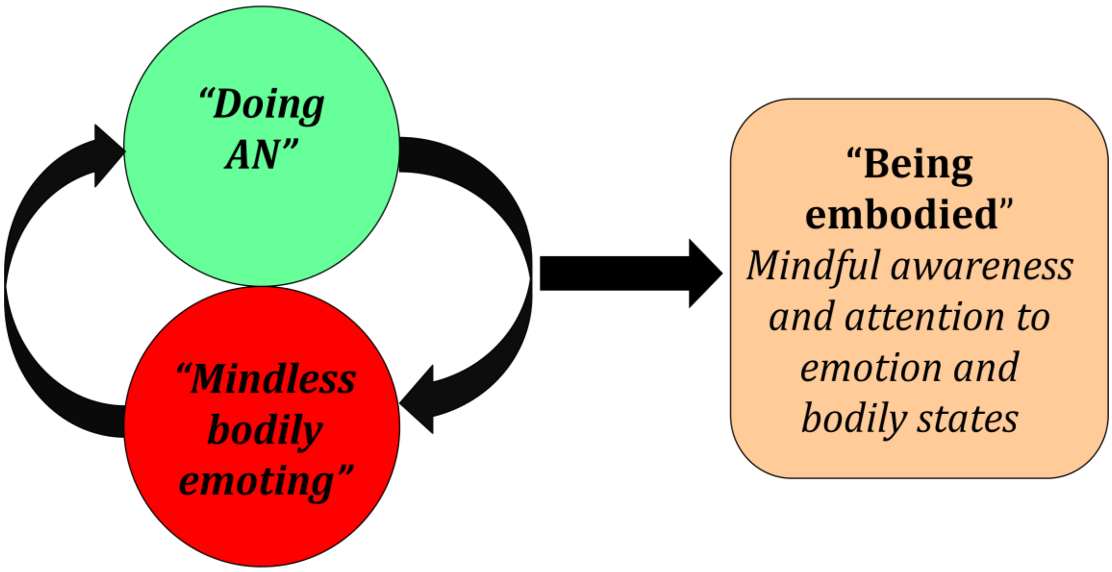


Figure 1.3
The ICS account applied to AN proposes that shifting individuals with AN into a mindful mode of processing, characterised by non-judgemental awareness of the present-moment, may be one route to recovery.

In terms of therapeutic strategies to facilitate the shift in modes, it is proposed that cautious use of mindfulness exercises and direct work with the senses and body state, such as mirror exposure or imagery, may be useful in combination with existing cognitive treatments (Park et al., 2012). The ICS account emphasises that the mode of mind sustained when any intervention in conducted is crucial to its success. Thus strategies proposed to be helpful, such as food diaries, could paradoxically be experienced as highly aversive if conducted in the wrong mode of processing (Park et al., 2012).

There is preliminary support for the hypothesis that careful disengagement of a ruminative doing AN mode of processing in favour of increased non-judgemental awareness of present-moment emotional and sensory experience may be beneficial in AN. For example, mindfulness practices which aim to train individuals to attend to the present-moment in a non-judgemental and non-elaborative manner have now been incorporated into therapies for EDs. It been demonstrated in pilot studies that mindful movement classes and yoga, which have an experiential emphasis, may increase mindfulness and decrease avoidance and ED psychopathology (Carei, Fyfe-Johnson, Breuner, & Brown, 2010; Rawal, Enayati, Williams, & Park, 2009). In addition, there is preliminary evidence that novel therapeutic interventions, such as Emotion Acceptance Behaviour Therapy and Dialectical Behaviour Therapy, which combine standard behavioural interventions with techniques to increase emotion awareness and decrease avoidance, may have potential utility in AN (Palmer et al., 2003; Wildes & Marcus, 2010; Wildes, Ringham, & Marcus, 2010). These preliminary studies support the importance of focusing on processes as well as content in AN treatment. This thesis will aim to build a stronger foundation for the development of such interventions through examination of specific processes which may underpin AN.

1.8 Overview of Part II: Rumination and reward

It has been suggested that a better understanding of the cognitive and affective maintaining mechanisms and their underlying neurobiology will contribute to the development of more effective strategies to augment existing treatment approaches for AN (Guarda, 2008; Kaye, Fudge, & Paulus, 2009; Park et al., 2011). Based on the predictions of the novel process account of AN proposed by Park and colleagues (2011, 2012), this thesis will focus on the role of rumination and reward in AN. As detailed in the ICS framework for AN outlined in Section 1.7, individuals with AN are preoccupied with *ruminative thoughts* about their body and eating control. In addition, individuals with AN have an *aberrant sense of reward*, for example they find aspects of their disorder rewarding which may contribute to the difficulties in relinquishing self-starvation behaviours. These features present a particular challenge in treatment yet remain poorly understood. Part II of the literature review considers the extant literature on rumination and reward processing and includes a selective review of relevant brain imaging studies in AN.

1.8.1 Rumination

Rumination is a cognitive or verbal activity that has been implicated in several psychological disorders (Aldao & Nolen-Hoeksema, 2010; Watkins & Moberly, 2009; Harvey, Watkins, Mansell, & Shafran, 2004), most notably in depression. Lyubomirsky and Nolen-Hoeksema (1993) define rumination as a negative form of self-focused attention which occurs in response to low or depressed mood. Whilst this is a more restricted and disorder-specific definition than employed by others (see Section 1.2 for a broader definition), the majority of research has investigated rumination in the context of Nolen-Hoeksema's Response Style Theory (RST) (Nolen-Hoeksema, 1991). Broadly, RST postulates that individual variation in that way people cope with depressed or low mood may explain differences in vulnerability to depressive symptomatology (Nolen-Hoeksema, 1991).

Rumination in depression

There is good evidence that rumination may be an important vulnerability and maintenance factor for depression. Prospective longitudinal studies have found that rumination predicts the onset of depression in adults (Lyubomirsky & Tkach, 2008) as well as children and adolescents (Abela, Brozina, & Haigh, 2002; Broderick & Korteland, 2004). Experimental work has shown that inducing rumination in depressed or dysphoric participants results in an elevation in their depressed mood compared to distraction, and also those who ruminate while depressed or dysphoric have longer and more severe periods of depressed mood (for example, Lyumbomirsky & Nolen-Hoeksema, 1993). Rumination has also been associated with a range of other negative outcomes in both clinical and non-clinical samples, such as impaired social problem solving, over general memory and suicidal ideation (Cribb, Moulds, & Carter, 2006; Park, Goodyer, & Teasdale, 2005; Surrence, Miranda, Marroquin, & Chan, 2009; Watkins & Baracaia, 2002).

Measuring rumination in depression

Studies examining rumination have typically employed the Ruminative Response Scale (RRS) (Nolen-Hoeksema & Morrow, 1991) which is a 22-item self-report questionnaire designed to capture rumination in response to low mood. It is a subscale of the more extensive Response Style Questionnaire (RSQ) (Nolen-Hoeksema, 1987).

The RRS has recently been subjected to further psychometric analyses as it was argued that many of the items on the RRS overlapped with items seen on measures of depressive symptomatology, such as the Becks Depression Inventory (BDI) (Beck, Ward, Memdelson, Mock, & Erbaugh, 1961). It was therefore questioned whether the observed relationships between depression and rumination was simply an artefact of similar item content (Treynor, Gonzalez, & Nolsen-Hoeksema, 2003). Following removal of 12 symptom-related items from the RRS, a principal component analyses provided support for a two factor model. The first component was defined as brooding as the items referred to a tendency to dwell on symptoms and compare the current situation with some other ideal. The second component was defined as reflection and referred to active attempts to gain insight into one’s problems and consider possible solutions to reduce depressive symptoms.

Ruminative brooding and reflection have been found to relate differently to concurrent and future depressive symptoms with brooding being associated with a maladaptive course and reflective pondering broadly demonstrating adaptive properties (for example, Crane, Barnhofer,& Williams, 2007). However, it is important to note that the relationship is not clear cut with some studies failing to find a differentiation between the factors (for example, Kwon & Olsen, 2007) and others finding the opposite associations (Selby, Connell, & Joiner, 2010; Surrence et al., 2009). Either way, it now seems common place for studies employing the RRS to explore possible differences between the two factors of rumination.

Rumination as a transdiagnostic processes

Whilst RST and the RRS have received empirical support, it has been argued recently that this conceptualisation restricts the exploration of ruminative experiences (Brinker & Dozois, 2009). For example, the focus on low mood in the RRS does not permit examination of other styles of repetitive thought such as worry which is typically associated with anxiety disorders (Brinker & Dozois, 2009). Martin and Tesser (1996) propose that whilst anxiety usually involves worry and depression involves rumination, all that actually differentiates the two is the temporal dynamics with the former focused more on the future and the latter involving the past. Other work has indicated that both disorders are characterised by a high degree of maladaptive self-focus (Ingram, 1990) and experimentally it has been found that both worry and rumination share the same processes and seem to differ only in content (Watkins, Moulds, & Mackintosh, 2005). Thus, authors have suggested that the same underlying style of thinking may manifest as different disorders depending on the content (for example, Brinker & Dezois, 2009; Segerstrom, Stanton, Alden, &

Shortridge, 2003; Watkins et al., 2005). Current measures of rumination, which primarily focus on rumination in response to low mood, may therefore be unable to capture adequately the repetitive negative thinking seen across different psychological disorders.

Theoretical accounts suggest that focusing on *ruminative processes* which maintain psychopathology could lead to novel treatment advances (Park et al., 2011; Teasdale, 1993, 1999). As detailed in Section 1.7, MBCT aims to train individuals to recognise negative thoughts and disengage from the ruminative patterns which could trigger a depressive episode (Segal, Williams, & Teasdale, 2002). Outcomes from randomized control trials have largely yielded promising results with significantly lower relapse in participants who have had three or more lifetime episodes of MDD (as reviewed recently by Beshai, Dobson, Bockting, & Quigley, 2011; Piet & Hougaard, 2011).

Rumination and avoidance

A number of the theoretical frameworks for AN discussed in Section 1.5 associate the process of rumination with avoidance. For example, Wolff and Serpell (1998) propose that rumination about food aims to suppress aversive emotions and similarly, Park, Dunn and Barnard (2011) suggest that rumination on themes of eating, weight and shape enable individuals to avoid emotional and body state cues (such hunger and coldness) which may threaten their control if attended to. The premise that rumination functions as a form of avoidance has been discussed in the context of a range of other psychological disorders. For example, Borkovec, Alcaine and Behar (2004) contend that like rumination, worry which characterises anxiety disorders, functions as motivated avoidance of aversive imagery and the somatic and physiological arousal which would be elicited by such imagery.

The avoidance of emotionally evocative material through repetitive negative thinking (such as rumination or worry) has been proposed to be problematic for several reasons. Perhaps most importantly, it provides a false sense of control over experience which is valued and reinforced. This stops individuals effectively responding to the emotional cues and thus has a paradoxical effect of increasing focus on the content of the material (Borkovec et al., 2004; Watkins & Moulds, 2005). As an example, in PTSD rumination involves thinking about the causes and consequences of the trauma, thus preventing direct reliving of the event which is proposed to interfere with the consolidation of the trauma memory (Ehlers & Clark, 2000). In support of this, it has been shown that employment of rumination in those with PTSD hinders emotional processing of negative events resulting in the maintenance of intrusive imagery (Williams & Moulds, 2007). In sum, it seems that rumination (and other forms of repetitive negative thinking) can be conceptualised as an avoidance strategy which exacerbates psychopathology.

1.8.1.1 Rumination in AN

Despite the fact that preoccupation with control of eating, weight and shape features prominently in cognitive behavioural accounts of AN (for example, Fairburn et al., 1999, 2003; Garner & Bemis, 1982), investigation of ruminative processes in AN has received markedly little attention. Rumination has been found to predict an increase in ED symptoms (Troop, Holbrey, & Treasure, 1998) and the onset of BN (Nolen-Hoeksema, Stice, Wade, & Bohon, 2007). Moreover it has been reported that women with EDs are more likely to use cognitive avoidance or rumination in response to a life crisis than HCs (Troop et al., 1998).

Recent research has shown that subclinical and clinical ED samples have a higher level of disorder-specific cognitions, depressive rumination, beliefs about the benefits of rumination and experiential avoidance compared to HCs (Rawal, Park, & Williams, 2010). This study also found that in participants who were followed up 10 months after initial participation, changes in self-reported ED symptoms were associated with changes in rumination and experiential avoidance (Rawal et al., 2010). From this it was suggested that rumination may be associated with avoidance of experience but it is also dependent on the severity of ED psychopathology (Rawal et al., 2010).

Further, in an experimental study using an imaginary meal paradigm, Rawal, Williams and Park (2011) manipulated the mode of self-focus in both an analogue ED sample and a partially weight-restored AN sample. The authors reported that a mindful experiencing mode of self-focus compared to a ruminative mode, reduced post-stressor reactivity and attempts to neutralise after imagining eating a large meal in both groups of participants (Rawal, Williams, & Park, 2011). Whilst this study was limited by a small sample of AN participants (*N* = 13) and no record of baseline levels of processing mode, it supports the notion that rumination is an important process in the maintenance of ED psychopathology.

It remains uncertain whether rumination has a distinct quality in those with EDs compared to other psychiatric disorders. This is particularly important given that depressive symptoms are common in individuals with EDs. As argued by Rawal, Park and Williams (2010), amendments to current measures of rumination would enable a more accurate assessment of rumination in EDs. As this thesis aims to investigate the role of ruminative processing in AN, it will be essential to develop and validate a new measure of rumination on eating, weight and shape (this work is described in Chapter 2).

1.8.2 Reward

As described in Section 1.2, rewards can be defined as objects or events that are advantageous or essential for survival and thus organisms will work to maximize their exposure to them (Schultz et al., 1997). Rewards in the primary domain are those which are innate to the organism and critical for survival such as food, drink and sex. Secondary, or higher-order rewards, derive their reinforcing value though associations with primary rewards and include money and social rewards (Delgado, Jou, & Phelps, 2011). Rewards not only have an effect on behaviour but they facilitate learning and positive emotional experience (Berridge, Robinson, & Aldridge, 2009).

A number of psychiatric disorders are characterised by aberrant processing and responding to rewarding stimuli. For example, a core feature of depression is anhedonia, or diminished ability to experience pleasure from activities or objects that are usually found rewarding (American Psychiatric Association, 1994). In drug addiction, it is thought that substance-related cues gain increased salience and thus become more attractive and wanted over time (Robinson & Berridge, 2001). It has therefore been proposed that examining reward processing may aid the understanding of psychological disorders characterised by significant deviations in mood and motivation (Berridge, Robinson, & Aldridge, 2009).

1.8.2.1 Reward processing in AN

As reviewed in Section 1.5 and 1.7, several accounts of AN identify aberrant reward processing as integral to the disorders onset and maintenance. More specifically, accounts discuss the rewarding sense of control and safety that weight loss initially provides and thus the positive beliefs which are often attributed to the anorectic state by sufferers (Garner & Bemis, 1982; Park et al., 2011; Wolff & Serpell, 1998). Furthermore, as AN is characterised by atypical cognitive and behavioural responses to primary rewarding food stimuli, this section will consider psychological theories and studies related to reward processing in AN (neuroimaging work will be discussed in Section 1.9).

There are some theories which aim to account specifically for the aberrant reward processing seen in AN. For example, Davis and Woodside (2002) propose that restriction and excessive exercise in AN function to alleviate anhedonia (diminished ability to experience pleasure) as these behaviours release β-endorphins which in turn stimulate dopaminergic (DA) neurons in mesolimbic reward structures. The authors provide some support for their hypothesis by showing that individuals with current AN report higher levels of anhedonia than BN participants and anhedonia is greatest in those who excessively exercise (Davis & Woodside, 2002). However, the conclusions that can be drawn are limited by the study's cross-sectional design, thus the inability to infer cause-effect relationships, and also its reliance on a single self-report measure.

The anhedonia hypothesis described above has been challenged by more recent theories of reward processing in AN. For example, it has been proposed that restriction in AN reflects the intense fear of weight gain associated with eating rather than an impaired ability to experience hedonic properties of food (Keating, Tilbrook, Rossell, Enticott, & Fitzgerald, 2012). According to this account, anhedonia may not characterise all individuals with AN as the reduced drive to obtain rewarding food stimuli is driven by higher-order concerns about weight gain (Kaye, Fudge, & Paulus, 2009; Keating et al., 2012). It may therefore be that over time, food becomes punishing as it is associated with weight gain, whilst weight control behaviours such as restriction and excessive exercise are positively reinforced.

In support of the notion that individuals with AN may be sensitive to both reward and punishment, a recent study has shown that individuals with current AN score higher on questionnaires of sensitivity to both reward and punishment compared to HC participants (Jappe et al., 2011). However, a study by Harrison, Treasure and Smillie (2011) reported that eating psychopathology in AN is associated with higher levels of punishment sensitivity and lower levels of reward sensitivity which supports the anhedonia hypothesis. There are several factors which could explain the diverging results which include medication status (in the study by Harrison et al. a large percentage of the participants were on antidepressants/anxiety medication which is relevant as a particular class of these drugs, the selective serotonin reuptake inhibitors, are thought to cause emotional blunting) and differences in rates of psychiatric comorbidity between the samples (45% of the participants in the study by Jappe et al. had a comorbid anxiety disorder, whilst Harrison et al. did not report data on this).

The next section will review a selection of behavioural studies which add weight to the notion of aberrant reward processing in AN. This selective review will also provide a foundation for the studies reported in the subsequent chapters of this thesis. Those reviewed use different types of paradigms. These will be examined in terms of symptom provoking and non-symptom provoking paradigms.

1.8.2.1.1 Experimental evidence examining reward processing in AN using symptom provoking paradigms

There is experimental evidence to suggest that processing of a range of rewarding stimuli is aberrant in individuals both currently diagnosed with AN and after recovery with the majority of these studies employing symptom provoking food paradigms. The results from food processing tasks in AN have been discussed in terms of general emotional reactivity, food craving, avoidance and reward processing (as discussed by Giel et al., 2011).

Jiang, Soussignan, Rigaud and Schaal (2010) found that AN participants reported significantly lower hedonic ratings of high calorie olfactory and visual food stimuli in states of hunger and satiety compared to HC participants. The authors suggested that unlike HC participants, homeostatic factors such as hunger do not affect the rewarding properties of high calorie foods in AN and instead behaviour are driven by top-down cognitive processes (Jiang Soussignan, Rigaud, & Schaal, 2010). Further, Eiber Berlin, de Brettes, Foulon, and Guelfi (2002) reported that hedonic (or 'liking') responses to sweet tastes in AN participants were significantly lower when participants when instructed to swallow the taste stimuli compared to when they were instructed to expel the solution. Interestingly, the differences in hedonic ratings were not significant when controlling for ratings of "fear to swallow" or "drive for thinness". Thus the authors suggested that the results may reflect an intense fear of gaining weight rather than an inability to respond to the pleasurable component from the sweet solutions (Eiber, Berlin, de Brettes, Foulon, & Guelfi, 2002).

Behavioural studies have also examined the reward value attached to body related stimuli, which is important as individuals with AN evaluate themselves largely in terms of their ability to control their shape and weight (Fairburn et al., 1999). Using a weight-restored sample, Watson, Werling, Zucker and Platt (2009) reported that individuals with AN found emaciated figures more rewarding to view than heavier figures whilst in HC participants, the attributed reward values were not associated with the body weight. This suggests that in AN, emaciated figures are found rewarding even in the absence of malnutrition.

1.8.2.1.2 Experimental evidence examining reward processing in AN using non-symptom provoking paradigms

An important consideration is whether deficits in reward processing are specific to disorder-relevant stimuli in AN, such as food and body images, or whether deficits can be seen across a range of modalities. Using eye tracking, Watson, Werling, Zucker and Platt (2009) found that weight-restored women with AN avoided looking at the face and eye regions of female figures, independent of observed body weight. The authors suggested that the findings indicate possible deficits in social reward processing in AN (Watson et al., 2009). However, a recent neuroimaging study has shown that after full recovery from AN there are no differences at the behavioural or neural level in processing positive or negative facial expressions thus suggesting that deficits in processing social rewards may be restricted to the ill phase (Cowdrey, Harmer, Park, & McCabe, 2011). Dissecting state versus trait features of AN will be discussed further in Section 1.10.

Several studies have found that individuals with current AN have impaired performance on the Iowa Gambling Task (for example, Cavedini et al., 2006; Tchanturia et al., 2007; Liao et al., 2009). The rationale for using this task is that it assesses how reward, punishment and uncertainty influence decision making in AN. Whilst impairment on the task has been shown to generalise to men with AN (Tchanturia et al., 2012), individuals recovered from AN have not been found to differ from HC participants in terms of their performance (Tchanturia et al., 2007; Linder, Fichter, & Quadflieg, 2012) thus suggesting impaired performance may be more of a state than trait feature. It is also difficult to determine to what extent results from such decision making tasks in the ill state are associated with other comorbid conditions or medication, as often these potential confounds are not taken into account. Interestingly, Guillaume and colleagues (2010) reported no difference in decision making abilities using the Iowa Gambling Task between ED (AN or BN) and HC participants or between the two AN subtypes. Importantly, the participants in this study were medication free and euthymic leading the authors to speculate that previous accounts of between-group differences in decision making abilities may have been driven by other clinical characteristics (such as medication and/or comorbid conditions) and not specifically ED psychopathology (Guillaume et al., 2010).

Steinglass and colleagues (2012) have investigated delay discounting for monetary rewards in current AN participants compared to HC participants. Delay discounting refers to the tendency for a delayed reward to be considered less valuable than an immediate reward of the same value. This is relevant for understanding AN as behaviour in AN seems to be guided more by future than immediate reward (for example, overriding the biological drive to consume palatable foods in the interest of the potential future reward of further weight loss). In line with the prediction, it was found that restricting AN participants reduced the value of a monetary reward significantly less than HC participants (Steinglass et al., 2012). Interestingly, Steinglass and colleagues (2012) reported no significant difference between the binge-eating/purging AN and HC participants in delay discounting. This finding fits with the clinical presentation of the subtypes as those with purely restricting AN tend to be more controlled and less impulsive than those with the binge-eating/purging subtype. Whilst speculative, the authors conclude that increased self-control may enable individuals with AN to delay reward and that this may facilitate prolonged food restriction (Steingalss et al., 2012).

1.8.2.1.3 Experimental evidence examining symptom provoking and non-symptom provoking reward processing in AN

Brooks, O'Daly, Uher, Schiöth and colleagues (2012) conducted a preliminary study in which the effect of subliminally presented stimuli (both symptom provoking and non-symptom provoking) were examined on working memory in restricting AN participants compared to HCs. It was reported that the AN participants had superior working memory compared to HCs, but this effect was lost when the subliminal food stimuli (and not the neutral or aversive stimuli) were presented (Brooks, O'Daly, Uher, Schiöth et al., 2012). The authors suggested that food stimuli may have heightened salience in AN and even if presented subliminally, it may trigger rumination on control of eating, weight and shape. Further, Brooks, O'Daly, Uher , Schiöth et al. proposed that the ruminative processing triggered by the food stimuli may compete for limited working memory resources, thus potentially explaining why individuals with AN show more errors in the working memory task after subliminal presentation of food stimuli. It was speculated that the process of rumination may underlie the cognitive inhibition of appetitive responses in AN (for example, the ability to restrict food intake despite being hungry) (Brooks, O'Daly, Uher, Schiöth et al., 2012) which also supports hypotheses derived from the ICS framework for AN (Park et al., 2011).

Whilst the results of the study by Brooks, O'Daly, Uher, Schiöth and colleagues (2012) have to interpreted cautiously due to the small sample size (*N* = 13), this study is important for two reasons. Firstly, it employed a combination of symptom provoking and non-symptom provoking stimuli and presented them subliminally thus tapping unconscious biases in AN. Secondly, it selected tasks that are known to activate areas of the brain, such as the dorsolateral prefrontal cortex (DLPFC), which have been hypothesised to underpin key symptoms of AN, such as excessive cognitive control (Kaye et al., 2009). As well as complementing the ICS account for AN (Park et al., 2011), the results support a neurobiological theory of AN which will be discussed in the next section.

1.9 What neural mechanisms control rumination and reward processing in AN?

1.9.1 Neurocircuit dysfunction in AN

A recent neurobiological framework for AN proposes that symptoms of the disorder can be explained by dysfunction in particular neural circuits (Kaye, Fudge, & Paulus, 2009). Using this framework in conjunction with the ICS for AN (Park et al., 2011), specific hypotheses regarding the neural underpinnings of rumination and reward processing can be generated and tested.

Broadly, the framework by Kaye and colleagues (2009) proposes that a dorsal cognitive neural circuit (for example, the DLPFC to the dorsal striatum) is over engaged in AN and this is manifested through rigid behaviours, elevated levels of anxiety about the future and increased preoccupation with eating, weight and shape. The dorsal cognitive neurocircuit overrides activity of a ventral neurocircuit (for example, insula and ventral striatum) which is crucial for identifying the emotional significance of salient stimuli and generating an appropriate affective response (Kaye et al., 2009). It is proposed that the unequal weighting of the two neurocircuits in AN may underpin the complex symptoms seen in AN, such as prolonged restriction despite the biological need to eat (Kaye et al., 2009).

One hypothesis derived from the neurobiological model by Kaye and colleagues (2009) is that exaggerated activity in the dorsal cognitive neurocircuit down-regulates information processing through reward pathways in AN, resulting in behaviour being directed by cognitive rules (for example, restricting eating to stay thin) rather than the immediate value of salient stimuli (for example, eating food to satisfy hunger).

1.9.2 Neurotransmitter alterations in AN

Drawing predominately on positron emission tomography (PET) and single photon emission computed tomography (SPECT) brain imaging studies in AN, Kaye, Fudge and Paulus (2009) propose that altered interactions between the serotonin (5-HT) and dopamine (DA) neurotransmitter systems may contribute to neurocircuit dysfunction in AN. A selection of studies examining the 5-HT and DA neurotransmitter systems in AN will therefore be considered briefly.

Serotonin is thought to contribute to a range of AN symptoms including depressed mood, increased satiety, obsessive compulsive behaviours and anxiety (Kaye et al., 2005). Studies have used PET in conjunction with selective radioligands to assess 5-HT receptor binding thus enabling a direct examination of 5-HT neurotransmission in specific brain regions. For example, using a selective 5-HT_{1A} receptor tracer, Bailer and colleagues (2007) reported increased binding potential in prefrontal, orbitofrontal and parietal areas of the brain in AN participants compared to HCs. This is relevant as it is thought that 5-HT_{1A} receptor activity has a role in anxiety and harm avoidance, both of which are often seen in AN (Kaye et al., 2009). However, a limitation of studies examining serotonin function in currently ill AN participants is that the results may be driven by current starvation, particularly as serotonin is synthesised from the amino acid tryptophan which is obtained through the diet (Bailer & Kaye, 2011). Therefore, studies in recovered AN participants may be more useful in revealing trait abnormalities in 5-HT function. As an example, Bailer and colleagues (2005) have also reported increased 5-HT_{1A} binding potential in recovered AN compared to HCs and further they found that binding potential in the AN participants positively correlated with self-reported harm avoidance. Such data raises the possibility that there are persistent alterations in the 5-HT system after recovery from AN and that these disturbances could be associated with increased anxiety.

Altered dopamine functioning is also thought to play a role in AN symptoms including depressed mood, restlessness and aberrant reward processing (Zinc & Weinberger, 2010). In support of this, using PET and a dopamine D2/D3 receptor antagonist, Frank and colleagues found that compared to HCs, women recovered from AN had increased binding potential in a core reward region of the brain–the ventral striatum. Based on this finding, the authors proposed that even after recovery, individuals with a history of AN may have difficulty in responding appropriately to salient stimuli (such as food reward) (Frank et al., 2005). This hypothesis is supported by recent FMRI studies which have shown altered neural activity in reward regions of the brain in AN to underweight body stimuli (Fladung et al., 2009) as well as sweet tastes (Frank et al., 2012).

As neurotransmitter systems do not operate alone, Kaye and colleagues (2009) propose that it may be more useful to consider the interaction between 5-HT and DA systems in AN than either system in isolation. More specifically, Kaye and colleagues (2009) speculate that 5-HT is the critical substrate of an aversive motivational system which might act against the DA-related reward system in AN and thus potentially contribute to neurocircuit dysfunction (as described in Section 1.9.1).

1.9.3 Parallels between Kaye et al.'s neurocircuit dysfunction and Park et al.'s ICS frameworks for AN

Whilst the framework by Kaye and colleagues (2009) takes a neurobiological perspective, parallels can be drawn with the ICS for AN described in Section 1.7 (Park et al., 2011). Rumination on eating weight and shape, which is conceptualized as a cognitive or verbal activity, may be an index of excessive activity in the dorsal neurocircuit (as described by Kaye et al., 2009). Thus over activity of the dorsal neurocircuit may reflect the ruminative "doing AN" mode which is suggested by Park and colleagues (2011) to be central to AN maintenance. Similarly, the ICS notion that rumination prevents individuals with AN directly experiencing bodily or emotional cues seems to conceptually map on to the neurobiological hypothesis that top-down control overrides activity in the ventral neurocircuit, resulting in aberrant processing of salient stimuli (such as palatable food).

The next section will review a selection of neuroimaging studies which support dysfunctional top-down and bottom-up processing networks in AN and provide rationale for the studies reported in subsequent chapters of this thesis. The studies reviewed use different kinds of paradigms which will be divided into symptom provoking paradigms and non-symptom provoking paradigms.

1.9.4 Results of symptom provoking paradigms

Symptom provoking paradigms are most frequently used in neuroimaging studies involving AN participants. Triggering stimuli have included food related stimuli (tastes or pictures) and body related stimuli, although only the literature on food related stimuli will be considered here as it is more relevant for the current thesis. By using food related stimuli, it is possible to study the neural activity associated with some of the core symptoms of AN.

1.9.4.1 FMRI with food images

Several studies have examined the neural correlates of processing visual food stimuli. Uher and colleagues (2004) presented images of savoury and sweet foods as well as aversive non-food images to participants with EDs (16 of whom had AN) and HC participants. At the behavioural level, the ED group rated the food stimuli as significantly less pleasant, more disgusting and more fear inducing than the HC group (Uher et al., 2004). At the neural level, both the AN and BN participants demonstrated significantly greater activation in the medial prefrontal cortex and the anterior cingulate cortex relative to HC participants specifically to the food stimuli (Uher et al., 2004). These regions have been implicated in the anticipation of reward and reward-based decision making (Rogers et al., 2004) thus suggesting a possible alteration in reward circuitry which is in line with the neurocircuit dysfunction model (Kaye et al., 2009).

A recent study reported that individuals with AN had increased activation in the DLPFC and right precuneus to food images versus non-food images (Brooks et al., 2011). The DLPFC is thought to be a critical part of the cognitive control network (Cole & Schneider, 2007) and thus increased activation in AN to food images may represent the increased control over food consumption. This supports the notion of excessive top-down control driving behaviours in AN. Interestingly, the precuneus has been implicated in self-referential processing (Cavanna & Trimble, 2006) and thus the increased activation in the AN participants may represent increased rumination on control of eating, shape and weight when presented with potentially threatening food images.

In support of this, Brooks, O'Daly, Uher, Friederich and colleagues (2012) conducted a novel FMRI study which instructed participants with AN (both restricting and binge-eating/purging type) and HCs to *think about* eating the food stimuli presented during the task. When thinking about eating, the AN participants showed reduced activation in the cerebellar vermis, part of the appetitive network, and increased activation in the visual cortex compared to HC participants. These findings suggest neural differences exist between AN and HC participants when instructed to ruminate about food. Interestingly, the purely restricting type AN participants had more DLPFC (control region) activation than those with the binge-eating/purging type of AN, consistent with the idea that this region is involved in the behavioural ability to restrict food intake. The authors tentatively suggest that the interactions between the bottom-up and top-down networks may determine the level of control an individual exerts over food and thus whether periods of restricting are interrupted with binge episodes (Brooks, O'Daly, Uher, Friederich et al., 2012).

Using a long term recovered sample in addition to a currently ill group, Uher and colleagues (2003) replicated their findings discussed earlier and found an increased neural response to food stimuli in the medial prefrontal cortex and the anterior cingulate cortex as well as a lack of activation in the inferior parietal lobe to food stimuli compared to HC participants. Interestingly, no significant between-group differences were reported for non-food related emotional stimuli suggesting that neural processing aberrancies are specific to food in both those currently ill with AN and after recovery (Uher et al., 2003). The fact that neural aberrancies were found after recovery from AN raises the possibility that neural activation to food, particularly in parts of the brain thought to have a regulatory role, may represent a neural biomarker or trait vulnerability for AN. Alternatively, these findings may represent a scar of the illness.

Studies have also examined the effect of manipulating hunger and satiety on the neural processing of food images in AN and HC participants (for example, Gizewski et al., 2010; Holsen et al., 2012; Santel, Baving, Krauel, Münte, & Rotte, 2006) as hunger state could influence the neural response to food. Using a repeated measures design, Santel and colleagues (2006) reported that AN participants showed decreased activation in the inferior parietal lobe to food images in a satiated state and decreased occipital activation to food images in a hungry state. The authors proposed that when satiated, individuals with AN show decreased gustatory-somatosensory processing, and when they are hungry individuals with AN can override the biological drive to eat by attending less to food stimuli (Santel et al., 2006). This suggests that levels of hunger may influence the neural response to food in AN and also that individuals with AN may process food stimuli differently at both a cognitive and sensory level to those never-ill.

1.9.4.2 FMRI with food tastes

Only three studies to date have administered food tastes in participants who have experienced AN (Frank et al., 2012; Vocks, Herpertz, Rosenberger, Senf, & Gizewaki, 2011; Wagner et al., 2008). This is surprising considering that gustatory processing may contribute to explanations of aberrant eating and reward related behaviour in AN. Vocks and colleagues (2011) administered liquid chocolate and water to participants with current AN and HCs in states of hunger and satiety. When hungry, the AN participants displayed significantly greater neural activation in the amygdala compared to HC participants (Vocks et al., 2011). This is of interest because in healthy adults, the recognition of emotionally salient stimuli is thought to recruit limbic structures such as the amygdala (Murphy, Nimmo-Smith, & Lawrence, 2003) and there is evidence that the amygdala is specifically involved in fear processing (leDoux, 2003). However, recent frameworks of emotion processing suggest that the amygdala may have a more general role in responding to emotionally salient information (Costafreda, Brammer, David, & Fu, 2008). Either way, it seems that consuming a high calorie drink in a state of hunger elicits a greater emotional response in AN compared to HCs.

Using a sample of individuals recovered AN from the restricting subtype of AN, Wagner and colleagues (2008) examined the neural response to sucrose, which is typically experienced as a pleasant taste, and a neutral water contrast. The stimuli were presented repeatedly and were thus predictable. The authors reported reduced activation to both the sucrose and water in the anterior insula, anterior cingulate and striatal regions (both ventral and dorsal) (Wagner et al., 2008). The authors also reported no correlation between subjective pleasantness ratings in the recovered AN group and the neural signal in the insula, unlike in the HC group (Wagner et al., 2008). Since the anterior insula has been shown previously to respond to the taste and physical properties of food in addition to coding the reward value of the food, these results are consistent with the hypothesis that the bottom-up system for perceiving rewards may be altered in AN.

Frank and colleagues (2012) employed a reward-conditioning paradigm that involved learning associations between conditioned visual stimuli (geometric shapes) and unconditioned taste stimuli (artificial saliva, sucrose, no solution control). After the learning phase, the stimuli were presented randomly and thus the participants could not predict exactly when they would receive the pleasant sucrose taste. It was found that individuals with current AN had a significantly greater neural response to the taste stimuli in the anteroventral striatum, insula and prefrontal cortex compared HC participants (Frank et al., 2012). The results suggested that brain reward circuits are more responsive to food stimuli in AN compared to those never ill.

It is intriguing that the results reported by Frank and colleagues (2012) diverge from those reported by Wagner and colleagues (2008) as both studies involved the administration of a sucrose solution. Differences in the predictability of sucrose receipt (repeated and predictable versus random and unpredictable) may explain the contrasting brain activations. It may be that when taste stimuli are delivered randomly to participants with AN (as in the study by Frank et al.), there is less opportunity for cognitive control strategies to modulate the reward response and thus increased neural activation in reward regions of the brain may occur. If it is the case that predictable food receipt leaves cognitive control intact, the findings may also contribute to explanations of why individuals with AN value strict eating routines and predictability.

1.9.5 Results of non-symptom provoking tasks

Whilst FMRI studies in AN have been primarily interested in the neural response to ED-related stimuli, Zastrow and colleagues (2009) examined the neural correlates of cognitive and behavioural flexibility in AN using a target detection task. This is of interest because numerous studies have shown that individuals with AN have an inflexible cognitive and behavioural profile which may in part account for symptom maintenance (for example, Tchanturia et al., 2011). In line with the hypothesis proposed by Zastrow and colleagues (2010), AN participants had significantly higher error rates on the task thus demonstrating poorer behavioural response shifting. Interestingly, the behavioural results were associated with decreased activation in brain regions including the ventral striatum and the anterior cingulate cortex, but increased activation in frontal and parietal areas (Zastrow et al., 2009). The authors concluded that the activation patterns in the AN compared to the HC participants may represent increased effortful cognitive control during task performance and decreased sensitivity to the motivational value of stimuli (Zastrow et al., 2009). Whilst it is difficult to conclude the extent to which these results were driven by current low weight, the data provides further support for the hypothesis that excessive activity in the dorsal cognitive neurocircuit drives AN symptom maintenance as proposed by Kaye and colleagues (Kaye et al., 2009).

Using participants recovered from AN, thereby avoiding the possible confound of starvation, Wagner and colleagues (2007) compared the behavioural and neural response to a guessing game paradigm in which participants could win or lose money. Unlike the HC participants, the recovered AN participants did not show a differential ventral striatal response to monetary wins versus losses (Wagner et al., 2007). The authors suggested that even after recovery, individuals with a history of AN may have difficulty evaluating the emotional significance of stimuli at the neural level (Wagner et al., 2007). Interestingly, the recovered AN participants demonstrated increased activation compared to the HCs in the caudate, part of the brain that is reliably activated by tasks which involve learning relationships between stimuli and response categories (Seger & Cincotta, 2005). Furthermore, regions of the brain involved in cognitive control, such as the DLPFC and parietal areas, project to the caudate (Cavada & Goldman-Rakic, 1991). It may therefore be that responses to rewarding stimuli are driven more by higher-level cognitive processes than hedonic evaluation in AN, even after recovery. Whilst a direct comparison is difficult to make due to the variation in task paradigms, the differences in the neural responses reported by Wagner and colleagues (2007) seem comparable to those reported in the currently ill AN participants by Zastrow and colleagues (2010) (discussed above). This poses the interesting question of whether increased activity in brain circuits involved in cognitive modulation are trait factors or alternatively scars of AN illness. This is important as identification of trait markers could enable the development of AN prevention strategies.

1.10 Research design in AN: The challenge of identifying state versus trait features

From the selected literature review on rumination and reward processing in AN, it is clear that there is value in studying those recovered from AN as well as those currently ill. Advantages and disadvantages of using currently ill and recovered AN participants in research which will be briefly considered.

Starvation effects

When individuals are severely underweight, as in AN, their cognitive and physiological systems are disturbed (Kaye et al., 2009). It is therefore difficult to determine whether any differences in research findings reflect state factors, predominantly driven by low weight, or whether they represent independent behavioural phenotypes. The cognitive and physiological effects of starvation pose a challenge for researchers in the AN field and this issue should be considered when interpreting research results.

Comorbidity

As detailed in Section 1.4, AN is highly comorbid with a range of other psychiatric disorders, particularly depression and anxiety disorders. Whilst symptoms may persist after weight restoration in a subset of individuals, being underweight is likely to exacerbate symptoms. Therefore, when comparing those with AN to HCs, any differences found between the groups may not be specific to the AN symptoms but rather to elevated levels of depression or anxiety. For example, a recent study reported that obsessive compulsive symptoms are a stronger predictor of discrimination accuracy of sad faces than AN diagnosis (Castro, Davies, Hale, Surguladze, & Tchanturia, 2010).

Medication

Medication effects are an important consideration as it is common for individuals with AN to be taking psychoactive medication (Aigner, Treasure, Kaye, & Kasper, 2011). There is a consistent body of research which has demonstrated that performance on experimental tasks are sensitive to antidepressants and other pharmacological agents (for example, Harmer, Hill, Taylor, Cowen, & Goodwin, 2003; McCabe, Cown, & Harmer, 2009). Failure to assess and control for medication status in statistical analyses may confound results when researching AN. This has been exemplified in a recent study by Jänsch, Harmer and Cooper (2009) who reported subtle differences in emotion processing between individuals with AN who were on antidepressants and/or antipsychotics and those who were not. However, it should be noted that the study by Jänsch and colleagues (2009) was limited by a small number of participants in the medicated (n = 16) and non-medicated (n = 12) AN subgroups. Nonetheless, by studying those recovered from AN and without any comorbid conditions, researchers are more likely to avoid the possible confound of current medication use. That said, it is also recognized that medication use may continue after recovery from AN.

Defining “recovery” from AN

Even if it is agreed that studying those recovered from AN is a useful way to understand the psychopathology of AN without data being confounded by low weight, there is no consensus regarding what constitutes recovery from AN. There are a number of issues that are apparent when trying to define recovery. Whether behavioural (for example, restricting), physiological (for example, healthy weight or menstrual status) as well as psychological (for example, concerns about controlling eating, weight and shape) indices should be included is an important consideration (as discussed by Bardone-Cone, et al., 2010). Several studies opt to use the term weight-restored opposed to recovered to denote participants who have regained weight to healthy level thereby avoiding the confounding factor of starvation. However, weight-restored individuals may continue to display the core psychological features of the ED, particularly concerns about eating, weight and shape. Thus they can be considered physically recovered but not psychologically recovered.

There is further variation in terms of the accepted weight threshold for weight restoration and recovery. For example, in a recent study by Friederich and colleagues (2012) participants in the weight-restored group had to have a BMI greater than 17.5 kg/m^2. In contrast, Bosanac and colleagues (2007) included participants with a BMI of greater than 18.5kg/m^2 in their weight-restored group. Variation can also be seen in duration of weight maintenance with some studies proposing that as little as 12 weeks is adequate (for example, Bosanac et al., 2007) whilst others requiring 12 months of weight maintenance (for example, Harrison, Tchanturia, & Treasure, 2010; Wagner et al., 2007). As relapse is common in AN, particularly in the first 12 months (Strober, Freeman, & Morrell, 1997), those studies using a shorter duration of weight maintenance may bias their results by including sub threshold cases in the recovered group.

Whether menstrual status is of diagnostic significance is controversial (as discussed by Attia & Roberto, 2009). The same applies when discussing its use as a criterion for recovery. More specifically, its use as a criterion for recovery is limited as it is not applicable to males, premenstrual females, those on the oral contraceptive or post-menopausal women. It is still often included in research studies using recovered samples and may be considered an additional check that the individual is physiologically recovered but not sufficient to judge recovery status on its own.

Perhaps most difficult to assess is psychological recovery, which is less quantifiable than behavioural symptoms. Psychological features refer to the level of ED cognitions that remain after weight restoration. This is crucial as both Carter, Blackmore, Sutandar-Pinnock, & Woodside (2004) and Channon and De Silva (1985) have identified residual concerns about shape and weight following treatment as a significant predictor of relapse. Again, the duration over which psychological recovery should be assessed and the measures used to assess AN cognitions over this time period are hugely variable in the literature. Most studies employ the Eating Disorder Examination (EDE) (Fairburn, 2008), or the questionnaire equivalent (Fairburn & Beglin, 2008). However, both versions focus on the past 28 days and so it is difficult to assess attitudes towards eating, weight and shape over a longer period of time. This is problematic when recruiting a sample of individuals recovered from AN, especially considering the findings of Carter and colleagues (2004) that the highest risk for relapse is 6-17 months post-treatment.

There is also the issue of remaining comorbid non-ED symptoms and disorders, such as depression or anxiety, after recovery. Bardone-Cone and colleagues (2010) reported in a recovered ED sample, elevated levels of current anxiety disorder. Although this sample was a mixed ED sample and not restricted to AN, it poses the important question of whether individuals who meet clinical criteria for a DSM psychiatric disorder should be included in recovered AN groups. By including such individuals it becomes difficult to tease apart whether results are due to the history of having an ED or driven by coexisting symptoms/disorder. Based on their findings that even after recovery from AN (using a rigorous 12 month criteria) individuals still display elevated anxiety, depression, and obsessive symptoms, Wagner, Barbarich-Marsteller and colleagues (2006) argue that such features are lifelong temperament and personality traits which may predispose an individual to AN. It could therefore be argued that excluding people who have recovered from AN but have other psychiatric diagnoses or symptoms may prevent recruitment of a representative and generalisable recovered AN sample.

Proposed definition of recovery

Bardone-Cone and colleagues (2010) have recently sought to operationalize and validate what is meant by recovery from AN. According to their definition, individuals should no longer meet DSM-IV criteria for AN, not report engaging in any ED behaviours for the past three months, have a BMI of at least 18.5 kg/m^2 and score within one standard deviation of aged matched community norms on all subscales of the EDE-Q. According to the authors, a partially recovered group would have to meet the same physical and behavioural criteria but not the psychological criteria (EDE-Q scores) (Bardone-Cone et al., 2010). The authors also argue that it is important to examine psychosocial functioning and Axis I psychopathology although these domains are not included in the definition (Bardone-Cone et al., 2010).

One problem with the definition proposed by Bardon-Cone and colleagues (2010) is that it does not specify the duration for which the healthy weight needs to be maintained. In addition, the measure of psychological recovery (EDE-Q) only covers the past 28 days. Lastly, there is evidence that three months of abstinence from ED behaviours may not be long enough to establish full recovery but rather remission (Kordy et al., 2002). Wagner and colleagues (2007) used a similar definition of recovery but used a 12 month time period and also stated that participants must not have used psychoactive medication or meet criteria for alcohol or drug abuse/dependence, MDD or severe anxiety disorder within 3 months of the study.

However, this study did not include a criterion directly tapping psychological recovery (such as the EDE-Q).

Trait versus scar effects

Whilst studying those recovered allows the data to be unconfounded by state factors, it is difficult to determine whether any differences found are stable trait characteristics or scar effects of previous periods of starvation or indeed previous ED treatment. Longitudinal studies recruiting vulnerable individuals before illness onset as well as during the acute stage are required to resolve this issue. However, it is recognised that prospective studies are a challenge in EDs due to the relative rarity of the disorder, a young average age of onset and also difficulty in identifying those at risk of developing the disorder (as discussed by Uher et al., 2003).

Section summary

Studying those recovered from AN has several advantages. Most importantly, it avoids confounding factors of low weight and so hypotheses regarding predisposing traits can be formulated more accurately. However, findings may be a residual scar of previous AN episodes. In addition, a helpful definition of AN recovery needs to be ascertained and guidelines and validated instruments to measure this construct need to be developed.

1.11 Part II summary

Despite contemporary psychological accounts of AN, the processes underpinning AN remain poorly understood and this in part has hindered the development of effective treatments for AN. Two features which present particular challenges to successful treatment include the intense preoccupation with thoughts about the body and eating control and an aberrant sense of reward, particularly in the primary domain of food. Both factors may contribute to the difficulty in relinquishing self-starvation behaviours and the high levels of relapse seen in AN. Previous behavioural studies have shown that rumination is associated with ED symptoms and whilst the results are not consistent, there is evidence that both behavioural and neural differences in response to rewarding stimuli might contribute to AN psychopathology. There is a good rationale for studying those ill and recovered in an attempt to differentiate between state and trait markers. The aim of this thesis is to build on such work in order to understand the processes involved in the maintenance of AN.

2 Principle component analysis of a minimally modified Ruminative Response Scale for Eating Disorders and the association with mindfulness and experiential avoidance

2.1 Overview

As identified in the literature review presented in Chapter 1, rumination is as a process that has been implicated in a number of psychological disorders, most notably depression. The ICS framework applied to AN suggests that ruminative preoccupation on eating, weight and shape characterises the "doing AN" mode and is central to the disorders maintenance (Park, Dunn, & Barnard, 2011). Few studies have investigated rumination in the context of EDs. This chapter therefore aims to develop and validate a novel measure of rumination on eating, weight and shape and test the association between rumination, mindfulness, experiential avoidance and ED symptoms. The specific questions addressed in this chapter are:

- Does rumination have a distinct quality in those with AN that is not captured adequately by existing measures of rumination?
- What is the relationship between rumination, mindfulness, experiential avoidance and ED symptoms?

2.2 Background

As reviewed in Section 1.5, theoretical frameworks for AN highlight the role that preoccupation on eating, weight and shape concerns have in the disorders onset and maintenance (for example, Fairburn et al., 1999, 2003). Behavioural and neuroimaging studies demonstrating altered processing of disorder-relevant stimuli (food and body images) in AN provide indirect support for this.

The ICS account of AN by Park, Dunn and Barnard (2011) conceptualises preoccupation in AN as a type of disorder-specific rumination which focuses on *thinking about* control of eating, weight and shape, rather than direct experiencing of bodily states and emotions associated with starvation. Rumination is thus proposed to have an avoidant function which would support studies showing that individuals with AN report greater avoidance of affect and difficulty tolerating emotions compared to HCs (Hambrook et al., 2011).

Rumination, and the associated avoidance of cognitions, emotions and bodily sensation (experiential avoidance), may be experienced positively by individuals with AN and thus facilitate symptom maintenance (Park et al., 2011; Schmidt & Treasure, 2006; Serpell, Treasure, Teasdale, & Sullivan, 1999). This hypothesis is difficult to test as to date there is no self-report measure to capture the unique content of rumination in AN which focuses on eating, weight, shape and control. Being able to accurately measure rumination and avoidance in AN is important as these processes tend to operate in parallel and are presumed to be correlates of the ruminative mode of processing (Williams, 2008).

The adaptive counterpart of rumination and avoidance is mindfulness, defined as purposefully and non-judgementally attending to the present-moment (Bishop, et al., 2004). Thus mindfulness is presumed to be a correlate of ‘being’ mode (Williams, 2008). Park, Dunn and Barnard (2012) suggest that in AN attending to the self and the body in a mindful way may be fundamental to recovery. In support of the association between mindfulness and ED symptoms, previous studies have shown that there is an inverse relationship between mindfulness and ED related cognitions (Lavender, Gratz, & Tull, 2011; Lavender, Jardin, & Anderson, 2009) and also that mindfulness mediates the link between ED cognitions and psychological distress (Masuda & Wendell, 2010). As discussed in Section 1.7, mindfulness practices are being incorporated into some aspects of ED treatments. However, to date no study has investigated the association between rumination, avoidance, mindfulness and ED symptoms.

2.2.1 Study aims

- To design and validate a minimally modified Ruminative Response Scale for EDs (RRS-ED) in a healthy sample and identify the factor structure and psychometric properties (Analysis 1).
- To conduct a preliminary assessment of the RRS-ED in those with AN (past and current) (Analysis 1).

- To examine the associations between rumination, experiential avoidance, mindfulness and ED symptoms in HC participants and in individuals with AN (past and current) (Analysis 2).

2.2.2 Hypotheses

- Principal component analysis (PCA) of the RRS-ED would yield a two factor solution in line with the original RRS.
- Greater ED symptoms would be associated with higher levels of ED-specific rumination, compared to depressive rumination.
- Participants with AN (past and current) would demonstrate significantly higher levels of ED-specific rumination compared to HCs.
- Rumination, as measured by the RRS-ED, and experiential avoidance would be positively associated with ED symptoms and trait mindfulness would be negatively associated with ED symptoms.

2.3 Method

2.3.1 Participants

Participants between the ages of 16 and 65 were included in this study. There were no other inclusion or exclusion criteria. Participants were recruited via posters, internet advertisements and email circulars.

2.3.2 Study procedure

The research protocol was reviewed and approved by the University of Oxford’s Research Ethics Committee (see Appendix 2.1). The survey was created using Bristol Online Surveys (Institute for Learning and Research Technology, University of Bristol, UK). The online web survey consisted of the new measure as well as self-report instruments of depression, anxiety and rumination (described below). The survey website was included as a link in internet advertisements as well as emails circulated to acquaintances and university colleges. The link took potential participants to an online information sheet and consent form (see Appendix 2.2 and Appendix 2.3). Data was stored automatically from the online programme. The questionnaires took approximately 25 minutes to complete. All data was analyzed using SPSS.

2.3.3 Measures

2.3.3.1 Ruminative Response Scale for EDs (RRS-ED)

The RRS-ED was adapted from a 10-item subset of the RRS for depression (Nolen-Hoeksema & Morrow, 1991; Treynor, Gonzalez, & Nolen-Hoeksema, 2003); five items from the reflection subscale and five items from the brooding subscale. The RRS was selected because it is a well validated measure and widely used in studies of dispositional tendencies to ruminate (for example, McMurrich & Johnson, 2008). Existing cognitive models and theoretical frameworks of AN were used to guide the modification of items (for example, Fairburn et al., 1999, 2003; Park et al., 2011). Permission to use the items was given by Professor Susan Nolen-Hoeksema, the senior author of the RRS for depression (Nolen-Hoeksema & Morrow, 1991; Treynor et al., 2003).

The items were reviewed by a panel of clinical psychologists (N = 2), research psychologists (N = 3) and psychiatrists (N = 2) in the ED field and also by a small sample of individuals (N = 6) who had recovered from an ED. They rated the items for clarity, relevance and significance using a series of Likert scales (1 = *not at all* to 5 = *very*). Further modifications were made based on their feedback.

The resulting RRS-ED required participants to indicate what they would generally do when they are concerned about controlling their eating, weight and shape. Response categories range from “almost never” to “almost always” and scores from 1 to 4 were assigned to each response category (see Appendix 2.4 for the final version of the RRS-ED).

2.3.3.2 ***Eating Disorder Examination-Questionnaire (EDE-Q)***

The EDE-Q (Fairburn & Beglin, 2008) is a 28-item self-report questionnaire (see Appendix 2.5). In addition to the global score, the EDE-Q comprises the following subscales: eating concerns, weight concerns, shape concerns and restraint. The measure also yields a global score. The global score was used in the current study for a measure of ED symptoms. The questionnaire focuses on the last 28 days and responses are on a 7-point scale with higher scores reflect greater eating-related symptoms. The questionnaire has good reliability and validity (Fairburn & Beglin, 2008) and acceptable internal consistency and test-retest reliability (Luce & Crowther, 1999).

2.3.3.3 Clinical Impairment Assessment (CIA)

The CIA (Bohn et al., 2008) is a 16-item measure to assess severity of psychosocial impairment due to ED psychopathology over the previous 28 days (see Appendix 2.6). The CIA has high levels of internal consistency, construct and discriminant validity, test-retest reliability and sensitivity to change (Bohn et al., 2008).

2.3.3.4 Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 (Kroenke, Spitzer, & Williams, 2001) is a 9-item brief scale for diagnosing and measuring severity of depression over a period of two weeks (see Appendix 2.7). Scores of 5, 10, 15 and 20 represent cut-off points for mild, moderate, moderately severe and severe depression respectively. The PHQ-9 has good validity and reliability (Kroenke et al., 2001).

2.3.3.5 Generalised Anxiety Disorder Assessment-7 (GAD-7)

The GAD-7 (Spitzer, Kroenke, Williams, & Lowe, 2006) is a 7-item brief scale for assessing the symptoms of generalised anxiety disorder over the last two weeks (see

Appendix 2.8). Scores of 5, 10 and 15 represent cut-points for mild, moderate and severe anxiety respectively. As well as a screening and severity measure for GAD, it has moderately good operating characteristics for three other common anxiety disorders: panic disorder, social anxiety disorder and post-traumatic stress disorder (Spitzer et al., 2006).

2.3.3.6 Ruminative Response Scale (RRS)

The RRS (Nolen-Hoeksema & Morrow, 1991) includes 22-items assessing three types of responses to depressed mood: focusing on the self, focusing on the symptoms, and focusing on the possible consequences and causes of depressed mood (see Appendix 2.9). The RRS has very high internal consistency (Cronbach‘s alpha ranging from .88 to .92) (Bagby et al., 1999; Nolen-Hoeksema & Davis, 1999), test-retest reliability (Nolen-Hoesema, Parker, & Larson, 1994), as well as convergent and predictive validity (Butler & Nolen-Hoeksema, 1994; Nolen-Hoeksema & Morrow, 1991).

2.3.3.7 Five Factor Mindfulness Questionnaire (FFMQ)

The FFMQ (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006) is a 39-item measure of everyday mindfulness (see Appendix 2.10). The five factors are: non reactivity to inner experience, observing thoughts and feelings, acting with awareness, describing/labelling with words and non-judging of experience. The FFMQ has been shown to have good internal consistency (Baer et al., 2006). Due to the multiple self-report measures used in this study, a combined score of the five factors was used as a measure of mindfulness (as in Sanders & Lam, 2010).

2.3.3.8 Acceptance and Action Questionnaire-II (AAQ-II)

The AAQ-II (Bond et al., 2011) is a 7-item measure of experiential avoidance and psychological inflexibility (see Appendix 2.11). Items are rated on a 7-point scale ranging from "never true" to "always true" with higher scores indicating greater levels of psychological inflexibility and avoidance. The AAQ-II has been designed to assess the same construct as the original AAQ-I (Hayes et al., 2004) and does correlate with the original scale (r =.97), but it has obtained better psychometric properties (Bond et al., 2011).

2.3.3.9 Other information

Participants voluntarily provided demographic information (age, ethnic origin, education and occupation) and self-reported height and weight (in order to calculate BMI = weight [kg]/height [m^2]). They also provided information on any current or past psychiatric diagnoses.

2.4 Results

2.4.1 Demographic characteristics

Data was collected from 375 participants. 100 (26.6%) participants were excluded from the main analysis because they reported a current or past diagnosis of one or more DSM Axis I or Axis II disorders (a subsample of these was used in subsequent analyses). Of the 275 healthy participants, 82.9% were female. There were significant gender differences in self-reported depression, anxiety and ED symptoms (p <.05), and thus only the data from the 228 females was analysed.

The sample consisted of undergraduate and postgraduate students as well as adults in full or part time employment. The mean age was 24.03 years (SD = 7.62, range = 16-64 years old). The mean BMI was 22.03 (SD = 2.75, range = 17.11 - 32.27)[1]. 165 (72%) of participants reported to have at least 16 years of education. 158 (69%) of the participants were students. The majority of the participants (87%) reported English as their first language. Descriptive statistics for the questionnaire measures are reported in Table 2.1.

---

1 Due to the large range in BMIs, participants were grouped into either a non-AN/healthy BMI group (defined as BMI 18-29) or an unhealthy BMI group (defined as either a BMI below 18 or above 29). Mann-Whitney *U* tests were used to determine whether ED, depression or anxiety symptoms significantly differed between the groups. There were no significant differences (p > .05) and therefore all participants were analysed together.

Table2.1 Descriptive statistics for the questionnaire variables in HCs

Variable	*M*	*SD*
EDE-Q		
Global	1.53	1.26
Restraint	1.43	1.40
Eating concern	.79	1.09
Weight concern	1.71	1.56
Shape concern	2.17	1.61
CIA	6.58	7.79
RRS-ED		
Total	12.35	4.48
Reflection	3.49	1.08
Brooding	8.86	3.84
RRS		
Total	40.38	13.19
Reflection	9.15	3.80
Brooding	9.09	3.47
Depression	22.14	7.63
PHQ-9	6.29	5.39
GAD-7	4.93	4.56
FFMQ	122.5	18.07
AAQ-II	18.86	7.65

Note. EDE-Q = Eating Disorder Examination Questionnaire; CIA = Clinical Impairment Assessment; RRS-ED = Ruminative Response Scale for Eating Disorders; RRS = Ruminative Response Scale; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder Questionnaire; FFMQ = Five Factor Mindfulness Questionnaire; AAQ-II = Acceptance and Action Questionnaire; BMI = body mass index.

2.4.2 Development of the RRS-ED

2.4.2.1 Principal component analysis (PCA)

Indices of sampling adequacy and sphericity confirmed that PCA was appropriate for the data. On PCA, two factors were identified. Items which demonstrated loadings of greater than 0.4 on both factors were excluded from the subsequent analyses as they could not be meaningfully interpreted. One item was excluded at this point ("Consider recent events to try and understand why you strive to control your eating, weight and/or shape"). The scree plot (Cattell, 1978) confirmed that the data was comprised of two factors. Initial eigen values for Factor 1 and Factor 2 were 5.08 and 1.24 respectively. The factors were subjected to rotation using the direct oblimin method. Direct oblimin was selected because it was expected that the resulting factors would correlate. The rotated factors accounted for 63.27% of the total variance divided as followed: Factor 1: 50.8%, Factor 2: 12.4%. Inspection of the factors led to labelling of brooding on eating, weight and shape concerns (Factor 1) and reflection on eating, weight and shape concerns (Factor 2) in line with the factors of the original RRS (Treynor, et al., 2003). The mean scores (*SD*) for the brooding and reflection subscales were 8.51(3.65) and 3.45 (1.05) respectively. The scales were moderately positively correlated ($r_s = .47$, $p < .001$). A copy of the scree plot together with the item numbers comprising each factor and the final measure can be seen in appendices 2.4, 2.12 and 2.13.

2.4.2.2 Internal Consistency

Cronbach coefficient alphas were computed for both the subscales. This was high for the brooding factor ($\alpha = .90$, average inter-item correlation = .58) and was moderate for the reflection factor ($\alpha = .61$, average inter-item correlation = .34).

2.4.2.3 Test-retest reliability

Participants who consented to be contacted again were asked to complete the RRS-ED a second time. The test-retest interval range from 3 to 12 weeks. 132 healthy female participants were approached and 54 completed the assessment, 24% of the total female healthy sample. The test-retest correlation coefficient for the brooding subscale of the RRS-ED was moderate to strong ($r_s = .64$, $p < .001$) and for the reflection subscale it was moderate ($r_s = .50$, $p < .001$). However, overall the RRS-ED had a moderate to strong structure ($r_s = .70$, $p < .001$).

Wilcoxon tests revealed a significant increase in brooding scores ($p < .001$) between Time 1 ($M = 9.24$, $SD = 3.97$) and Time 2 ($M = 10.56$, $SD = 4.21$). There was no significant change in reflection factor scores between Time 1 and Time 2 ($p > .05$) (Time 1: $M = 3.50$, $SD = .93$; Time 2: $M = 3.50$, $SD = .91$).

2.4.2.4 Construct validity

2.4.2.4.1 Convergent validity

Convergent validity was assessed by correlating RRS-ED scores with the EDE-Q subscale and CIA scores using non-parametric Spearman‘s correlation coefficient. As shown in Table 2.2, significant positive correlations were found between mean brooding scores on the RRS-ED and EDE-Q subscale scores. The reflection factor of the RRS-ED also had significant positive correlations with the measures of ED symptoms (EDE-Q subscales) and impairment (CIA), although the correlations were weaker (as shown in Table 2.2).

Table 2.2 Correlations between RRS-ED factors and ED symptoms in HCs

Spearman's rho (r_s)	RRS-ED brooding	RRS-ED reflection	EDE-Q restraint	EDE-Q eating	EDE-Q weight	EDE-Q shape	CIA
RRS-ED brooding	1.00						
RRS-ED reflection	.47**	1.00					
EDE-Q restraint	.54**	.35 **	1.00				
EDE-Q eating	.73**	.41 **	.53**	1.00			
EDE-Q weight	.70 **	.45**	.65**	.69**	1.00		
EDE-Q shape	.70**	.44*	.64**	.71**	.87**	1.00	
CIA	.78**	.46**	.58**	.73**	.75**	.78**	1.00

Note. EDE-Q = Eating Disorder Examination Questionnaire; RRS-ED = Ruminative Response Scale for Eating Disorders; CIA = Clinical Impairment Assessment.
** p < .001

2.4.2.4.2 Divergent validity

In order to assess divergent validity, RRS-ED subscale scores were correlated with participants BMI and age using Spearman‘s correlation coefficient. Neither of the subscales correlated significantly with age, although the RRS-ED brooding subscale correlated significantly with BMI, $r_s = .27$, $p < .001$. However, the absolute value for this correlation is small. Overall, the correlations suggest adequate divergent validity.

2.4.2.5 Ability of the RRS-ED to predict symptoms in healthy females

A series of stepwise linear regressions were performed. Since all analyses were exploratory in nature, the stepwise procedure was chosen with entry set at .05 and removal at .10. The regressions tested the ability of the RRS-ED subscales to predict (a) scores on the EDE-Q when controlling for common variance associated with clinical impairment, depression and anxiety (b) scores on the PHQ-9 when controlling for common variance associated with ED symptoms, clinical impairment and anxiety, and (c) scores on the GAD-7 when controlling for variance associated with ED symptoms, clinical impairment and depression. BMI was also included as a potential predictor and this variable was entered on Step 1 along with the other covariates. RRS-ED subscales scores were entered on Step 2. Ability of the original rumination scale (the RRS) to predict ED, depression and anxiety symptoms was included as an additional validity check, with the expectation that RRS subscales would significantly predict depression but not ED symptoms.

2.4.2.5.1 Global EDE-Q as a dependent variable

On Step 1, only the total CIA scores were entered into the model, $R^2 = .61$, $F = 355.91$, $p < .001$. In the final model, it was shown that RRS-ED brooding scores and BMI made additional significant contributions to the model, $R^2 = .67$, $F = 62.32$, $p < .001$. Subscales of the RRS for depression were not significant predictors of global EDE-Q scores. Summary statistics for significant predictors are shown in Table 2.3.

Table 2.3 Final model for prediction of global EDE-Q scores in HCs

Variable	*β* (standardized)	*T*	*p*
Constant		-3.05	.003
CIA	.59	8.54	<.001
RRS-ED- brooding	.20	3.19	<.001
RRS-ED reflection	-.01	-.23	.82
RRS depression	0.03	.48	.63
RRS reflection	.004	.07	.94
RRS brooding	-.034	-.57	.57
BMI	.17	4.13	<.001

Note. EDE-Q = Eating Disorder Examination Questionnaire; CIA = Clinical Impairment Assessment; RRS-ED = Ruminative Response Scale for Eating Disorders; RRS = Ruminative Response Scale; BMI = body mass index.

2.4.2.5.2 *PHQ-9 scores as a dependent variable*

For this analysis, CIA and GAD-7 scores (entered on Step 1) produced a significant model, $R^2 = .53$, $F = 254.28$, $p < .001$. In the final model, the depression subscale of the original RRS and the GAD-7 scores were further significant predictors, $R^2 = .66$, $F = 52.38$, $p < .001$. RRS-ED subscale scores were not able to explain variance in depression symptoms. Summary statistics for significant predictors in the final model are shown in Table 2.4.

Table 2.4 Final model for prediction of PHQ-9 scores in HCs

Variable	*β* (standardized)	*t*	*p*
Constant		-1.84	.07
GAD-7	.45	8.55	<.001
CIA	.09	1.30	.19
RRS-ED brooding	.004	.07	.95
RRS-ED reflection	.01	.15	.88
RRS depression	.40	6.19	<.001
RRS reflection	-.11	-1.89	.06
RRS brooding	.05	.87	.38
BMI	.02	.53	.60

Note. EDE-Q = Eating Disorder Examination Questionnaire; CIA = Clinical Impairment Assessment; RRS-ED = Ruminative Response Scale for Eating Disorders; RRS = Ruminative Response Scale; BMI = body mass index.

2.4.2.5.3 GAD-7 scores as a dependent variable

PHQ-9 and CIA scores produced a significant model when entered on Step 1, $R^2 = .53$, $F = 254.28$, $p < .001$. The brooding and reflection subscales from the original RRS for depression were further significant predictor of anxiety, $R^2 = .57$, $F = 37.99$, $p < .001$. Summary statistics for prediction of GAD-7 scores are shown in Table 2.5.

Table 2.5 Final model for prediction of GAD-7 scores in HCs

Variable	β (standardized)	t	p
Constant		-.01	.99
PHQ-9	.55	8.55	<.001
CIA	.19	2.34	.02
RRS-ED brooding	-.14	-1.91	.06
RRS-ED reflection	-.01	-.15	.88
RRS depression	-.02	-.19	.85
RRS reflection	.13	2.03	.04
RRS brooding	.15	2.23	.03
BMI	-.01	-.11	.92

Note. EDE-Q = Eating Disorder Examination Questionnaire; CIA = Clinical Impairment Assessment; RRS-ED = Ruminative Response Scale for Eating Disorders; RRS = Ruminative Response Scale; BMI = body mass index.

2.4.2.6 Content overlap between the RRS-ED and the EDE-Q

To test whether the RRS-ED is redundant when analysed with the EDE-Q, a PCA with varimax rotation and a factor cut-off of .4 was conducted with all the items from both the measures. The PCA with the RRS-ED items and EDE-Q items resulted in one brooding factor (containing all RRS-ED brooding items; eigen value = 2.44), one reflection factor (containing all RRS-ED reflection items; eigen value = 1.3) one shape/weight concern factor (containing seven shape concern and four weight items from the EDE-Q; eigen value = 14.28), one restraint factor (containing three restraint items from the EDE-Q; eigen value = 1.33) and one eating factor (containing four eating, two restraint and one joint shape/weight concern item from the EDE-Q; eigen value = 1.69). These five factors together accounted for 67.9% of the variance.

2.4.3 Evaluating the performance of the RRS-ED in AN

Data from 42 participants who were removed from the main analysis because they reported an episode of AN were analysed as a preliminary test of the RRS-ED's validity in individuals with a history of AN (mean age = 24 years, *SD* = 8.31; mean BMI = 19.60, *SD*= 2.46). To examine between group differences, non-parametric Mann-Whitney *U* tests were used as the data from the AN group was not normally distributed and could not be corrected by transformations. The AN group had significantly higher scores on the brooding (AN mean rank = 202.7, HC mean rank = 123.1) and reflection (AN mean rank = 179.4, HC mean rank = 127.41) subscales of the RRS-ED compared to the HC group. Results gave Mann-Whitney *U* statistics of

1965 for the brooding subscale and 2944.5 for the reflection subscale, both with an associated probability value of $p < .001$.

2.4.3.1 Ability of the RRS-ED to predict symptoms in AN.

Hierarchical regression analysis was used to explore the relationship between rumination and the level of ED symptoms in the AN group[2]. Based on the variance inflation factor (VIF) and tolerance statistics, it was apparent that the assumption of no multicollinearity had been met (VIF values were all below 10 and the tolerance statistics were all above 0.2). In addition, the assumption of independent errors was met (Durbin-Watson [*d*] =2.3). For this analysis, PHQ-9 and CIA scores (entered in Block 1) produced a significant model, $R^2 = .60$, $F = 28.80$, $p < .001$. Both brooding and reflection, as measured by the RRS-ED, were further significant predictors, $R^2 = .78$, $F = 32.92$, $p < .001$. The RRS for depression was not able to explain variance in ED symptoms ($p > .05$).

[2] Hierarchical regression was selected opposed to stepwise (as used in 2.4.2.5). It is recommended stepwise regression is only appropriate for preliminary or exploratory work.

2.4.4 Summary of Analysis 1

The RRS-ED was developed to measure rumination on eating, weight and shape as to date no measures exist to capture rumination in EDs. The findings provide psychometric support for the novel measure as well as support for the importance of considering disorder-specific rumination. The 9-item scale is non-redundant in content when analysed with EDE-Q items and it captures two aspects of rumination: reflection and brooding. The next section will examine the association between rumination, as measured by the RRS-ED, and related cognitive-affective constructs (mindfulness and experiential avoidance).

2.4.5 Analysis 2

2.4.5.1 The association between rumination, experiential avoidance, mindfulness and ED symptoms.

As the study variables were not normally distributed (Kolmogorov Smirnov = $p < .001$) and they could not be corrected by transformations, non-parametric Spearman's Rho (r_s) was used to examine the association between study variables. Significance levels were corrected for multiple comparisons[3].

As shown in Table 2.6, experiential avoidance and mindfulness were significantly correlated with the brooding subscale of the RRS-ED (AAQ-II: $r_s = .20$, $p < .001$; FFMQ: $r_s = -.40$, $p < .05$). The relationship was in a positive direction for the AAQ-II and in a negative direction for the FFMQ scores. AAQ-II scores also correlated significantly with the reflection factor of the RRS-ED ($p = .03$), however the correlation lost its significance when controlling for multiple comparisons ($p > .05$).

3 In order to reduce Type 1 error each of the p values were multiplied by the number of correlation coefficients tested for significance ($N = 21$). The corrected p values were deemed significant if $p < .05$.

Experiential avoidance and mindfulness were significantly associated with ED symptoms as measured by the EDE-Q. The relationship was in a positive direction for the AAQ-II ($r_s = .18$, $p < .05$) and in a negative direction for the FFMQ scores ($r_s = -.31$, $p < .05$) and the associations remained after controlling for multiple comparisons.

Depression and anxiety scores were significantly and positively correlated with global EDE-Q scores. These variables were therefore included as covariates in subsequent analysis.

Table 2.6 Means, standard deviations and correlations of self-reported symptoms, rumination, experiential avoidance and mindfulness in HCs

Spearman's r_s	Global EDE-Q	RRS-ED brooding	RRS-ED reflection	AAQ-II	FFMQ	PHQ-9	GAD-7
Global EDE-Q	1.00						
RRS-ED brooding	.74 *	1.00					
RRS-ED reflection	.47 *	.47 *	1.00				
AAQ-II	.18 *	.20	.14 ^{ns}	1.00			
FFMQ	-.31 *	-.40 *	-.11 ^{ns}	-.12 ^{ns}	1.00		
PHQ-9	.40 *	.43 *	.20*	.03 ^{ns}	-.46 *	1.00	
GAD-7	.34 *	.34 *	.24 *	.58 ^{ns}	-.36 *	.63 *	1.0
M	1.53	8.86	3.48	18.86	122.5	6.29	4.93
SD	1.26	3.84	1.08	7.65	18.07	5.39	4.56

Note. EDE-Q = Eating Disorder Examination Questionnaire; RRS-ED = Ruminative Response Scale for Eating Disorders; AAQ-II = Acceptance and Action Questionnaire-II; FFMQ = Five Factor Mindfulness Questionnaire; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder Assessment
* $p < .05$ (corrected for multiple comparisons); ns = non-significant

2.4.5.2 Does rumination, experiential avoidance or mindfulness predict ED symptoms in healthy females?

To determine the independent contributions of rumination (brooding or reflection), experiential avoidance and mindfulness to ED symptoms, a hierarchical regression analysis was conducted. The EDE-Q global scores were entered as the dependent variable and the RRS-ED brooding, RRS-ED reflection, FFMQ and AAQ-II scores were entered as four independent variables. Scores on the PHQ-9 and GAD-7 were controlled for in the analysis and thus entered in the first block.

Based on the VIF and tolerance statistics, it was apparent that the assumption of no multicollinearity had been met (VIF values were all below 10 and the tolerance statistics were all above 0.2). In addition, the assumption of independent errors was met (Durbin-Watson [d] =2.1). Controlling for the covariates, the addition of the four independent variables in Block 2 accounted for an additional 33% of the variance in ED symptoms (as shown in Table 2.7). With regard to the unique contributions of each of the four variables of interest, only brooding on eating, weight and shape was uniquely associated with ED symptoms in the final step of the model, RRS-ED brooding: β =.57, t = 9.62, p < .001. Reflection, mindfulness and experiential avoidance did not uniquely predict ED symptoms in the analysis (p > .05).

Table 2.7 Hierarchical multiple regression analysis predicting ED symptoms in HCs

Variable	R^2	β (standardized)	t	p
Block 1	.21			
PHQ-9		.36	4.19	.001
GAD-7		.12	1.43	.154
Block 2	.54			
PHQ-9		.15	2.12	.04
GAD-7		.08	1.17	.24
RRS-ED brooding		.57	9.62	.001
RRS-ED reflection		.08	1.45	.15
FFMQ		-.01	-.10	.92
AAQ-II		.04	.84	.40

Note. EDE-Q = Eating Disorder Examination Questionnaire; RRS-ED = Ruminative Response Scale for Eating Disorders; AAQ-II = Acceptance and Action Questionnaire-II; FFMQ = Five Factor Mindfulness Questionnaire; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder Assessment

2.4.5.3 ED symptoms, rumination, experiential avoidance and mindfulness in AN

Data from the 42 participants who were removed from the main analysis because they reported episodes of AN were analysed as a preliminary test of the association between ED symptoms, mindfulness, experiential avoidance and rumination in individuals with a history of AN.

Correlations for the variables of interest are shown Table 2.8. As the variables were normally distributed, Pearson's r was used to examine the associations. Significance levels were corrected for multiple comparisons.

Mindfulness, as measured by the FFMQ, was significantly and negatively correlated with ED symptoms, brooding on eating, weight and shape, and experiential avoidance (EDE-Q: $r = -.59$, $p < .05$; RRS-ED brooding: $r = -.66$, $p < .05$;
AAQ-II: $r = -.58$, $p < .05$). Experiential avoidance was significantly and positively associated with ED symptoms, although this association did not withstand correction for multiple comparisons ($p > .05$). Experiential avoidance was however significantly and positively associated with ruminative brooding on eating, weight and shape even after correction for multiple comparisons (Brooding: $r = .67$, $p < .05$). As PHQ-9 and GAD-7 scores were significantly correlated with ED symptoms measured by the EDE-Q, they were controlled for in subsequent analyses.

Table 2.8 Means, standard deviations and correlations of self-reported symptoms, rumination, experiential avoidance and mindfulness in AN

Pearson's *r*	Global EDE-Q	RRS-ED brooding	RRS-ED reflection	AAQ-II	FFMQ	PHQ-9	GAD-7
Global EDE-Q	1.00						
RRS-ED brooding	.75 *	1.00					
RRS-ED reflection	.55 *	.33 ns	1.00				
AAQ-II	.47 ns	.67 *	.30 ns	1.00			
FFMQ	-.59 *	-.66 *	-.22 ns	-.58 *	1.00		
PHQ-9	.79 *	.81 *	.30 ns	.49 ns	-.67 *	1.00	
GAD-7	.65 *	.58 *	.25 ns	.43 ns	-.37 ns	.75 *	1.0
M	2.36	14.43	4.95	23.73	118.43	12.15	10.31
SD	1.76	6.08	2.31	7.50	20.6	6.82	4.74

Note. EDE-Q = Eating Disorder Examination Questionnaire; RRS-ED = Ruminative Response Scale for Eating Disorders; AAQ-II = Acceptance and Action Questionnaire-II; FFMQ = Five Factor Mindfulness Questionnaire; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder Assessment
* $p < .05$ (corrected for multiple comparisons); ns = non-significant

2.4.5.4 Does rumination or mindfulness predict ED symptoms in AN?

A hierarchical regression analysis was conducted to determine the independent contributions of rumination (brooding or reflection) and mindfulness on ED symptoms in individuals with a history of AN. EDE-Q global score was entered as the dependent variable and the RRS-ED brooding, RRS-ED reflection and FFMQ scores were entered as three independent variables. Scores on the PHQ-9 and GAD-7 were controlled for in the analysis. AAQ-II scores were not included as a predictor as it did not significantly correlate with the outcome variable.

Based on the VIF and tolerance statistics, it was apparent that the assumption of no multicollinearity had been met (VIF values were all below 10 and the tolerance statistics were all above 0.2). In addition, the assumption of independent errors was met (Durbin-Watson [d] =1.9). Controlling for the covariates, the addition of the three independent variables in block two accounted for an additional 15% of the variance in ED symptoms (as shown in Table 2.9). With regard to the unique contributions of each of the four variables of interest, only reflection on eating, weight and shape was uniquely associated with ED symptoms in the final step of the model (RRS-ED reflection: β =.38, t = 2.99, p = .007). Brooding and mindfulness did not uniquely predict ED symptoms in the analysis (p > .05).

Table 2.9 Hierarchical multiple regression analysis predicting ED symptoms in AN participants

Variable	R^2	β (standardized)	t	p
Step 1	.58			
PHQ-9		.59	2.93	.008
GAD-7		.21	1.05	.303
Step 2	.73			
PHQ-9		.36	1.61	.123
GAD-7		.12	.67	.511
RRS-ED brooding		.22	1.25	.27
RRS-ED reflection		.36	2.99	.007
FFMQ		-.14	-.91	.370

Note. EDE-Q = Eating Disorder Examination Questionnaire; RRS-ED = Ruminative Response Scale for Eating Disorders; FFMQ = Five Factor Mindfulness Questionnaire; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder Assessment.

2.4.6 Summary of Analysis 2

In an effort to extend the existing literature and test specific hypotheses generated from the ICS account of AN by Park and colleagues (Park et al., 2011, 2012), this analysis utilized a novel measure of rumination on eating, weight and shape, as well as validated measures of experiential avoidance and mindfulness. As predicted, rumination on eating weight and shape, experiential avoidance and low mindfulness were associated with ED symptoms in a healthy sample. Further, brooding on eating, weight, and shape accounted for unique variance in ED symptoms. The results were similar in those with a history of AN, although experiential avoidance was associated with ruminative brooding on eating, weight and shape and not ED symptoms as measured by the EDE-Q. Lastly, in the AN participants, reflection on eating, weight and shape accounted for unique variance in ED symptoms.

2.5 Summary of results from Analysis 1 and Analysis 2

- The two factor RRS-ED measures rumination on eating, weight and shape and has adequate psychometric properties when examined in a large healthy female sample.
- Brooding and reflection, as measured by the RRS-ED, explains variance in ED symptoms whilst rumination on depressive symptoms does not.
- Rumination on ED themes is associated with greater experiential avoidance and lower mindfulness in both healthy participants and those with experience of AN.
- Rumination is a stronger predictor of ED symptoms than either experiential avoidance or mindfulness in both healthy participants and those with experience of AN.

2.6 Discussion

Does rumination have a distinct quality in those with AN that is not captured by measures of rumination in depression?

The first aim of this study was to develop a useful measure of rumination on ED symptoms and establish its psychometric properties. To this end, the 9-item RRS-ED comprised of a brooding and reflection factor was developed. The brooding factor connotes regretful thinking about the ED psychopathology, more specifically, comparing the current situation which is predominantly focused on control of eating, weight and/or shape with some other ideal standard. Reflection was made up of three items which represented active attempts to gain insight into ED symptoms. The results indicate that the RRS-ED has good criterion related validity and internal consistency, adequate test-retest reliability and is non-redundant in content when analysed with EDE-Q items.

In the regression analysis with the HC participants, impairment as measured by the CIA and BMI emerged as significant predictors of ED symptoms when entered as control variables. Depression symptoms did not emerge as a predictor. This is important as a frequent criticism of ED research is that findings could also be explained by co morbid depression (for example, Corcos et al., 2000). Moreover, even when rumination in response to low mood was included as potential predictor of ED symptoms, only the RRS-ED brooding subscale emerged as significant. This supports the hypothesis that ED symptoms are associated with a higher level of ED-specific rumination compared to depressive rumination and suggests that rumination in EDs is distinct from rumination in depression. In further support of this, in the AN sample the RRS-ED brooding and reflection subscales were also able to predict variance in the EDE-Q global scores, whilst the RRS for depression or the measure of depressive symptoms did not significantly contribute to the model.

The finding that the RRS-ED is a better predictor of ED symptoms than an existing measure of rumination has implications for the recent debate surrounding repetitive negative thought as a transdiagnostic phenomenon (for example, Brinker and DeZois, 2009; Harvey, Watkins, Mansell, & Shafran, 2004; Hoyer, Gloster & Herzberg, 2009; McEvoy, Mahoney & Moulds, 2010). It suggests that not only is there unique variance in ruminative thinking in AN but also that the RRS-ED may be a useful tool for capturing it. This finding is also consistent with the ICS account of AN which proposes that in AN, ruminative tendencies become attached to themes of eating, weight, shape and their control (Park et al., 2011). Whilst there may be overlap between ruminative processing in EDs and depression, results indicate that there are also important differences in content and focus, as much thinking in EDs centres on perceived self-discrepancies and imperfections over control of eating, weight, and shape. Rumination, as measured by the RRS-ED, may therefore be important when examining mechanisms which maintain EDs.

Correlations: Brooding and reflection on eating, weight and shape and ED symptoms

Brooding, and to a lesser extent reflection, on ED symptoms was significantly associated with the CIA and EDE-Q scores, suggesting that brooding on disorder-specific symptoms may be more pertinent. This provides further evidence that brooding is a more maladaptive form of rumination than reflection (Pearson, Watkins, Mullan, & Moberly, 2010; Treynor et al., 2003). Whilst speculative, this could reflect the tendency for people with ED symptoms to attend more to discrepancy-based information (Park et al., 2011), as the items on the brooding factor referred to comparing discrepancies between current state with some other "ideal state".

What is the relationship between rumination, mindfulness, experiential avoidance and ED symptoms?

As predicted, rumination on eating weight and shape, experiential avoidance and low mindfulness was associated with ED symptoms in a healthy sample. Only brooding on eating, weight, shape, and not mindfulness or experiential avoidance, accounted for unique variance in ED symptoms in the HC participants. The results were similar in the AN group, although experiential avoidance was associated with ruminative brooding on eating, weight and shape and not ED symptoms as measured by the EDE-Q. Lastly, in the AN participants, reflection on eating, weight and shape and not mindfulness or experiential avoidance accounted for unique variance in ED symptoms.

The findings are largely consistent with previous findings that ED symptoms are positively associated with rumination and experiential avoidance (Corstorphine, Mountford, Tomlinson, Waller, & Meyer, 2007; Nolen-Hoeksema et al., 2007; Rawal et al., 2010; Wildes et al., 2010) and negatively associated with mindfulness (Lavender et al., 2009, 2011). The findings are in line with the predictions of Park, Dunn and Barnard (2011) that disorder-specific rumination may function as a cognitive avoidance strategy and facilitate restriction as individuals are able to tune out from the physical and emotional symptoms associated with starvation. Non-judgmental awareness of present-moment experience, including one's sensations, thoughts and bodily states may foster a more accepting stance and help counter the ruminative and avoidant processes which are associated with ED symptoms (Park et al., 2012).

Despite providing evidence for the expected associations between rumination, experiential avoidance, mindfulness and ED symptoms, only ruminative brooding in the healthy sample and reflection in the AN participants, were able to uniquely predict ED symptoms. Mindfulness and experiential avoidance did not uniquely contribute to the regression models. One explanation for this may be that the associations between experiential avoidance, mindfulness and ED symptoms are driven in part by the anxiety and depression symptoms which often co-occur with ED symptoms (Herzog, Keller, Sacks, Yeh, & Lavori, 1992; Kaye et al., 2004). In support of this, maladaptive strategies such as experiential avoidance are proposed to contribute to the maintenance of many emotional disorders, including anxiety and depression (Bishop et al., 2004; Hayes & Feldman, 2004). Self-reported anxiety and depression were not controlled for in the correlation analyses yet were controlled for in the regression analyses and thus could potentially explain the results. The findings reported here therefore highlight the importance of controlling for comorbid symptoms in AN research, particularly when examining cognitive-affective processes.

It is intriguing that different subscales of the RRS-ED predicted ED symptoms in the HC and AN groups. It has been suggested that brooding may be the more maladaptive subtype of rumination. For example, Treynor, Gonzalez and Nolen-Hoeksema (2003) conducted a longitudinal analysis and found that brooding was associated with more depression both concurrently and over time, whereas reflection was associated with less depression overtime but more depression concurrently. It is therefore surprising that reflection and not brooding predicted ED symptoms in the AN participants. However, reflection is not consistently found to be an adaptive cognitive style. For example, Surrence, Miranda, Marroquin and Chan (2009) found that in individuals with suicidal intent, reflection was positively associated with suicidal ideation. Further, Joorman, Dkane and Gotlib (2006) argued that in clinical samples, brooding and reflection may perpetuate each other thus erasing the adaptive function of reflection. Since both brooding and reflection were positively associated with ED symptoms in this study it is possible that the two components of rumination may have perpetuated each other resulting in reflection becoming as maladaptive as brooding. It has also been suggested that when the active attempts to solve current problems are unsuccessful, reflection may turn to persistent and maladaptive negative thoughts (Miranda & Nolen-Hoeksema, 2007).

2.6.1 Limitations

RRS item modification was largely driven by previous theoretical work and therefore topics important to individuals with EDs may have not been captured. Reliance on a cross-sectional design means that causal inferences cannot be made. Prospective longitudinal research would permit refined hypothesis testing with regard to the role of rumination, mindfulness and avoidance in the maintenance of ED symptoms. The study relied on self-report and this methodology may lead to inaccurate reporting. Additionally, the results may not be generalizable because the study was confined to a female, largely student and non-clinical sample. Although disordered eating behaviors and cognitions are pervasive in this group (Vohs, Heatherton, & Herrin, 2001), floor effects were observed on some of the measures. Lastly, the diagnosis of AN was based purely on self-report and whilst there is evidence to suggest that the EDE-Q may be used in place of an interviewer-based measure when assessing overall diagnosis (Binford, Le Grange, & Jellar, 2005; Wolk, Loeb, & Walsh, 2005), replication using researcher-assessed samples would be beneficial.

2.7 Conclusions

Rumination in AN has a disorder-specific content which is captured by the RRS-ED. Rumination on eating weight and shape, experiential avoidance and low mindfulness are processes associated with ED symptoms. Experimental studies manipulating the way in which information is processed in AN (for example, rumination versus mindful processing) and examining the effect of such processing modes on ED symptoms, would be a useful next step in determining the role of rumination in the maintenance of AN.

3 Rumination and modes of processing around meal times in women with anorexia nervosa: quantitative and qualitative results from a pilot study

3.1 Overview

The study reported in Chapter 2 demonstrated that rumination on control of eating, weight and shape is associated with ED symptoms and with avoidance of experience. As discussed in Chapter 1 and Chapter 2, rumination and avoidance are seen as hallmarks of a ruminative mode of processing and this mode of processing has been found to have adverse effects on psychopathology. This chapter investigates qualitative aspects of modes of processing in individuals with AN and explores whether the tendency to process information about the self in a ruminative way (for example, rumination about exercise regimes or calorie intake) can be shifted in individuals with AN with beneficial effects on the meal time experience. Three specific questions are addressed:

- Can a ruminative mode of processing be interrupted by focusing attention on the breath in AN?
- Is focusing attention on the breath more effective at facilitating awareness of the present-moment compared to a distraction exercise in AN?

- Do different modes of processing effect the experience of the body and meal time management in AN?
- How do individuals with AN perceive the process of rumination and what is their experiences of an intervention designed to interrupt it?

3.2 Background

As reviewed in Section 1.7, the ICS account of AN predicts that rumination on eating, weight and shape and their control is a process that operates persistently in AN and may be central to the disorders maintenance (Park et al., 2011, 2012). The data in Chapter 2 lends some support to this by showing that higher levels of ED symptoms are associated with greater ED specific rumination, compared to depressive rumination, and also that ED specific rumination is associated with avoidance of experience and low mindfulness.

A second prediction derived from the ICS model for AN is that ED symptoms can be attenuated by interrupting the ruminative “doing AN” mode and enhancing a “being embodied” mode of processing characterised by mindful awareness of the present-moment (Park et al., 2012). This shift in the pattern of processing is thought to be characterised by a reduction in rumination and avoidance and an increase in experiential insight and non-judgemental attention to the body (Park et al., 2012). In support of this proposition, Rawal, Enayati, Williams and Park (2009) demonstrated that a mindful movement class, aiming to facilitate non-judgemental awareness of the body, increased feelings of at oneness with self and body in AN participants compared to psychoeducation. Further, an experimental study with AN participants which involved manipulating the mode of processing, demonstrated that ruminative processing (i.e., analytical thinking about the self) exacerbated cognitive and behavioural reactivity after an imaginary meal procedure, whereas a mindful mode of processing had the opposite effect (Rawal et al., 2011).

Whilst the studies reviewed above are limited by their preliminary nature, support for the role of processing patterns (or modes) in the maintenance of AN can also be obtained indirectly from the depression literature. In depression, adopting a mindful mode of processing has been shown to reduce relapse when trained regularly in the remitted condition (Kuyken et al., 2008; Teasdale et al., 2000). In line with ICS frameworks, such effects may result from a reduction in rumination and avoidance in the mindful mode thus enabling more adaptive information processing (Teasdale, 1999; Teasdale & Barnard, 1993; Williams, 2008; Williams, 2010).

As reviewed in Section 1.7, the ICS account of AN suggests that a mindful mode of processing is crucial for AN recovery (Park et al., 2012). Therefore training a qualitative shift in the experience of self and body, away from an object to be controlled (as in doing AN mode) to a subjective experience of embodiment (being embodied mode), may be beneficial for individuals with AN (Park et al., 2011, 2012; Rawal et al., 2009). However, Park et al. (2012) highlight that with ill and underweight AN patients who tend to be highly ruminative and avoidant of experience (as shown in Chapter 2), attending mindfully to experience (for example, the body or emotional states) may be aversive. Therefore in the acute stages of AN, alternative strategies may be more practical in the short term, with training in mindful awareness introduced gradually.

In terms of alternative strategies that may be more practical, Response Style Theory (RST) postulates that distraction and problem-solving are more adaptive responses to negative emotional states than rumination (Nolen-Hoeksema, 1991). Distraction involves engaging in benign or pleasurable activities that direct attention away from the negative emotional state, whereas problem-solving involves active attempts to generate solutions to alter one's negative mood. It has been proposed by Nolen-Hoeksema (1991) that distraction may offer a brief relief from distress and enable an individual to engage more effectively in problem-solving. This hypothesis has been supported by a range of laboratory studies which typically induce rumination and then instruct participants to engage in different response styles (as discussed by Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). However, on its own any beneficial effects of distraction are unlikely to last as distraction procedures simply redirect the focus of attention temporarily (Nolen-Hoeksema, 1991). In contrast, exercises that aim to induce a mindful mode of processing are thought to have more sustained effect as there is evidence that mindful 'being' mode facilitates emotional processing, allowing the development of more adaptive schematic models of the self (Teasdale, 1999). The sustained effect of mindful mode processing has been evidenced by the success of MBCT on depression relapse (Kuyken et al., 2008; Teasdale et al., 2000).

A recent laboratory study examined the effect of three different strategies (mindfulness, distraction and problem-solving) on state rumination in healthy participants (Hilt & Pollak, 2012). It was reported that both the distraction and mindfulness interventions were associated with significantly reduced rumination, whereas problem-solving had no effect on rumination (Hilt & Pollak, 2012). Whilst the study was unable to determine the duration of the effects, the authors reasoned that even if the effects of the interventions were short, they may be useful if practiced frequently by those who have a tendency to ruminate. Applied to AN, distraction may therefore be an adaptive alternative to rumination and a more comfortable response style than mindful awareness in acute illness.

3.2.1 Study aims

- To examine the effects of a single rumination, mindful breathing and distraction exercise on analytical self-focus and present-moment awareness in AN.
- To examine the effects of these different exercises on the experience of the body and meal time management in AN.
- To analyse the qualitative experience of AN participants in the study.

3.2.2 Hypotheses

- Rumination compared to mindful breathing will increase analytical self-focus.
- Mindful breathing compared to distraction will increase experiential self-focus.
- Compared to mindful breathing, rumination will be associated with significantly greater feelings of fatness and more behavioural and cognitive reactivity around the meal.

- Significant differences in the outcome variables (i.e., mode of processing and the meal time experience) will be observed between those who are currently underweight compared to those who are partially weight-restored.

3.3 Method

3.3.1 Overall design

This study employed a quasi-experimental within-participant design to examine the effects of rumination, mindful breathing and distraction on processing styles and the meal time experience in participants with a history of AN.

3.3.2 Participants

Participants (16-years-old or above) with a history of AN were recruited through three main sources. First, participants were recruited from a database of individuals with current or past AN maintained by the research team at the University of Oxford. All individuals on this database were sent an advertisement for the study and were invited to apply if they currently had AN or considered themselves as partially/recently recovered or weight-restored but felt the study may be of interest and/or useful for them. Second, participants were recruited from the inpatient and outpatient services provided by Oxford Health NHS Foundation Trust. Third, an advertisement was place on BEAT's (national ED charity) website and also sent to their research contacts.

3.3.3 Study procedure

Ethical permission from the study was obtained from the Outer West London Research Ethics Committee (see Appendix 3.1) and Oxford Health NHS Foundation Trust (see Appendix 3.2). After complete description of the study (see Appendix 3.3), all the participants provided written, informed consent (see Appendix 3.4). Participants first completed a questionnaire battery (described below) and were asked to return this to the researcher. Participants who returned the completed questionnaires were then invited to attend an introductory session for the study. In the introductory session, the researcher described the study procedure and provided the participants with three coloured compact discs (CDs), each with a brief exercise recorded onto it, and a practice diary (for an example of the practice diary see Appendix 3.5). If participants were unable or unwilling to travel to the researcher, the introductory session would be conducted using a recorded study introduction combined with telephone and/or email support.

There were three phases in the study, each lasting one day, and there were a number of different tasks to complete within each phase. All participants completed all three phases. Figure 3.1 shows the tasks which were employed within each phase.

Figure 3.1 Tasks included in Phase 1, Phase 2 and Phase 3

Monday						Tuesday						Wednesday					
Phase 1 (First CD)						Phase 2 (Second CD)						Phase 3 (Third CD)					
Familiarise	Listen to CD	Pre-meal VAS	Dinner	Post-meal VAS	Feedback	Familiarise	Listen to CD	Pre-meal VAS	Dinner	Post-meal VAS	Feedback	Familiarise	Listen to CD	Pre-meal VAS	Dinner	Post-meal VAS	Feedback

Note. All participants completed all three phases on different, but consecutive, days.

During Phase 1, participants were instructed to listen to the first exercise (marked on the CD as "First CD") at some point in the day to familiarise themselves with it. Following this, participants were asked to listen to the same exercise before the evening meal and complete a series of visual analogue scales (VAS) in the practice diary before and after listening to the exercise, in addition to after the meal. After the VAS had been completed post-meal, participants were encouraged to provide written feedback on their experience of the exercise and the meal time in the practice diary. Phase 2 and Phase 3 of the study followed the same procedure as Phase 1 but involved the use of the other exercises on the subsequent two days. The order of the exercises used across the study phases was counterbalanced between participants. When participants returned the diary to the researcher at the end of the study they were debriefed via phone or email and sent a £10 gift voucher.

3.3.4 *Exercises*[4]

3.3.4.1 *Mindful breathing*

The mindful breathing exercise, designed to induce a mindful 'experiential' mode, was based on a script used in the MBCT programme (Segal, Williams, & Teasdale, 2002) (the script is shown in Appendix 3.6). Participants were guided through three steps: (1) bringing awareness to the whole experience (including the body, cognitions and emotions), (2) narrowing the focus to the breath, and (3) expanding again to a wider focus, but intending to take a sense of openness and awareness to the rest of the day. This three minute exercise embodies the central features of mindfulness: bringing attention into the present-moment and developing greater awareness with an attitude of acceptance (Kabat-Zinn, 1994). In MBCT, participants are taught to draw on this three minute practice particularly when faced with stressful and/or challenging situations and thus may be useful around meal times for those with AN.

3.3.4.2 *Rumination*

The rumination exercise, designed to induce a 'ruminative' mode, was based on the analytical self-focus manipulations developed by Watkins and Teasdale (2004) (the script is shown in Appendix 3.7). In this, participants are guided through 28-items which have been adapted from Morrow and Nolen-Hoeksema's (1990) rumination task. All the items are symptom focused, for example directing attention to "the

[4] The exercises were matched in length (3 minutes and 7 seconds each).

physical sensations in your body”. The initial instructions for the recorded version used in this study were:

> For the next few minutes, try your best to think about each of the following items. As you listen to the items, use your imagination and concentration to think about the causes, meanings and consequences of the items. Spend a few moments visualising and concentrating on each item, attempting to make sense of and understand the issues raised by each item.

The instruction, “think about” preceded each specific item, for example, ‘‘think about the way you feel inside” (Watkins & Teasdale, 2004).

3.3.4.3 Distraction

The distraction exercise was a modified version of the filler task used by Holmes, Mathews, Dalgleish, and Mackintosh (2006). Participants were instructed to rate three short extracts of classical music for pleasantness (on a scale of 1 [*extremely unpleasant*] to 9 [*extremely pleasant*]) (the script is shown in Appendix 3.8). Each extract lasted 40 seconds. In pilot work, the three extracts used were rated by healthy participants (N = 8) as the “most neutral” out of a possible fifteen extracts. In order to keep participants focused on the exercise and control for the language used in the other two exercises, verbal prompts were given to rate the music between each extract.

3.3.5 Measures

3.3.5.1 ED symptoms

In order to measure ED symptoms, the EDE-Q (Fairburn & Beglin, 2008) and the CIA (Bohn, et al., 2008) were used (as described in Section 2.3.3).

3.3.5.2 Beck Depression Inventory-II (BDI-II)

The BDI-II (Beck, Steer, & Brown, 1996) is a validated 21-item self-report questionnaire, which measures depressive symptom severity in the past two weeks (see Appendix 3.9). Participants rate their answers using a 0 to 3 scale with higher scores indicating greater depression severity (range 0 to 63). The standard cut offs used are as follows: 0 to 13, minimal depression; 14 to 19, mild depression; 20 to 28, moderate depression; and 29 to 63, severe depression (Beck et al., 1996).

3.3.5.3 State Trait Anxiety Inventory (STAI)

The STAI (Spielberger, 1983) is a 40-item self-report questionnaire that measures state anxiety (STAI-S) and trait anxiety (STAI-T) (see Appendix 3.10). Items are scored from 0 (*not at all*) to 3 (*a lot*). The STAI has good reliability and discriminate validity has a good internal consistency (between 0.90 and 0.93 for the STAI-S and between 0.84 and 0.87 for the STAI-T). The convergent validity with respect to other measures of anxiety ranges from 0.73 to 0.85 (Spielberger, 1983). The present study used the trait scale only.

3.3.5.4 Process measures

In order to measure relevant cognitive-affective processes participants completed the FFMQ (Baer et al., 2006) the AAQ-II (Bond et al., 2011) and the RRS-ED (see section 2.3.3 for more details).

3.3.5.5 Other information

Participants voluntarily provided demographic information (age and gender) and self-reported height and weight (in order to calculate BMI). Participants also provided information on whether they currently had an ED diagnosis, what the diagnosis was and whether they were receiving treatment for the ED. In addition to the self-reported diagnosis, frequencies of behaviours reported on the EDE-Q and current weight were used to assess severity of ED psychopathology.

3.3.5.6 Visual analogue scales (VAS)

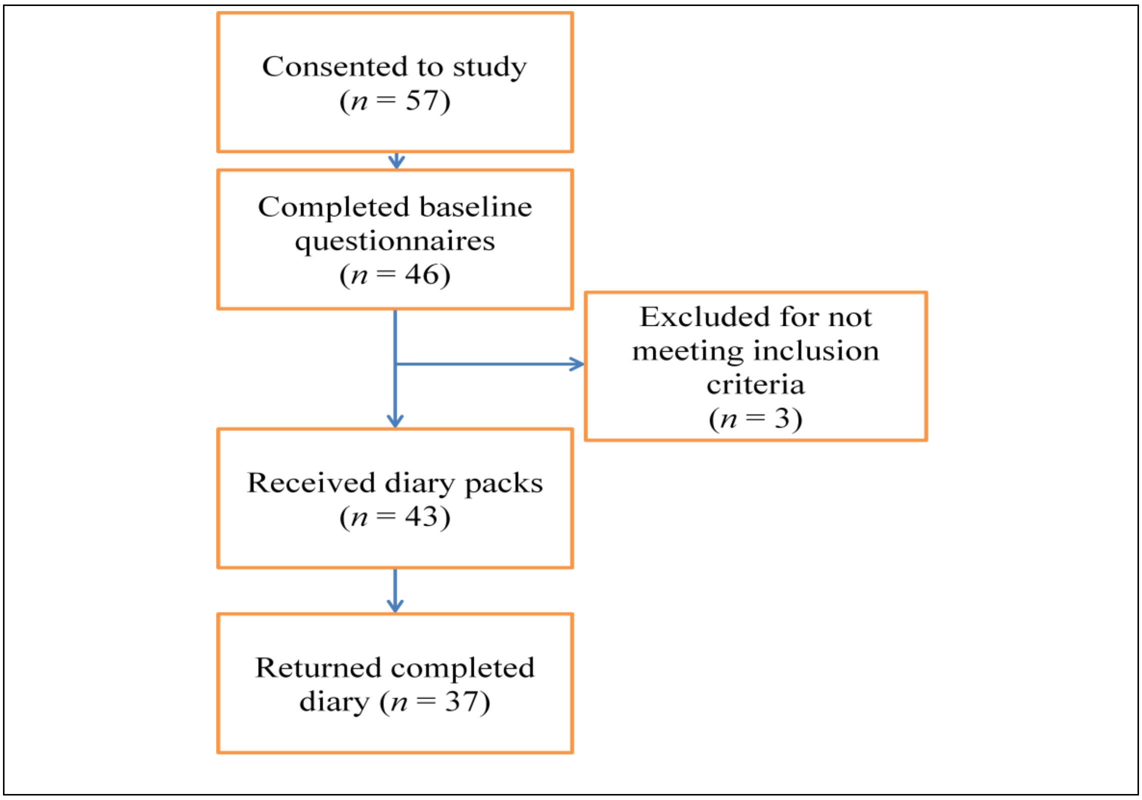
On each of the days that participants were enrolled in the study, they completed a series of VAS (with a scale of 0 [*not at all*] to 100 [*extremely*]) which were presented in the practice diary. Similar measures have been used in previous studies (for example, Rawal et al., 2011). In order to fit into the A5 sized practice diary, the VAS were 68mm in length. Two of the VAS aimed to examine whether the exercises influenced the way in which participants were focusing on themselves and were completed before and after each of the exercises (analytical check: proportion of thoughts concerned with trying to understand explain or make sense of things*;* experiential check: degree of focus on present-moment experience). A VAS was included to index feelings towards the body before and after each of the exercises ("feeling fat"). After the meal, participants also rated whether they thought that the exercise helped them manage the meal (defined as reducing cognitive and behavioural reactivity after the meal).

3.4 Results

3.4.1 Participants

In total, 57 female participants with a history of AN gave written informed consent to participate in the study and were sent the questionnaire pack. Forty-six of the participants completed and returned the questionnaire pack. Of these, three were excluded due to a current self-reported diagnosis of BED or BN. These three participants were however offered copies of the exercises to try. Forty-three participants were therefore invited to complete the introductory session for the study (10 of these participants opted to attend the introductory session in person). Thirty-seven of the 43 participants went on to complete and return the diary (88% of those who were sent the diary, 65% of the total who gave consent, see Figure 3.2). Eleven of these participants who were entered into the study had started to regain weight and therefore no longer meet full DSM-IV criteria for AN. The six who did not complete the diary were considered non-completers. Of the completers, 22 were currently receiving outpatient support for their ED, two were inpatients and 13 were not currently receiving any professional support for their ED.

Figure 3.2 Participant flow through the study



3.4.2 Demographic and questionnaire data

Questionnaire data was assessed for normality using the Kolmogorov-Smirnov test. Data was found to be normally distributed ($p > .05$) and so parametric tests were employed. Independent samples *t*-tests indicated a significant difference between the completers and non-completers in terms of global EDE-Q scores,

t (44) = 3.66, p =.001, and CIA scores, t (44) = 2.15, p =.04. The mean scores showed that participants who only completed the questionnaire pack and not the diary scored significantly lower on these ED-related measures than those who completed the diary. There were no other significant differences between the completers and non-completers. Demographic information, clinical variables and questionnaire scores for the 37 completers can be seen in Table 3.1.

Table 3.1 Demographic information and questionnaire scores for the AN participants who completed the study

Variable	*n*	*M*	*SD*
Age (years)	37	29.71	10.51
BMI	33	17.19	2.26
EDE-Q	37	3.90	1.20
CIA	37	32.10	11.96
BDI-II	37	32.41	14.52
STAI-T	37	43.97	9.63
AAQ-II	37	34.84	8.49
FFMQ	37	106.24	19.64
RRS-ED	37	21.95	5.81
Duration of illness (months)	29	159.03	145.65
Time in treatment (months)	25	111.82	116.22
Age of onset	22	16.92	5.40

Note. The variation in sample size is due to variation in the number of women who provided information on clinical variables.

3.4.3 VAS data analysis

VAS scales in each participant's diary were hand measured by the researcher and scores ranging from 0 to 68 were entered into SPSS. The Kolmogorov-Smirnov test indicated that not all of the variables were normally distributed ($p < .05$). In an attempt to correct the data, logarithmic and square root transformations were conducted. However, after transforming the data, the variables were still not normally distributed. The decision was made to cautiously proceed with the data set in its raw form and to verify any significant results using non-parametric tests.

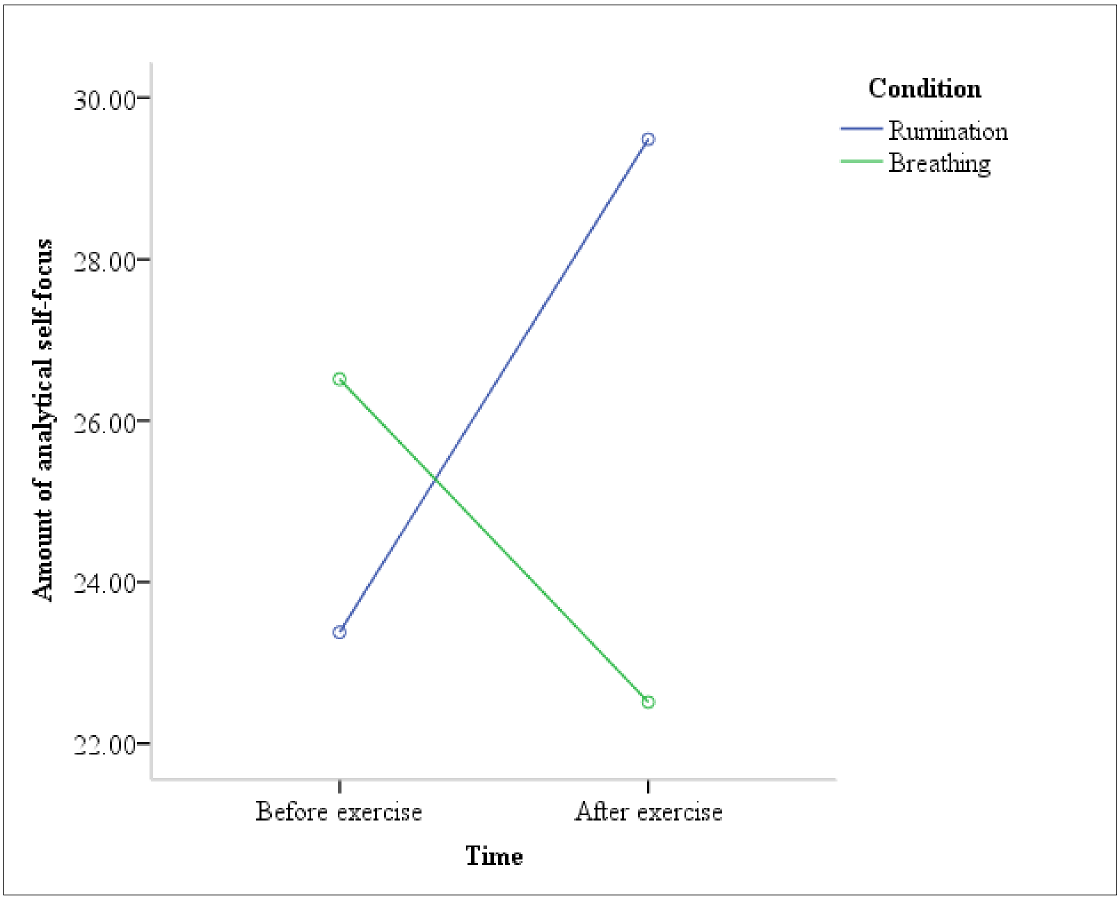
Repeated measures ANOVAs were used to explore differences in participants' VAS ratings across the time points (pre-post) for the three conditions. To avoid the statistical problems resulting from multiple testing, the data was analysed in such a way that only specific questions, based on the hypotheses, were addressed. The significance level was set at $p < .05$. The analyses which yielded significant results were re-run controlling for self-reported depression (BDI-II) and anxiety (STAI-T). In addition, separate analyses were performed on those who were underweight (henceforth "full criteria AN") compared to those who no longer met full DSM criteria for AN due to their BMI (henceforth "partially weight-restored AN").

3.4.4 VAS results

3.4.4.1 Does rumination increase analytical thinking compared to mindful breathing in AN?

Changes in analytical thinking before and after the rumination and mindful breathing exercises were analysed using a 2 x 2 repeated measures ANOVA with condition (rumination, breathing) and time (before, after) as the within-participant variables. There were no main effects of time or condition. There was a significant condition x time interaction, F (1, 36) = 9.63, p = .004 (as shown in Figure 3.3). Controlling for multiple comparisons (α = .05/2), planned comparisons using t-tests confirmed that participants showed significantly greater analytical self-focus after using the rumination exercise compared to the mindful breathing exercise, (After rumination M = 29.49, SD = 16.2; After mindful breathing, M = 22.51, SD = 15.84; t [36] = 2.42, p = .02). The planned comparisons also showed that there was no difference before using the exercises in ratings of analytical self-focus (Before rumination, M = 23.38, SD = 16.34; Before mindful breathing, M = 26.51, SD = 18.0; t [36] = -.97, p = .34). It should be noted that a non-parametric Wilcoxon Signed-ranks test confirmed that analytical self-focus was greater after the rumination exercise compared to the mindful breathing exercise (Z = -2.49, p = .01).

Figure 3.3 Analytical self-focus before and after the rumination and mindful breathing exercises



Controlling for depression and trait anxiety

When the analysis was re-run controlling for scores on the BDI-II and STAI-T the interaction between condition and time became non-significant, F (1, 34) = .21, p = .07.

Full criteria AN compared to partially weight-restored AN[5]

To examine whether the rumination exercise had a different effect on analytical self-focus in those who met full DSM-IV criteria for AN compared to those who did not due to their BMI, the repeated measures ANOVA was re-run on subgroups of participants. In the participants who met full criteria for AN (n = 22), there was a significant condition x time interaction, F (1, 21) = 7.64, p = .01. None of the planned comparisons reached significance although there was a trend for more analytical self-focus after the rumination exercise compared to the mindful breathing exercise (After rumination, M = 29.36, SD = 15.76; After mindful breathing, M = 20.96, SD = 16.98; t [21] = -1.78, p = .09). Again this interaction was lost when controlling for BDI-II and STAI-T scores. The condition x time interaction was not found in the partially weight-restored participants (n = 11).

3.4.4.2 Is mindful breathing more effective at reducing analytical self-focus compared to distraction?

Changes in analytical thinking before and after the mindful breathing exercise and the distraction exercise was analysed using a 2 x 2 repeated measures ANOVA with condition (breathing, music) and time (before, after) as the within-participant variables. There were no main effects. The condition x time interaction was not significant.

[5] Four participants did not provide information on their height and weight and so BMI could not be calculated. These participants were not included in the subgroup analysis.

Full criteria AN compared to partially weight-restored AN

There were no significant main effects or interactions when running the repeated measures ANOVA on the subgroups of AN participants.

3.4.4.3 Is mindful breathing more effective at increasing experiential self-focus than distraction?

Changes in experiential thinking before and after the mindful breathing exercise and distraction exercise was analysed using a 2 x 2 repeated measures ANOVA with condition (breathing, music) and time (before, after) as the within-participant variables. There was no main effect of condition but there was a significant main effect of time, F (1, 36) = 37.67, $p < .001$. There was significantly greater experiential self-focus after using either the mindful breathing or distraction exercises compared to baseline (Before exercises, M = 39.89, SD = 27.12; After exercises, M = 68.57, SD = 28.38). A non-parametric Wilcoxon Signed-ranks test confirmed that experiential self-focus was greater after using the exercises compared to before using the exercises (Z = - 4.51, $p < .001$). There was no significant condition x time interaction.

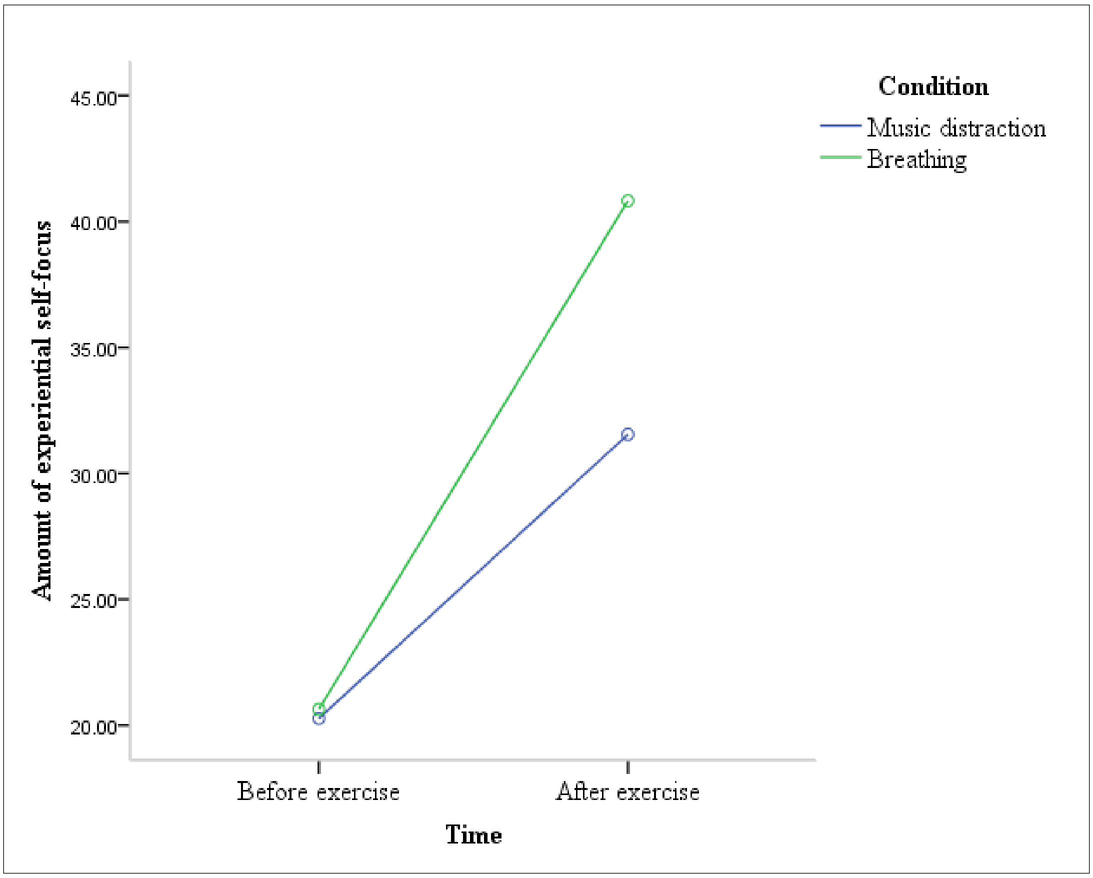
Controlling for depression and trait anxiety

When the analysis was re-run controlling for scores on the BDI-II and STAI-T the main effect of time was lost, F (1, 34) = 2.41, p = .13.

Full criteria AN compared to partially weight-restored AN

To examine whether the mindful breathing and distraction exercises differed in effect on experiential processing at different stages of AN, the repeated measures ANOVA was re-run on subgroups of participants. In the participants who met full criteria for AN (n = 22), there was a significant main effect of time, F (1, 21) = 7.64, p = .01. This was due to greater experiential processing after using either of the exercises (Before exercises, M = 39.77, SD = 28.02, After exercises, M = 68.41, SD = 30.92). A non-parametric Wilcoxon test confirmed this finding (Z = -3.30, p = .001). For the partially weight-restored AN participants (n = 11), again there was a main effect of time, F (1, 10) = 7.64, p = .01. As with the full criteria AN participants, this was due to greater experiential processing after using either of the exercises (Before exercises, M = 40.91, SD = 28.11; After exercises, M = 72.37, SD = 27.07) and this was confirmed by a non-parametric test (Z = -2.67, p < .01). Interestingly, the condition x time interaction was significant in the partially weight-restored group (p < .05). Figure 3.4 shows that this result was due to greater experiential self-focus after using the mindful breathing exercise compared to the music distraction exercise. These effects were lost when controlling for BDI-II and STAI-T scores.

Figure 3.4 Experiential self-focus before and after the mindful breathing and distraction exercises in the partially weight-restored participants (*n* = 11)



3.4.4.4 Does rumination increase feelings of fatness compared to mindful breathing in AN?

Changes in "feeling fat" before and after the rumination and mindful breathing exercise was analysed using a 2 x 2 repeated measures ANOVA with condition (rumination, breathing) and time (before, after) as the within-participant variables. Contrary to the hypothesis, there were no significant main effects or interactions.

Full criteria AN compared to partially weight-restored AN

When examining changes in “feeling fat” before and after the rumination and breathing exercise in the subgroups of participants, it was found that there were no significant main effects or interactions for the full criteria AN participants when using repeated measures ANOVA ($p > .05$). In the partially weight-restored group, there was a main effect of time, F (1, 10) = 5.56, $p < .05$. This was due to a decrease in “feeling fat” after using either of the exercises (Before exercises, M = 70.46, SD = 27.08; After exercises, M = 62.46, SD = 24.44) and this was confirmed by a non-parametric test (Z = -2.14, $p < .05$). However, the effect did not remain significant when the controlling for BDI-II and STAI-T scores.

3.4.4.5 Which of the exercises help participants with AN to manage the meal?

Participants VAS ratings of whether the exercises helped manage the meal, rated after the meal, were compared across the three conditions (rumination, mindful breathing, distraction) using a one-way repeated measures ANOVA. There were no significant differences in self-reported management of the meal between any of the conditions ($p > .05$).

3.4.5 Summary of quantitative results

- The rumination exercise led to significantly greater analytical self-focus compared to the mindful breathing.
- The effect of mindful breathing was not significantly different from distraction when examining all AN participants together.
- When examining only the partially weight-restored AN participants, mindful breathing did lead to significantly greater experiential self-focus compared to distraction.
- There was no significant effect of any of the exercises on feelings of fatness.
- According to reports from the VAS, there were no significant differences following any of the exercises in terms of meal time management.

3.5 Qualitative analysis of the experience of being in different modes around the meal time

In order to better understand the quantitative results and also to gain further insight into the experience of the different exercises designed to encourage different modes of processing around meal times, the comments provided by the participants on the exercises were analysed qualitatively.

3.6 Method for qualitative analysis

Thirty-six of the 37 participants who completed the study provided written feedback on their experiences of using the exercises. The instruction to participants was: "Please comment on the [second] exercise. Continue on a separate sheet if necessary*"*. Written feedback provided in the diaries was transcribed verbatim by the principal researcher (FC). The minimum and maximum number of words from the feedback varied for each exercise (Rumination, 13 to 195 words; Mindful breathing, 19 to 287 words; Distraction, 13 to 253 words).

Data was coded by hand and analysed thematically using a modified grounded theory approach (Strauss & Corbin, 1990), incorporating constant comparison (Pope, Ziebland, & Mays, 2000) (for full details see Appendix 3.11). Initially, all 36 transcripts were read and re-read line-by-line and key words or phrases were noted in the margin of the transcripts as codes (open coding) (Strauss & Corbin, 1990). Following this, the researcher (FC) compared the codes and began to organise them into categories depending on whether the themes were overlapping. The content of the categories were then used to devise an appropriate title and where appropriate, words used by the participants were included in the category titles. The separate categories were compared and in order to reduce the total number of categories, those which were similar in content were pooled and formed seven higher order categories. The three conditions (rumination, mindful breathing and distraction) were coded and analysed separately. However, non-specific themes that emerged across conditions were also noted (i.e., themes which were not related specifically to one of the exercises) and formed higher order categories. Following this, a final coding scheme was devised (see Table 3.2 for the coding scheme) and this was applied to all the text.

To ensure that the researcher’s coding was valid, 20% of the transcripts were randomly selected and given to an independent researcher to check. The independent researcher was an educational psychology graduate student who had previous experience in the grounded theory approach but was unfamiliar with the specific hypotheses of this study. Following credibility checking, the interpretation of the data and the conclusions drawn were made in a meeting between the researcher (FC) and the researcher’s supervisor (RJP) – a psychiatrist with extensive clinical and research experience in EDs.

3.7 Qualitative results

3.7.1 Overview of qualitative results

The final hierarchical coding scheme consisted of seven higher order categories and 17 lower order categories. Five categories emerged as relevant for only one of the three exercises as indicated in Table 3.2. The remaining two higher order categories were more general and included the usual meal time experience and suggestions as to what would be helpful around meal times. Each higher order category is presented below and supported by verbatim excerpts. In order to situate the sample, demographic and clinical variables relating to the participants from whom the excerpts were taken is provided in Table 3.3.

Table 3.2 Categories extracted from the qualitative analysis

Exercise	**Higher order category**	**Lower order category**
Rumination	Thinking about myself	*Avoidance/distraction*
		Negative emotional response
Breathing	Being in the moment	*Familiarity with meditation and/or mindfulness*
		Relaxing/calming
		Overwhelming
	Increased awareness of eating and food	*Feeling more at ease*
		More realistic about food quantities
		Changing behaviour around meal times
		Taking time out
	A pleasant break in a hectic day	*Changing routines*
Music distraction	Not focusing on myself	*Avoidance*
Non-specific	The usual meal time experience	*Stress/anxiety*
		Rumination/avoidance
		Rigid routines
	Suggesting what may be helpful	*Practicing the exercise/familiarity*
		Longer exercises
		Using the exercise at different time points

Table 3.3 Demographic information, clinical variables and questionnaire scores on quoted qualitative data

Participant code	Age	Self-reported BMI	Duration of illness (months)	EDE-Q	CIA	BDI-II
1	37	15.2	192	3.46	21	13
2	20	19.5	60	3.22	28	32
3	29	17.5	24	3.92	25	29
5	58	15.5	492	4.40	36	21
12	17	20	--	3.86	31	25
15	36	15.5	--	3.65	35	13
19	16	19	288	3.91	27	23
20	41	14.5	320	4.16	16	39
24	42	15	28	3.33	43	38
25	22	--	32	3.33	33	15
26	--	20	--	4.49	40	44
34	29	19.5	192	2.09	43	4
39	30	18	20	5.45	25	26
51	22	16.5	24	4.18	37	51

Note. A number of participants failed to provide demographic and/or illness-related information.

3.7.2 Themes arising from the rumination exercise

Thinking about myself

The first category focused particularly upon participants' experiences of *thinking about* themselves. Some participants found ruminative thinking about the self aversive and reported that it had a negative impact on the meal time experience. One reason for this was that the exercise brought into conscious awareness disturbing or unpleasant thoughts and feelings which tend to be avoided. Some participants also felt that focusing on the self elicited unpleasant feelings of guilt about their current state and pessimism about the future.

> *"…having to think about myself and my feelings e.t.c., made me aware of how I was feeling during every mouthful, which made eating very difficult. I prefer not to think at all when I eat so I can just get on with it."* [Participant 3, rumination][6]

In contrast, following the rumination exercise other participants commented that they found it beneficial to have focused thinking about the self as it acted as a distraction from the upcoming meal.

> *"….becoming aware of how tense, anxious and stressed I was did help me for a short while as it made me focus on something other than the meal."*
>
> [Participant 51, rumination]

[6] Refers to the participant code and the condition.

3.7.3 Themes arising from the mindful breathing exercise

Being in the moment

Becoming more aware of the present-moment was a theme which emerged from the mindful breathing exercise. Some participants felt that the experience of being in the present-moment was positive as it interrupted ruminative processing cycles. Parallels were made between the mindful breathing exercise and previous experiences with yoga practices and meditation. There was some indication that these participants found the exercise useful because of its familiarity and that it had a positive effect on the meal time experience.

> *"Like coming home to a 'safe' place. I have used mindfulness before, and the voice was familiar and felt reassuring. It felt like a relief to be in the moment (as far as I could) for a while as I am in a low mood this morning and ruminating- being in my own head. I found using this CD and prior reflecting on how I was in this diary helpful as a means of stopping a while and taking stock of the present moment and my own condition, rather than just hurling myself into my meal in a stressed state, as I usually do."* [Participant 5, breathing]

Conversely, the mindful breathing exercise was experienced negatively by some participants. Participants commented that they would lapse into negative rumination and consequently were unable to focus on their breathing.

> *"I initially found this distressing because this practice automatically made me dwell on things that cause me anxiety, guilt, shame or hopelessness. I struggled to narrow my concentration to my breathing especially when I had started to dwell on my thoughts and feelings."* [Participant 15, breathing]

Participants also found that the mindful breathing exercise made them too aware of their body and feelings of discomfort with their body. Some participants reported that rather than being aware of the body before a meal, they prefer to use other strategies to cope, such as rumination or distraction.

> *"This was my least favourite exercise because it made me focus too much on my body and so I felt fatter than before. Sometimes I had to listen to CD1* [rumination] *after CD3* [breathing] *just so I could cope with the meal."* [Participant 12, breathing]
>
> *"I didn't find it helpful. In fact quite the opposite. I don't see the benefit of focusing on what makes you feel terrible. I would rather have a distraction.* "
> [Participant 20, breathing]

Increased awareness of food and eating

As well as becoming more aware of the present-moment, participants felt that they became more aware of the amount that they were eating or the way in which they were eating and for some this made the meal time less challenging.

"Although the meal was still difficult I was much more focused on what I was eating and I seemed a lot more realistic about what I was eating (i.e., I often look at my small portion and it seems enormous whereas today, when I was calmer I could appreciate that it was a manageable amount so it seemed a little less daunting)."
[Participant 24, breathing]

"Narrowing the focus on breathing and posture helped me to concentrate on how I was feeling about myself and I felt a little more at ease when eating"
[Participant 3, breathing]

There was also some evidence that that increasing awareness of eating following the mindful breathing exercise had an effect on post-meal urges to engage in compensatory behaviours, such as binge-eating or maladaptive thoughts about weight gain.

"*I was more aware of what I was eating afterward which made me think that I was eating a larger amount of food because I wasn't dreaming as much. I think it helped me not to have a full blown binge"* [Participant 26, breathing]

"It relaxed me and forced me and forced me to focus on something other than the panic of food. I realised that eating a normal amount wasn't going to change my weight." [Participant 19, breathing]

A pleasant break in a hectic day

Participants commented on the benefits of stopping what they were doing and focusing on their breath. Some participants valued the break that the mindful breathing exercise provided in their busy days. Whilst it was evidently difficult for participants to break out of their usual routines around meal times and fit in a short meditation practice, for some of those who managed, it seemed a positive experience.

"I found listening to the CD really made me stop rushing around and focus on the present. The voice was soothing and it was good to stop what I was doing and become aware of my breath and be in the present." [Participant 26, breathing]

"I found it quite therapeutic to sit and focus on myself and breathing but this allowed me to focus on my thoughts which I try to avoid. However, I found it hard not following my usual routine. Changing even the slightest thing like listening to a CD was difficult." [Participant 39, breathing]

3.7.4 Themes arising from the distraction exercise

Not focusing on myself

A category that emerged from the distraction exercise was the use of distraction in facilitating avoidance of aversive meal time emotions. This seemed to be valued by some participants. Participants described that during the distraction exercise they were not focused on themselves or the upcoming meal but rather their reactions to the music.

> *"I think this was helpful because it took the focus away from self-analysis/how I was feeling and made me concentrate on something else which I think is so helpful".*
> [Participant 1, distraction]
>
> *"All my mental faculties were directed to analytically reflecting on the pieces of music rather than being engaged in thinking about myself."*
> [Participant 15. distraction]

In some cases, participants reported not liking classical music, but they still found that by focusing on how much they did not like the music they were distracted from thinking about themselves and the meal ahead.

> *"I did not particularly enjoy the pieces of music so I did not find them very relaxing. However, I do think that thinking about how I would rate them in my head kept me focused on the exercise and prevented my mind from wondering."*
>
> [Participant 25. distraction]

3.7.5 Non-specific themes

The usual meal time experience

When providing feedback on the exercises, participants reflected on their usual meal time experience. Participants described a general tendency to ruminate before the meal. There were indications that the content of rumination was often on eating, shape and weight concerns. The first extract also points to the perceived importance of emotional avoidance in AN.

> *"I focus on thoughts about feelings of weight gain and about distracting myself from emotions surrounding these thoughts."* [Participant 51]
>
> *"I have been feeling a bit preoccupied with thoughts about my body/eating and some self disgust/sense of greed."* [Participant 5]

Participants reported high levels of stress and anxiety preceding the meal and the negative impact that this has on the meal time experience.

"I am usually incredibly stressed prior to a meal and by the time I sit down to eat, I am so anxious that it makes things extra hard". [Participant 24]

Suggesting what may be helpful

Participants felt that using the exercises at different or additional points in the day would be useful, particularly after the meal as this would distract them from negative emotions or urges to engage in maladaptive behaviours.

"I think it would have been helpful to listen to the CD again after the meal to help me deal with the guilt and anxiety I felt after eating." [Participant 26]

"The exercise did help me prevent compensatory behaviours for a little longer than usual and I would perhaps find it useful to use the exercise after as well as before." [Participant 51]

Some participants also found that anxiety and stress experienced at the meal time was so overwhelming that they were unable to concentrate on the exercise. Therefore, participants felt that they would benefit from practicing the exercise over a longer period of time, enabling them to become more familiar with the exercise and/or provide more of an opportunity to incorporate it into their daily routine. Participants also suggested that longer exercises would be needed to have a significant effect on the meal time.

“I often found it difficult to fully let go of anxieties/thoughts to carry out the exercise, but that may be something that would improve if I continued to use the CD regularly.” [Participant 3]

“Before a real sense of own breathing and awareness could develop we were into the next thing and then it was all over. For a fairly distracted mind more time to calm my thoughts may have had a bigger impact.” [Participant 34]

“I feel that the music extracts were a little bit too short and that there could have been more of them to make the CD more effective.” [Participant 32]

3.8 Summary of qualitative analysis

- Thinking about the self in a ruminative way elicited a range of negative cognitions and emotions.
- Increasing awareness of the present-moment following the mindful breathing exercise was experienced positively by some participants. Others were unable to get into or stay in the present-moment and found emotions overwhelming, triggering rumination.
- Participants valued being distracted from their cognitions, emotions and also the upcoming meal.
- The usual meal time experience for individuals with AN is characterised by rumination, aversive emotions and rigid routines.
- Using longer exercises and at different times may be required to have a significant effect on the meal time experience in AN.

3.9 Discussion of quantitative and qualitative data

The aim of this exploratory study was to examine different modes of processing in individuals with AN around meal times. The analysis highlighted how difficult it is to interrupt a ruminative processing mode and enhance a more accepting stance, particularly around meal times, in individuals with current symptoms of AN. The qualitative component of the analysis enabled a more detailed analysis of the meal time experience for participants with AN and more specifically, the experience of different modes of processing at this challenging time. The results from the qualitative analysis supports key predictions from the ICS account of AN such as the tendency to process self-material in a ruminative way, the perceived value of avoidance, as well as the difficulties associated with experiential mode processing when ill with AN (Park et al., 2011, 2012).

What effect does rumination compared to mindful breathing have on analytical self-focus?

It was hypothesised that the rumination exercise would lead to greater analytical self-focus compared to the mindful breathing exercise. In line with previous work using similar rumination inductions (for example, Rawal et al., 2011; Watkins & Moulds, 2005; Watkins & Teasdale, 2001), the rumination exercise in this study did significantly increase analytical self-focus, unlike the mindful breathing exercise. This supports the validity of the exercise in inducing rumination and the proposal that it is the analytical flavour of self-focus in rumination, not self-focus *per se*, which may be detrimental in psychological disorders (Watkins & Teasdale, 2001).

The qualitative analysis indicated that some individuals with AN valued the rumination exercise because “thinking about” themselves in an analytical and evaluative way facilitated avoidance of difficult emotions and cognitions that were elicited by the meal. This supports theories which suggest that repetitive negative thinking, such as rumination or worry, functions to escape or avoid aversive experiences (as discussed in Section 1.8.1). Applied more specifically to AN, it supports the ICS framework which suggests that rumination on themes of eating, weight and shape enable individuals to avoid emotions and body-state cues associated with starvation (Park et al., 2011). It also adds weight to the findings of Chapter 2 that reported a relationship between rumination, avoidance and ED symptoms.

In the quantitative analysis, the mindful breathing exercise did not lead to a significant reduction in analytical self-focus overall. As cautioned by Park et al. (2012), interrupting ruminative cycles in currently ill AN participants is challenging. There are several potential explanations for why the mindful breathing exercise used in this study failed to disrupt ruminative processing in AN. One possibility is that when confronted with salient situational cues, such as food for individuals with AN, an increase in analytical rumination may be triggered (state-related rumination). The contribution of state-related rumination, triggered by the food, to trait levels of rumination would make it more difficult to disengage from the ruminative thoughts and adopt a more experiential mode of processing.

The second possible explanation is that with increasing duration of illness, rumination may become a habitual mode of thinking. In addition, increased negative mood associated with AN or comorbid depression may augment the intensity of rumination, making switching out of this mode too effortful, especially when unpractised and severely underweight. As can be seen in Table 3.1, the mean score for the BDI-II as well as the duration of illness for the sample is high (BDI-II, M = 34.9; Duration of illness, M = 159.03 months). If it is the case that chronicity and depressed mood are related to the inability to disrupt ruminative processing, interventions aimed to help AN participants “switch out” of such thought patterns may be more effective if implemented either in the first episode of AN, before ruminative processing styles become too entrenched, or after partial weight-restoration. This would support the notion that in the acute stages of illness, strategies such as distraction may be more comfortable.

The fact that the mindful breathing exercise employed in this study was brief and not usually used as a standalone intervention (i.e., without more comprehensive training in mindfulness skills) may also explain why it did not significantly reduce analytical self-focus in this study. There are laboratory studies which have used mindful breathing exercises and found significant changes in the outcome variables of interest (for example, Arch & Craske, 2006; Erisman & Roemer, 2010; Feldman, Greeson, & Senvill, 2011). However, these studies are generally conducted in non-clinical participants and the exercises used are longer and supplemented with direct guidance from the researchers. In the present study, participants with clinical EDs worked through the brief exercises at home and thus without much guidance from the researcher. As the qualitative analysis indicated, some participants did report difficulties engaging with the exercises because of such factors. It has also been found that the amount of time spent practicing guided meditations (such as the mindful breathing exercise) is related to improvements in levels of mindfulness and also measures of psychological wellbeing (Carmody & Baer, 2008; Kristeller & Hallett, 1999). Whilst this study was not trying to implement a mindfulness treatment program, it is likely that the brevity of the mindful breathing exercise combined with its standalone use explains why it did not reduce analytical self-focus. Extensive training in experiential mode processing and in less emotionally-laden situations (i.e., not meal times) may be more beneficial for participants with AN.

Does mindful breathing facilitate greater present-moment awareness compared to distraction in AN?

In quantitative analysis there was no overall difference between the mindful breathing exercise and the distraction exercise on experiential self-focus when considering all the participants together. However, there was a main effect of time suggesting greater experiential self-focus after listening to either the mindful breathing or distraction exercise. This supports the notion that in the short term, currently ill patients with AN may benefit as much from distraction-based strategies as training in different modes of processing. This parallels the literature in depression, where distraction has been shown to provide short term relief from depressive symptoms (Nolen-Hoeksema, 1991). Significantly greater experiential self-focus following the mindful breathing exercise in the partially weight-restored AN participants supports the proposition that mindfulness-based practices may be more suitable for those working towards recovery. This interpretation needs to be treated cautiously due to the small sample size in the partially weight-restored subgroup. Nonetheless if this is the case, it would correspond with the depression literature which supports the use of mindfulness-based practices in the context of remitted depression (as reviewed by Besahai et al., 2011; Piet & Hougaard, 2011).

One problem with interpreting the results from the distraction exercise is that it is difficult to know exactly how the exercise had its effect. Distraction tasks are designed to be affectively neutral. However, as reviewed by Koelsch (2010), findings from psychophysiological and neuroimaging research have shown that music elicits intense emotional responses. Therefore, despite selecting the “most neutral” musical extracts for the distraction exercise, it is unlikely that they were non emotional. It is therefore possible that when asked to rate their present-moment awareness (including sensory experiences and feelings), participants were reflecting on emotions elicited by the music.

Another possibility is that the distraction exercise had similar qualities to the mindful breathing exercise. More specifically, the music in the distraction exercise and the mindful breathing may have both facilitated more sensory-based processing. As shown by Figure 1.1 (Section 1.7, Chapter 1), Williams (2010) has associated the “doing” and “being” modes with conceptual (language-based) processing and sensory-perceptual processing respectively. This is relevant as it may be that both the sound-based distraction exercise and the mindful breathing exercise, directed attention to sensory-based processing whilst the rumination exercise increased language-based processing.

Whilst an increase in experiential self-focus, as indexed by the VAS, was found after both the mindful breathing and the distraction exercises in the quantitative analysis, in the qualitative analysis the theme of “being in the moment” was extracted only from the mindful breathing data. Some participants identified an increased awareness of the present-moment and considered this an adaptive alternative to their typical ruminative processing style. This supports a fundamental premise of ICS frameworks that shifting attention to present-moment experience, with a compassionate and non-judgemental stance, may interrupt ruminative processing cycles (Park et al., 2011; Teasdale, 1999; Teasdale, Segal, & Williams, 1995; Williams, 2008). However, other AN participants reported feeling emotionally overwhelmed following the breathing exercise and in certain cases there was evidence that this aversive experience led to increased rumination. Thus it seems that some participants did not switch into a mindful mode of processing. Rather they may have shifted into what Park, Dunn and Barnard (2011) refer to as “mindless emoting”- overwhelmed by body state and needing to reinstate doing AN mode of mind characterised by high levels of rumination and avoidance of bodily cues. The heterogeneity in the effect of the mindful breathing exercise may explain in part why there was no statistical difference between the mindful breathing and distraction exercise in terms of experiential self-focus.

Do different modes of processing have an effect on the experience of the body and meal time management in AN?

There was no evidence from the overall quantitative analysis that any of the exercises (rumination, mindful breathing or distraction) had a significant effect on the experience of the body or meal time management in the AN participants. The lack of significant results may be explained by the brevity of the exercises, the lack of training in the different modes, and/or the chronicity of the sample recruited (as discussed above). Similar to the findings reported here, Wildes, Marcus, Bright, Dapelo and Psychol (2012) conducted an experimental paradigm with AN participants in which mood was manipulated before eating and reported that whilst a negative mood induction influenced the expression of cognitive ED symptoms, this was not translated into changes in overt eating behaviours. Thus it may be that the brief exercises used in the present study are better for examining the ability to switch modes of processing, rather than examining the challenging issue of whether such mode changes can then alter behaviour and cognitions around meal times.

Whilst not supported by the statistical analysis, the qualitative analysis indicated that there were some positive outcomes of the exercises (particularly the mindful breathing and distraction exercises), including feeling more at one with the body and being more at ease when eating. This supports the prediction of Park et al. (2012) that for some individuals with AN, training a qualitative shift in awareness of the self and body away from an object to be controlled as in doing AN may be beneficial. It would be of interest to examine whether more guidance on the different modes of processing would be of use in AN participants, for example guidance on how to approach the meal in a mindful way. This is especially relevant given that some participants who reported previous experience of meditation-based activities seemed to find the mindful breathing practice useful before the meal time (see Section 3.7.3)

The effect of anxiety and depression

The quantitative results reported did not remain significant when controlling for self-reported symptoms of depression and anxiety. It is difficult to determine with any certainly whether anxiety and depression did actually effect the mode of processing given the small shifts in *p* values from what was just over compared to what was just under significant. Future studies with larger sample sizes may enable more accurate evaluations of the effect of depression and anxiety symptoms on modes of processing.

The usual meal time experience

In terms of the usual meal time experience, women with AN described a variety of negative cognitions and emotions experienced around the meal. More specifically, participants experienced high levels of stress and anxiety before the meal time. This supports the continued development of novel interventions which aim to reduce meal time anxiety. For example, Cardi and colleagues (2012) have recently reported on the use of vodcasts (a video podcast) to support eating and reduce anxiety in people with EDs.

Participants reported engaging in rumination before the meal. It is difficult to know from the analysis to what extent this rumination was triggered by contextual factors (i.e., the upcoming meal), and thus state-related, or alternatively reflected trait ruminative tendencies. Either way, this finding adds to the contention that rumination is a maladaptive process in EDs which may escalate symptoms and supports previous theoretical and empirical work (Park et al., 2011; Rawal et al., 2011). In line with previous studies and the results reported in Chapter 2, the data also illustrates that maladaptive strategies, such as rumination and avoidance, are used by some individuals with AN to manage aversive experiences such as eating (Lavender & Anderson, 2010; Rawal et al., 2010). This qualitative finding therefore provides a further rationale for the development of strategies to reduce avoidance and rumination whilst promoting emotional processing, thereby enhancing awareness and acceptance of the body, cognitions and emotions.

Suggesting what may be helpful

Participants suggested that making the exercises longer and having more time to practice the exercises, particularly the mindful breathing exercise, may improve the effectiveness. The MBCT for depression manual highlights the importance of regular training and out of class practice for yielding the benefits of mindfulness (Segal et al., 2002) and empirical research shows that time spent engaging in practice of formal meditation exercises is related to extent of improvement in mindfulness and general well-being (Carmody & Baer, 2008). Thus it is expected that greater effects on the meal time experience would result from more guidance and regular practice of longer exercises.

3.9.1 Limitations

Limitations of quantitative analysis

Due to the challenges of recruiting participants currently ill with AN, a power calculation was not conducted a priori and thus the study may have been underpowered. This is particularly applicable to the subgroup analyses and when running the analyses controlling for anxiety and depression. Further, parametric tests were used on the data despite some variables being not normally distributed. Therefore results from the quantitative analysis should be interpreted cautiously. Future studies would benefit from larger sample sizes.

Limitations of qualitative analysis

The material provided by participants consisted mainly of brief comments and short sentences, thus individual themes could not be examined in great depth. Some of the themes extracted were not directly supported by the statistical analysis and therefore need to be interpreted cautiously. Lastly, as with all qualitative analyses, researcher bias may have influenced the coding and interpretation of the data.

Overall limitations

Overall limitations of this study include a relatively small sample size and a self-selected sample. Thus generalisations cannot be made to other contexts. Due to the reliance of self-report, it is also difficult to reliably determine the effect of co morbid diagnoses on the results. This is especially important given that the sample was heterogeneous in terms of age, severity and chronicity. Data on clinical variables (for example, duration of illness, lowest ever BMI) were missing from some participants and therefore inferences about the characteristics of the sample may be distorted. Lastly, there was no control group to compare the results to and so it is uncertain how a non-AN participant group would respond to the exercises.

3.10 Conclusions

This study explored the effects of different modes of processing in AN around meal times. The results show that interrupting rumination around meal times is challenging and that fostering more mindful processing in such stressful circumstances may lead individuals with AN to feel overwhelmed and out of control. The main limitation of this study (and that reported in Chapter 2) is the reliance on self-report to index complex psychological processes. To better understand the processes which drive aberrant responses to food in AN, the next step is to seek more objective evidence, for example by examining the neural response to food stimuli in AN. This work is described in Chapter 4.

4 Neural response to pleasant and aversive food stimuli in recovered anorexia nervosa

4.1 Overview

The study reported in Chapter 3 demonstrated that the aberrant response to food in those with AN manifests as intense rumination around meal times which is difficult to shift. Examining how food cues are processed by the brain in individuals with AN may add to the findings described in Chapter 3. Using neuroimaging it may also be possible to further elucidate the processes which drive the aberrant responses to food and eating in AN. Therefore, the key questions which will be addressed in this chapter include:

- What are the neural responses to rewarding and aversive food tastes and pictures in AN?
- Does brain imaging aid understanding of the complex eating-related behaviours and attitudes that characterise AN?

4.2 Background

As reviewed in Chapter 1, individuals with AN have a puzzling relationship with food: they are intensely preoccupied with thoughts about food yet paradoxically they can severely restrict their intake. Addressing the question of how individuals with AN are able to refrain from eating energy-dense foods, which are typically experienced as rewarding by healthy individuals, whilst they remain so preoccupied with food may be important in understanding the disorders maintenance. The process account of AN suggests that rumination may be one process which facilitates restrictive behaviours in AN (Park et al., 2011) and Chapter 2 provided preliminary evidence that rumination on eating, weight and shape is associated with ED symptoms.

Chapter 3 examined ruminative processing around meal times in AN. The results demonstrated that interrupting rumination around meal times is challenging as eating in AN is associated with a range of aversive cognitions, emotions and behaviours. As suggested by Park et al. (2011, 2012), it is therefore likely that food stimuli, which are highly valued and experienced as rewarding by those without AN, are processed differently by those with the disorder. This hypothesis has been supported by a range of behavioural and neuroimaging studies (as reviewed in Chapter 1). The atypical processing of rewarding stimuli, particularly in the primary domain of food, is also consistent with the neurobiological account of AN by Kaye and colleagues (Kaye et al., 2009) (as discussed in Section 1.9.1). This account suggests that aberrant interactions between reward regions of the brain, such as the ventral striatum, and top-down neural circuits involved in cognitive control, may explain the disordered eating behaviours that characterise AN.

A major limitation of the studies reported in Chapters 2 and 3 is that the data was collected via self-report. Some studies have found that individuals with AN have difficulty in accurately recognising and labelling emotional states (Speranza, Loas, Wallier, & Corcos, 2007) although it is noted that this is not a consistent finding (for example, Parling, Mortazavi, & Ghaderi, 2010). Therefore self-reported psychological processes may be even more susceptible to biases and inaccuracies in AN participants compared to other participant groups. This may be especially apparent around meal times which are typically experienced as overwhelming by individuals with AN and may be associated with an increase in rumination and avoidance (as suggested by the data in Chapter 3). Neuroimaging studies allow the neural response to stimuli to be detected even without conscious awareness (as discussed by Critchley, 2005) and thus are not dependent on subjective report. This study aimed to use neuroimaging in those recovered from AN to examine the neural response to food stimuli. A well validated paradigm which has been shown in previous work to directly activate reward regions of the brain such as the ventral striatum was employed (McCabe, Cowen, & Harmer, 2009; McCabe, Mishor, Cowen, & Harmer, 2010). Therefore, the results from this study will help to understand the role of the brain in relation to both reward processing in AN and the cognitive processes described in Chapters 2 and 3.

.

4.3 Study aim

The main aim of this study was to examine the neural response to rewarding and aversive food tastes and pictures in individuals recovered from AN compared to HCs.[7]

4.4 Hypothesis

Women with a history of AN would have aberrant neural responses to the sight and taste of pleasant chocolate and aversive strawberry stimuli in the brain regions which have been shown to be activated by this task, such as the ventral striatum, caudate, insula, medial prefrontal and orbitofrontal cortices (for example, McCabe, Cowen, & Harmer, 2009; McCabe, Mishor, Cowen, & Harmer, 2010; Rolls & McCabe, 2007).

[7] Recovered AN were selected to avoid the confounds introduced by scanning currently ill AN participants and also to examine trait/scar neural markers of AN (see Section 1.10 for further discussion on this).

4.5 Method

4.5.1 Overall design

This study used a between-participants design to examine the neural response to pleasant chocolate and aversive strawberry visual and taste stimuli in women recovered from AN compared to HC participants.

4.5.2 Participants

Sixteen female participants who had met DSM-IV criteria for AN (American Psychiatric Association, 1994) but had been recovered for 12 months and sixteen female HC participants were recruited for the study. Participants were recruited via posters, internet advertisements and email circulars. The study was approved by the Central London Research Ethics Committee (see Appendix 4.1).

4.5.2.1 Inclusion and exclusion criteria

Inclusion criteria for the HC participants included, (1) a current BMI between 18.5 and 25 kg/m^2, (2) no first-degree relative with a current or past ED diagnosis (assessed by self-report), (3) no lifetime history of any Axis I psychiatric disorder on the Structured Clinical Interview for DSM-IV (SCID) (Spitzer, Williams, Gibbon, & First, 2004), (4) maintenance of a weight in the healthy range (define by the WHO) since menarche (assessed by self-report).

As there is no consensus as to how recovery from AN should be measured (see Section 1.10), the criteria used in this study was in line with the definition used in previous brain imaging studies involving recovered AN participants (for example, Wagner et al., 2007, 2008). Therefore, in addition to having a history of DSM-IV AN assessed by the SCID (Spitzer et al., 2004), in order to be considered recovered, for the previous 12 months participants had to have (1) maintained a BMI of between 18.5 and 25 kg/m^2 for 12 months (assessed by self-report), (2) had regular menstrual cycles (assessed by self-report), (3) not used psychoactive medications for 12 months prior to the study (assessed by self-report). In addition, recovered participants had to score within one standard deviation of the EDE-Q global mean scores for young women (Mond, Hay, Rodgers, & Owen, 2006).

General exclusion criteria for all participants included a history of head injury, neurological or other severe medical illness, pregnancy, and any contradictions to MRI (for example, metallic implants).

4.5.3 Study procedure

4.5.3.1 Screening phase

All participants underwent a screening process that involved a brief email screening and a face to face assessment using the SCID (Spitzer et al., 2004). At the screening session, participants also had their height and weight recorded in order to calculate BMI and completed an assessment of IQ and a questionnaire to assess chocolate eating (detailed below). Recovered AN participants also reported on their duration of illness, lowest ever BMI, age of onset and length of recovery. All participants provided written informed consent (see Appendix 4.2 and Appendix 4.3).

As part of the screening process, all participants were invited to practice the task in the laboratory. This involved rating the visual and taste stimuli using the keys on a laptop. The researcher observed the ratings and if any of the participants responses were in opposition to that expected (for example, if they found the liquid chocolate aversive or the mouldy strawberry picture pleasant) they would not be included in the study.

If participants met inclusion criteria, they were invited to attend a scanning session and availability for the scan was discussed. Participants left the screening session with a battery of questionnaires to fill in at home consisting of the BDI-II (Beck et al., 1996), EDE-Q (Fairburn & Beglin, 2008), STAI-T (Spielberger, 1983) and the Fawcett-Clark Pleasure Capacity Scale (FCPS) (Fawcett, Clark, Scheftner, & Gibbons, 1983).

4.5.3.2 Pre-scan phase

On arrival, participants were invited to complete the Positive and Negative Affect Scale (PANAS) (Watson, Clark, & Tellegen, 1988), the STAI-S (Spielberger, 1983) and a series of visual analogue scales (VAS) to assess current mood state (detailed in Section 4.5.4). Participants also completed an MRI safety questionnaire to ensure they did not present with any contradictions to MRI. Participants were once again given a copy of the task instructions to read.

4.5.3.3 Scan phase

Participants were shown into the scanner control room and introduced to the radiographer who conducted safety checks with the participant. The participants were then taken into the magnet room and asked to lay head first in the scanner bore. The radiographer placed the head coil on participants and attached a viewing mirror. Meanwhile, the researcher prepared both the materials required for the taste task and the computer and projection screen for the visual presentations. Participants were then passed the delivery tubes and the button box and were able to practice swallowing the tastes while laying down and rating the stimuli using the button box. The radiographer and the researcher ensured participants could see the whole screen and made adjustments as necessary. The researcher and radiographer left the magnet room and communicated with the participants through the intercom. Before the tasks started, the researcher reviewed the instructions for a final time using the intercom. The researcher stayed in the control room, apart from during the reward task. During this task, the researcher was positioned in the magnet room in order to administer the taste stimuli.

4.5.3.4 Post-scan phase

Participants were removed from the scanner and completed a payment form. Participants were thanked and debriefed.

4.5.4 Measures

4.5.4.1 National Adult Reading Test (NART-R)

The NART-R (Nelson & Willison, 1991) contains 50 irregular words (see Appendix 4.5). For each word, participants are asked to pronounce the word and each response is marked as correct or incorrect by the researcher. Using the number of words pronounced correctly, a score of IQ can be calculated.

4.5.4.2 Fawcett Clark Pleasure Capacity Scale (FCPS)

The FCPS (Fawcett et al., 1983) contains 36-items describing pleasurable situations (see Appendix 4.6). For each item, participants are asked to rate on a 5-point scale how much pleasure they would experience from each situation, regardless of the likelihood of the situation actually occurring.

4.5.4.3 Chocolate Scale

This is a brief questionnaire that contains questions based on those found in the Food Cravers Questionnaire (Cepeda-Benito, Gleaves, Williams, & Erath, 2000). Participants are asked to rate on a scale from 1 to 10 how much they like chocolate, how often they crave chocolate and how frequently they eat chocolate. Higher scores indicate more chocolate liking, craving and eating. This version of the questionnaire used in this study is taken from McCabe and colleagues work (McCabe, Cowen, & Harmer, 2009; McCabe, Mishor, Cowen, & Harmer, 2010) (see Appendix 4.7).

4.5.4.4 The Positive and Negative Affect Schedule (PANAS)

The PANAS (Watson et al., 1988) consists of two 10-item mood scales and provides a brief measures of positive and negative affect (see Appendix 4.8). Respondents are asked to rate the extent to which they have experienced each particular emotion within a specified time period, with reference to a 5-point scale. The scale points are: 1 (*very slightly or not at all*), 2 (*a little*), 3 (*moderately*), 4 (*quite a bit*) and 5 (*very much*). A number of different time frames have been used with the PANAS, but in the current study the time frame adopted was “in the last hour”.

4.5.4.5 Visual analogue scales (VAS)

Mood was rated using four VAS (happy, despondent, anxious, and alert). The VAS were 10mm in length and labelled at each end from “not at all” to “extremely”.

Participants were asked to mark a cross on the line at the point that best represents how they were currently feeling.

4.5.5 ***Reward task*** *(as described previously in McCabe et al., 2009)*

4.5.5.1 Stimuli

Taste stimuli were delivered to the participant's mouth through three Teflon tubes (one for the tasteless rinse control, one for the chocolate taste and one for the strawberry taste). The tubes were held between the lips. Each tube was connected to a separate reservoir via a syringe and a one-way syringe activated check valve (Model 14044-5, World Precision Instruments, Inc), which allowed 0.5ml of any stimulus to be delivered manually at the time indicated by the computer. The chocolate was formulated to be liquid at room temperature (whole milk, chocolate powder, cocoa, sugar, milk powder). A control tasteless solution 0.5ml of a saliva-like rinse solution (25 x 10^{-3} mol/L KCl and 2.5 x 10^{-3} mol/L $NaHCO_3$ in distilled H_20) was used between trials (for an overview of the conditions see Appendix 4.9) and when subtracted from the effects of the other stimuli, allowed somatosensory and any mouth movement effects to be subtracted from the effects produced by the other oral stimuli. This allows the taste, texture, and olfactory areas to be shown independently of any somatosensory effects produced by introducing a fluid into the mouth (as demonstrated previously by de Araujo, Kringelbach, Rolls, & McGlone, 2003; O'Doherty, Rolls, Francis, Bowtell, & McGlone, 2001). The aversive taste condition was a strawberry drink (glycol, glycerol, mannitol, hydrobenzoate; manufactured by

Rosemont Pharmaceuticals LTD) and this was rated as intense as the chocolate taste but unpleasant in valence (McCabe et al., 2009). Both the liquid chocolate and the strawberry had approximately the same sweetness and texture which enabled them to pass freely through the tubes.

4.5.5.2 Task procedure (as described previously in McCabe et al., 2009)

At the beginning of each trial, one of the six stimuli chosen by random permutation was presented. If the trial involved a taste stimulus, this was delivered in a 0.5ml aliquot to the participant's mouth. At the same time at the start of the trial, a visual stimulus was presented. This would either be the picture of chocolate, of mouldy strawberries or a grey control image. The visual stimulus was presented by a computer running the Presentation software package (Neurobehavioral Systems, Davis, CA). The image was turned off after 7 seconds at which time a small green cross appeared on a visual display to indicate to the participant to swallow what was in the mouth. After a delay of 2 seconds, the participant was asked to rate each of the stimuli for "pleasantness" on that trial (with +2 being very pleasant and -2 very unpleasant), for "intensity" on that trial (0 to +4), and for "wanting" (+2 for wanting very much, 0 for neutral, and -2 for very much not wanting). The ratings were made with a VAS in which the participant moved the bar to the appropriate point using a button box. After the last rating, the grey visual stimulus indicated that there would be a delivery of the tasteless control solution and this was also used as a rinse between stimuli. The rinse was administered in the same way as the test stimulus and the participant was cued to swallow after 7 seconds by the green cross. The tasteless control was always accompanied by the grey visual stimulus. On trials in which only the picture of chocolate was shown, there was no rinse but the grey visual stimulus was shown in order to allow an appropriate contrast as described below. There was then a 2 second delay period that allowed for swallowing followed by a 1 second gap until the start of the next trial. A trial was repeated for each of the 6 stimulus conditions shown in Appendix 4.9, and the whole cycle was repeated 9 times.

The instruction given to the participant was (on taste trials) to move the tongue once as soon as a stimulus or tasteless solution was delivered in order to distribute the solution round the mouth to activate the receptors for taste and smell. Following this, participants were instructed to keep still for the remainder of the 7 second period until the green cross was shown, at which point the participant could swallow. This procedure has been shown in previous work to allow taste effects to be demonstrated clearly with FMRI, using the procedure of subtracting any activations produced by the tasteless control from those produced by a taste or other stimulus (for example, de Araujo et al., 2003; O'Doherty et al., 2001).

4.5.6 FMRI scan[8]

Data was collected using a Siemens Avanto 1.5T whole-body scanner at the Oxford Centre for Magnetic Resonance Imaging. T_2* weighted echo planar imaging (EPI) slices were acquired every 2 seconds (T_R [repetition time] = 2). Axial slices with in-

[8] A brief explanation of FMRI is provided in Appendix 4.10.

plane resolution of 3x3mm and between-plane spacing of 3mm were obtained. The matrix size was 64 x 64 and the field of view was 192x192 mm. Acquisition was carried out during the task performance yielding 972 volumes in total. In addition to collection of T_2*-weighted echo planar imaging slices, a Turbo FLASH (Fast Low Angle SHot) sequence (T_R = 12ms, T_E [echo time] = 5.64ms), voxel size = $1mm^3$, was also acquired to facilitate co-registration of the FMRI data into standard space.

*4.5.7 **Data analysis** (as described previously in McCabe et al., 2009)*

The data from the reward paradigm were analysed using Statistical Parametric Mapping software (SPM 8, Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). Pre-processing involved realignment, reslicing with sinc interpolation, normalisation to the MNI coordinate system (Montreal Neurological Institute) and spatial smoothing with a 6mm full width at half maximum isotropic Gaussian kernel. Time series non-sphericity at each voxel was estimated and corrected for (Friston et al., 2002), and a high-pass filter with a cut-off period of 128 seconds was applied. In the single event design, a general linear model was then applied to the time course of activation where stimulus onsets were modelled as single impulse response functions and then convolved with the canonical haemodynamic response function (Friston, Worsley, Frackowiak, Mazziotta, & Evans, 1994). Linear contrasts were defined to test specific effects. Time derivatives were included in the basic functions set. Following smoothness estimation, linear contrasts of parameter estimates were defined to test the specific effects of each condition with each individual dataset. Voxel values for each contrast resulted in a statistical parametric map (SPM) of the corresponding *t*-statistic, which was then transformed into the unit normal distribution (SPM *Z*). The statistical parametric maps from each individual dataset were then entered into second-level, random effects analyses accounting for both scan-to-scan and participant-to-participant variability. The simple main effects of group were examined with one-sample *t*-tests. To assess the between-group differences for each condition two-sample *t*-tests were used. Corrected *p* values were based on the spatial extent of clusters of 30 or more contiguous voxels above a threshold of $p < .05$ and fully corrected for the number of comparisons (resels) in the entire brain volume ("whole-brain" multiple comparisons for which $p < .05$ family-wise error, EDE-Q scores added as a covariate of no interest). Plots of contrast estimates were extracted using the plots tool in SPM8. Coordinates of the activations are listed in the stereotactic space of the MNI's ICBM152 brain.

4.6 Results for the reward task

4.6.1 Demographic characteristics

Data was collected from 16 recovered AN participants and 16 HC participants. The groups consisted of undergraduate and postgraduate students as well as adults in full or part time employment. The two groups were matched for age, IQ, current BMI and chocolate eating/liking (as shown in Table 4.1). There was no significant differences between the control group and the recovered AN group in the measures of anhedonia (FCPS), depression (BDI-II), anxiety (STAI) or ED symptoms (EDE-Q). Baseline mood ratings on visual analogue scales and the PANAS did not differ between the groups.

All sixteen recovered AN participants had met criteria for restricting type AN. Four of the recovered AN participants had also met criteria for BN and one for EDNOS during their lifetime. In addition, nine of the recovered participants had fulfilled the criteria for MDD during their lifetime and three participants had fulfilled the criteria for obsessive compulsive disorder (OCD).

One participant from the recovered AN group was excluded from the analysis of the data from the reward paradigm due to a technical error. After this participant was removed, there was a trend for the recovered AN participants to score higher on the EDE-Q that the HC participants (p = .05, Mann-Whitney U). EDE-Q global scores were therefore controlled for in the analysis.

Table 4.1 Group demographic and questionnaire measures for the recovered AN and HC participants

	Group			
	Recovered AN (*n* = 15)		HCs (*n* = 16)	
Measure	*M*	*SD*	*M*	*SD*
Age	23.33	3.50	24.10	2.90
BMI	21.33	2.17	21.19	1.56
IQ	115.94	4.66	113.30	4.24
EDE-Q	1.11	1.13	.33	.46 *
BDI-II	5.87	6.81	2.25	2.54
STAI-T	16.47	10.27	13.27	8.50
STAI-S	12.67	7.31	9.93	4.27
FCPS	134.53	10.90	135.31	20.27
PANAS +ve	24.81	5.05	26.00	7.62
PANAS -ve	12.75	4.45	12.0	4.69
VAS-alert	8.36	11.05	4.91	2.90

Table 4.1 Group demographic and questionnaire measures for the recovered AN and the HC participants (continued)

	Recovered AN (n = 15)		HCs (n = 16)	
Measure	*M*	*SD*	*M*	*SD*
VAS-happy	9.31	10.64	6.80	1.93
VAS-despondent	.60	.74	.50	.65
VAS-anxious	1.62	1.60	1.40	1.30
Choc craving	5.13	2.53	6.56	1.46
Choc liking	7.27	2.05	8.06	1.39
Choc eating frequency	3.38	2.41	2.51	1.66
Lowest BMI (kg/m^2)	14.27	1.94	---	--
Recovery length (months)	42	28.57	---	--

Note. * $p < .05$ Mann-Whitney *U*
BDI-II = Beck Depression Inventory-II; FCPS = Fawcett-Clarke Pleasure Capacity Scale; STAI-T = State Trait Anxiety Inventory - trait subscale; STAI-S = State Trait Anxiety Inventory - state subscale; EDE-Q = Eating Disorder Examination questionnaire; PANAS +ve = Positive and Negative Affect Scale, positive scale; PANAS -ve = Positive and Negative Affect Scale, negative scale; VAS = Visual analogue scale; BMI = Body Mass Index.

4.6.2 Ratings of the stimuli

Using repeated measures ANOVAs for the pleasantness, intensity, and wanting ratings, there were no significant differences between the two groups and their ratings of pleasantness over the six stimuli, F (1, 29) = 3.08, p = .09, intensity over the six stimuli, F (1, 29) = 0.95, p = .34, or wanting over the six stimuli, F (1, 29) = 2.80, p = .11. Subjective ratings are shown in Appendix 4.11.

4.6.3 FMRI response

Appendix 4.12 provides a summary of the results for each contrast across all participants to indicate the main effect of task. Table 4.2 provides a summary of the results of the interaction with group (recovered AN versus HCs). The FMRI results remained significant when global EDE-Q scores were added as a covariate.

4.6.4 Main effects of task

As expected, the taste stimuli of chocolate and strawberry activated an overlapping region of the anterior insula in both HCs and recovered AN participants. Both chocolate and strawberry picture stimuli activated bilaterally regions of the occipital cortex. The chocolate taste and chocolate picture activated areas of reward relevant circuitry, more specifically the ventral striatum and anterior cingulate cortex. By contrast, the aversive stimuli of strawberry taste and the sight of mouldy strawberries activated areas involved in aversive processing including lateral orbitofrontal cortex, the caudate and insula cortex.

4.6.5 Effect of group

As expected, there was no significant difference in response to the taste of chocolate between the two groups in the primary taste cortex (i.e., anterior insula) (Small, Jones-Gotman, Zatorre, Petrides, & Evans, 1997) confirming that the sensory experience of chocolate was associated with a similar neural response across groups.

Table 4.2 Regions showing significant effect of group on each condition

Brain region	MNI coordinates			*Z* score	Significance (*p* value)
	X	*Y*	*Z*		
Chocolate in mouth:					
Recovered AN > HCs					
Ventral striatum	12	8	0	4.28	< .001
Putamen	-20	2	8	4.65	< .001
Posterior cingulate	0	-36	20	4.28	< .001
Sight of chocolate:					
Recovered AN > HCs					
Occipital cortex	38	-80	−10	3.66	= .001
Anterior prefrontal cortex	12	66	12	3.70	= .003
Subgenual cingulate/ Medial prefrontal cortex	-1	28	-12	3.49	=.003*
Chocolate taste and sight:					
Recovered AN > HCs					
Pallidum	14	10	-4	2.92	= .04

Table 4.2 Regions showing significant effect of group on each condition (continued)

Brain region	MNI coordinates			*Z* score	Significance (*p* value)
	X	*Y*	*Z*		
Strawberry in mouth:					
Recovered AN > HCs					
Posterior insula	42	-14	4	3.20	< .001
Putamen	24	4	14	3.49	<.001 *
Strawberry taste and sight:					
Recovered AN > HCs					
Anterior cingulated cortex	10	6	34	3.8	< .001
Operculum	42	-14	20	3.74	< .001
Caudate	14	12	12	3.45	< .001
DLPFC	8	46	22	3.34	= .004

Note. DLPFC, Dorsolateral prefrontal cortex
p value clusters whole-brain fully corrected (family-wise error $p < .05$ [EDE-Q added as covariates of no interest]).
Coordinates are defined in the MNI stereotactic space (Montreal Neurological Institute, Canada).
*$p > .05$ after adding EDE-Q global scores as a covariate.

4.6.5.1 Chocolate reward: taste and sight

The recovered AN group showed increased responses to the taste of chocolate in areas known to play a key role in reward, including the ventral striatum (as shown in Table 4.2 and Figure 4.1) and cingulate cortex. There was also increased activation to the sight of chocolate alone in the recovered group compared to the HC group in the occipital cortex (shown in Figure 4.2), anterior prefrontal cortex and medial prefrontal cortex. There were no areas where the HCs showed increased responses relative to the recovered AN group for the chocolate reward condition. After correcting for multiple comparisons, there were no significant correlations between the FMRI response in the recovered AN group and duration of illness, lowest ever BMI, age of onset or length of recovery in the brain regions that demonstrated increased responses to the taste and sight of chocolate.

Figure 4.1 Chocolate in the mouth condition for the recovered AN versus HCs

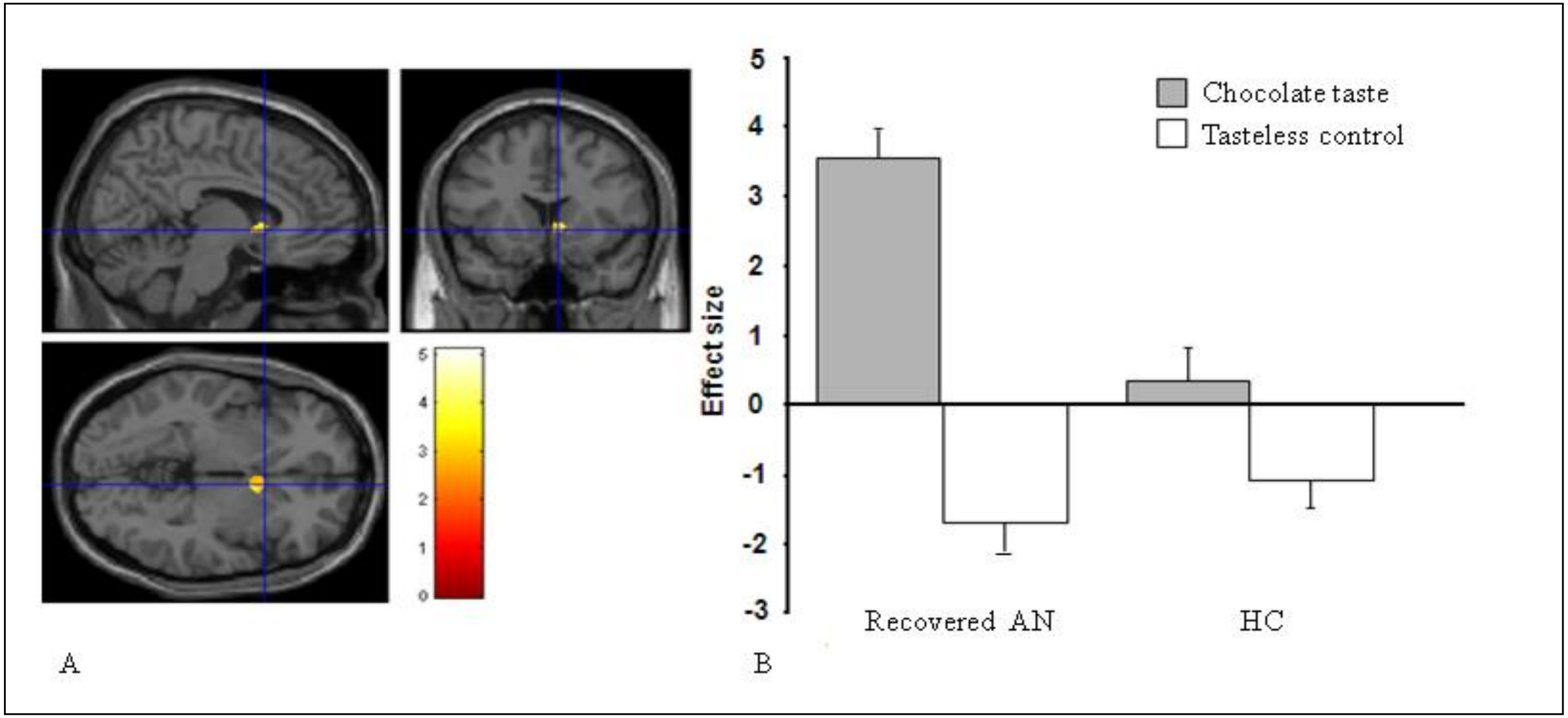


Figure 4.1

A. Axial, sagittal, and coronal image of significantly increased ventral striatum activation in the recovered AN group compared to the HC group.

B. Contrast estimates centred at 12, 8, 0 for the recovered AN group compared to HC group ($p < .001$).

Figure 4.2 Sight of chocolate condition for the recovered AN versus HCs

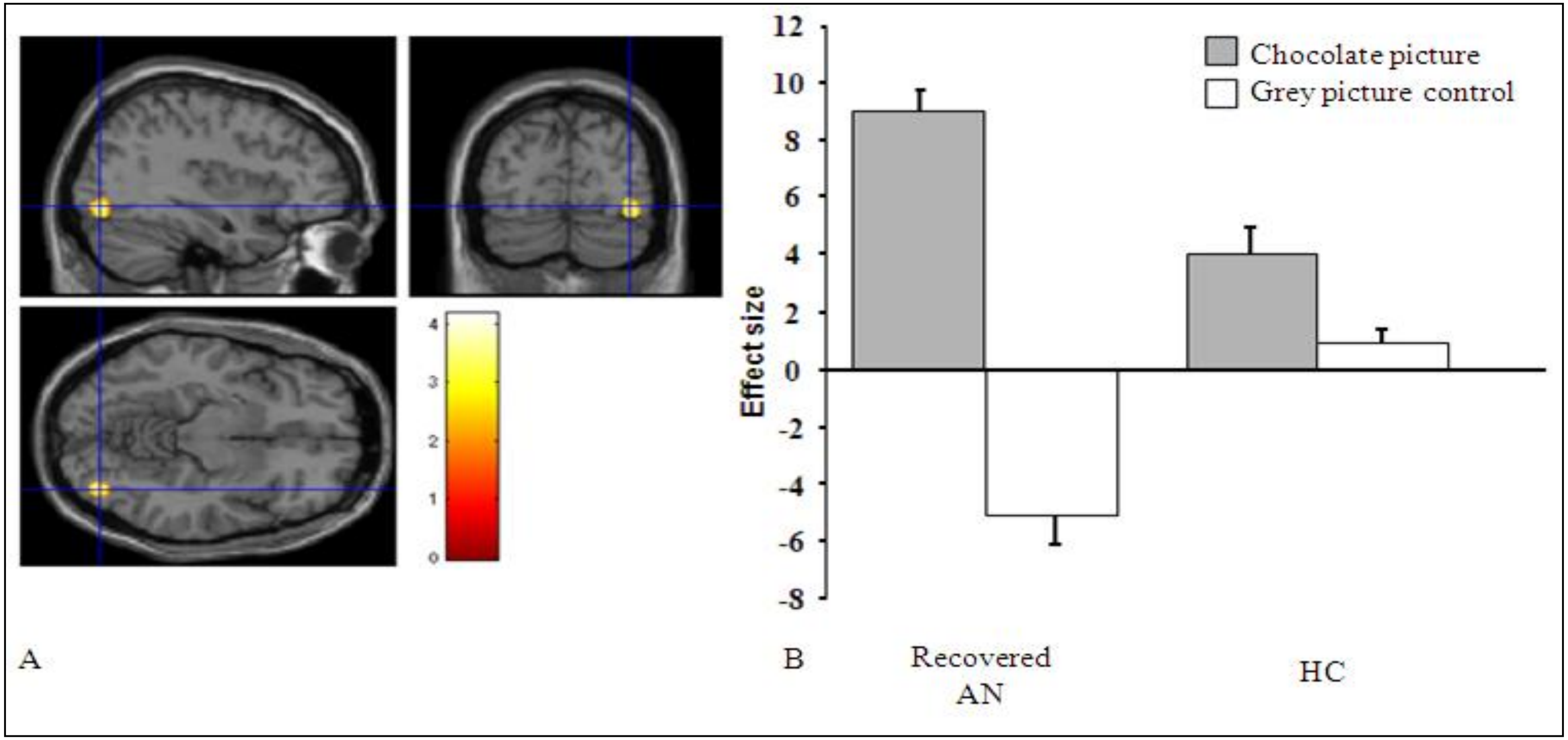


Figure 4.2

A. Axial, sagittal, and coronal image of increased occipital activation in the recovered AN group compared to the HC group.

B. Contrast estimates centred at 38, -80, -10 for the recovered AN group compared to the HC group (*p* = .001).

4.6.5.2 Aversive strawberry: taste and sight

There was increased activation in the recovered AN group compared to the HC group for the unpleasant strawberry taste conditions (taste alone and taste with picture), specifically in the anterior cingulate cortex, the lateral posterior insula, putamen, caudate and the DLPFC (as shown in Table 4.2 and Figure 4.3). There were no group differences for the strawberry picture alone. There were no areas where the HCs showed increased responses relative to the recovered group for the aversive strawberry condition. After correcting for multiple comparisons there were no significant correlations between the FMRI response in the recovered AN group and duration of illness, lowest ever BMI, age of onset or length of recovery in the brain regions that demonstrated increased responses to the taste and sight of strawberry.

Figure 4.3 Strawberry in the mouth with the sight of mouldy strawberry condition for the recovered AN versus HCs

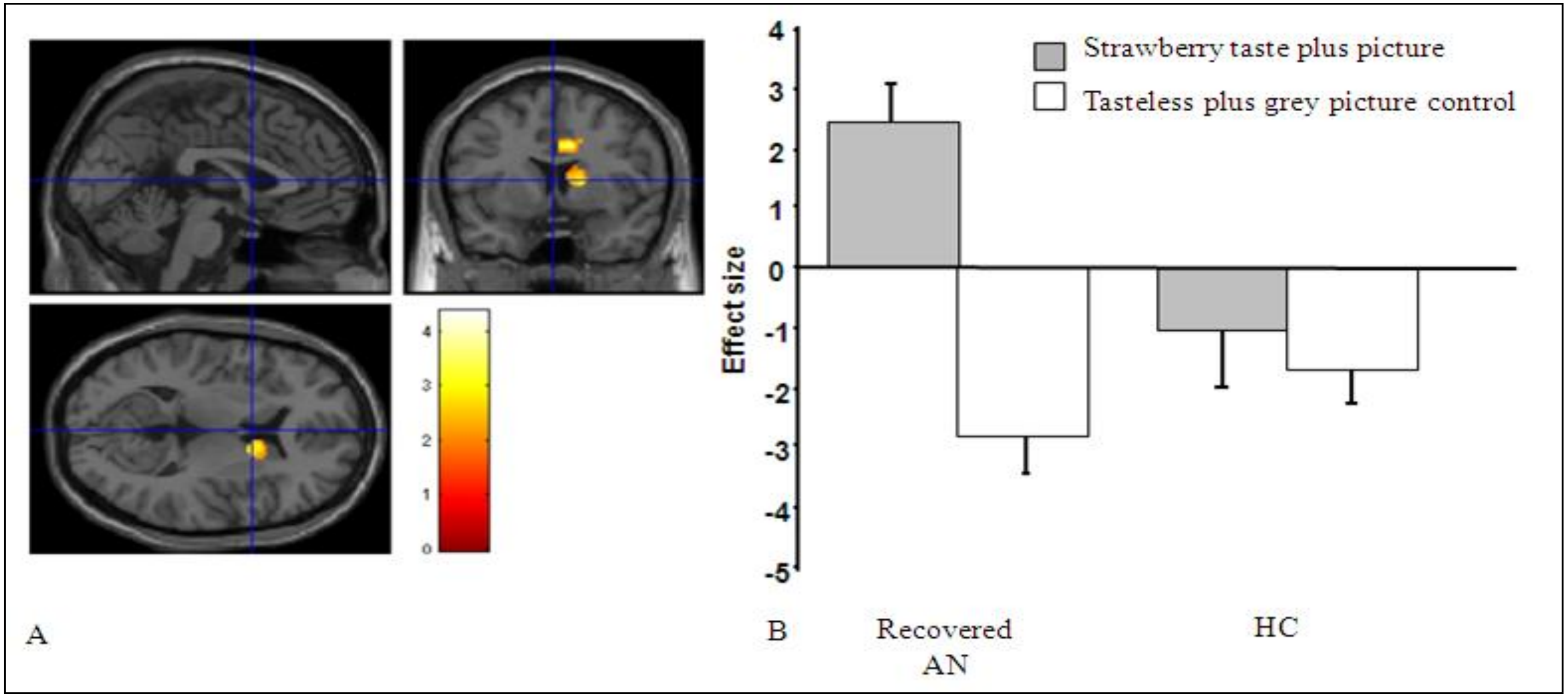


Figure 4.3

A. Axial, sagittal, and coronal image of increased caudate and anterior cingulate in the recovered AN group compared to the HC group.

B. Contrast estimates centred at 14, 12, 12 (Caudate) for the recovered AN group compared to the HC group ($p < .001$).

4.7 Summary of results

- There were no significant differences between the groups in subjective ratings of intensity, wanting or liking for the taste and picture stimuli.
- Women recovered from AN have increased neural activity to the pleasant taste and pictures of chocolate compared to HC participants in reward areas of the brain, such as the ventral striatum.
- Women recovered from AN have increased posterior insula and caudate activity to the unpleasant strawberry conditions compared to HCs.

4.8 Discussion

This study examined the neural regions involved in processing pleasant and aversive food tastes and pictures in women recovered from AN compared to HC participants. The findings demonstrate that those recovered from AN have increased ventral striatal activity to the pleasant taste of chocolate compared to HC participants despite no difference in subjective experience or primary taste cortex activations to the stimuli. Furthermore, the results show that those recovered also have increased posterior insula and caudate activity to the unpleasant conditions compared to HCs. These results are largely consistent with studies employing food stimuli in individuals with current AN (as reviewed in Section 1.9.4) and therefore pose the important question of whether aberrant processing of food stimuli represents a neural biomarker for AN or alternatively whether such neural activations are a scar of the illness.

Neural response to chocolate tastes

The ventral striatum has been shown to respond to a range of rewarding stimuli in healthy volunteers including money (Knutson, Adams, Fong, & Hommer, 2001), music (Blood & Zatorre, 2001) pleasant touch (McCabe, Rolls, Bilderbeck, & McGlone, 2008) as well as the perceived reward value of food (Berthoud & Morrison, 2008). This is in line with animal work which shows that DA activity in this brain region is critical for mediating the reinforcing effects of rewarding stimuli (as reviewed by Schultz, 2002). The increased neural response in the ventral striatum reported in this study indicates alterations in the brains reward system even after recovery from AN. It may be that women with a history of AN attribute increased salience to chocolate taste stimuli, thus potentially explaining the increased neural response in the ventral striatum. More generally, this finding provides support for the notion that DA dysfunction in reward regions of the brain (such as the ventral striatum) may contribute to core symptoms of AN (Kaye et al., 2009). That said, this study involved recovered AN participants and it is therefore uncertain whether increased activation would be seen to the chocolate taste in those currently ill with AN. However, Frank and colleagues (2012) reported that current AN participants had a significantly greater neural response in the ventral striatum to a pleasant sucrose taste compared to HCs. If one assumes similar increased activity would be seen to the chocolate taste in currently ill AN participants, future studies may consider what additional processes are operating to prevent individuals with AN from actually consuming the rewarding food stimuli.

The recovered AN group also demonstrated significantly greater activation in the posterior cingulate to the chocolate taste. This is of interest because the posterior cingulate has been associated with self-referential thinking. For example, Johnson and colleagues (2006) conducted a within-subjects FMRI study with two conditions: self-reflection and distraction. The authors reported that in healthy participants, self-reflection resulted in greater activity in the posterior cingulate, as well as other brain regions, compared to the distraction condition (Johnson et al., 2006). This finding has clinical implications as the posterior cingulate has also been associated with rumination in depression. For example, it has been shown that neural activity in the posterior cingulate during a rumination induction versus distraction was greater in depressed participants compared to HCs (Cooney, Joormann, Eugène, Dennis, & Gotlib, 2010). Johnson et al. (2006) therefore concluded that ruminative self-focus is associated with enhanced activity in regions of the brain including the posterior cingulate. Whilst speculative, the increased activity found in the posterior cingulate to the chocolate taste in the recovered AN participants could reflect increased rumination when presented with energy-dense food. This would fit with the hypothesis that rumination functions as an avoidance strategy in AN to maintain control over salient food stimuli (Park et al., 2011).

Comparison to depression

Using the same task, it has previously been shown that those who are recovered from depression have *decreased* ventral striatum to chocolate reward (McCabe et al., 2009). Therefore symptoms of depression (currently or in the past) are unlikely to explain the results reported here. This is important considering the high level of comorbidity between MDD and AN (as discussed in Section 1.4).

Comparison to other eating-related disturbances

The results reported here are similar to a previous study examining the neural response to chocolate in chocolate cravers (Rolls & McCabe, 2007). Like the cravers, the recovered AN participants also show increased response to chocolate in the ventral striatum but unlike cravers, those recovered from AN also had increased neural response to the aversive food stimuli, despite no subjective differences. This supports the idea that individuals with AN may have a hypersensitive neural response to food stimuli, irrespective of valence, and therefore may practice restraint in order to control exposure to stimuli which would otherwise be experienced as overwhelming and aversive. However, this explanation fails to account for the fundamental differences in eating-related behaviours between cravers and AN sufferers, more specifically why a chocolate craver consumes chocolate whereas individuals with AN severely restrict their intake despite being intensely preoccupied with it. One hypothesis is that higher-level cognitive processes (such as rumination) have an inhibitory effect in AN enabling these individuals to avoid consumption of the salient food stimuli. This would support the theoretical work of Park et al. (2011) as well as the studies reported in Chapter 2 and 3 that highlight the role of rumination in the maintenance of AN.

Interestingly, studies examining the neural response to taste stimuli in obese individuals have also found increased activations in areas such as the insula, anterior cingulate and parietal cortex (DelParigi et al., 2003; Rothemund et al., 2007). However, unlike the recovered AN participants, obese participants show less activation in the striatum in response to consumption of a chocolate drink (Stice, Spoor, Bohon, Veldhuizen, & Small, 2008) or a sucrose solution (Frank et al., 2012). Since this brain region contributes to the motivational salience of stimuli, it has been suggested that obese individuals may overeat to compensate for the hypofunctioning of the striatum (Stice, Spoor, Ng, & Zald, 2009; Stice, Yokum, Blum, & Bohon, 2010). Whilst a full discussion is beyond the scope of this thesis, it should be noted that a contrasting hypothesis for obesity, the reward-surfeit hypothesis, proposes that obese individuals overeat due to an overactive reward system (Stice, Yokum, Burger, Epstein, & Small, 2011).

Bohon and colleague have shown using a chocolate taste paradigm that individuals with both sub threshold BN (Bohon & Stice, 2012b) and full threshold BN (Bohon & Stice, 2012a) show lower activity as compared to HCs in reward-related brain regions. The authors suggest that the binge-eating which characterizes BN functions to compensate for an underactive reward system (Bohon & Stice, 2012a, 2012b). However, it is uncertain what factors determine whether an individual with a hypofunctioning reward system will develop BN or obesity. It is possible that over evaluation of the control of shape and weight, as detailed in cognitive models of EDs (Fairburn et al., 1999, 2003), may account for this difference between the BN and obesity as this as this is a feature of core psychopathology in BN (along with other EDs) but is absent in obesity.

Whether individuals with the binge-eating/purging type of AN would show hypoactivity (as in the BN and obese participants) or hyperactivity (as in the restricting type AN participants reported in this study) in reward regions of the brain is a further consideration. Brooks O'Daly, Uher, Friederich et al. (2012) compared the neural response to food images between AN restricting and AN binge-eating/purging type. Whilst the authors do not report differences in ventral striatum between the groups, the restricting type AN participants did show increased activation in regions of the brain involved in integrating top-down (cognitive) and bottom-up (appetitive) arousal responses to salient stimuli, such as the anterior cingulate (Brooks, O'Daly, Uher, Friederich et al., 2012). Brooks, O’Daly, Uher, Friederich and colleagues (2012) suggested that those who purely restrict have more conflict between cognitive strategies and appetitive responses than those who also engage in binge-eating. As this subgroup analysis was conducted on a small number of participants with the binge-eating/purging type of AN (n = 7), examining the neural response to food-related tastes and pictures in a larger sample would be a useful next step, especially as this subtype is more resistant to treatment (Peat, Mitchell, Hoek, & Wonderlich, 2009).

Neural response to images of chocolate

Consistent with the findings reported here for the chocolate picture, previous studies in current or past AN have shown increased activations to disorder-relevant visual stimuli, such as food pictures and body figures in reward-related areas (for relevant studies see Section 1.9.4). More specifically, increased activation in the occipital cortex to the chocolate picture in the recovered AN group compared to the HC participants was found in the current study. This replicates the findings reported previously in both currently ill participants and those recovered from AN (Brooks, O'Daly, Uher, Friederich et al., 2012; Gordon et al., 2001; Uher et al., 2003, 2004). Since occipital cortex activation has been linked to early recognition of emotionally salient stimuli (Paradiso et al., 1999), the increased activation in AN may represent cognitive biases to food stimuli, even after recovery.

Increased activation in the medial prefrontal cortex to the chocolate picture in the recovered AN group compared to the HCs was also found. These results are similar to that reported by Uher and colleagues (2003, 2004) in currently ill and recovered AN participants. The medial prefrontal cortex subserves a variety of behaviors guided by emotional and motivational factors, including feeding (McClure, Laibson, Loewenstein, & Cohen, 2004). The increased prefrontal cortex activation to the visual chocolate stimuli may represent the need for increased top-down cognitive control in AN to emotionally salient cues, such as food, which may otherwise be experienced as overwhelming (Kaye et al., 2009). Interestingly, Brooks, O'Daly, Uher, Friederich et al. (2012) have proposed that continued functional aberrancies in frontal areas after recovery may explain why cognitive symptoms often remain long after weight restoration.

Neural response to sucrose in AN

There have also been studies examining reward processing in AN that have found results inconsistent with those reported here. As reviewed in Section 1.9.4.2, Wagner and colleagues (2008) found *reduced* insula, ventral striatal and anterior cingulate activations in recovered AN participants compared to HCs in response to a sucrose solution. It may be that compared to a sucrose solution, the chocolate drink used in the current study is much more salient and evokes a greater reward response. It may also be that the chocolate drink results in a greater emotional response as it has strong connotations with real world experiences (greater ecological validity). However, a study with currently ill AN participants also used a sucrose solution and in line with the results reported in this chapter, found increased neural activation in reward regions of the brain (for example, the ventral striatum) compared to a HC group (Frank et al., 2012). The diverging results may therefore be better explained by differences in experimental design. Wagner and colleagues (2008) used a block design with more predictable taste administrations than in either the current study or Frank and colleague’s (2012) study. Whilst speculative, it may be that there is less opportunity for cognitive processes to influence the rewarding properties of taste representations in the brain when the stimuli are administered randomly compared to when they are presented repeatedly.

Aversive strawberry conditions

The recovered AN group showed increased responses in the caudate nucleus and posterior insula. This is of interest because the emotion of disgust has been shown to activate both the caudate nucleus and the posterior regions of the insula (Phillips et al., 1997) and this suggests that individuals recovered from AN show increased processing of aversive cues. This is also consistent with reports of greater sensitivity in AN to both punishing (Harrison, O'Brien, Lopez, & Treasure, 2010) and disgusting (Aharoni & Hertz, 2012) stimuli.

Whilst the experience of disgust to the aversive condition may be heightened in the recovered AN group, it could also be that increased activation may be linked to other negative emotions such as anxiety (Davey & Chapman, 2009). In line with this, eating elicits high levels of anxiety in individuals with EDs (as discussed in Chapter 3) and at the neural level it has been shown that individuals with high levels of anxiety demonstrate heightened activation in the insula cortex to emotionally salient stimuli (Stein, Simmons, Feinstein, & Paulus, 2007).

The dorsolateral prefrontal cortex (DLPFC), which also showed exaggerated activity to the strawberry taste and picture in the recovered AN group, is an important node in the cognitive control network (Cole & Schneider, 2007). More specifically, it is considered the highest cortical area responsible for information retrieval, motor planning, sequencing and regulation (Hoshi & Tanji, 2004). The DLPFC is also extensively connected to a variety of brain areas including the striatum, and it has been suggested that it may modulate striatal activity that underlies the approach or avoidance of food (as suggested by Kaye et al., 2009). In line with this, it has been reported that postoperative gastric bypass patients have significantly reduced striatal and DLPFC activation and reduced desire to eat high compared to low calorie food stimuli (Ochner et al., 2012). This may reflect a decrease need for inhibitory control when the anticipated reward value of food and desire to eat is reduced due to the effects of bypass on the gastric regulation of appetite. Thus it supports the notion that the DLPFC may have a critical role in limiting consumption of energy-dense food.

It could therefore be that the increased activation in the DLPFC to the aversive stimuli in the recovered AN group represents an enhanced attempt to control exposure (and in the case of the aversive stimuli perhaps minimize exposure). This would be in line with the proposal that even after recovery, individuals with AN have higher levels of harm avoidance and respond to such stimuli in a strategic way, opposed to relying on the stimuli's hedonic properties (Kaye et al., 2009).

Group differences in anterior cingulate activation to the aversive stimuli were also found. The anterior cingulate is thought to interact with the DLPFC in order to effectively evaluate stimuli, control attentional resources and guide appropriate actions (Critchley, Tang, Glaser, Butterworth, & Dolan, 2005; Wallis & Kennerley, 2011). The increased activation reported here may represent heightened regulatory control when presented with food that is aversive in nature compared to HC participants. The anterior cingulate has also been consistently implicated in the pathogenesis of anxiety and depressive disorders (van Tol et al., 2010), symptoms of which are commonly present in those with AN (Kaye et al., 2004). It may therefore be that the anterior cingulate represents part of a dysfunctional network associated with anxious and affective phenomena in a group of related disorders (Uher et al., 2004).

4.8.1 Limitations

Differing levels of hunger between the participants were not controlled for. As reviewed in Section 1.9.4, studies have shown that manipulating levels of hunger and satiety can affect the neural response to food stimuli in AN. Secondly, whilst all participants met the criteria for inclusion, there was a trend towards significantly higher EDE-Q scores in the AN recovered group compared to HCs. Therefore, one interpretation of the results is that the "recovered" individuals may still be engaging in some level of restriction, at least relative to the HCs, and this may be related to the increased responsivity in reward-related brain regions to food. This is particularly relevant as it has recently been reported in a healthy sample that dietary restraint scores were positively correlated with activation in the right orbitofrontal cortex and DLPFC in response to chocolate tastes (Burger & Stice, 2011). However, in the current study using a sample of recovered AN participants, correlations between the neural activations and both duration of recovery and the restraint subscale scores on the EDE-Q did not yield any significant associations.

Since this study used food stimuli only, it is uncertain whether the results reflect increased salience of all emotional stimuli or just those that are associated with food. However, it has been shown that the neural response to emotional face stimuli does not differ between a HC and recovered AN sample (Cowdrey et al., 2011) which suggests the differences may be specific to disorder-relevant stimuli. It is also difficult to determine whether the neural responses to the food stimuli are driven by top-down cognitive (for example, rumination about weight gain) or bottom-up hedonic responses to the food stimuli (or both). Employing a task which directly dissociates hedonically-driven versus cognitively-driven responses would complement the data reported here and aid understanding of eating behaviour in AN (this work is described in Chapter 5). Lastly, it is difficult to determine if the neural dysfunction is a stable trait characteristic or a scar effect. Longitudinal designs or studies recruiting cohorts of individuals at different stages of illness would help to resolve this issue.

4.8.2 Conclusions

Women recovered from AN showed increased neural responses to both rewarding and aversive food stimuli which supports the notion of increased salience of food stimuli in AN. The results may explain why self-denial and restraint, as a way of controlling and reducing exposure to food, characterises AN. The results aid the neurobiological understanding of AN and more specifically support the view that the response to food reward may constitute a neural biomarker for AN. Experimental studies which can directly tease apart hedonic versus cognitive responses to food would be a useful next step in determining what processes drive aberrant eating-related behaviours in AN.

5 Liking versus wanting for high and low calorie food in anorexia nervosa

5.1 Overview

The study reported in Chapter 4 demonstrated that individuals with past AN have an aberrant neural response to pleasant and aversive food stimuli. Current approaches for understanding food reward recognise the role of both affective (liking) and motivational (wanting) processes in driving human eating behaviour (Berridge & Robinson, 2003). Few studies have applied this framework to AN, yet separate assessment of liking and wanting may further the understanding of eating-related behaviour in AN. Therefore this study aims to address the following questions:

- Do individuals currently experiencing the psychopathological symptoms of AN display aberrant liking (affective salience) and wanting (motivational salience) responses to high and/or low calorie food stimuli compared to those recovered from AN and those never ill?
- Do explicit and/or implicit processes drive differences in liking and wanting for food in AN?
- Are differences in food liking or wanting dependent on the stage of AN?

5.2 Background

As reviewed in Chapter 1, symptom-provoking food paradigms have been used in behavioural and neuroimaging studies to further the understanding of reward-related behaviours, including eating, in AN (as reviewed by Brooks, Prince, Stahl, Campbell, & Treasure, 2011; Giel et al., 2011; Keating et al., 2012; van Kuyck et al., 2009). The previous chapter reported that individuals recovered from AN had an increased neural response to pleasant food tastes and pictures in reward regions of the brain compared to HC participants. Importantly, no significant between group differences were found in subjective ratings of pleasantness or wanting for the stimuli. This suggests that dissociation between objective and subjective reward responses exist even after weight restoration and psychological recovery.

Whilst the study reported in Chapter 4 was conducted using participants recovered from AN, similar discrepancies have been shown in the currently ill AN state. For example, Holsen and colleagues (2012) examined both subjective ratings and neural activations to high calorie food images in HC and AN participants in states of hunger and satiety. The authors reported significant correlations between percent blood oxygen level-dependent (BOLD) signal change in the insula and appetite-related ratings (for example, desire to eat and hunger) in HC participants but not those with active AN. Thus in states of hunger, when the motivation to eat should be high, greater activation in the insula does not seem to correspond to subjective evaluations of the food stimuli in AN participants. As with findings reported Chapter 4, it is difficult to determine whether these results are due to an inability to detect the physical sensations such as hunger or due to higher cognitive processes modulating or overriding reward-related neural activation. This separation between the objective state and the subjective experience of food stimuli, presents a significant challenge for treatment, thus understanding the exact mechanisms through which the experience of reward becomes distorted in AN is potentially very important.

The semantics of language describing eating-related pleasure imply that food reward is more than simply liking the taste of a food. Humans also talk about wanting, craving and impulsive desires for food. Research using nonhuman species have shown neuro-chemical dissociations between the mediation of affective responses to the hedonic impact of primary reinforcers (such as food), and those substrates responsible for attributing motivational significance to such stimuli (Berridge et al., 2009). This suggests that reward is not a unitary process but may consist of subcomponents. In broad terms, distinct psychological components have been identified termed: liking (hedonic pleasure or affect), wanting (hedonic motivation or desire to eat) and learning (predictive associations). Berridge (2009) reviews evidence suggesting liking and wanting can occur at both an explicit conscious (wanting and liking) an implicit unconscious level (‘wanting’ and ‘liking’). It is suggested that the term ‘wanting’ be used to refer to the unconscious incentive salience of a stimulus, as distinct from conscious wanting, reflecting a cognitively-driven explicit desire (Berridge, 2009). It is proposed that to experience reward in the fullest sense, liking and wanting must operate in parallel (Berridge & Robinson, 2003). However, the possibility for these components to separate leads to novel explanations of disorders characterised by atypical responses to reward such as depression, addictions and EDs

(Berridge, 2009; Berridge, Ho, Richard, & DiFeliceantonio, 2010; Robinson & Berridge, 2001).

In terms of AN, the paradoxical avoidance of eating yet obsession with food suggests there could be an exaggerated separation between hedonic and motivational processes. This would support the current frameworks for AN (for example, Kaye et al., 2009; Keating et al., 2012; Park et al., 2011), previous research (as reviewed by, Brooks, Prince, Stahl, Campbell, & Treasure, 2011; Giel et al., 2011; Keating et al., 2012; van Kuyck et al., 2009) as well as the data provided in Chapters 2-4. However, to comprehensively understand the complex response to food in AN, it is important to consider not only liking and wanting for foods typically experienced as highly palatable and rewarding but also for foods with low energy density or “diet-compatible foods”. In those with AN, a common additional strategy to control hunger is excessive and driven consumption of low energy-dense foods, whilst restricting intake of high energy-dense foods (Hetherington & Rolls, 1991; Jauregui Lobera & Bolanos Rios, 2009). This suggests a perversion in the homeostatic need for high energy-dense foods in AN, which is manifest as increased desire and preference to consume low energy-dense foods. Directly examining implicit ‘liking’ and ‘wanting’ and explicit liking and wanting for high and low calorie foods may therefore provide a richer understanding of the mechanisms underlying these abnormal eating behaviours.

Specific paradigms have been developed that aim to capture the dual components of food reward. For example, in the Leeds Food Preference Questionnaire (LFPQ) participants are asked to explicitly rate liking (explicit hedonic ratings) and wanting (explicit desires) for food images and then asked to choose between pairs of food stimuli according to which one they 'want' more in the moment (Finlayson et al., 2008; Finlayson, King, & Blundell, 2007). Reaction times to choose between the stimuli are interpreted as implicit 'wanting' responses, due to the measure being covert and the participants' inability to consciously monitor or interfere with the speed and pattern of their responses. Thus implicit 'wanting' can be considered more of a conditioned approach or cue-triggered 'wanting' than the explicit wanting response (Berridge, 2009). The issue of whether it is possible to isolate liking and wanting processes and at both an explicit and implicit level using experimental platforms (such as the LFPQ) is relevant and thus will be discussed briefly.

In a proof of concept study, Finlayson, King and Blundell (2007) used the LFPQ and manipulated the level of hunger and satiety in healthy participants using a test-meal procedure. The authors reported that when satiated, participants liked, but did not 'want' high fat savoury food more than low fat savoury food. When satiated participants also reported wanting, but not liking, low fat sweet foods more than high fat sweet foods (Finlayson et al., 2007). The authors therefore provided evidence that liking and wanting processes can be partially uncoupled using the LFPQ. Subsequently the authors reported an extension of the LFPQ which aimed to distinguish implicit 'wanting' and explicit wanting responses (Finlayson et al., 2008). Implicit 'wanting' was indexed by the reaction time of choices made for different food categories with the rationale being that participants will be motivated to respond to the foods which are desired more, thus reaction times will be shorter for the more implicitly ‘wanted’ foods (Finlayson et al., 2008). Again the authors were able to demonstrate using a hunger-satiety manipulation that liking could be partially dissociated from wanting. Further, it was reported that the differences in implicit ‘wanting’ responses under conditions of hunger and satiety were not correlated with the explicit liking or wanting measure. The authors therefore cautiously drew the conclusion that the processes of wanting and liking can be *partially* dissociated using behavioural tasks (Finlayson et al., 2008).

To date, studies employing the LFPQ have been largely concerned with identifying behavioural markers of appetite and food reward in healthy individuals or those at risk of overconsumption (Finlayson, Arlotti, Dalton, King, & Blundell, 2011; Finlayson, Bordes, Griffioen-Roose, de Graaf, & Blundell, 2012; Griffioen-Roose, Finlayson, Mars, Blundell, & de Graaf, 2010; Griffioen-Roose et al., 2012). However, it is hoped that the current study will demonstrate equally that such measures may be adapted to identify behavioural markers of appetite and food reward in AN, in whom the risk of sustained under consumption of energy dense foods is of clinical concern.

5.2.1 Study aims

- To examine separately liking and wanting for foods of different energy densities in women with experience of AN and HCs at both an implicit and explicit level.

- To compare liking and wanting for food in women at different stages of AN illness (currently ill, weight-restored and recovered) as well as HC participants.

5.2.2 Hypothesis

- Individuals currently experiencing symptoms of AN (either underweight or weight-restored) would show reduced explicit liking and wanting for high calorie foods and increased implicit ‘wanting’ for low calorie foods compared to recovered AN participants and those never ill. The different responses would be most evident in the currently underweight group of AN participants.

5.3 Method

5.3.1 Participants

Sixty four participants who had experienced AN were recruited as well as HC participants (*n* = 41). The AN participants were divided into three subgroups: recovered from AN (AN-R) (*n* = 22), weight-restored AN (AN-W) (*n* = 22) and current AN (AN-C) (*n* = 20). Participants were recruited through four main sources. First, participants were recruited from the database maintained by the research team of individuals with current or past AN (as described in Chapter 3). All participants on this database were sent an advertisement for the study and were invited to apply. Second, participants were recruited using advertisements in the University environment. Third, an advertisement was placed on BEAT's website and also sent to their research contacts. Lastly, advertisements were placed in the local paper.

General exclusion criteria for all participants included: age below 16 or above 65 years, insufficient English language skills or male gender. The specific inclusion and exclusion criteria described below were designed to enable a valid differentiation between the three AN groups and between the AN groups and the HC participants. All psychiatric diagnoses were assessed using the SCID (Spitzer et al., 2004). Ethical permission from the study was obtained from the South Central Research Ethics Committee (see Appendix 5.1). After complete description of the study (see information sheet in Appendix 5.2), all participants provided written, informed consent (see Appendix 5.3).

Current AN participants

The specific inclusion criteria were a current diagnosis of AN according to DSM-IV, as indexed by the SCID (either binge-eating/purging or restricting type) (Spitzer et al., 2004) and not currently receiving inpatient treatment.

The AN-C sample had a mean duration of illness of 116.45 months (*SD* = 111.59 months). These participants (n = 20) had a mean age of 26.40 (10.56) years and a mean BMI of 16.33 kg/m^2 (*SD* = 1.10 kg/m^2). Four of the participants currently met criteria for the binge-eating/purging type of AN with the remaining 16 meeting criteria for the restricting type. Four participants were currently taking antidepressant medication and 11 met criteria for current depression. Eight of the current AN participants had met criteria for two or more psychiatric disorders in their life time (in addition to EDs).

Weight-restored AN participants

In order to be considered weight-restored, participants had to have a history of DSM-IV AN (either binge-eating/purging or restricting type) assessed by the SCID (Spitzer et al., 2004) and currently have a BMI greater than or equal to 18 kg/m^2. In addition, participants had to report significant ED symptoms, defined either as: a global EDE-Q score greater than one standard deviation above the community norms (Mond et al., 2006), a CIA score of 16 or above (cut off for clinical ED) (Bohn et al., 2008) or episodes of binge-eating, restrictive eating patterns, purging behaviour or excessive/driven exercise (as reported on the EDE-Q).

The AN-W sample (n = 22) had a mean age of 25.01 (SD = 6.03) years and a mean BMI of 21.05 kg/m^2 (SD = 1.89 kg/m^2). Four of the participants previously met criteria for binge-eating/purging type AN with the remaining 18 meeting criteria for restricting type. Seven participants were currently taking antidepressant medication and 12 met criteria for current depression. Ten participants had met criteria for two or more psychiatric disorders in the life time (in addition to EDs).

Recovered AN participants

All recovered participants had a history of DSM-IV AN (either binge-eating/purging or restricting type) assessed by the SCID (Spitzer et al., 2004). In order to be considered recovered participants had to have: maintained a BMI of between 18.5 and

25 kg/m^2 for 12 months (assessed by self-report), scored within one standard deviation of the EDE-Q global mean scores for young women (Mond et al., 2007) and not met criteria currently for a DSM-IV disorder (assessed using the SCID).

The AN-R sample (n = 22) had a mean age of 23.73 (SD = 5.76) years and a mean BMI of 21.03 kg/m^2 (SD = 1.53 kg/m^2). Four of the participants had previously met criteria for binge-eating/purging type AN with the remaining 18 meeting criteria for the restricting type. Participants who were on maintenance antidepressant medication (n = 2) were not excluded from this group as long as they did not meet current criteria for a depressed mood assessed using the SCID and BDI-II (Beck et al., 1996) scores. Whilst none of the recovered participants met the current criteria for depression, 17 had had a depressed episode in their lifetime. Whilst no current psychiatric disorders were diagnosed, six participants had a lifetime history of two or more psychiatric disorders (in addition to EDs). The 22 participants included in the analysis had been recovered for a mean of 39.45 months (SD = 35.45). In addition, two participants were excluded before the testing session as they reported that they were currently receiving psychological treatment for another psychiatric disorder.

Healthy control participants

Inclusion criteria for the HC participants included: a current BMI between 18.5 and 25 kg/m^2, no first-degree relative with a current or past ED diagnosis (assessed by self- report), no lifetime history of any Axis I psychiatric disorder on the SCID for DSM-IV (Spitzer et al., 2004), maintenance of a BMI in the healthy range (18.5-25) since menarche (assessed by self-report), not currently engaging in dieting behaviour (assessed by self-report) and not suffering from multiple food intolerances or allergies (assessed by self-report).

Six HC participants were excluded at screening due to violation of one or more of the criteria detailed above (leaving 41 participants for the analysis). The HC sample (n = 41) had a mean age of 24.29 (SD = 6.46) years and a mean BMI of 21.70 kg/m^2 (SD = 1.88 kg/m^2).

5.3.2 Measures

5.3.2.1 ED symptoms

In order to measure ED symptoms, the EDE-Q (Fairburn & Beglin, 2008) and the CIA (Bohn et al., 2008) was used (see Section 2.3.3 in Chapter 2 for more details).

5.3.2.2 Depression and anxiety symptoms

In order to measure depression and anxiety symptoms, the BDI-II (Beck et al., 1996) and the STAI (Spielberger, 1983) was used (see Section 3.3.5 in Chapter 3 for more details).

5.3.2.3 Pleasure capacity

In order to measure the participants' capacity to experience reward or pleasure across different domains, the FCPS (Fawcett et al., 1983) was used (see Section 4.5.4.2 in Chapter 4 for more details).

5.3.2.4 Visual analogue scales (VAS)

To assess subjective states immediately before and after the task, participants completed a series of 100mm VAS assessing "in the moment" mood (happiness, despondency, anxiety) and appetite-related variables (hunger, thirst, desire to eat and level of fullness). The VAS were anchored at each end by "not at all" to "extremely" (see Appendix 5.4).

5.3.2.5 Other information

All participants provided demographic information (age, ethnicity and years in education). Height and weight (fully clothed) were taken in order to calculate BMI. Participants who were unable to be weighed provided self-report estimates. AN participants also provided information on their duration of AN illness, their lowest ever BMI, time in treatment, age of onset and where applicable the duration of recovery (defined as the period of time in which problems with eating, weight and shape did not significantly impact on daily functioning).

5.3.3 Assessment of food reward: Leeds-Oxford Food Preference Questionnaire (LO-FPQ)

Components of food reward were assessed by specifically adapting the original LFPQ (as described by Finlayson et al., 2008). The original procedure presented photographic food stimuli based on two key dimensions: fat content and taste (Finlayson et al., 2008). For this study, the task was modified such that separate measures of liking and wanting were assessed using food stimuli varying along the dimensions of calorie content (high or low) and taste (savoury or sweet). The modified task will be referred to as the Leeds-Oxford Food Preference Questionnaire (LO-FPQ).

High resolution digital colour photographs of 16 foods were used and could be organised either equally into separate generic categories of high calorie (HCa), low calorie (LCa), savoury (SA) and sweet (SW) or combined categories of high calorie savoury (HCaSA), high calorie sweet (HCaSW), low calorie savoury (LcaSA) or low calorie sweet (LCaSW) (for details of the foods included in each category see Appendix 5.5). The photographs selected for use were based on pilot work in which 14 women who had experience of AN rated a database of 28 images, with each of the four categories equally represented. Decisions of which stimuli to use were based on mean ratings of taste, calorie content, appeal and familiarity. Only one of the participants who completed the piloting went on to complete the full study.

Stimuli were presented using E-Prime (v2.0) on a 14.1 inch laptop screen and each of the food images measured 75 x 57mm^2. The presentation of food images during the task was programmed automatically (in a random order for measures of explicit liking and wanting and in randomized combination for the forced choice measure of implicit 'wanting') and responses were logged online.

5.3.3.1 Explicit liking and wanting trials

For the explicit rating trials, each of the 16 stimuli were presented one at a time on the computer screen and rated using a 100mm VAS anchored at each end by the statements "not at all" to "extremely". Separate questions were used to distinguish ratings of liking versus wanting for the food stimuli and these were presented in contrasting colours to encourage discrimination. For liking trials participants were asked: "How pleasant would it be to experience the taste of this food now?", and for the wanting trials participants were asked: "How much do you want to eat some of this food now?" The VAS were positioned below the stimuli and participants would use the mouse to move a centred cursor to the desired location on the scale. After a response had been made, the procedure automatically cycled to the next trial and the cursor would return to the centre of the rating scale. Mean ratings for each of the categories (HCaSA, HCaSW, LCaSA, LCaSW) were automatically computed by the software (minimum-maximum: 0-100).

5.3.3.2 Implicit 'wanting' trials

A behavioural 'forced choice' methodology was employed whereby each of the food stimuli was paired with another from a different food category. Participants were then asked to select the food that they "most want to eat now" using a keyboard response. Participants were instructed to respond as accurately and quickly as possible and reaction time (in milliseconds) of each choice was measured. Reaction time data was used as an implicit measure of 'wanting'; by covertly measuring reaction time to the food stimuli, participants remained unaware of implicit changes in their behaviour on the task, whilst remaining free to determine the direction of their choices. Reaction times were transformed to standardized "*d*-score" (D-RT) using a validated algorithm (Greenwald, Nosek, & Banaji, 2003) (for further information on how D-RT is calculated, see Appendix 5.6). Final scores were inverted for ease of interpretation and therefore the higher the D-RT, the greater the implicit wanting for that food category relative to other categories in the task (with a score of 0 indicating no difference in speed of response relative to alternative categories in the task).

5.3.4 Study procedure

Participants attended the department for one visit lasting approximately 90 minutes. Upon arrival, participants were made comfortable in a testing room and were asked to complete the battery of questionnaires. The SCID (Spitzer et al., 2004) was then administered by a graduate research student and weight and height was recorded. Instructions for the LO-FPQ were shown to the participant on the computer and participants completed a practice block of both the programs. Pre-test VAS were then completed. Following this, the LO-FPQ was delivered. To reduce order effects, both the stimuli and stimulus pairs were fully randomised across participants. Participants were navigated through the task at all times by instructions on the screen. Following the task, participants completed the VAS scale for a second time. Participants were reimbursed and were debriefed before leaving the department.

5.3.5 Data analysis

Data from the LO-FPQ, collected using E-prime, were exported to MS Excel via E-Data aid. MS Excel was used to calculate the variables for export to SPSS. Data was analysed using SPSS 18 for Windows. Parametric data was analysed by separate three-way analysis of covariance ANCOVAs (group x taste x calorie content) with depression and anxiety (trait) as covariates. Interactions were verified by *t*-tests with Bonferroni correction to control for Type I error. Results from the task are reported with size effect (ηp^2). Analyses were run for a second time excluding participants currently on antidepressants (n = 13) and excluding participants who were diagnosed with the binge-eating/purging type of AN (n = 12). Significant changes in the results after excluding participants on antidepressant medication and/or the binge-eating/purging type of AN are highlighted.

The pre-test VAS were compared across the groups using between group ANOVAs with post-hoc tests to identify any differences in mood or appetite-related variables at baseline. To compare changes in pre- and post-test VAS between the groups a series of repeated measures ANOVAs were conducted.

5.4 Results

5.4.1 Demographic characteristics

Ninety percent of the participants were right handed and 63.8% defined their ethnic origin as White British. Table 5.1 shows the demographic and questionnaire data for the four groups. As the data did show normal distribution within groups (Kolmogorov -Smirnov, $p > .05$), parametric group comparisons were conducted using a between-groups ANOVA followed by paired samples *t*-tests (Bonferroni corrected).

The four groups were comparable in term of years in education, age and ratings on the pleasure scale. Significant group differences were observed in terms of depression, anxiety (state and trait), ED symptoms, clinical impairment and BMI (as shown in Table 5.1). The AN-C and AN-W groups had significantly higher scores on the EDE-Q, CIA, STAI and BDI-II than the AN-R or HC group. With mean EDE-Q and CIA scores above clinical cut offs, both the AN-C and the AN-W showed significant ED symptomatology. In addition, with mean BDI-II scores of 18.90 and 15.55 respectively, both these groups showed mild depression (Beck et al., 1996). The AN-R group reported significantly higher trait anxiety than the HC group ($p = .02$). This was the only significant difference in terms of demographic variables between the AN-R and the HC participants.

There was no significant differences between the three AN groups in terms of age of onset, time in treatment or lowest ever BMI ($p > .05$). However, there was a main effect of duration of illness, F (2, 63) = 6.47, $p = .003$, and post-hoc tests revealed that the AN-C group reported a significant longer duration of illness than either the AN-W or the AN-R (see Appendix 5.7).

Table 5.1 Demographics and questionnaire scores stratified by group

	AN-C		AN-W		AN-R		HC		*p*	Pair wise post-hoc
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*(two tailed)*	group comparisons
Age (years)	26.40	10.56	25.1	6.03	23.73	5.76	24.29	6.46	.276	---
BMI*	16.33	1.10	21.05	1.89	21.03	1.53	21.70	1.88	<.001	AN-C < AN-W, AN-R, HC
Education (years)	16.85	3.08	17.23	2.43	17.14	2.64	17.22	2.20	.954	---
EDE-Q	3.09	1.15	2.80	1.24	.85	.43	.43	.32	<.001	AN-C, AN-W > AN-R, HC

Table 5.1 Demographics and questionnaire scores stratified by group (continued)

CIA	24.0	11.20	16.96	10.89	4.32	3.05	1.42	1.43	<.001	AN-C >AN-W>AN-R, HC
BDI-II	18.90	12.62	15.55	10.51	4.18	4.04	2.46	2.11	<.001	AN-C, AN-W >AN-R, HC
STAI-S	23.85	11.34	21.77	11.54	12.36	7.04	8.10	6.60	<.001	AN-C,AN-W > AN-R, HC
STAI-T	36.05	12.02	32.27	13.32	20.18	9.22	12.15	6.98	<.001	AN-C,AN-W>AN-R > HC
FCPS	130.40	18.15	126.36	25.12	132.50	17.96	131.95	19.15	.452	---

Note. AN-C = Current anorexia nervosa; AN-W = Weight restored anorexia nervosa; AN-R = Recovered anorexia nervosa; BMI = Body mass index; EDE-Q = Eating Disorder Examination Questionnaire (global score); CIA = Clinical Impairment Assessment; BDI-II = Beck Depression Inventory II; STAI-T = State-Trait Anxiety Inventory – trait subscale; STAI- S = State- Trait Anxiety Inventory-state subscale; FCPS = Fawcett Clark Pleasure Capacity Scale.
*Seven participants from the AN-C (n = 4) and AN-W group (n = 3) were not weighed and so BMI was calculated based on self-reported height and weight.

5.4.2 Visual analogue scales (VAS)

The distributions of six of the parameters measured by the VAS violated the assumption of homogeneity (Levene's test statistic < . 05). Data was successfully transformed using square root transformations. A series of one-way ANOVAs were used to examine the difference in mood and appetite-related ratings (happiness, despondency, anxiety, desire to eat, hunger, thirst and level of fullness) between the groups at baseline. In order to take into account of multiple testing, the criterion used for significance testing was set at $p < .007$ (.05/7). The analyses revealed that there was a significant difference between the groups in ratings of happiness, despondency and anxiety (all at $p \leq .001$). Post-hoc *t*-tests showed that HCs were significantly less despondent, less anxious and happier than the AN-W and the AN-C groups. There were no significant differences in the ratings of happiness, despondency or anxiety between the AN-R and the HCs.

To examine the change in ratings from pre- to post-test within the groups, a series of repeated measures ANOVAs were conducted. For the AN-C group there was no significant main effect of time and no significant time x rating interaction. For the AN-W group there was a significant main effect of time,
F (1, 21) = 13.63, $p = .001$, and this was qualified by a significant time x rating interaction, F (6, 16) = 3.23, $p = .03$. Post-hoc *t*-tests (corrected for multiple comparisons) showed that the AN-W group were significantly more hungry post-test compared to pre-test, t (21) = - 5.19, $p < .001$. For the AN-R group there was no

significant main effect of time and no significant time x rating interaction. Lastly, for the HC group there was a significant main effect of time, F (1, 40) = 17.21, $p < .001$, and this was qualified by a significant time x rating interaction, F (6, 35) = 4.07, $p = .003$. Post-hoc t-test (corrected for multiple comparisons) showed that there was a significant increase in hunger, t (40) = -4.56, $p < .001$; desire to eat, t (40) = - 4.40, $p < .001$; and thirst, t (40) = -2.87, $p = .007$, from pre- to post-test in the HC participants. Untransformed means and standard deviations for the VAS ratings before and after the task are shown in Appendix 5.8.

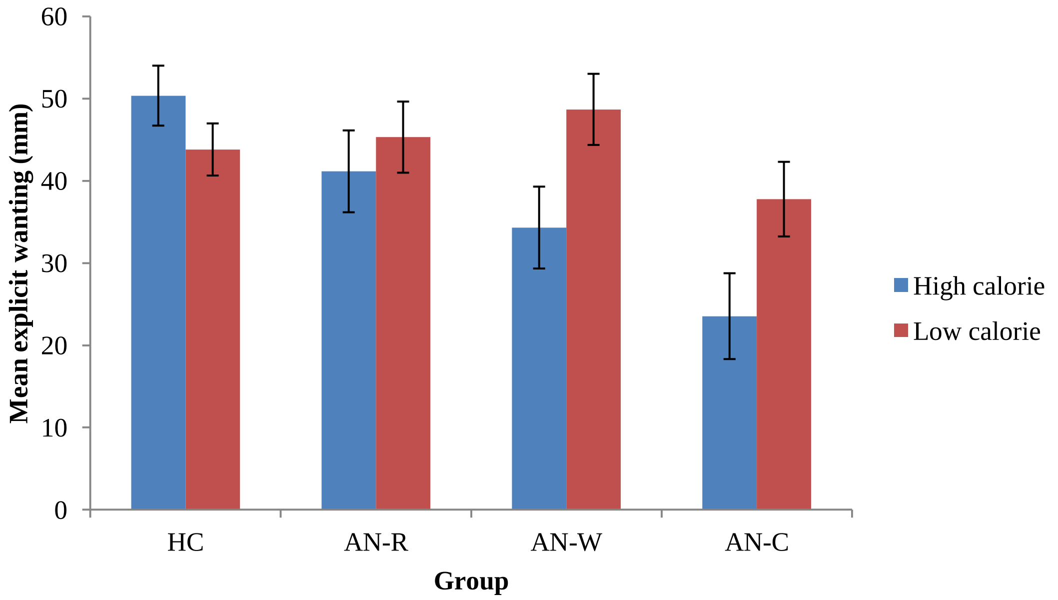
5.4.3 Explicit liking

Mean ratings of explicit liking was significantly greater for the sweet food category (M = 51.84, SD = 19.1) than the savoury food category (M = 40.73, SD = 19.2), F (1, 99) =5.25, $p < .05$, $\eta p^2 = .05$. The results remained unchanged when removing the participants who were currently taking antidepressant medication from the analysis. When the participants diagnosed with the binge-eating/purging type of AN were removed from the analysis, a significant calorie x group interaction emerged, F (3, 89) = 3.26, $p < .05$, $\eta p^2 = .10$. When examining the restricting type participants only, post-hoc comparisons using the Games-Howell test (due to unequal sample size) revealed that the restricting AN-C participants explicitly liked high calorie foods less than HC participants ($p < .05$). Means and standard deviations for all the ratings are shown in Appendix 5.9.

5.4.4 Explicit wanting

There was a significant main effect of calorie content. Mean ratings of explicit wanting were significantly greater for the low calorie food category than the high calorie food category, F (1, 99) =5.56, p <.05, ηp^2= .05. The significant main effect of calorie content was qualified by a significant calorie x group interaction, F (3, 99) = 4.39, p < .01, ηp^2 = .12. Post-hoc comparisons using the Games-Howell test (due to unequal sample size) revealed that the AN-C and the AN-W explicitly wanted high calorie foods less than HC participants (p < .05) (as shown in Figure 5.1). The results remained unchanged when removing the participants who were currently taking antidepressant medication or those diagnosed with the binge-eating/purging AN from the analysis. There were no other significant main effects or interactions.

Figure 5.1 Mean explicit wanting across the groups for high and low calorie foods



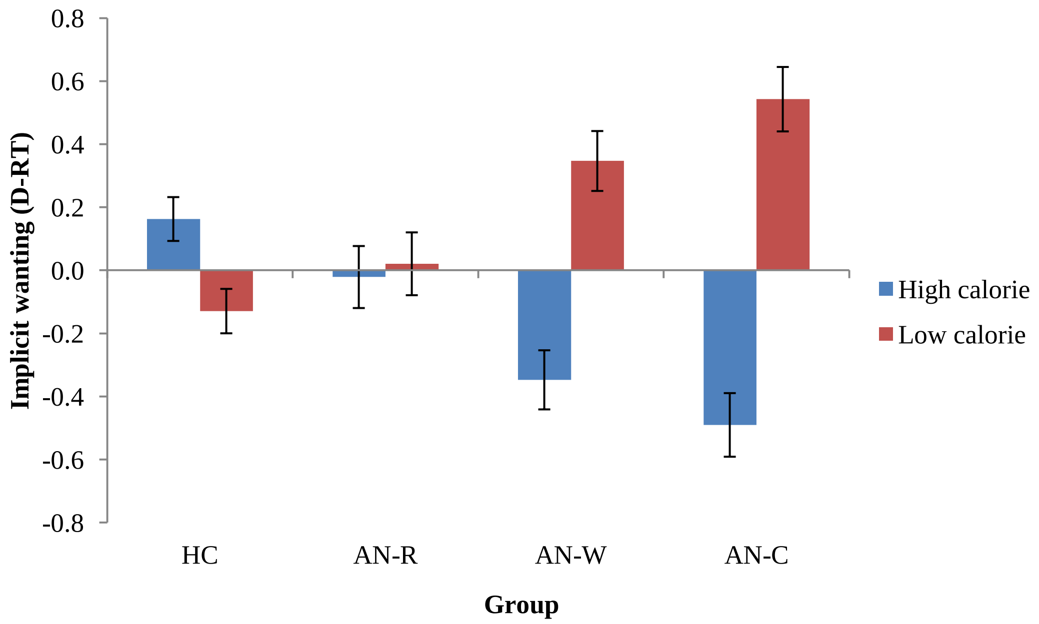
Note. HC = Healthy control; AN-R = Recovered anorexia nervosa; AN-W = Weight restored anorexia nervosa; AN-C = Current anorexia nervosa. Error bars show *SD*.

5.4.5 Implicit 'wanting' (D-RT)

For implicit 'wanting', there was a significant calorie x group interaction, F (3, 95) = 5.1, p < .01, ηp^2 = .14. Post-hoc tests revealed that the AN-C and the AN-W participants showed slower reaction times towards high calorie food images, indicating less implicit 'wanting', compared to HC participants (p < .001) (as shown in Figure 5.2). The AN-C group also showed slower reaction times towards high calorie food images compared to the AN-R participants (p = .02). For low calorie foods, post-hoc tests revealed significantly faster reaction times in the AN-C and AN-W groups compared to the HC participants indicating greater implicit 'wanting'

(p < .001). AN-C and AN-W participants were also significantly faster at responding to the low calorie foods compared to the AN-R participants, which again suggests greater 'wanting' for low calorie foods in those with current AN psychopathology (p < .05). These results remained significant when removing the participants who were currently taking antidepressant medication or diagnosed with the binge-eating/purging type from the analysis. There were no other significant main effects or interactions.

Figure 5.2 Standardized reaction time (D-RT) across the groups for high and low calorie foods



Note. Implicit 'wanting' scores assessed by transformed reaction time in forced choice paradigm (D-RT).A larger D-RT value means a faster reaction time (greater implicit 'wanting') for that food category relative to other categories in the task. HC = Healthy control; AN-R = Recovered anorexia nervosa; AN-W = Weight restored anorexia nervosa; AN-C = Current anorexia nervosa. Error bars show *SD*.

5.4.6 Correlating clinical variables with liking and'wanting responses within each group

After correcting for multiple comparisons, no significant associations were found between mean explicit liking or wanting or implicit 'wanting' responses for high and low calorie foods within each group and restraint (as measured by the EDE-Q), current BMI, pre-test hunger, duration of illness or lowest ever BMI.

5.5 Summary of results

- Individuals currently experiencing clinically significant symptoms of AN showed significantly reduced explicit wanting (AN-C only) and implicit ‘wanting’ (AN-C and AN-W) for high calorie food and increased implicit ‘wanting’ (AN-C and AN-W) for low calorie foods compared to HCs.
- When the participants with the binge-eating/purging type of AN were removed from the analysis, the AN-C participants also reported significantly less explicit liking for high calorie foods
- The AN-R participants did not significantly differ from the HC participants on any indexes food reward.
- Clinical variables (such as restraint, lowest ever BMI) were not significantly associated with liking or wanting.

5.6 Discussion

Few previous studies have attempted to distinguish liking versus wanting for food in AN which is surprising considering the successful application of the liking/wanting framework to other eating disturbances (for example, Berridge, 2009; Berridge et al., 2010; Finlayson et al., 2011; Finlayson et al., 2012; Mela, 2006). A recent study using visual and olfactory food cues found that AN participants (restricting type) reported decreased sensory pleasure for high energy-dense food compared to HC participants but no differences were found in liking response for the low energy-dense foods (Jiang et al., 2010). With regard to the motivation to eat, the AN participants showed lower wanting for low and high energy-dense foods (Jiang et al., 2010). Therefore this study did not reveal the inverted wanting response to low versus high calorie foods that was shown in the AN participants in the current study. The variance in results is likely to be due to the different experimental paradigms but may also be explained by heterogeneity in the clinical characteristics of the AN participants or the sample size (which was larger in our study). Nonetheless Jiang and colleagues (2010) concluded that cognitive symptoms of the disorder, for example concern about weight gain, may influence food intake more than a general inability to experience pleasure.

Interestingly, a review of behavioural and neurophysiological data on responsiveness to food-related cues in obesity concludes that eating behaviour in obese individuals may be associated with increased motivation for food consumption, without necessarily any greater explicit pleasure derived from the actual tastes properties of the food (Mela, 2006). In a similar manner, the data reported here supports the notion that AN is associated with decreased motivation to engage in eating high calorie foods and increased wanting for low calorie foods accompanied by a lesser change in the liking response. Thus it could be that in both obesity and AN, attitudinal and/or cognitive factors override or modulate the hedonic value of food. This would support current frameworks of AN which propose that ruminative concern with control of eating and the body override sensory information, such as the palatability of food (Kaye et al., 2009; Keating et al., 2012; Park et al., 2011) and challenge the notion that eating behaviours in AN are driven primarily by disturbances in gustatory processing (Wagner et al., 2008) or a general inability to experience reward (Davis & Woodside, 2002).

The study shows that both individuals currently meeting full criteria for AN and those who have had AN and restored some weight yet continue to have clinically significant ED psychopathology (thus meeting criteria DSM-IV criteria for EDNOS but not AN), displayed similarly aberrant explicit and implicit wanting responses to food reward compared to the AN-R and HC participants. Moreover there was no correlation between current BMI and the liking/wanting indexes. This suggests that the findings are not driven purely by low weight, but rather by the psychopathology itself or processes underpinning it (Park et al., 2011, 2012). Potentially, aberrant wanting responses to food could contribute to the high rates of relapse seen in AN after weight restoration (Carter et al., 2007; Sysko et al., 2005). This hypothesis is in part supported by the finding that the AN-R participants, who had healthy weights and low ED symptoms, did not differ from the HC participants in liking or wanting for high or low calorie foods.

It is interesting that currently underweight AN participants reported significantly lower explicit and implicit wanting for the high calorie foods compared to the recovered AN and never ill participants, whereas the weight-restored participants only showed significantly lower implicit ‘wanting’ compared to HC participants. One possible explanation is that when asked explicitly about wanting to eat high calorie foods, individuals who have regained weight following AN may be able to modulate their response, perhaps due to successful cognitive treatment, so that they are more in line with those never ill. However, the subconscious reaction to low versus high calorie food (as measured by the implicit ‘wanting’ task) remains unchanged. Alternatively, it could be that the biological effects of starvation in the current AN participants may impact on appetite and/or taste and thus high calorie food becomes less wanted implicitly and explicitly compared to the weight-restored participants.

The study did not reveal any significant differences in terms of liking and wanting for high or low calorie foods between the HC participants and the AN-R. This diverges from the neuroimaging literature, including that reported in Chapter 4, in which neural differences between those AN-R and HC participants in processing food–related stimuli has been demonstrated (Uher et al., 2003; Wagner et al., 2008). In the previous chapter, no differences in subjective reports of liking and wanting for food tastes and pictures were found between HCs and AN-R participants despite significantly different neural activation in reward regions of the brain. It could be that after recovery, individuals are able to modulate or override their responses to food stimuli in a more adaptive manner despite underlying neural differences in reward circuitry. This may reflect successful ED treatment and whilst speculative, it may explain why differences can be detected at the neural level but not at the behavioural level. Alternatively, it could be that the objective nature of brain imaging, or the use of tastes as well as pictures in Chapter 4, captures valid differences in food processing that are lost through subjective biases in behavioural studies. In order to further examine food processing in recovered participants; it would of interest to use the same food reward task at both the neural and behavioural level to enable direct comparison.

It is intriguing that when the participants with the binge-eating/purging type of AN were removed from the analyses, a significant difference emerged in the explicit liking responses: the restricting type AN-C participants reported significantly less liking for the high calorie foods compared to the HCs. Whilst this finding has to be treated as preliminary, one possibility is that individuals with restrictive AN engage a greater degree of explicit strategies to override appetitive drives to eat compared to those who lose control on occasion and binge-eat on energy-dense foods. This would support the results of a recent neuroimaging study which found greater activation in regions of the brain involved in rumination and regulating both cognitive and emotional processing in restricting type AN participants compared to those who binge-eat/purge (Brooks, O'Daly, Uher, Friedercih et al., 2012).

The LO-FPQ measured liking and wanting for food, yet the learning subcomponent of reward was not measured. Learning is an essential component in decision-making regarding eating-related behaviour and may therefore also be important in AN (Berridge, 2009). For example, in AN it may be that over time a previously liked food (such as chocolate) is associated with an adverse reaction (for example, feeling ‘fat’). In an attempt to prevent the negative outcome (feeling ‘fat’), individuals with AN may learn to avoid eating such foods and thus want high calorie palatable foods less. Thus avoidance (or restriction) of high calorie foods may be negatively reinforced. Therefore, future work examining reward processing in AN would benefit from measuring learning as well as liking and wanting.

5.6.1 Limitations

This limitations section will first consider general limitations of the study reported and following this, the specific question of whether reaction time data is an accurate measure of implicit ‘wanting’ will be considered.

Hunger ratings before the test relied on self-report measures and this may be considered a limitation especially as research has identified that individuals with AN have deficits in interoceptive awareness and thus may be impaired in detecting hunger (Fassino, Pierò, Gramaglia, & Abbate-Daga, 2004). Future studies would benefit from manipulating levels of satiety using a preload, as has been done in previous studies using a similar task (Finlayson et al., 2011; Finlayson et al., 2012; Griffioen-Roose et al., 2010). It should however be noted that there were no significant group differences in pre-test hunger and no significant correlations between hunger levels and task responses. A small number of participants were currently taking antidepressant medication and this could be considered a limitation as there is evidence that such psychoactive medication can affect performance on information processing tasks in AN (Jänsch et al., 2009). However, analysing the data without these participants did not change the results suggesting that antidepressants did not significantly contribute to the between-group differences reported. The number of participants in each group was small resulting in modest effect sizes. This also meant that we were unable to compare the binge-eating/purging AN participants and the pure restricting type separately. Future, research with larger sample sizes of each subtype of AN would therefore be advantageous. Lastly, the LO-FPQ did not include a measure of implicit ‘liking’ (objective affective reactions) yet such unconscious responses may be important in AN. Future studies may consider including an implicit measure of ‘liking’, for example measuring facial affective reactions in AN to food stimuli of different energy densities.

Is reaction time data an accurate measure of implicit ‘wanting’?

Whilst other studies have used reaction time as a measure of implicit processes, there are a number of competing explanations as to what these reaction times actually mean. Applied to the data reported here, it may be that participants currently experiencing symptoms of AN, whether underweight or weight-restored, are more familiar with the low calorie foods and/or have an attentional bias towards them. Alternatively, it may be that individuals with AN have learnt to avoid high calorie foods which have in the past led to feelings of being out of control. Thus high calorie foods may have become associated with aversive cognitions and emotions. Faster reaction times to the low calorie foods may therefore not reflect more implicit ‘wanting’ for low calorie foods but rather an increased attempt to reduce exposure to the threatening high calorie foods. Whilst it is not possible to determine whether the reaction times to the food stimuli do index subconscious ‘wanting’ processes, combining behavioural tasks which aim to capture ‘liking’ and ‘wanting’ processes, such as the LO-FPQ, with neuroimaging may further substantiate the conscious and subconscious processes involved in eating.

5.7 Conclusions

This study provides support for the hypothesis that liking and wanting for food reward are two separate psychological processes that may contribute to the aberrant eating behaviours seen in individuals with AN. Whilst conclusions must be considered cautiously due to the limitations highlighted, the data suggests that aberrant explicit and implicit wanting, rather than hedonic liking for food may be more pertinent for individuals with current AN and after weight restoration.

6 Resting state functional connectivity in recovered anorexia nervosa: Implications for understanding rumination and reward processing

6.1 Overview

The current chapter reports the results of a neuroimaging study examining resting state functional connectivity in recovered AN and HC participants. Specifically, it aims to draw together the themes of rumination and reward processing which have been central to this thesis. The following question arising from the studies reported in Chapters 2-5 is addressed:

- What differences are there in neural networks underpinning rumination and cognitive control after recovery from AN in comparison to those never ill?

6.2 Background

Rumination and reward processing in AN are themes which have been discussed throughout this thesis. Results from the studies reported in Chapters 2-5 suggest that individuals with AN are highly ruminative on eating, weight and shape and this is associated with avoidance (Chapters 2 and 3). This ruminative mode of processing is difficult to shift in AN, particularly in the presence of food which is typically experienced by individuals with AN as overwhelming (Chapter 3). Even after recovery from AN, differences at the neural level can be detected when presented with food stimuli compared to those never ill. Such aberrancies are particularly apparent in brain regions involved in reward processing (such as the ventral striatum) and cognitive control (such as the DLPFC) (Chapter 4). It may be that aberrant cognitive processes (such as rumination about food and the body), rather than hedonic (or liking) experiences, drive the restrictive eating practices that characterise the disorder (Chapter 5). This would be consistent with the theoretical work suggesting that a ruminative ‘doing AN’ mode, or top-down neurocircuits, regulate the response to salient stimuli in AN (such as food) and therefore drive restrictive eating practices (Kaye et al., 2009; Park et al., 2011).

Recent advances in neuroimaging techniques have enabled the investigation of neural networks which are thought to correspond to critical brain functions, such as executive control and salience detection. Given the hypothesis that the anorexic state can be explained by complex interactions between different modes of processing (Park et al, 2011), which may be underpinned by distinct neural networks (Kaye et al., 2009), such neuroimaging techniques may further the understanding of how cognitive processes (such as rumination) and appetitive responses interact in AN.

Resting state functional connectivity

Resting state functional connectivity is an FMRI approach that utilises spontaneous fluctuations in the resting brain, enabling temporal correlations between brain areas to be mapped (Biswal et al., 2010; Greicius, Supekar, Menon, & Dougherty, 2009). Brain regions showing a strong temporal coherence (spontaneous co activation) are termed “resting state networks” and are thought to reflect intrinsic properties of functional brain organisation (Damoiseaux et al., 2006; Gusnard & Raichle, 2001). For example, the default mode network (DMN) which encompasses brain regions including the posterior cingulate, the precuneus and parts of the prefrontal cortex, is more active at rest than during attention-demanding tasks and is therefore thought to be associated with stimulus-independent thought and self-reflection (Raichle et al., 2001). Networks have been consistently demonstrated across different resting state conditions, including sleep and anaesthesia (Boly et al., 2008), and thus support the contention that BOLD activity during resting states cannot simply be a manifestation of conscious activity.

Resting state functional connectivity in neuropsychiatric disorders

Although there is no data on resting state functional connectivity in AN, it has been examined in other neuropsychiatric disorders including depression, bipolar disorder and schizophrenia (Greicius, 2008). Identification of neural networks at rest is relevant for neuropsychiatric research for several reasons. One exciting possibility is that the strength of functional connectivity in resting state networks may underpin the activity of neural responses observed in task-based FMRI studies. For example, increased functional connectivity has been found in the DMN in depressed patients highlighting a potential neural mechanism for the negative self-focus, or rumination, that characterises the disorder (Sheline, Price, Yan, & Mintun, 2010; Veer et al., 2010). Increased functional connectivity has also been shown to correlate with self-reported levels of ruminative brooding in depressed participants (Berman et al., 2010; Hamilton et al., 2010). It has also been found that current psychoactive treatments can modulate resting state functional connectivity in healthy volunteers and depressed patients, thus demonstrating a mechanism by which psychiatric medications may be having their therapeutic effects (Anand et al., 2005; McCabe & Mishor, 2011; McCabe et al., 2011).

Highlighting the potential importance of resting state functional connectivity for neuropsychiatric research, Zhou and colleagues (2010), as well as others, have suggested that this FMRI approach could be used to detect potential biomarkers for diagnosis, prognosis and treatment evaluation (Hasler & Northoff, 2011; Zhou et al., 2010). Furthermore, considering the practical advantages of resting state functional connectivity for clinical populations (good signal to noise BOLD, brief acquisition, minimal participant compliance), it seems that this is a valuable approach for extending the neurobiological understanding of AN.

Interim summary

Taken together the findings reported in Chapters 2-5 suggest that there could be alterations in networks modulating cognitive control and rumination. Identifying neural network dysfunction using resting state functional connectivity may aid understanding of the complex processes which underpin AN.

6.3 Study aim

- To examine neural networks in non-medicated women recovered from AN compared to HCs using resting state functional connectivity.

6.4 Hypothesis

Based on the results of the studies reported in Chapters 2-5, in addition to the neurobiological and theoretical frameworks for AN (for example, Kaye et al., 2009; Park et al., 2011), the hypothesis is that increased resting state functional connectivity would be seen in networks that encompass brain regions underpinning self-referential processing (rumination) and cognitive control (such as the DMN) in recovered AN compared to HC participants.

6.5 Method

6.5.1 Overall design

The data reported in this chapter was collected as part of the study described in Chapter 4. A between-groups design was used to examine whole-brain functional connectivity in women recovered from AN compared to HC participants.

6.5.2 Participants

See Chapter 4 (Section 4.5.2) for participant information. Due to technical errors, resting-state scans from two HC participants could not be included in this analysis. Therefore, 16 recovered AN participants and 14 HC participants were included in the final analysis (Appendix 6.1 shows the demographic and questionnaire data for these participants).

6.5.2.1 Inclusion and exclusion criteria

See Chapter 4 (Section 4.5.2.1) for details on inclusion and exclusion criteria.

6.5.3 Measures

See Chapter 4 (Section 4.5.4) for details on the measures used. Data from the RRS-ED (see Chapter 2 for more information on this measure) is also reported (as shown in Appendix 6.1).

6.6 FMRI scan

Imaging data were acquired using the same Sieman's Avanto 1.5T whole body scanner as described in Chapter 4. Resting state FMRI data were acquired at the end of the imaging protocol: after completing two task-related MRI runs (reported in Chapter 4 and Cowdrey et al., 2011) and an anatomical scan. Participants were instructed to lie in dimmed light with their eyes open, think of nothing in particular, and not to fall asleep.

T_2* weighted EPI slices were acquired every 3 seconds (T_R=3). Axial slices (35) with in-plane resolution of 3×3mm and between plane spacing of 4mm were obtained. The matrix size was 64×64 and the field of view was 192×192mm. Acquisition was carried out during the resting scan yielding 140 volumes in total (acquisition time = 5 minutes). As described in Chapter 4, an anatomical T_1-weighted sequence with axial plane slice, thickness 1mm and in-plane resolution of 1×1mm was acquired to improve the registration process and also for grey matter analysis.

6.6.1 ***Resting state data analysis*** *(as described previously by Filippini et al., 2009)*

FMRI analysis was carried out using FSL (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2011) with resting-state networks identified using the independent component analysis (ICA) tool MELODIC (Multivariate Exploratory Linear Optimized Decomposition into Independent Components) (Beckmann, DeLuca, Devlin, & Smith, 2005). Individual prestatistical processing consisted of motion correction, brain extraction, spatial smoothing using a Gaussian kernel of full-width at half-maximum 6mm, and high-pass temporal filtering equivalent to 150 s (0.007 Hz). FMRI volumes were registered to the individual's structural scan and standard space images using FMRIB's Nonlinear Image Registration Tool (FNIRT).

Pre-processed functional data containing 140 time-points for each participant were temporally concatenated across participants, creating a single 4D dataset, in order to carry out group-wise ICA. Group-ICA was carried out at a dimensionality of 60. RSNs (resting-state networks) of interest covered the entire brain and were selected using spatial correlation against sets of previously defined maps (Beckmann et al., 2005).

The participant-specific analysis of the resting data was carried out using a regression technique (dual regression) (Filippini et al., 2009) that allows for voxel-wise comparisons of resting functional connectivity between participants or participant-groups. This approach proceeds in three stages: first, the (group wise) concatenated multiple FMRI data sets are decomposed using ICA in order to identify large-scale patterns of functional connectivity in the population of participants (as described above). Second, dual regression approach is used to identify, within each participant's FMRI data set, participant-specific temporal dynamics and spatial maps that are associated with each group IC map. This involves (A) using the full set of group-ICA spatial maps in a linear model fit (spatial regression) against the separate FMRI data sets, resulting in matrices describing temporal dynamics for each component for each participant and (B) using these participant-specific time-course matrices in a linear model fit (temporal regression) against the associated FMRI data set to estimate participant-specific spatial maps. Finally, the different component maps are collected across participants into single 4D files (one per original ICA map, with the 4th dimension being participant ID) and tested voxel wise for statistically significant differences between the groups using non-parametric permutation testing (5000 permutations) (Nichols & Holmes, 2002).

Clusters were determined by using threshold-free cluster enhancement (TFCE) (Smith & Nichols, 2009) and a family-wise-error (FWE) corrected cluster significance threshold of p = .05. This results in spatial maps characterizing the between-participant/group differences. Non-parametric tests were used (10,000 permutations), to safeguard against the possibility that the between-participants effects were non-Gaussian, and because such non-parametric inference has greater robustness against spatial non-stationarity than commonly used parametric methods (Hayasaka, Phan, Liberzon, Worsley, & Nichols, 2004).

6.6.2 Grey matter data analysis

Abnormalities in grey matter volume have been found previously in those recovered from AN (Joos et al., 2011; Katzman, Zipursky, Lambe, & Mikulis, 1997; Roberto et al., 2011) although this finding is not always reported (Castro-Fornieles et al., 2006; Wagner, Greer et al., 2006). To test whether altered functional connectivity in this study may be explained by differences between the groups in grey matter volume, voxel-based morphometry (VBM) analysis was run on the high resolution T_1-weighted data sets (Douaud et al., 2007). In brief, brain extraction and tissue-type segmentation were performed, and resulting grey matter partial volume images were aligned to standard space using FMRIB's Linear Image Registration Tool (FLIRT) and then nonlinear (FNIRT) registration tools. The resulting images were averaged, modulated to correct for nonlinear warp-field expansion, and smoothed with an isotropic Gaussian kernel of full width at half maximum 4 mm to create a study-specific template. Finally, voxel-wise GLM was applied using permutation nonparametric testing (5,000 permutations), correcting for multiple comparisons across space.

6.7 Results

6.7.1 Demographic characteristics

The 14 HC participants and the 16 recovered AN participants did not significantly differ in terms of age, body mass index or IQ ($p > .05$). There were no significant differences between the groups for measures of ED symptoms[9], depression, state or trait anxiety, positive affect or negative affect ($p > .05$). However, the recovered AN group scored significantly higher than the HC in terms of rumination on control of eating and body shape and weight ($p < .05$) (see Appendix 6.1).

6.7.2 Resting state functional connectivity main effects

Independent component analysis (ICA) defined sixty independent components. Of these, twelve components were identified as RSNs (covering the majority of grey matter) and were evaluated further (Figure 6.1 shows eight RSNs). The other components reflected distinct artefacts resulting from head motion and physiological or scanner noise. The RSNs of interest included: medial visual, lateral visual, auditory, sensory-motor, DMN, cognitive control and fronto-parietal (right and left). These networks corresponded to resting state networks which have been described previous and show high stability over time (Beckmann et al., 2005).

[9] It is noted that the results in terms of ED symptoms are discrepant to that reported in Chapter 4. This is due to two HC participants being excluded from the analysis and an additional recovered AN participant being included in the analysis.

Figure 6.1 Sagittal, coronal and axial slices for the main RSNs detected, overlaid onto a standard EPI functional template

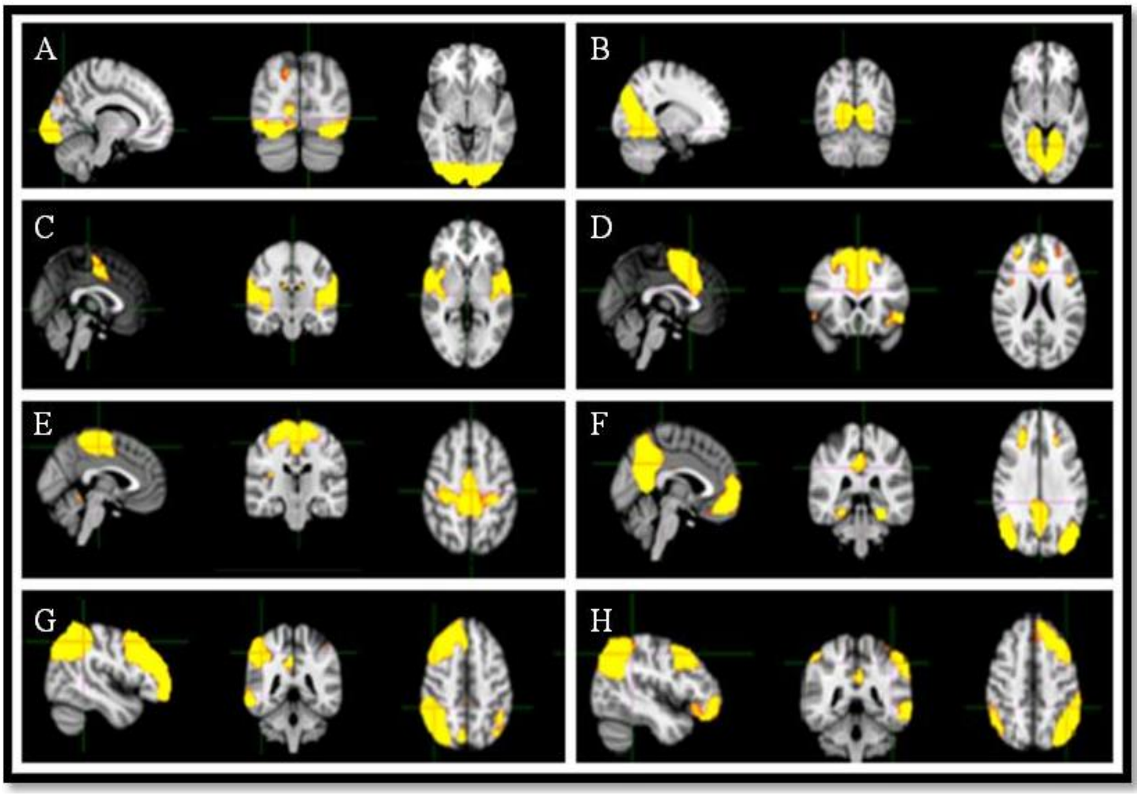


Figure 6.1

Networks identified include:

(A) lateral visual, (B) medial visual, (C) auditory, (D) cognitive control, (E) sensory-motor,(F) DMN, (G) left fronto- parietal, (H) right fronto-parietal

6.7.3 Resting state functional connectivity: between-group effects

Significant between-group differences in the voxel-wise spatial distribution of the functional connectivity maps were subsequently revealed in the DMN. Significantly increased temporal correlation (coherence) was observed in recovered AN relative to healthy controls between the DMN functional connectivity map and in a region of the right precuneus close to the border of the posterior cingulate gyrus (t = 4.84, BA31, [8,-60, 24]) and the dorsolateral prefrontal cortex / inferior frontal gyrus (DLPFC/IFG) (t = 4.99, BA9, [44, 6, 26]) (Figure 6.2 and Figure 6.3). Clusters were determined by using threshold-free cluster enhancement (TFCE) (Smith & Nichols, 2009) and an FWE corrected significance threshold of p = .05 (i.e., fully corrected for multi-comparisons across voxels, within the DMN). These significant results would not survive *further* corrections for multiple comparisons, for example, correcting for *all* RSNs identified, or for two-tailed testing (i.e., the HC > AN contrast). However, as it was expected that increased connectivity in the recovered AN group would be found in brain regions of the DMN, it is thought that further corrections are not necessary.

The lack of difference in the other RSNs identified (including purely visual and sensory-motor) argues against the DMN difference being caused by *non-neural* physiological group differences such as global perfusion or heart rate differences.

Figure 6.2 Average DMN map from both groups combined and between-group differences

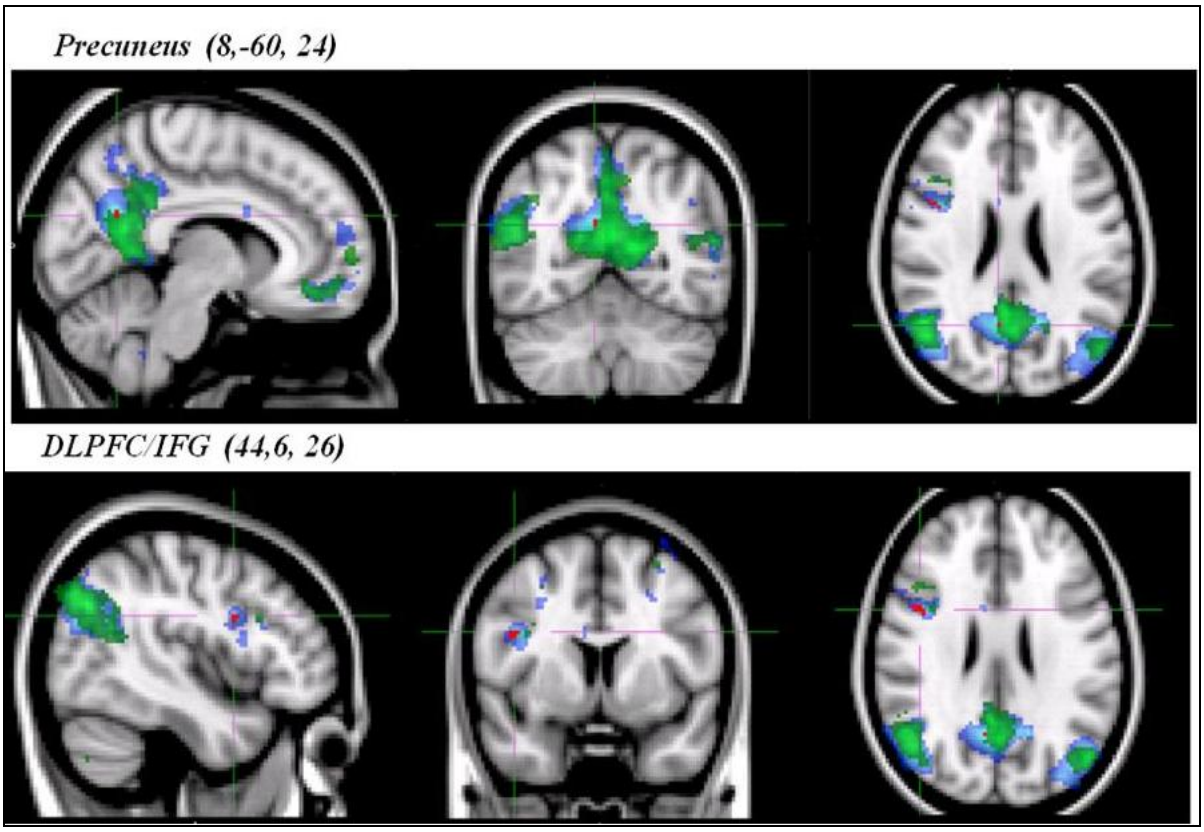


Figure 6.2

Recovered AN group average DMN map ($Z > 5$)

HC group average DMN map ($Z > 5$)

Group differences in functional connectivity between the DMN and the precuneus and the DLPFC / IFG: Recovered AN > HCs, corrected ($p < .05$) (i.e., fully significant for multiple comparisons across voxels, within the DMN).

Note. Networks are overlaid onto the MNI-152 standard brain.

Figure 6.3 BOLD fluctuation in the DMN in the recovered AN and HC participants in the precuneus and DLPFC/IFG

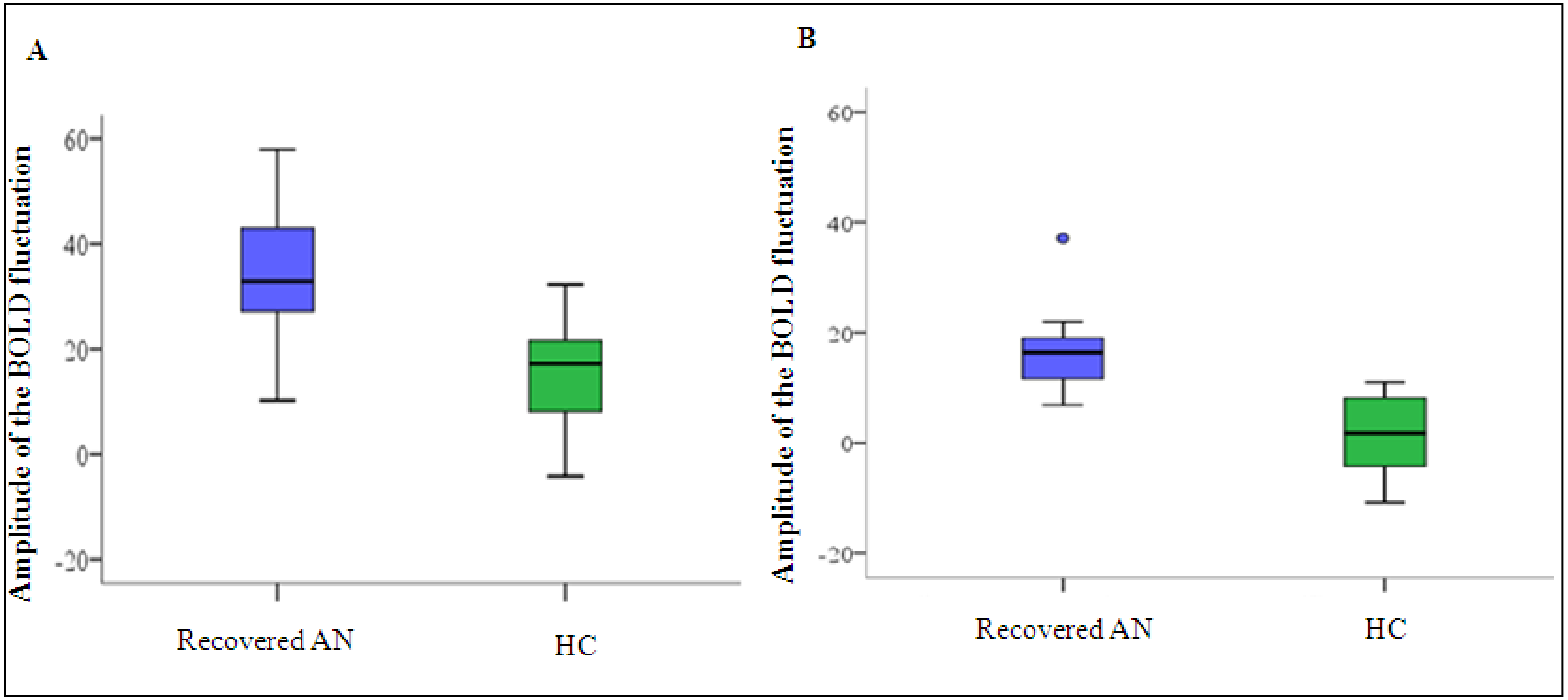


Figure 6.3

Box plots show an increase in the amplitude of the BOLD fluctuation (the average beta-value within the regions exhibiting statistical group differences-‘connectivity strength’) in the recovered anorexia nervosa participants compared to the healthy control participants between the DMN and the (A) precuneus (8, -60, 24) and, (B) DLPFC/IFG (44, 6, 26).

6.7.4 Grey matter

No differences in grey matter were observed between the HCs and those recovered from AN. This indicates that the altered functional connectivity within the network discussed above is unlikely to be related to macroscopic (i.e., MRI observable) structural grey matter abnormalities.

6.7.5 Correlations with self-reported rumination and ED symptoms

Total scores on the RRS-ED, BDI-II and EDE-Q were examined for correlations with the precuneus and DLPFC dual regression output. Collapsing across participant group there was a positive correlation between the DLPFC output and the RRS-ED (r_s = .46, p = .001) and EDE-Q (r_s = .58, p=.01) scores but there was no significant correlation with scores on the BDI-II. There were no significant correlations between any of the questionnaire measures and the precuneus. When examining the two groups separately, the correlation between the DLPFC output and the EDE-Q score in the recovered AN group was at trend level (r_s = .49, p = .054). As shown in Appendix 6.2, there were no other significant correlations when examining the two groups separately.

6.8 Summary of results

- Individuals recovered from AN had increased resting state functional connectivity between the DMN and the precuneus and DLPFC, compared to HC participants.
- There were no between-group differences in grey matter morphology.
- RRS-ED and EDE-Q scores significantly correlated with the DLPFC but not the precuneus output.

6.9 Discussion

Increased resting state functional connectivity between the DMN and the precuneus and DLPFC, was found in those recovered from AN compared to HC participants. The results support the hypothesis that resting state networks involving rumination and cognitive control may be dysfunctional in AN, even after recovery. These findings further support the thesis that rumination, and the potential link between rumination and reward processing, may contribute to the maintenance of AN.

Increased resting state functional connectivity in the precuneus

The precuneus has a pivotal role in the DMN and therefore is involved in processes that are self-referential in nature (Greicius et al., 2009). It has been posited that a decrease in DMN activity during an effortful task reflects the need to turn off self-referential processing in order to deploy attention to the demands of the task (Gusnard, Akbudak, Shulman, & Raichle, 2001; Shulman et al., 1997).Thus it may be that the increased functional connectivity in the precuneus might underpin the rumination seen in AN. If this is the case, it would support the data reported in Chapters 2-5 and the notion that rumination on eating, weight and shape is an important maintaining factor in AN (Park et al.,2011). However, the precuneus output did not correlate with scores on the RRS-ED. One possibility is that there was not enough variance to in RRS-ED scores to model in this way. If there was more variance in terms of scores on the rumination measure, it is possible that a relationship between the precuneus output and scores on the RRS-ED may have been found. It may be that if the study was repeated in a currently ill AN sample, and not those recovered from AN, there would be more variance in RRS-ED scores.

Increased resting state functional connectivity in the DLPFC /IFG

Recovered AN participants also showed significantly greater resting state functional connectivity in the DLPFC/IFG compared to the HCs. In fact, as can be seen from the group-average DMN maps in Figure 6.2, and the box plot in Figure 6.3, the DLPFC/IFG is barely (if at all) involved in the DMN in the control group. As reported in Chapter 4, the DLPFC is an important node in the cognitive control network (Cole & Schneider, 2007) and has been implicated in response inhibition (Swick, Ashley, & Turken, 2008), risk aversion (Christopoulos, Tobler, Bossaerts, Dolan, & Schultz, 2009) and emotion control (Wang et al., 2008). It is possible that the result of increased activity in the DLPFC area might contribute to the excessive inhibitory control seen in AN and supported by the data in Chapters 4 and 5. The results support the idea of an imbalance between top-down cognitive control and bottom-up appetitive processing in AN (Kaye et al., 2009).

DMN in depression

There is emerging evidence of altered resting state functional connectivity in the DMN in depression. There have been reports of increased resting state functional connectivity in the DMN in depression which authors have related to the increased self-focus and rumination seen in depression (Greicius et al., 2007; Sheline et al., 2010; Zhou et al., 2010). For example, Greicius and colleagues (2007) found increased functional connectivity in the thalamaus and the subgenual cingulate cortex in the depressed participant group compared to HCs. Sheline et al. (2010) similarly found increased functional connectivity in regions of the DMN in depressed participants, but the differences were located in the medial prefrontal cortex and the posterior cingulate regions of the DMN.

As increased resting state functional connectivity was also found in the recovered AN participants in this study, it could be argued that the results may have been driven by current or past depression symptoms. However, the differences between the recovered AN and HC participants were located in the DLPFC/IFG and precuneus regions of the DMN. These regions are not typically found to show aberrant functional connectivity in the DMN in depression. Whilst speculative, the differences may pertain to disorder-specific feature of AN and depression. For example, unlike depression AN is characterised by excessive cognitive control and rumination on themes of eating, weight and shape. It should also be noted that increased resting state functional connectivity in the DMN in depression is not consistently reported and studies have also reported decreased DMN resting state functional connectivity in depression (for example, Anand et al., 2005; Bluhm et al., 2009; Veer et al., 2010; Zhu et al., 2011). It is possible that heterogeneous depressed samples, for example differing in severity or comorbidity, and/or differences in medication status of the depressed participants or variation in analysis method (i.e. ICA versus seed-based analysis) could explain the inconsistencies in the depression literature.

6.9.1 Limitations

As discussed in Chapter 4, from studying individuals recovered from AN, it is difficult to determine whether the increased functional connectivity effects are ‘scars’ of previous illness episodes or premorbid risk factors which exist before illness onset. Whilst they are difficult to conduct in AN, longitudinal studies would be advantageous to tease apart trait, state and scar effects.

It is important to consider the possible effect that the previous FMRI tasks had on the resting state data. Whilst the optimal method of collecting resting data is debated, there is some evidence that prior task engagement may affect activity in subsequent resting scans. For example, one study using a working memory task reported that memory load had a significant impact resting state functional connectivity data collected immediately after task engagement (Pyka et al., 2009). In the current study, a ten minute anatomical scan was conducted between the end of the tasks and the start of the resting scan, thus minimising the chance of residual effects. However, it would be beneficial to replicate the results using resting scans acquired at the beginning of the experimental procedure (especially as the food-related task reported in Chapter 4 may have increased rumination in the recovered AN participants).

Lastly, there is no consensus as to what is the optimal number of components that should be generated by the ICA analysis (Beckmann et al., 2005). This study estimated a relatively high number (60) of components to reduce the chance of under fitting the data and thus not validly separating the individual networks. Equally, it is possible that this high number of components resulted in over fitting (i.e., forcing the data to decompose into too many components and potentially dividing valid resting state networks). However, the analysis was re-run using a lower number of components but it was found that the resulting networks did not replicate those shown in previous studies.

6.9.2 Conclusions

This chapter has demonstrated that participants with a history of AN have increased resting state functional connectivity between the DMN and the precuneus and DLPFC. As the DMN has been implicated in self-referential processing, the results are compatible with the core symptoms of AN including ruminative preoccupation on eating weight and shape and impaired cognitive flexibility (Kaye et al., 2009; Park et al., 2011, 2012). These findings further support the contention that rumination overrides basic appetitive drives in AN.

7 General discussion

7.1 Overview of thesis

As discussed in Chapter 1, there is an urgent need to develop and disseminate effective treatments for adult AN, as the prognosis remains poor. A range of theories have outlined the content of cognition in AN, but the processes which generate such content and contribute to the persistence of the disorder remain poorly defined and understood. The ICS account of AN was therefore developed to delineate the *processes* which are thought to underpin AN psychopathology (Park et al., 2011, 2012). Using this framework a number of novel and specific hypotheses can be generated and these have been used to guide the studies reported in this thesis.

The extant literature on AN identifies different processes that may be involved in the development and maintenance of AN. For example, interoceptive deficits, emotion dysregulation and alexithymia have all been associated with the onset and maintenance of AN. However, this thesis was restricted to just two complementary processes discussed by Park, Dunn and Barnard (2011, 2012): intense rumination on control of eating, weight and shape and disrupted reward processing, particularly in the primary domain of food. These processes were selected because of the premise that rumination has an avoidant function and enables individuals to transcend salient cues (such as hunger) (Park et al., 2011). The process of rumination may explain why individuals with AN exhibit aberrant responses to stimuli that are typically experienced as rewarding (such as energy-dense foods). Therefore, the overarching aim of the thesis was to investigate the role of rumination and reward processes in the context of AN maintenance and by doing so further the understanding of how higher cognitive processes (such as rumination) and appetitive processes may interact and modulate the response towards food stimuli.

A series of five studies employing different experimental strategies and participant groups (non-clinical as well as AN samples) explored the role of rumination and reward processing in AN. A summary of each study will be provided in the next section together with an attempt to integrate the principal findings from each chapter.

7.2 Summary of the principal findings

The studies reported in Chapters 2 and 3 explored the nature and function of ruminative processing in individuals with varying levels of ED psychopathology. Specifically, the study reported in Chapter 2 considered the content of rumination in AN and how rumination may be associated with avoidance. The results suggested that rumination in AN is distinct from rumination in depression as it focuses on control of eating, weight and shape. Therefore existing measures of rumination which predominately focus on rumination on depressive symptoms may not adequately capture rumination in AN. A novel measure of rumination on ED themes (the RRS-ED) was therefore developed and validated using a large non-clinical sample in addition to a smaller AN sample. Using the new measure, it was found that ED symptoms were positively associated with rumination on eating, weight and shape (particularly ruminative brooding) and experiential avoidance, and negatively associated with trait mindfulness. These results were supportive of the process account of AN which suggests that for individuals with AN, analytical cognitions about eating, weight and shape prevail, with a relative lack of emotional or bodily experience (Park et al., 2011). Based on the process account of AN and the data reported in Chapter 2, it was hypothesised that the ruminative mode of processing may contribute to escalation of ED symptoms. Therefore, Study 2 (reported in Chapter 3) investigated whether individuals with AN could disengage from rumination around meal times and whether this would have an effect on the meal time experience.

As explained in Chapters 1 and 2, in contrast to ruminative processing, fostering a mindful mode of processing in which attention is directed to the present-moment experience in a non-elaborative or non-judgemental way may reduce AN symptoms. A previous experimental study by Rawal, Williams and Park (2011) involving an imaginary meal procedure supported this hypothesis. In this study, AN participants demonstrated less cognitive and behavioural reactivity after the imaginary meal procedure following a experiential mode manipulation compared to a ruminative mode manipulation. However, it has been suggested that when ill and underweight with AN, experiential manipulations which aim to increase attention to present-moment experiences, may be experienced as overwhelming and aversive (Park et al., 2012). Simply distracting individuals from ruminative thoughts may be a more fruitful strategy in the short term, particularly at times when ruminations may increase due to stress or anxiety (such as meal times) and when individuals are not practiced in mindfulness. However, simple distraction is less likely to be of long term benefit.

In Study 2 (Chapter 3) individuals currently diagnosed with AN adopted different exercises before meal times which aimed to manipulate the mode of processing (rumination versus experiential processing). In addition, the effect of a distraction exercise was examined. The results suggested that the rumination exercise did lead to more analytical self-focus. However, mindful breathing (the experiential exercise) did not significantly reduce analytical processing. As well as it being very difficult to shift individuals out of rumination at meal times, there were several potential explanations for this finding that largely focus on the practical attributes of the mindful breathing exercise (for example, the experiential exercise being too short and not suitable as a standalone intervention without guidance). Furthermore, it was found that an increase in experiential processing was not specific to the mindful breathing exercise, but found after the distraction exercise as well. Overlap between the two exercises may have explained this result. In short, the distraction exercise had a strong sensory non-verbal element (i.e., music) and so may not have been the optimal exercise to use as a comparison. To complement the statistical analysis, a qualitative analysis was also conducted on the feedback from the participants on their experiences of being in the different modes of processing around the meal time. This analysis highlighted that for some individuals, being focused on the present-moment in a mindful way was a valuable experience before the meal, however as cautioned by Park et al. (2012), for some it was experienced as overwhelming and aversive especially in the context of severe starvation or depression.

The study reported in Chapter 4 used an alternative methodology, namely neuroimaging. It was hoped that by gaining insight into the brain regions specifically involved in responding to rewarding and aversive food stimuli, objective evidence would be provided that cognitive processes (such as rumination) may be associated with symptom maintenance in AN (such as avoidance of eating).

As discussed in Chapter 1 (in Section 1.9), neuroimaging work relating to AN has employed tasks which include disorder-specific stimuli (for example, food and body images) as well as and non disorder-specific stimuli (for example, monetary rewards). Despite heterogeneity in the tasks, in addition to the status of the AN participants included (i.e., recovered, weight-restored or currently ill), consistent themes are starting to emerge from the data. The insula (particularly anterior insula), ventral striatum, anterior cingulate and the DLPFC all appear to be implicated in AN. This supports the neurobiological framework of Kaye, Fudge and Paulus (2009) which proposes that top-down neural circuits (prefrontal and cingulate regions) override the basic appetitive drives (for example, insula and ventral striatum).

Whether aberrant functioning of these regions can be demonstrated after recovery from AN is an important questions and was examined in Study 3 (Chapter 4) using a novel paradigm involving tastes and pictures of pleasant and aversive food stimuli. The neuroimaging data in Study 3 demonstrated that women with a history of AN had an aberrant neural response to the sight and taste of pleasant chocolate and aversive strawberry stimuli in regions of the brain involved in reward processing (ventral striatum) and cognitive control (prefrontal areas). The study also showed that some additional areas (namely the posterior cingulate, the putamen and the pallidum) exhibited increased activity when processing food related stimuli. Of particular interest was the increased activation in the posterior cingulate as this is an area which has been implicated in self-referential processing or rumination in the context of depression (Cooney et al., 2010; Johnson et al., 2006). One possible interpretation of the data reported in Chapter 4 was that food stimuli has increased salience in AN, but regions of the brain involved in cognitive control and rumination may be over engaged and function to control exposure to the salient stimuli. Thus reward related neural activation may not be able to override the inhibitory signals from cognitive control regions. As the study involved recovered AN participants, the possibility that there may be trait alterations in neural circuitry was raised and thus the results had potential implications for understanding the processes which maintain AN. Whilst speculative, it was suggested that the imbalance between the two neurocircuits becomes greater in line with starvation. Therefore, when individuals are currently ill with AN they may experience an even stronger conflict between the need to eat and the need to maintain control over eating, shape and weight. The clinical observation that individuals with AN often talk about wanting to recover but are unable to change their behaviours supports the notion that cognitive processes predominate in the ill state. However, in order to test this, the task would need to be replicated in those recovered alongside currently ill participants and those never-ill. This would also help tease apart trait versus scar effects of AN on neural circuitry.

The neuroimaging data in Chapter 4 suggested that that processing of rewarding stimuli may be aberrant in individuals with AN, even after recovery. The aim of

Chapter 5 was to further unpick the processes which may explain the aberrant responses to food rewards. Recent research from the neuroscience field has suggested reward is not a unitary process but may consist of subcomponents with separate neural underpinnings. In broad terms, it is thought that reward can be broken down into liking (hedonic pleasure or affect) and wanting (hedonic motivation or desire) processes (Berridge & Robinson, 2003; Berridge et al., 2009). These dual processes provide a novel framework for studying the response to food reward in AN. The study reported in Chapter 5 therefore employed a computer-based task which aims to measure the processes of liking and wanting for food reward at both an implicit and explicit level (Finlayson et al., 2008). Individuals at different stages of AN illness (current AN, weight-restored and recovered) as well as a HC group completed the study. The data suggested that individuals with AN (both underweight and weight-restored) had decreased explicit wanting and implicit 'wanting' for high calorie foods compared to those recovered from AN and HC participants, despite no difference in liking responses for the same food. Thus it was concluded that the aberrant response to food stimuli in AN may be associated more with decreased motivational wanting than hedonic liking and this may not be related purely to starvation.

For the final chapter of the thesis, neural networks were examined in participants recovered from AN using a FMRI technique called resting state functional connectivity. This technique, which studies neural activity in the absence of a task, had not been applied to data from AN participants before the study reported in Chapter 6. In line with the main propositions of this thesis, it was found that individuals recovered from AN showed increased functional connectivity between neural regions thought to be implicated in cognitive control and rumination. This final chapter therefore suggested that even in the absence of disorder-relevant stimuli (such as food), increased top-down processing can be indentified in individuals who have recovered from AN.

7.2.1 Integration of the principal findings

Figure 7.1 presents a tentative framework which attempts to integrate the main findings of the studies reported in Chapters 2 to 6. Figure 7.1 illustrates that rumination on eating, weight and shape may function to cognitively control the response to salient stimuli (such as chocolate). Based on the findings of Chapter 4 and Chapter 6, it is proposed that brain regions including the DLPFC, the posterior cingulate and the precuneus may underpin ruminative processing in AN. These regions have been associated with cognitive control and self-referential processing in previous studies (Cooney et al., 2010; Johnson et al., 2006). The increased top-down response may interact with somatosensory/appetite related processes which respond to the rewarding properties of the stimulus. At the neural level, the ventral striatum and the anterior insula are thought to be critically involved in this bottom-up processing circuit (as shown in Chapter 4). Akin to the role of rumination in depression and anxiety (Borkovec et al., 2004; Williams, 2010), thinking about the stimulus in a ruminative way may enable individuals with AN to avoid direct experience of the salient stimulus (as discussed in Chapter 2 and Chapter 3). Although there is a conflict between the cognitively driven need for control and the reward driven need to consume the food (as indicated in Chapter 5), cognitive processes override reward processes and bias the response to food. Thus individuals with AN are able to refrain from consuming energy-dense food, contributing to the maintenance of AN.

Figure 7.1 A proposed framework for understanding the role of rumination and reward processes in AN

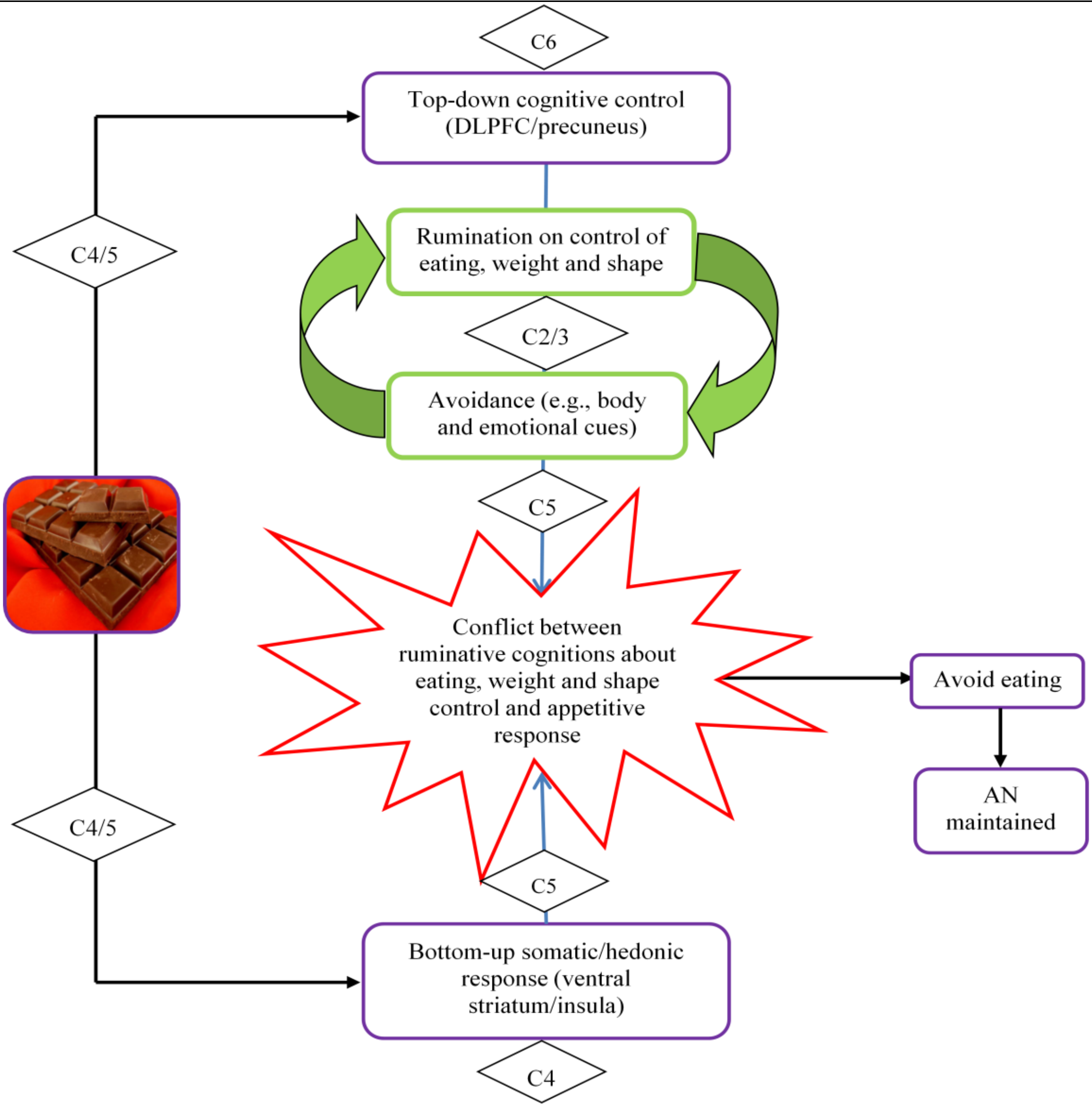


Figure 7.1
Interactions between top-down and bottom-up processes, each with distinct neural underpinnings, may explain control over food intake in AN. More specifically, cognitive processes (in the form of rumination about control of eating, weight and shape) override bottom-up reward processes. This may enable individuals with AN to severely restrict their intake despite their acute need for nourishment. Thus, rumination and reward processing are thought to contribute to the maintenance of AN.
Note. DLPFC: Dorsolateral prefrontal cortex
C: Relevant thesis chapter

7.3 Theoretical and clinical implications of the findings

7.3.1 Theoretical implications

Incorporating processes into cognitive theories of AN

Cognitive theories of AN have outlined the content of cognition which contribute to the onset and maintenance of the disorder. According to Fairburn, Cooper and Shafran's (2003) transdiagnostic theory, individuals with EDs over evaluate the importance of eating, weight shape and their ability to control them. For example, individuals may believe that their self-worth is entirely related to the ability to control eating. According to this account, distorted cognitions (for example, "in order to feel in control of my life I must control my eating") result in strict dieting and additional weight control behaviours (Fairburn et al., 2003). It is proposed that the reinforcing effect of weight loss, combined with the physiological effects of starvation, leads to the development and maintenance of AN (Fairburn et al., 2003). Whilst the content of cognition in AN can be identified using such theories, the specific processes through which distorted cognitions are translated into ED behaviours, such as dietary restriction, remain undefined. Frameworks of AN maintenance which highlight the underlying processes may therefore augment cognitive theories.

The aim of Figure 7.2 is to show how the processes examined in this thesis may complement existing cognitive accounts of the disorder, such as those described in Chapter 1. As suggested by Park et al. (2011, 2012), Figure 7.2 illustrates how rumination on disorder-specific themes may enable individuals with AN to avoid salient somatic (for example, hunger) and emotional cues. The process of rumination may therefore become highly valued and reinforced as it enables individuals to maintain strict control over their eating, weight and shape. Thus rumination on control of eating, weight and shape may be a process which enables AN symptoms to escalate.

Figure 7.2 Modified cognitive model of AN including the proposed maintaining process of rumination (and subsequent avoidance)

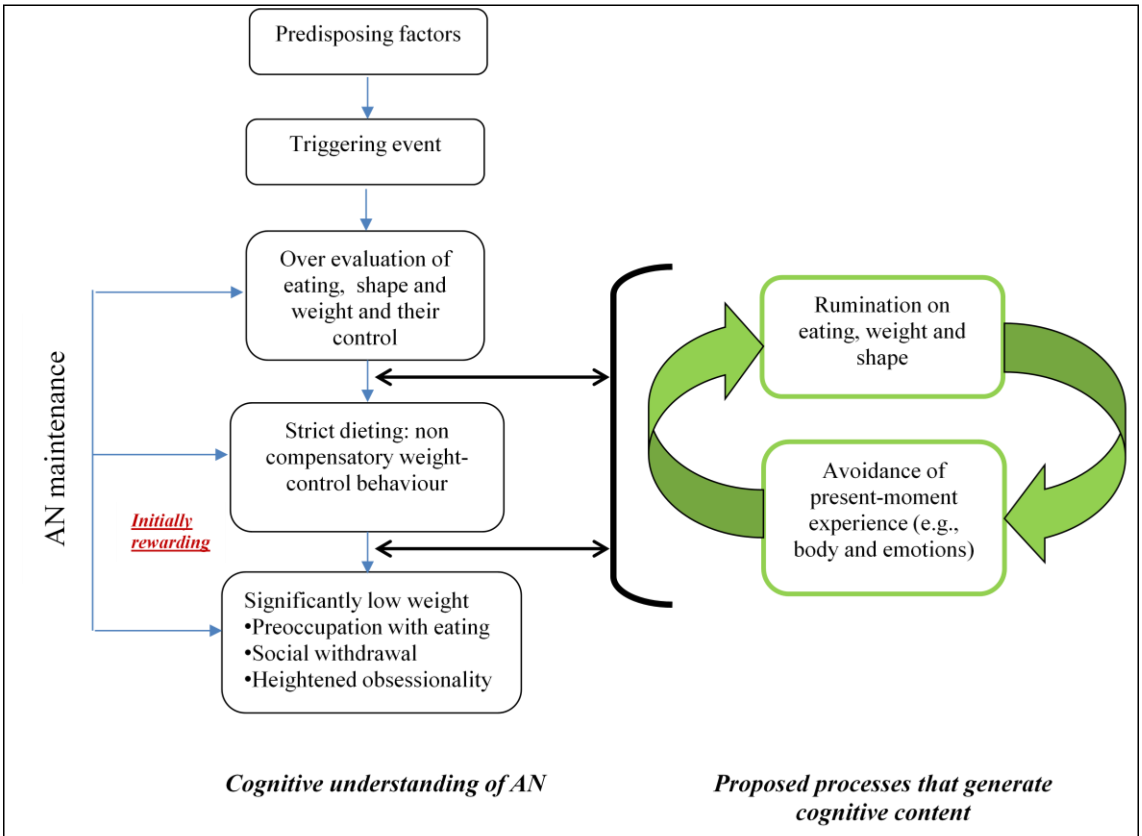


Figure 7.2
The processes of rumination and avoidance may facilitate dietary restriction in AN and therefore contribute to the maintenance of AN.

7.3.2 Clinical implications

Implications for cognitive-behavioural approaches to AN treatment

The data in this thesis suggests that AN symptoms may be maintained, at least in part, by ruminative processes. Whilst speculative, this may have implications for the treatment of AN. With regard to psychological treatments, CBT is often used in AN despite the evidence-base for its use being sparse (Fairburn, 2005). As part of CBT, a range of verbally-based strategies, such as food diaries and thought records, are used. It may be unrealistic to assume that such verbal interventions can readily change habitual cognitions and behaviours in AN if the mode of processing is not addressed first. For example, if a client with AN is ruminating about the need to control eating, weight and shape, it may be ineffective and possibly unhelpful to ask them to record their dietary intake as this could potentially trigger further restriction and ruminations about the need to control intake. As discussed by Park and colleagues (2011, 2012), using cognitive strategies whilst in a ruminative mode of mind may therefore contribute to symptom maintenance and potentially prevent engagement of the client in the therapeutic process. Instead, teaching strategies to help the client to shift from a ruminative mode to an experiential mode before the use of such verbal interventions may be helpful. Rather than ruminating and trying to avoid any aversive aspects of experience, the emphasis on self-acceptance and non-judgemental awareness of the present-moment may facilitate less emotional and behavioural reactivity to such cognitive interventions.

There is preliminary evidence that acceptance and mindfulness-based approaches may be useful in the treatment of non-underweight forms of EDs such as BED (as discussed by Baer, Fischer, & Huss, 2005; Kristeller & Wolever, 2010). However, as exemplified by a recent literature review, studies examining the application of mindfulness strategies to AN are sparse (Wanden-Berghe, Sanz-Valero, & Wanden-Berghe, 2010) and do not extend beyond pilot studies or case-reports (Heffner, Sperry, Eifert, & Detweiler, 2002; Rawal et al., 2009). As shown in Chapter 3, there are unique challenges of using such techniques in AN consistent with the predictions of Park et al. (2012). For example, using experiential strategies when individuals are currently ill with AN, particularly at difficult times such as meals, may increase the likelihood of individuals feeling emotionally overwhelmed. Further it was demonstrated in Chapter 3 that it is very difficult for individuals with AN to “switch out” of ruminative thought patterns.

Instead of proposing that mindful- and acceptance-based strategies *per se* may help reduce AN psychopathology, it is more useful to consider how strategies from these approaches can be adapted to address the unique challenges presented by clients with AN and at what stage of illness. As suggested by Park and colleagues (2012), training in awareness of senses which are not as emotionally-laden as the body in AN, such as sights and sound, may be a useful first step. Overtime, experiential training could move through a hierarchy of avoided and distressing experiences, with experiences such as aversive emotions, salient body parts (for example, stomach or hips) and energy-dense foods being worked on last and only after substantial training in cultivating an experiential mode of mind.

The hypothesis that non affect-laden strategies could be used to switch individuals with AN out of rumination has some preliminary evidence. Clave-Brule, Mazloum, Park, Harbottle, and Birmingham (2009) conducted a qualitative study examining the effect of a visuospatial activity (knitting) on anxious preoccupations in AN. Cognitive models of working memory suggest that visuospatial tasks selectively compete for limited processing capacity (Baddeley, 2003). Thus by engaging in a concurrent visuospatial task, it is plausible that the intensity of ruminative preoccupations on eating, weight and shape may decline due to the limited processing capacity of working memory. Indeed, the study reported that knitting did reduce anxious preoccupations about eating, weight and shape (Clave-Brule et al., 2009). As the study did not include a control condition, results should be interpreted cautiously. However, an earlier study with a similar rationale did include a control condition. In this study, it was found that different visuospatial tasks, such as a pattern tapping, reduced the vividness of food related imagery in a non-clinical sample compared to the control condition (Kemps, Tiggemann, Woods, & Soekov, 2004).

The relationship with the body is a challenging aspect of experience in AN which would eventually need to be addressed in the therapeutic process. There is preliminary evidence that helping clients shift from a mind-set which is dominated by thoughts about controlling the body, to a more accepting mind-set may be beneficial. Delinsky and Wilson (2006) compared mindful mirror exposure with a discussion-based body image intervention in women with extreme weight and shape concerns. Whilst both conditions resulted in reduced body checking, dieting, depression, avoidance and weight and shape concerns, the effect was significantly greater for the mindful mirror exposure compared to the non-exposure condition (Delinsky & Wilson, 2006). Whilst these results are encouraging, a study employing a dismantling design is needed to ascertain whether the results can be explained by exposure to the body alone or whether the mindfulness instructions are a fundamental component.

Whilst bearing in mind the limitations, findings from the preliminary studies discussed above support the contention that gradually training clients with AN to process salient information in a mindful and accepting way may be beneficial. It is important to reiterate that the suggestion here is not to replace existing cognitive and behavioural techniques used in AN treatment. Rather the suggestion is to supplement core therapeutic tasks with process-oriented strategies and thereby potentially increase their effectiveness.

Reward processing as a treatment target in AN

The studies reported in Chapters 4 and 5 examined the processing of food stimuli at both the behavioural and neural level and differences were identified between those with experience of AN and those never ill. More specifically in Chapter 5 it was found that individuals with AN may not have difficulties experiencing the hedonic (liking) properties of rewarding food, but rather they show a reduced desire to consume these foods and instead exhibit a greater motivational drive (implicit ‘wanting’) to consume low-calorie foods. This is likely to reflect the overvalued ideation about controlling eating, weight and shape that is central to cognitive theories of AN. The data in Chapters 4 and 5 therefore emphasises the need to move beyond conceptualising eating behaviour in AN as a symptom of anhedonia and rather examine the processes which may motivate approach or avoidance of low and high calorie foods. Using this approach, it may be possible to develop targeted strategies to augment existing interventions that make balanced, appropriate eating something that is liked and wanted, rather than the restrictive eating practices which are seemingly valued by individuals with AN, even after weight restoration.

Neuromodulation as a potential treatment strategy in AN

Data from Studies 3 and 5 (Chapters 4 and 6) tentatively identified neurobiological markers associated with increased rumination and aberrant food reward processing in AN. This neuroimaging data also has potential treatment implications as there is emerging research suggesting that neuromodulatory techniques, focusing on areas thought to be involved in cognitive control and reward processing, may influence core ED symptoms. For example, Van den Eynde, Guillaume, Broadbent, Campbell, and Schmidt (2012) conducted a pilot study in which repetitive transcranial magnetic stimulation (rTMS) was administered to the left DLPFC in participants with the binge-eating/purging type of AN following exposure to food stimuli. It was found that after one session of rTMS focusing on the left DLPFC, participants with AN reported significantly reduced anxiety as well as feelings of fullness and fatness (Van den Eynde, Guillaume, Broadbent, Campbell, & Schmidt, 2012). Whilst not investigated in this exploratory study, it would be of interest to examine whether the reduction in core symptoms of AN following rTMS were associated with changes in processes style, for example reductions in rumination, and also whether these changes translate into behavioural modification (such as increased food consumption).

Further, whilst not yet subject to empirical investigation, it has been hypothesised that deep brain stimulation (DBS) in regions of the brain implicated in feeding behaviour and reward processing, may be a fruitful avenue for AN treatment development (Benabid & Torres, 2012). In sum, it seems that the brain regions implicated in reward processing and cognitive control, identified in Studies 3 and 5 (Chapters 4 and 6), may be key targets for brain modulation techniques in the future.

7.4 General limitations of the research presented

Specific limitations have been identified for each study in the respective chapter. This section will therefore detail more general limitations of the research presented.

One limitation of the research presented in the current thesis is the use of self-report to measure complex psychological processes in AN. This is particularly pertinent to Chapters 2 and 3. Beyond the general limitations of self-reporting (for example, social desirability biases, demand characteristics, extreme versus moderacy response styles and concerns about the reliability and/or validity of questionnaires), there are additional concerns in using this methodology in AN participants. Cognitive impairment due to low weight, medication, and degree of psychopathology are just a few of the variables that are likely to influence the accuracy of self-report. Further, as detailed by Vitousek and Manke (1994), individuals with AN typically have poor introspective skills and this may interfere with the ability to accurately report on their internal experiences. Lastly, Teasdale and Barnard (1993) have made a distinction between cognitions that are “intellectual” (not associated with emotion production) and "emotional" (with emotional content and meaning). It is possible that questionnaires, particularly those that measure complex processes such as avoidance or rumination, only access intellectual meaning, whereas the emotional response and personal meaning of the cognitions may be more relevant for understanding AN maintenance. Whilst self-report has significant limitations, especially when employed in AN samples, the conclusions derived from the studies relying on self-report in this thesis were corroborated by using more objective methodologies, such as neuroimaging.

As well as self-reporting on processes such as rumination and avoidance, Studies 1 and 2 (Chapters 2 and 3) relied on self-reported diagnosis. An important question therefore is whether self-reported diagnoses are as accurate as those obtained through clinician/researcher administered interviews. Several studies have investigated this issue by comparing self-report measures (such as the EDE-Q) with diagnoses arrived through interviews. Whilst the results from these studies are not entirely consistent, the general consensus seems to be that self-reported overall diagnosis (for example AN or BN) is usually credible and in line with the diagnosis arrived at through interview (for example, Wolk et al., 2005). However, it seems that specific features of EDs which are harder to define objectively, such as binge-eating, and comorbid conditions are less likely to be captured accurately by self-report. Therefore, despite being more labour intensive, diagnosis based on interviews by trained clinicians or researchers are more likely to result in accurate diagnoses, including subtype classifications and comorbidities. In this thesis, whilst some studies relied on self-reported diagnosis and thus should be treated with caution, others employed researcher-led diagnostic interviews.

Akin to the participants recruited for the initial RRS-ED validation (Chapter 2), a number of studies in the ED literature have used analogue/non-clinical participants. The debate as to whether studies using non-clinical participant can contribute to the understanding of AN is therefore relevant for this thesis and may be considered a limitation. On the one hand, the processes examined in this thesis may be conceptualised as essentially normal processes that have gone awry or exaggerated in AN. For example, Watkins (2008) suggests that engaging in prolonged and repetitive thinking about one's self is a normative process, but it becomes exaggerated in psychopathological conditions. There is also some evidence that regards eating, weight and shape concerns on a continuum. For example, Cooper and Turner (2000) reported that participants with AN had significantly greater assumptions about shape and weight than non-dieting controls, but that essentially healthy dieters score in-between the AN and non-dieters on the same subscale. Therefore, whilst using non-clinical participants to examine cognitive-affective components in AN cannot substitute clinical data, there seems to be some value in using such participants, particularly when considering the practical advantages (for example, collecting a large sample in a short period of time).

This thesis did not set out to directly evaluate whether rumination and/or reward processing function differently in the AN subtypes (restriction versus binge-eating/purging). There is evidence that the different subtypes of AN may differ in some psychological characteristics which potentially have different neural underpinnings. For example, people with the binge-eating/purging type of AN are often found to be more impulsive and higher in novelty seeking than those with restricting type AN (Fassino, Amianto, Gramaglia, Facchini, & Daga, 2004). At the neural level, structural and functional differences have been found between the two subtypes which may reflect the varying levels of appetite restraint (Brooks et al., 2011; Brooks, O'Daly, Uher, Friederich et al., 2012). Thus by including both types of AN in some of the studies reported in this thesis (for example, Chapter 5), additional variability (or noise) may have been introduced. Future studies may benefit from having purer AN samples and devising specific hypotheses about the processes which differ between AN subtypes. However, this would be challenging due to the relative rarity of the disorder, particularly the binge-eating/purging type (Favaro, Ferrara, & Santonastaso, 2003), as well as the high levels of migration between ED diagnoses (Milos, Spindler, Schnyder, & Fairburn, 2005). Similarly, in this thesis there was limited discussion of whether rumination and/or reward processing are expected to operate differently in other forms of EDs (such as BN or BED) and thus the results cannot generalise to other EDs. However, given the pressing need to develop effective evidence-based treatments for AN, there is a clear rationale for the specific focus on AN in this thesis.

7.5 Future directions

As demonstrated in this thesis, there is emerging psychological and neurobiological evidence highlighting the relevance of aberrant reward processing and rumination on eating weight and shape in AN. Although a number of future directions for research have been identified within the respective chapters, general future directions will be outlined below.

The focus of the current thesis was restricted to rumination and aberrant reward processing as these been hypothesised by the ICS account to make significant contributions to the maintenance of AN (Park et al., 2011, 2012). Whilst the data in this thesis has been able to demonstrate that such processes are important in understanding AN psychopathology, a number of other potentially relevant processes were not studied. This provides a clear avenue for further research. For example, interoceptive processes, referring to the perception and representation of bodily signals, are thought to be relevant for modulating approach and avoidance behaviours (Herbert & Pollatos, 2012). By examining interoception in AN it would be possible to test the hypothesis from the ICS account of AN that altered feedback from the body interacts with cognitive processes (such as rumination) and potentially contributes to the maintenance of the disorder (Park et al., 2012).

A range of cross-sectional data highlighting a possible link between cognitive processes and symptoms of AN (such as dysfunctional processing of rewarding food stimuli) have been presented in the thesis. An important area for future research will be to test directional hypotheses, for example, whether the process of rumination contributes to relapse in AN. Therefore, follow-up studies are required to examine whether the mode of processing changes across course of the illness and whether this is associated with changes in AN symptoms. By doing so it may be possible to test bidirectional hypotheses between rumination and AN symptoms.

Repetitive negative thinking (i.e., rumination, worry and preoccupation) has been examined across a range of psychological disorders and it has been suggested that this thinking style may be more usefully conceptualised as a transdiagnostic process (Harvey, Watkins, Mansell, & Shafran, 2004). The studies reported in Chapter 2 and 3 examined rumination in AN and found that whilst rumination has a similar function to that of other psychological disorders (i.e., rumination has an avoidant function), the content or flavour of the rumination is different in AN as it specifically focuses on eating, weight and shape and the ability to control these indices. It may therefore be that previous studies examining rumination in the context of EDs (for example, Aldao, Nolen-Hoeksema, & Schweizer, 2011; Nolen-Hoeksema et al., 2007; Rawal et al., 2010) which have employed measures which examine rumination in the context of depression, do not accurately capture the unique content of rumination found in AN. Future studies employing the RRS-ED may help further delineate the role that ruminative processing has in the maintenance of ED symptoms and contribute to the understanding of repetitive negative thinking as a transdiagnostic process.

The neuroimaging work reported in Chapters 4 and 6 recruited participants recovered from AN to avoid the confound of starvation associated with the currently ill state and also to examine potential trait markers. However, without also using the same paradigm with a currently ill sample, it is difficult to determine whether the neural aberrancies found in the recovered AN participants can explain the ED behaviours that characterise the ill state. Whilst other studies have employed paradigms which involve the presentation of food stimuli in current AN, the heterogeneity between the paradigms mean that a direct comparison cannot be made. Further, no study to date has investigated resting state functional connectivity in current AN. It would therefore be of value to study individuals currently ill with AN using the same approaches as reported in Chapters 4 and 6. This would determine whether the same neural aberrancies are seen when the individuals are currently engaging in ED behaviours (such as restriction) and thus lead to more accurate hypotheses about how these neural regions are implicated in the maintenance of AN.

Whilst not the central aim of this thesis, both the process of rumination and the aberrant response to rewarding stimuli have been investigated in the context of other psychopathologies which are often found coexist with AN, such as depression. Thus by studying rumination and reward processing in AN, consideration can be given as to how AN may differ at a process level from depression and determine what the characteristic psychological features of AN are. For example, a previous study using the reward paradigm described in Chapter 4, identified that participants recovered from depression have a decreased neural response in the ventral striatum to the rewarding chocolate taste compared to a HC group (McCabe et al., 2009). This is the opposite of that reported in the recovered AN participants in Chapter 4 and therefore suggests that there may be important differences in processing rewarding stimuli between the two disorders. Similarly, in terms of rumination, the data in this thesis suggests that the content of rumination in AN is different to that seen in depression, despite it serving a similar avoidant function. As well as future studies including a depressed control group allowing direct comparisons to be made across disorders, future studies could systematically explore the differences in rumination and reward processing between those with AN, those with AN and comorbid depression, as well as HCs. This is particularly important given that psychiatric comorbidity has been shown to be an unfavourable prognostic factor for AN (Papadopoulos, Ekborn, Brandt, & Ekselius, 2010).

7.6 Summary and conclusion of the thesis

To improve the outcome of AN, effective evidence-based treatments need to be developed. Before effective treatments can be developed, a better appreciation of how complex processes shape behaviours in AN needs to be gained. This thesis therefore explored the role of rumination and aberrant reward processing in the maintenance of AN. The findings of the thesis suggest that individuals with AN are ruminative on themes of eating, weight and shape and that a modified version of the Ruminative Response Scale may provide a useful tool to capture ruminative processing in AN. The findings confirm that it is difficult to interrupt rumination in AN when untrained in mindfulness and that fostering greater awareness of present-moment experience may leave individuals with AN feeling overwhelmed and out of control. Brain regions involved in rumination and reward processing were found to function aberrantly even after recovery from AN and this could in part explain why individuals with AN display altered motivational ‘wanting’ responses to high calories foods.

In sum, the findings of this thesis suggest that AN maintenance might involve the interplay between cognitive processes, such as rumination, and altered appetitive drives. It is hoped that the work in this thesis will refine current theoretical knowledge and this will in turn lead to a better understanding of AN and eventually the development of novel treatment strategies.

References

Abela, J. R. Z., Brozina, K., & Haigh, E. P. (2002). An examination of the response styles theory of depression in third- and seventh-grade children: A short-term longitudinal study. *Journal of Abnormal Child Psychology, 30*(5), 515-527.

Aharoni, R., & Hertz, M. M. (2012). Disgust sensitivity and anorexia nervosa. *European Eating Disorders Review*, *20*(2), 106-110.

Aigner, M., Treasure, J., Kaye, W., & Kasper, S. (2011). World federation of societies of biological psychiatry (WFSBP) guidelines for the pharmacological treatment of eating disorders. *World Journal of Biological Psychiatry, 12*(6), 400-443.

Aldao, A., & Nolen-Hoeksema, S. (2010). Specificity of cognitive emotion regulation strategies: A transdiagnostic examination. *Behaviour Research and Therapy, 48*(10), 974-983.

Aldao, A., Nolen-Hoeksema, S., & Schweizer, S. (2011). Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clinical Psychology Review, 30*(2), 217-237.

American Psychiatric Association (1994). *Diagnostic and statistical manual of mental health disorders* (4th ed.). Washington, DC: American Psychiatric Publishing.

Anand, A., Li, Y., Wang, Y., Wu, J., Gao, S., Bukhari, L., et al. (2005). Activity and connectivity of brain mood regulating circuit in depression: A functional magnetic resonance study. *Biological Psychiatry, 57*(10), 1079-1088.

Arch, J. J., & Craske, M. G. (2006). Mechanisms of mindfulness: Emotion regulation following a focused breathing induction. *Behaviour Research and Therapy, 44*(12), 1849-1858.

Arcelus, J., Mitchell, A. J., Wales, J., & Nielsen, S. (2011). Mortality rates in patients with anorexia nervosa and other eating disorders: A meta-analysis of 36 studies. *Archives of General Psychiatry*, *68*(7), 724-731.

Attia, E., & Roberto, C. A. (2009). Should amenorrhea be a diagnostic criterion for anorexia nervosa? *International Journal of Eating Disorders, 42*(7), 581-589.

Baddeley, A. (2003). Working memory: looking back and looking forward. *Nature Review Neuroscience, 4*(10), 829-839.

Baer, R., Fischer, S., & Huss, D. (2005). Mindfulness and acceptance in the treatment of disordered eating. *Journal of Rational-Emotive & Cognitive-Behavior Therapy, 23*(4), 281-300.

Baer, R. A., Smith, G. T., Hopkins, J., Krietemeyer, J., & Toney, L. (2006). Using self-report assessment methods to explore facets of mindfulness. *Assessment, 13*(1), 27-45.

Bagby, M. R., Rector, N. A., Segal, Z. V., Joffe, R. T., Levitt, A. J., Kennedy, S. H., et al. (1999). Rumination and distraction in major depression: assessing response to pharmacological treatment. *Journal of Affective Disorders, 55*(2-3), 225-229.

Bailer, U. F., Frank, G. K., Henry, S. E., Price, J. C., Meltzer, C. C., Mathis, C. A., et al. (2007). Exaggerated 5-HT1A but normal 5-HT2A receptor activity in individuals ill with anorexia nervosa. *Biological Psychiatry, 61*(9), 1090-1099.

Bailer, U. F., Frank, G. K., Henry, S. E., Price, J. C., Meltzer, C. C., Weissfeld, L., et al. (2005). Altered brain serotonin 5-HT1A receptor binding after recovery from anorexia nervosa measured by positron emission tomography and [Carbonyl11C]WAY-100635. *Archives of General Psychiatry, 62*(9), 1032-1041.

Bailer, U., & Kaye, W. (2011). Serotonin: Imaging findings in eating disorders. In R. Adan & W. Kaye (Eds.), *Behavioral neurobiology of eating disorders* (1 ed., Vol. 6, pp. 59-79). New York: Springer.

Bardone-Cone, A. M., Harney, M. B., Maldonado, C. R., Lawson, M. A., Robinson, D. P., Smith, R., et al. (2010). Defining recovery from an eating disorder: Conceptualization, validation, and examination of psychosocial functioning and psychiatric comorbidity. *Behaviour Research and Therapy*, *48*(3), 194-202.

Beck, A. T. (1972). *Depression: Causes and treatment*: University of Pennsylvania Press.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck depression inventory-II* (2nd ed.). San Antonio, Texas: Psychological Corporation.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*(6), 561-571

Becker, A. E., Thomas, J. J., & Pike, K. M. (2009). Should non-fat-phobic anorexia nervosa be included in DSM-V? *International Journal of Eating Disorders, 42*(7), 620-635.

Beckmann, C. F., DeLuca, M., Devlin, J. T., & Smith, S. M. (2005). Investigations into resting-state connectivity using independent component analysis. *Philosophical Transactions of the Royal Society B: Biological Sciences, 360*(1457), 1001-1013.

Benabid, A. L., & Torres, N. (2012). New targets for DBS. *Parkinsonism & Related Disorders, 18, Supplement 1*, S21-S23.

Berman, M. G., Peltier, S., Nee, D. E., Kross, E., Deldin, P. J., & Jonides, J. (2010). Depression, rumination and the default network. *Social Cognitive and Affective Neuroscience, 6*(5), 548-555.

Berridge, K. C. (2009). Liking and wanting food rewards: Brain substrates and roles in eating disorders. *Physiology & Behavior, 97*(5), 537-550.

Berridge, K. C., Ho, C.-Y., Richard, J. M., & DiFeliceantonio, A. G. (2010). The tempted brain eats: Pleasure and desire circuits in obesity and eating disorders. *Brain Research, 1350*, 43-64.

Berridge, K. C., & Robinson, T. E. (2003). Parsing reward. *Trends in Neurosciences, 26*(9), 507-513.

Berridge, K. C., Robinson, T. E., & Aldridge, J. W. (2009). Dissecting components of reward: 'liking', 'wanting', and learning. *Current Opinion in Pharmacology, 9*(1), 65-73.

Berthoud, H.-R., & Morrison, C. (2008). The brain, appetite, and obesity. *Annual Review of Psychology, 59*(1), 55-92.

Beshai, S., Dobson, K. S., Bockting, C. L. H., & Quigley, L. (2011). Relapse and recurrence prevention in depression: Current research and future prospects. *Clinical Psychology Review, 31*(8), 1349-1360.

Binford, R. B., Le Grange, D., & Jellar, C. C. (2005). Eating disorders examination versus eating disorders examination-questionnaire in adolescents with full and partial-syndrome bulimia nervosa and anorexia nervosa. *International Journal of Eating Disorders, 37*(1), 44-49.

Bishop, S., Lau, M., Shapiro, S., Carlson, L., Anderson, N., Carmody, J., et al. (2004). Mindfulness: a proposed operational definition. *Clinical Psychology: Science and Practice, 11*(13), 230-241.

Biswal, B. B., Mennes, M., Zuo, X.-N., Gohel, S., Kelly, C., Smith, S. M., et al. (2010). Toward discovery science of human brain function. *Proceedings of the National Academy of Sciences, 107*(10), 4734-4739.

Blood, A. J., & Zatorre, R. J. (2001). Intensely pleasurable responses to music correlate with activity in brain regions implicated in reward and emotion. *Proceedings of the National Academy of Sciences, 98*(20), 11818-11823.

Bluhm, R., Williamson, P., Lanius, R., Théberge, J., Densmore, M., Bartha, R., et al. (2009). Resting state default-mode network connectivity in early depression using a seed region-of-interest analysis: Decreased connectivity with caudate nucleus. *Psychiatry and Clinical Neurosciences, 63*(6), 754-761.

Bohn, K., Doll, H. A., Cooper, Z., O'Connor, M., Palmer, R. L., & Fairburn, C. G. (2008). The measurement of impairment due to eating disorder psychopathology. *Behaviour Research and Therapy, 46*(10), 1105-1110.

Bohon, C., & Stice, E. (2012a). Negative affect and neural response to palatable food intake in bulimia nervosa. *Appetite, 58*(3), 964-970.

Bohon, C., & Stice, E. (2012b). Reward abnormalities among women with full and subthreshold bulimia nervosa: A functional magnetic resonance imaging study. *International Journal of Eating Disorders, 44*(7), 585-595.

Boly, M., Phillips, C., Tshibanda, L., Vanhaudenhuyse, A., Schabus, M., Dang-Vu, T. T., et al. (2008). Intrinsic brain activity in altered states of consciousness. *Annals of the New York Academy of Sciences, 1129*(1), 119-129.

Bond, F. W., Hayes, S. C., Baer, R. A., Carpenter, K. M., Guenole, N., Orcutt, H. K., et al. (2011). Preliminary psychometric properties of the Acceptance and Action Questionnaire-II: A revised measure of psychological inflexibility and experiential avoidance. *Behavior Therapy, 42*(4), 676-688.

Borkovec, T. D., Alcaine, O., & Behar, E. (2004). Avoidance theory of worry and generalized anxiety disorder. In R. G. Heimberg, C. L. Turk & D. S. Mennin (Eds.), *Generalized anxiety disorder: Advances in research and practice* (pp. 77-108). New York: Guilford.

Bosanac, P., Kurlender, S., Stojanovska, L., Hallam, K., Norman, T., McGrath, C., et al. (2007). Neuropsychological study of underweight and “weight-recovered” anorexia nervosa compared with bulimia nervosa and normal controls. *International Journal of Eating Disorders, 40*(7), 613-621.

Brinker, J. K., & Dozois, D. J. A. (2009). Ruminative thought style and depressed mood. *Journal of Clinical Psychology, 65*(1), 1-19.

Broderick, P. C., & Korteland, C. (2004). A prospective study of rumination and depression in early adolescence. *Clinical Child Psychology and Psychiatry, 9*(3), 383-394.

Brooks, S. J., O Daly, O. G., Uher, R., Friederich, H.-C., Giampietro, V., Brammer, M., et al. (2011). Differential neural responses to food images in women with bulimia versus anorexia nervosa. *PLoS ONE, 6*(7), e22259.

Brooks, S. J., O'Daly, O., Uher, R., Friederich, H.-C., Giampietro, V., Brammer, M., et al. (2012). Thinking about eating food activates visual cortex with reduced bilateral cerebellar activation in females with anorexia nervosa: An fMRI study. *PLoS ONE, 7*(3), e34000.

Brooks, S. J., O' Daly, O. G., Uher, R., Schiöth, H. B., Treasure, J., & Campbell, I. C. (2012). Subliminal food images compromise superior working memory performance in women with restricting anorexia nervosa. *Consciousness and Cognition, 21*(2), 751-763.

Brooks, S., Prince, A., Stahl, D., Campbell, I. C., & Treasure, J. (2011). A systematic review and meta-analysis of cognitive bias to food stimuli in people with disordered eating behaviour. *Clinical Psychology Review, 31*(1), 37-51

Bruch, H. (1978). *The golden cage. The enigma of anorexia nervosa*. Cambridege, Massachusetts: Harvard University Press.

Butler, L. D., & Nolen-Hoeksema, S. (1994). Gender differences in responses to depressed mood in a college sample. *Sex Roles, 30*(5), 331-346.

Burger, K. S., & Stice, E. (2011). Relation of dietary restraint scores to activation of reward-related brain regions in response to food intake, anticipated intake, and food pictures. *Neuroimage, 55*(1), 233-239.

Cardi, V., Kan, C., Roncero, M., Harrison, A., Lounes, N., Tchanturia, K., et al. (2012). Mealtime support in anorexia nervosa: A within- subject comparison study of a novel vodcast intervention. *Psychotherapy and Psychosomatics, 81*(1), 54-55.

Carei, T. R., Fyfe-Johnson, A. L., Breuner, C. C., & Brown, M. A. (2010). Randomized controlled clinical trial of yoga in the treatment of eating disorders. *Journal of Adolescent Health, 46*(4), 346-351.

Carmody, J., & Baer, R. (2008). Relationships between mindfulness practice and levels of mindfulness, medical and psychological symptoms and well-being in a mindfulness-based stress reduction program. *Journal of Behavioral Medicine, 31*(1), 23-33.

Carter, F. A., Jordan, J., McIntosh, V. V. W., Luty, S. E., McKenzie, J. M., Frampton, C. M. A., et al. (2011). The long-term efficacy of three psychotherapies for anorexia nervosa: A randomized, controlled trial. *International Journal of Eating Disorders, 44*(7), 647-654.

Carter, J. C., Blackmore, A. D., Sutandar-Pinnock, K., & Woodside, D. B. (2004). Relapse in anorexia nervosa: a survival analysis. *Psychological Medicine, 34*(04), 671-679.

Castro-Fornieles, J., Bargalló, N., Lázaro, L., Andrés, S., Falcon, C., Plana, M. T., et al. (2009). A cross-sectional and follow-up voxel-based morphometric MRI study in adolescent anorexia nervosa. *Journal of Psychiatric Research, 43*(3), 331-340.

Castro, L., Davies, H., Hale, L., Surguladze, S., & Tchanturia, K. (2010). Facial affect recognition in anorexia nervosa: is obsessionality a missing piece of the puzzle? *Australian and New Zealand Journal of Psychiatry, 44*(12), 1118-1125.

Cattell, R.B. (1978). The scientific use of factor analysis. New York: Plenum.

Cavada, C., & Goldman-Rakic, P. S. (1991). Topographic segregation of corticostriatal projections from posterior parietal subdivisions in the macaque monkey. *Neuroscience, 42*(3), 683-696.

Cavanna, A. E., & Trimble, M. R. (2006). The precuneus: a review of its functional anatomy and behavioural correlates. *Brain, 129*(3), 564-583.

Cavedini, P., Zorzi, C., Bassi, T., Gorini, A., Baraldi, C., Ubbiali, A., et al. (2006). Decision-making functioning as a predictor of treatment outcome in anorexia nervosa. *Psychiatry Research, 145*(2-3), 179-187.

Cepeda-Benito, A., Gleaves, D. H., Williams, T. L., & Erath, S. A. (2000). The development and validation of the state and trait food-cravings questionnaires. *Behavior Therapy, 31*(1), 151-173.

Channon, S., & DeSilva, W. P. (1985). Psychological correlates of weight gain in patients with anorexia nervosa. *Journal of Psychiatric Research, 19*(2-3), 267-271.

Christopoulos, G. I., Tobler, P. N., Bossaerts, P., Dolan, R. J., & Schultz, W. (2009). Neural correlates of value, risk, and risk aversion contributing to decision making under risk. *The Journal of Neuroscience, 29*(40), 12574-12583.

Clave-Brule, M., Mazloum, A., Park, R. J., Harbottle, E. J., & Birmingham, C. L. (2009). Managing anxiety in eating disorders with knitting. *Eating and Weight Disorders, 14*(1), 1-5.

Cole, M. W., & Schneider, W. (2007). The cognitive control network: Integrated cortical regions with dissociable functions. *Neuroimage, 37*(1), 343-360.

Cooney, R., Joormann, J., Eugène, F., Dennis, E., & Gotlib, I. (2010). Neural correlates of rumination in depression. *Cognitive, Affective, & Behavioral Neuroscience, 10*(4), 470-478.

Cooper, M., & Turner, H. (2000). Underlying assumptions and core beliefs in anorexia nervosa and dieting. *British Journal of Clinical Psychology, 39*(2), 215-218.

Corcos, M., Guilbaud, O., Speranza, M., Paterniti, S., Loas, G., Stephan, P., et al. (2000). Alexithymia and depression in eating disorders. *Psychiatry Research, 93*(3), 263-266.

Corstorphine, E., Mountford, V., Tomlinson, S., Waller, G., & Meyer, C. (2007). Distress tolerance in the eating disorders. *Eating Behaviors, 8*(1), 91-97.

Costafreda, S. G., Brammer, M. J., David, A. S., & Fu, C. H. Y. (2008). Predictors of amygdala activation during the processing of emotional stimuli: A meta-analysis of 385 PET and fMRI studies. *Brain Research Reviews, 58*(1), 57-70.

Cowdrey, F. A., Harmer, C. J., Park, R. J., & McCabe, C. (2011). Neural responses to emotional faces in women recovered from anorexia nervosa. *Psychiatry Research: Neuroimaging*. doi: 10.1016/j.psychresns.2011.08.009

Crane, C., Barnhofer, T., & Williams, J. M. G. (2007). Reflection, brooding, and suicidality: A preliminary study of different types of rumination in individuals with a history of major depression. *British Journal of Clinical Psychology, 46*(4), 497-504.

Cribb, G., Moulds, M., & Carter, S. (2006). Rumination and experiential avoidance in depression. *Behaviour change, 23*(3), 165-176.

Crisp, A. H., & Fransella, F. (1972). Conceptual changes during recovery from anorexia nervosa. *British Journal of Medical Psychology, 45*(4), 395-405.

Critchley, H. D. (2005). Neural mechanisms of autonomic, affective, and cognitive integration. *The Journal of Comparative Neurology, 493*(1), 154-166.

Critchley, H. D., Tang, J., Glaser, D., Butterworth, B., & Dolan, R. J. (2005). Anterior cingulate activity during error and autonomic response. *Neuroimage, 27*(4), 885-895.

Damoiseaux, J. S., Rombouts, S. A. R. B., Barkhof, F., Scheltens, P., Stam, C. J., Smith, S. M., et al. (2006). Consistent resting-state networks across healthy subjects. *Proceedings of the National Academy of Sciences, 103*(37), 13848-13853.

Davey, G. C. L., & Chapman, L. (2009). Disgust and eating disorder symptomatology in a non-clinical population: The role of trait anxiety and anxiety sensitivity. *Clinical Psychology & Psychotherapy, 16*(4), 268-275.

Davis, C., & Woodside, D. B. (2002). Sensitivity to the rewarding effects of food and exercise in the eating disorders. *Comprehensive Psychiatry, 43*(3), 189-194.

de Araujo, I. E. T., Kringelbach, M. L., Rolls, E. T., & McGlone, F. (2003). Human cortical responses to water in the mouth, and the effects of thirst. *Journal of Neurophysiology, 90*(3), 1865-1876.

Delgado, M. R., Jou, R. L., & Phelps, E. A. (2011). Neural systems underlying aversive conditioning in humans with primary and secondary reinforcers. *Frontiers in Neuroscience, 5*(71), 1-10.

Delinsky, S. S., & Wilson, G. T. (2006). Mirror exposure for the treatment of body image disturbance. *International Journal of Eating Disorders, 39*(2), 108-116

DelParigi, A., Chen, K., Salbe, A. D., Hill, J. O., Wing, R. R., Reiman, E. M., et al. (2003). Persistence of abnormal neural responses to a meal in postobese individuals. *International Journal of Obesity & Related Metabolic Disorders, 28*(3), 370-377.

Douaud, G. l., Smith, S., Jenkinson, M., Behrens, T., Johansen-Berg, H., Vickers, J., et al. (2007). Anatomically related grey and white matter abnormalities in adolescent-onset schizophrenia. *Brain, 130*(9), 2375-2386.

Eddy, K. T., Dorer, D. J., Franko, D. L., Tahilani, K., Thompson-Brenner, H., & Herzog, D. B. (2008). Diagnostic crossover in anorexia nervosa and bulimia nervosa: Implications for DSM-V. *American Journal of Psychiatry, 165*(2), 245-250.

Eddy, K. T., Keel, P. K., Dorer, D. J., Delinsky, S. S., Franko, D. L., & Herzog, D. B. (2002). Longitudinal comparison of anorexia nervosa subtypes. *International Journal of Eating Disorders, 31*(2), 191-201.

Ehlers, A., & Clark, D. M. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy, 38*(4), 319-345.

Eiber, R., Berlin, I., de Brettes, B., Foulon, C., & Guelfi, J. D. (2002). Hedonic response to sucrose solutions and the fear of weight gain in patients with eating disorders. *Psychiatry Research, 113*(1-2), 173-180.

Erisman, S. M., & Roemer, L. (2010). A preliminary investigation of the effects of experimentally induced mindfulness on emotional responding to film clips. *Emotion, 10*(1), 72-82.

Fairburn, C. G. (2008). *Cognitive Behavior Therapy and Eating Disorders*. New York: The Guilford Press.

Fairburn, C. G. (2005). Evidence-based treatment of anorexia nervosa. *International Journal of Eating Disorders, 37*(S1), S26-S30.

Fairburn, C. G., & Beglin, S. J. (2008). Eating disorder examination questionnaire (EDE-Q 6.0). In C. Fairburn (Ed.), *Cognitive behaviour therapy and eating disorders* (pp. 309-313). New York: Guildford Press.

Fairburn, C., & Bohn, K. (2005). Eating disorder NOS (EDNOS): an example of the troublesome "not otherwise specified" (NOS) category in DSM-IV. *Behaviour Research and Therapy, 43*(6), 691-701.

Fairburn, C. G., & Cooper, Z. (2011). Eating disorders, DSM-5 and clinical reality. *The British Journal of Psychiatry, 198*(1), 8-10.

Fairburn, C., G, Cooper, Z., & Shafran, R. (2003). Cognitive behaviour therapy for eating disorders: a "transdiagnostic" theory and treatment. *Behaviour Research and Therapy, 41*(5), 509-528.

Fairburn, C. G., & Harrison, P. J. (2003). Eating disorders. *The Lancet, 361*(9355), 407-416.

Fairburn, C. G., Shafran, R., & Cooper, Z. (1999). A cognitive behavioural theory of anorexia nervosa. *Behaviour Research and Therapy, 37*(1), 1-13.

Fassino, S., Pierò, A., Gramaglia, C., & Abbate-Daga, G. (2004). Clinical, psychopathological and personality correlates of interoceptive awareness in anorexia nervosa, bulimia nervosa and obesity. *Psychopathology, 37*(4), 168-174.

Favaro, A., Ferrara, S., & Santonastaso, P. (2003). The spectrum of eating disorders in young women: A prevalence study in a general population sample. *Psychosomatic Medicine, 65*(4), 701-708.

Fawcett, J., Clark, D. C., Scheftner, W. A., & Gibbons, R. D. (1983). Assessing anhedonia in psychiatric patients: The pleasure scale. *Archives of General Psychiatry, 40*(1), 79-84.

Feldman, G., Greeson, J., & Senvill, J. (2011). Differential effects of mindful breathing, progressive muscle relaxation, and loving kindness meditation on decentering and negative reactions to repetitive thoughts. *Behaviour Research and Therapy, 48*(10), 1002-1011.

Filippini, N., MacIntosh, B. J., Hough, M. G., Goodwin, G. M., Frisoni, G. B., Smith, S. M., et al. (2009). Distinct patterns of brain activity in young carriers of the APOE-ε4 allele. *Proceedings of the National Academy of Sciences, 106*(17), 7209-7214.

Finlayson, G., Arlotti, A., Dalton, M., King, N., & Blundell, J. E. (2011). Implicit wanting and explicit liking are markers for trait binge eating. A susceptible phenotype for overeating. *Appetite, 57*(3), 722-728.

Finlayson, G., Bordes, I., Griffioen-Roose, S., de Graaf, C., & Blundell, J. E. (2012). Susceptibility to overeating affects the impact of savory or sweet drinks on satiation, reward, and food intake in nonobese women. *The Journal of Nutrition, 142*(1), 125-130.

Finlayson, G., King, N., & Blundell, J. (2008). The role of implicit wanting in relation to explicit liking and wanting for food: Implications for appetite control. *Appetite, 50*(1), 120-127.

Finlayson, G., King, N., & Blundell, J. E. (2007). Is it possible to dissociate 'liking' and 'wanting' for foods in humans? A novel experimental procedure. *Physiology and Behavior, 90*(1), 36-42.

Fladung, A.-K., Gron, G., Grammer, K., Herrnberger, B., Schilly, E., Grasteit, S., et al. (2009). A neural signature of anorexia nervosa in the ventral striatal reward system. *American Journal of Psychiatry* (167), 206-212.

Flament, M. F., Bissada, H., & Spettigue, W. (2011). Evidence-based pharmacotherapy of eating disorders. *The International Journal of Neuropsychopharmacology, 15* (2), 189-207.

Fornaro, M., Perugi, G., Gabrielli, F., Prestia, D., Mattei, C., Vinciguerra, V., et al. (2010). Lifetime co-morbidity with different subtypes of eating disorders in 148 females with bipolar disorders. *Journal of Affective Disorders, 121*(1-2), 147-151.

Frank, G. K., Bailer, U. F., Henry, S. E., Drevets, W., Meltzer, C. C., Price, J. C., et al. (2005). Increased dopamine D2/D3 receptor binding after recovery from anorexia nervosa measured by positron emission tomography and [11C]raclopride. *Biological Psychiatry, 58*(11), 908-912.

Frank, G. K. W., Reynolds, J. R., Shott, M. E., Jappe, L., Yang, T. T., Tregellas, J. R., et al. (2012). Anorexia nervosa and obesity are associated with opposite brain reward response. *Neuropsychopharmacology*. doi: 10.1035/npp.2012.51.

Franko, D. L., Keel, P. K., Dorer, D. J., Blais, M. A., Delinsky, S. S., Eddy, K. T., et al. (2004). What predicts suicide attempts in women with eating disorders? *Psychological Medicine, 34*(05), 843-853.

Friederich, H-C., Walther, S., Bendszus, M., Biller, A., Thomann, P., Zeigermann, S., et al. (2012). Grey matter abnormalities within cortico-limbic-striatal circuits in acute and weight-restored anorexia nervosa patients. *Neuroimage 59*(2), 1106-1113.

Friston, K. J., Glaser, D. E., Henson, R. N. A., Kiebel, S., Phillips, C., & Ashburner, J. (2002). Classical and bayesian inference in neuroimaging: applications. *Neuroimage, 16*(2), 484-512.

Friston, K. J., Worsley, K. J., Frackowiak, R. S. J., Mazziotta, J. C., & Evans, A. C. (1994). Assessing the significance of focal activations using their spatial extent. *Human Brain Mapping, 1*, 214-220.

Garner, D. M., & Bemis, K. M. (1982). A cognitive-behavioral approach to anorexia nervosa. *Cognitive Therapy and Research, 6*(2), 123-150.

Giel, K., Teufel, M., Friederich, H.-C., Hautzinger, M., Enck, P., & Zipfel, S. (2011). Pictorial food stimuli and eating disorders. *International Journal of Eating Disorders, 44*(2), 105-117.

Gizewski, E. R., Rosenberger, C., de Greiff, A., Moll, A., Senf, W., Wanke, I., et al. (2010). Influence of satiety and subjective valence rating on cerebral activation patterns in response to visual stimulation with high-calorie stimuli among restrictive anorectic and control women. *Neuropsychobiology, 62*(3), 182-192.

Godart, N. T., Perdereau, F., Rein, Z., Berthoz, S., Wallier, J., Jeammet, P., et al. (2007). Comorbidity studies of eating disorders and mood disorders. Critical review of the literature. *Journal of Affective Disorders, 97*(1-3), 37-49.

Gordon, C. M., Dougherty, D. D., Fischman, A. J., Emans, S. J., Grace, E., Lamm, R., et al. (2001). Neural substrates of anorexia nervosa: A behavioral challenge study with positron emission tomography. *The Journal of Pediatrics, 139*(1), 51-57.

Greenwald, A. G., Nosek, B. A., & Banaji, M. R. (2003). Understanding and using the implicit association test: I. An improved scoring algorithm: Correction to Greenwald et al. (2003). *Journal of Personality and Social Psychology, 85*(3), 481.

Greicius, M. D. (2008). Resting-state functional connectivity in neuropsychiatric disorders. *Current Opinion in Neurology, 21*(4), 424-430.

Greicius, M. D., Supekar, K., Menon, V., & Dougherty, R. F. (2009). Resting-state functional connectivity reflects structural connectivity in the default mode network. *Cerebral Cortex, 19*(1), 72-78.

Griffioen-Roose, S., Finlayson, G., Mars, M., Blundell, J. E., & de Graaf, C. (2010). Measuring food reward and the transfer effect of sensory specific satiety. *Appetite, 55*(3), 648-655.

Griffioen-Roose, S., Mars, M., Siebelink, E., Finlayson, G., Tome, D., & de Graaf, C. (2012). Protein status elicits compensatory changes in food intake and food preferences. *The American Journal of Clinical Nutrition, 95*(1), 32-38.

Guarda, A. S. (2008). Treatment of anorexia nervosa: Insights and obstacles. *Physiology & Behavior, 94*(1), 113-120.

Guillaume, S., Sang, C., N-T, Jaussent, I., Raingeard, I., Bringer, J., Jollant, F., et al. (2010). Is decision making really impaired in eating disorders? *Neuropsychology, 24*(6), 808-812.

Gusnard, D. A., Akbudak, E., Shulman, G. L., & Raichle, M. E. (2001). Medial prefrontal cortex and self-referential mental activity: Relation to a default mode of brain function. *Proceedings of the National Academy of Sciences, 98*(7), 4259-4264.

Gusnard, D. A., & Raichle, M. E. (2001). Searching for a baseline: Functional imaging and the resting human brain. *Nature Review Neuroscince, 2*(10), 685-694.

Hambrook, D., Oldershaw, A., Rimes, K., Schmidt, U., Tchanturia, K., Treasure, J., et al. (2011). Emotional expression, self-silencing, and distress tolerance in anorexia nervosa and chronic fatigue syndrome. *British Journal of Clinical Psychology, 50*(3), 310-325.

Hamilton, J. P., Furman, D. J., Chang, C., Thomason, M. E., Dennis, E., & Gotlib, I. H. (2010). Default-mode and task-positive network activity in major depressive disorder: Implications for adaptive and maladaptive rumination. *Biological Psychiatry, 70*(4), 327-333.

Harmer, C. J., Hill, S. A., Taylor, M. J., Cowen, P. J., & Goodwin, G. M. (2003). Toward a neuropsychological theory of antidepressant drug action: Increase in positive emotional bias after potentiation of norepinephrine activity. *American Journal of Psychiatry, 160*(5), 990-992.

Harrison, A., O'Brien, N., Lopez, C., & Treasure, J. (2010). Sensitivity to reward and punishment in eating disorders. *Psychiatry Research, 177*(1-2), 1-11.

Harrison, A., Tchanturia, K., & Treasure, J. (2010). Attentional bias, emotion recognition, and emotion regulation in anorexia: State or trait? *Biological Psychiatry, 68*(8), 755-761.

Harrison, A., Treasure, J., & Smillie, L. D. (2011). Approach and avoidance motivation in eating disorders. *Psychiatry Research, 188*(3), 396-401.

Harvey, A., Watkins, E., Mansell, W., & Shafran, R. (2004). *Cognitive behavioural processes across psychological disorders: A transdiagnostic approach to research and treatment* Oxford: Oxford University Press.

Hasler, G., & Northoff, G. (2011). Discovering imaging endophenotypes for major depression. *Molecular Psychiatry, 16*(6), 604-619.

Hayasaka, S., Phan, K. L., Liberzon, I., Worsley, K. J., & Nichols, T. E. (2004). Nonstationary cluster-size inference with random field and permutation methods. *Neuroimage, 22*(2), 676-687.

Hayes, A. M., & Feldman, G. (2004). Clarifying the construct of mindfulness in the context of emotion regulation and the process of change in therapy. *Clinical Psychology: Science and Practice, 11*(3), 255-262.

Hebebrand, J., & Bulik, C. M. (2011). Critical appraisal of the provisional DSM-5 criteria for anorexia nervosa and an alternative proposal. *International Journal of Eating Disorders*, *44*(8), 665-678.

Heffner, M., Sperry, J., Eifert, G. H., & Detweiler, M. (2002). Acceptance and commitment therapy in the treatment of an adolescent female with anorexia nervosa: A case example. *Cognitive and Behavioral Practice*, *9*(3), 232-236.

Herbert, B. M., & Pollatos, O. (2012). The body in the mind: On the relationship between interoception and embodiment. *Topics in Cognitive Science*. doi:10.111/j.1756-87652012.01189.x.

Herzog, D. B., Keller, M. B., Sacks, N. R., Yeh, C. J., & Lavori, P. W. (1992). Psychiatric comorbidity in treatment-seeking anorexics and bulimics. *Journal of the American Academy of Child & Adolescent Psychiatry, 31*(5), 810-818.

Hetherington, M. M., & Rolls, B. J. (1991). Eating behavior in eating disorders: Response to preloads. *Physiology & Behavior, 50*(1), 101-108.

Hilt, L. M., & Pollak, S. D. (2012). Getting out of rumination: Comparison of three brief interventions in a sample of youth. *Journal of Abnormal Child Psychology*.

Holmes, E. A., Mathews, A., Dalgleish, T., & Mackintosh, B. (2006). Positive interpretation training: Effects of mental imagery versus verbal training on positive mood. *Behavior Therapy, 37*(3), 237-247.

Holsen, L. M., Lawson, E. A., Blum, J., Ko, E., Makris, N., Fazeli, P. K., et al. (2012). Food motivation circuitry hypoactivation related to hedonic and nonhedonic aspects of hunger and satiety in women with active anorexia nervosa and weight-restored women with anorexia nervosa. *Journal of Psychiatry Neuroscience, 37*(3), 1-11.

Hoshi, E., & Tanji, J. (2004). Area-selective neuronal activity in the dorsolateral prefrontal cortex for information retrieval and action planning. *Journal of Neurophysiology, 91*(6), 2707-2722.

Hoyer, J., Gloster, AT, Herzberg, PY (2009). Is worry different from rumination? Yes, it is more predictive of psychopathology! *Psychosocial medicine, 5*(6), 1-9.

Hudson, J. I., Hiripi, E., Pope Jr, H. G., & Kessler, R. C. (2007). The prevalence and correlates of eating disorders in the national comorbidity survey replication. *Biological Psychiatry, 61*(3), 348-358.

Ingram, R. E. (1990). Self-focused attention in clinical disorders: Review and a conceptual model. *Psychological Bulletin, 107*(2), 156-176.

Jänsch, C., Harmer, C., & Cooper, M. J. (2009). Emotional processing in women with anorexia nervosa and in healthy volunteers. *Eating Behaviors, 10*(3), 184-191.

Jappe, L. M., Frank, G. K. W., Shott, M. E., Rollin, M. D. H., Pryor, T., Hagman, J. O., et al. (2011). Heightened sensitivity to reward and punishment in anorexia nervosa. *International Journal of Eating Disorders, 44*(4), 317-324.

Jauregui Lobera, I., & Bolanos Rios, P. (2009). Choice of diet in patients with anorexia nervosa. *Nutrición Hospitalaria, 24*(6), 682-687.

Jenkinson, M., Beckmann, C. F., Behrens, T. E. J., Woolrich, M. W., & Smith, S. M. (2011). FSL. *Neuroimage*. doi:10.1016/j.neuroimage.2011.09.015.

Jiang, T., Soussignan, R., Rigaud, D., & Schaal, B. (2010). Pleasure for visual and olfactory stimuli evoking energy-dense foods is decreased in anorexia nervosa. *Psychiatry Research, 180*(1), 42-47.

Johnson, M. K., Raye, C. L., Mitchell, K. J., Touryan, S. R., Greene, E. J., & Nolen-Hoeksema, S. (2006). Dissociating medial frontal and posterior cingulate activity during self-reflection. *Social Cognitive and Affective Neuroscience, 1*(1), 56-64.

Joormann, J., Dkane, M., & Gotlib, I. H. (2006). Adaptive and maladaptive components of rumination? Diagnostic specificity and relation to depressive biases. *Behavior Therapy, 37*(3), 269-280.

Joos, A., Hartmann, A., Glauche, V., Perlov, E., Unterbrink, T., Saum, B., et al. (2011). Grey matter deficit in long-term recovered anorexia nervosa patients. *European Eating Disorders Review, 19*(1), 59-63.

Kabat-Zinn, J. (1994). *Wherever you go, there you are: Mindfulness meditation in everyday life.* New York: Hyperion.

Kalm, L. M., & Semba, R. D. (2005). They starved so that others be better fed: Remembering Ancel Keys and the Minnesota experiment. *The Journal of Nutrition, 135*(6), 1347-1352.

Katzman, D. K., Zipursky, R. B., Lambe, E. K., & Mikulis, D. J. (1997). A longitudinal magnetic resonance imaging study of brain changes in adolescents with anorexia nervosa. *Archives of Pediatrics and Adolescent Medicine, 151*(8), 793-797.

Kaye, W. H., Bulik, C. M., Thornton, L., Barbarich, N., Masters, K., & the Price Foundation Collaborative Group (2004). Comorbidity of anxiety disorders with anorexia and bulimia nervosa. *American Journal of Psychiatry, 161*(12), 2215-2221.

Kaye, W. H., Frank, G. K., Bailer, U. F., Henry, S. E., Meltzer, C. C., Price, J. C., et al. (2005). Serotonin alterations in anorexia and bulimia nervosa: New insights from imaging studies. *Physiology & Behavior, 85*(1), 73-81.

Kaye, W. H., Fudge, J. L., & Paulus, M. (2009). New insights into symptoms and neurocircuit function of anorexia nervosa. *Nature Review Neuroscience, 10*(8), 573-584.

Keating, C., Tilbrook, A. J., Rossell, S. L., Enticott, P. G., & Fitzgerald, P. B. (2012). Reward processing in anorexia nervosa. *Neuropsychologia, 50*(5) 567-575.

Kemps, E., Tiggemann, M., Woods, D., & Soekov, B. (2004). Reduction of food cravings through concurrent visuospatial processing. *International Journal of Eating Disorders, 36*(1), 31-40.

Knutson, B., Adams, C. M., Fong, G. W., & Hommer, D. (2001). Anticipation of increasing monetary reward selectively recruits nucleus accumbens. *The Journal of Neuroscience, 21*(16), RC159.

Klump, K. L., Strober, M., Bulik, C. M., Thornton, L., Johnson, C., Devlin, B., et al. (2004). Personality characteristics of women before and after recovery from an eating disorder. *Psychological Medicine, 34*(08), 1407-1418.

Koelsch, S. (2010). Towards a neural basis of music-evoked emotions. *Trends in Cognitive Sciences, 14*(3), 131-137.

Kordy, H., Krämer, B., Palmer, R. L., Papezova, H., Pellet, J., Richard, M., et al. (2002). Remission, recovery, relapse, and recurrence in eating disorders: Conceptualization and illustration of a validation strategy. *Journal of Clinical Psychology, 58*(7), 833-846.

Kristeller, J. L., & Hallett, C. B. (1999). An exploratory study of a meditation-based intervention for binge eating disorder. *Journal of Health Psychology, 4*(3), 357-363.

Kristeller, J. L., & Wolever, R. Q. (2010). Mindfulness-based eating awareness training for treating binge eating disorder: The conceptual foundation. *Eating Disorders: The Journal of Treatment & Prevention, 19*(1), 49-61.

Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ-9. *Journal of General Internal Medicine, 16*(9), 606-613.

Kuyken, W., Byford, S., Taylor, R. S., Watkins, E., Holden, E., White, K., et al. (2008). Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *Journal of Consulting and Clinical Psychology, 76*(6), 966-978.

Kwon, P., & Olson, M. L. (2007). Rumination and depressive symptoms: Moderating role of defence style immaturity. *Personality and Individual Differences, 43*(4), 715-724.

Lavender, J. M., & Anderson, D. A. (2010). Contribution of emotion regulation difficulties to disordered eating and body dissatisfaction in college men. *International Journal of Eating Disorders, 43*(4), 352-357.

Lavender, J. M., Gratz, K. L., & Tull, M. T. (2011). Exploring the relationship between facets of mindfulness and eating pathology in women. *Cognitive Behaviour Therapy, 40*(3), 174-182.

Lavender, J. M., Jardin, B. F., & Anderson, D. A. (2009). Bulimic symptoms in undergraduate men and women: Contributions of mindfulness and thought suppression. *Eating Behaviors, 10*(4), 228-231.

leDoux, J. (2003). The emotional brain, fear, and the amygdala. *Cellular and Molecular Neurobiology, 23*(4), 727-738.

Liao, P-C., Uher, R., Lawrence, N., Treasure, J., Schmidt, U., Campbell, I. C., et al. (2009). An examination of decision making in bulimia nervosa. *Journal of Clinical and Experimental Neuropsychology, 31*(4), 455 - 461.

Lindner, S. E., Fichter, M. M., & Quadflieg, N. (2012). Decision-making and planning in full recovery of anorexia nervosa. *International Journal of Eating Disorders*. doi:10.1002/eat.22025.

Luce, K. H., & Crowther, J. H. (1999). The reliability of the eating disorder examination – Self-report questionnaire version (EDE-Q). *International Journal of Eating Disorders, 25*(3), 349-351.

Lyubomirsky, S., & Nolen-Hoeksema, S. (1993). Self-perpetuating properties of dysphoric rumination. *Journal of Personality and Social Psychology, 65*(2), 339-349.

Lyubomirsky, S., & Tkach, C. (2008). The consequences of dysphoric rumination. In C. Papageorgiou, A. Wells (Eds.), *Depressive Rumination. Nature, Theory and Treatment* (pp. 21-41): John Wiley & Sons Ltd: UK.

Martin, L. L., & Tesser, A. T. (1996). Some ruminative thoughts. In R. S. Wyer (Ed.), *Ruminative thoughts: Adavances in social cognition* (Vol. IX, pp. 1-47): Lawrence Erlbaum Associates.

Masuda, A., & Wendell, J. W. (2010). Mindfulness mediates the relation between disordered eating-related cognitions and psychological distress. *Eating Behaviors, 11*(4), 293-296.

McCabe, C., Cowen, P. J., & Harmer, C. J. (2009). Neural representation of reward in recovered depressed patients. *Psychopharmacology, 205*, 667-677.

McCabe, C., & Mishor, Z. (2011). Antidepressant medications reduce subcortical-cortical resting-state functional connectivity in healthy volunteers. *Neuroimage, 57*(4), 1317-1323.

McCabe, C., Mishor, Z., Cowen, P. J., & Harmer, C. J. (2010). Diminished neural processing of aversive and rewarding stimuli during selective serotonin reuptake inhibitor treatment. *Biological Psychiatry, 67*(5), 439-445.

McCabe, C., Mishor, Z., Filippini, N., Cowen, P. J., Taylor, M. J., & Harmer, C. J. (2011). SSRI administration reduces resting state functional connectivity in dorso-medial prefrontal cortex. *Molecular Psychiatry, 16*(6), 592-594.

McCabe, C., Rolls, E. T., Bilderbeck, A., & McGlone, F. (2008). Cognitive influences on the affective representation of touch and the sight of touch in the human brain. *Social Cognitive and Affective Neuroscience, 3*(2), 97-108.

McClure, S. M., Laibson, D. I., Loewenstein, G., & Cohen, J. D. (2004). Separate neural systems value immediate and delayed monetary rewards. *Science, 306*(5695), 503-507.

McEvoy, P. M., Mahoney, A. E. J., & Moulds, M. L. (2010). Are worry, rumination, and post-event processing one and the same?: Development of the repetitive thinking questionnaire. *Journal of Anxiety Disorders, 24*(5), 509-519.

McIntosh, V. V. W., Jordan, J., Carter, F. A., Luty, S. E., McKenzie, J. M., Bulik, C. M., et al. (2005). Three psychotherapies for anorexia nervosa: A randomized, controlled trial. *American Journal of Psychiatry, 162*(4), 741-747.

McMurrich, S., & Johnson S. L. (2008). Dispositional rumination in individuals with a depression history. *Cognitive Therapy and Research, 32*(4), 542-555.

Mela, D. J. (2006). Eating for pleasure or just wanting to eat? Reconsidering sensory hedonic responses as a driver of obesity. *Appetite, 47*(1), 10-17.

Milos, G., Spindler, A., Schnyder, U., & Fairburn, C. G. (2005). Instability of eating disorder diagnoses: prospective study. *The British Journal of Psychiatry, 187*(6), 573-578.

Miranda, R., & Nolen-Hoeksema, S. (2007). Brooding and reflection: Rumination predicts suicidal ideation at 1-year follow-up in a community sample. *Behaviour Research and Therapy, 45*(12), 3088-3095.

Mischoulon, D., Eddy, K. T., Keshaviah, A., Dinescu, D., Ross, S. L., Kass, A. E., et al. (2011). Depression and eating disorders: Treatment and course. *Journal of Affective Disorders, 130*(3), 470-477.

Mond, J. M., Hay, P. J., Rodgers, B., & Owen, C. (2006). Eating disorder examination questionnaire (EDE-Q): Norms for young adult women. *Behaviour Research and Therapy, 44*(1), 53-62.

Mond, J. M., Hay, P. J., Rodgers, B., & Owen, C. (2007). Self-report versus interview assessment of purging in a community sample of women. *European Eating Disorders Review*, *15*(6), 403-409.

Morrow, J., & Nolen-Hoeksema, S. (1990). Effects of responses to depression on the remediation of depressive affect. *Journal of Personality and Social Psychology, 58*(3), 519-527.

Murphy, F. C., Nimmo-Smith, I., Lawrence, A.D (2003). Functional neuroanatomy of emotions: A meta-analysis. *Cognitive Affective & Behavioral Neuroscience 3*(3), 207-233.

Nelson, H. E., & Willison, J. R. (1991). *The revised National Adult Reading Test-Test Manual.*Windor UK: NFER-Nelson.

Nichols, T. E., & Holmes, A. P. (2002). Nonparametric permutation tests for functional neuroimaging: A primer with examples. *Human Brain Mapping, 15*(1), 1-25.

Nolen-Hoeksema, S. (1987). Sex differences in unipolar depression: Evidence and theory. *Psychological Bulletin, 101*(2), 259-282.

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *Journal of Abnormal Psychology, 100*(4), 569-582.

Nolen-Hoeksema, S., & Davis, C. G. (1999). "Thanks for sharing that": Ruminators and their social support networks. *Journal of Personality and Social Psychology, 77*(4), 801-814.

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster: The 1989 Loma Prieta earthquake. *Journal of Personality and Social Psychology, 61*(1), 115-121.

Nolen-Hoeksema, S., Parker, L. E., & Larson, J. (1994). Ruminative coping with depressed mood following loss. *Journal of Personality and Social Psychology, 67*(1), 92-104.

Nolen-Hoeksema, S., Stice, E., Wade, E., & Bohon, C. (2007). Reciprocal relations between rumination and bulimic, substance abuse, and depressive symptoms in female adolescents. [longitudinal study]. *Journal of Abnormal Psychology, 116*(1), 198-207.

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*(5), 400-424.

Ochner, C. N., Stice, E., Hutchins, E., Afifi, L., Geliebter, A., Hirsch, J., et al. (2012). Relation between changes in neural responsivity and reductions in desire to eat high-calorie foods following gastric bypass surgery. *Neuroscience, 209*, 128-135.

O'Doherty, J., Rolls, E. T., Francis, S., Bowtell, R., & McGlone, F. (2001). Representation of pleasant and aversive taste in the human brain. *Journal of Neurophysiology, 85*(3), 1315-1321.

Palmer, R. L., Birchall, H., Damani, S., Gatward, N., McGrain, L., & Parker, L. (2003). A dialectical behavior therapy program for people with an eating disorder and borderline personality disorder-description and outcome. *International Journal of Eating Disorders, 33*(3), 281-286.

Papadopoulos, F. C., Ekbom, A., Brandt, L., & Ekselius, L. (2009). Excess mortality, causes of death and prognostic factors in anorexia nervosa. *The British Journal of Psychiatry, 194*(1), 10-17.

Paradiso, S., Johnson, D. L., Andreasen, N. C., O'Leary, D. S., Watkins, G. L., Boles Ponto, L. L., et al. (1999). Cerebral blood flow changes associated with attribution of emotional valence to pleasant, unpleasant, and neutral visual stimuli in a PET study of normal subjects. *American Journal of Psychiatry, 156*(10), 1618-1629.

Park, R. J., Dunn, B. D., & Barnard, P. J. (2011). Schematic models and modes of mind in anorexia nervosa I: A novel process account *International Journal of Cognitive Therapy, 4*(4), 415-437.

Park, R. J., Dunn, B. D., & Barnard, P. J. (2012). Schematic models and modes of mind in anorexia nervosa II: Implications for treatment and course. *International Journal of Cognitive Therapy, 5*(1), 86-98.

Park, R. J., Goodyer, I. M., & Teasdale, J. D. (2004). Effects of induced rumination and distraction on mood and over general autobiographical memory in adolescent major depressive disorder and controls. *Journal of Child Psychology and Psychiatry, 45*(5), 996

Parling, T., Mortazavi, M., & Ghaderi, A. (2010). Alexithymia and emotional awareness in anorexia nervosa: Time for a shift in the measurement of the concept? *Eating Behaviors, 11*(4), 205-210.

Pearson, K. A., Watkins, E. R., Mullan, E. G., & Moberly, N. J. (2010). Psychosocial correlates of depressive rumination. *Behaviour Research and Therapy, 48*(8), 784-791.

Peat, C., Mitchell, J. E., Hoek, H. W., & Wonderlich, S. A. (2009). Validity and utility of subtyping anorexia nervosa. *International Journal of Eating Disorders, 42*(7), 590-594.

Phillips, M. L., Young, A. W., Senior, C., Brammer, M., Andrew, C., Calder, A. J., et al. (1997). A specific neural substrate for perceiving facial expressions of disgust. *Nature, 389*(6650), 495-498.

Piet, J., & Hougaard, E. (2011). The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: A systematic review and meta-analysis. *Clinical Psychology Review, 31*(6), 1032-1040.

Pope, C., Ziebland, S., & Mays, N. (2000). Analysing qualitative data. *British Medical Journal, 320*(7227), 114-116.

Pyka, M., Beckmann, C. F., Schoning, S., Hauke, S., Heider, D., Kugel, H., et al. (2009). Impact of working memory load on fMRI resting state pattern in subsequent resting phases. *PLoS ONE, 4*(9), e7198.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences, 98*(2), 676-682.

Rawal, A., Enayati, J., Williams, J. M. G., & Park, R. J. (2009). A mindful approach to eating disorders. *Healthcare Counselling and Psychotherapy Journal, 9*(4), 16-20.

Rawal, A., Park, R. J., & Williams, J. M. G. (2010). Rumination, experiential avoidance, and dysfunctional thinking in eating disorders. *Behaviour Research and Therapy, 48*(9), 851-859.

Rawal, A., Williams, J. M. G., & Park, R. J. (2011). Effects of analytical and experiential self-focus on stress-induced cognitive reactivity in eating disorder psychopathology. *Behaviour Research and Therapy, 49*(10), 635-645.

Roberto, C. A., Mayer, L. E. S., Brickman, A. M., Barnes, A., Muraskin, J., Yeung, L.-K., et al. (2011). Brain tissue volume changes following weight gain in adults with anorexia nervosa. *International Journal of Eating Disorders, 44*(5), 406-411.

Robinson, T. E., & Berridge, K. C. (2001). Incentive-sensitization and addiction. *Addiction, 96*(1), 103-114.

Rogers, R. D., Ramnani, N., Mackay, C., Wilson, J. L., Jezzard, P., Carter, C. S., et al. (2004). Distinct portions of anterior cingulate cortex and medial prefrontal cortex are activated by reward processing in separable phases of decision-making cognition. *Biological Psychiatry, 55*(6), 594-602.

Rolls, E. T., & McCabe, C. (2007). Enhanced affective brain representations of chocolate in cravers vs. non-cravers. *European Journal of Neuroscience, 26*(4), 1067-1076.

Root, T. L., Pinheiro, A. P., Thornton, L., Strober, M., Fernandez-Aranda, F., Brandt, H., et al. (2010). Substance use disorders in women with anorexia nervosa. *International Journal of Eating Disorders, 43*(1), 14-21.

Rothemund, Y., Preuschhof, C., Bohner, G., Bauknecht, H.-C., Klingebiel, R., Flor, H., et al. (2007). Differential activation of the dorsal striatum by high-calorie visual food stimuli in obese individuals. *Neuroimage, 37*(2), 410-421.

Sanders, W. A., & Lam, D. H. (2010). Ruminative and mindful self-focused processing modes and their impact on problem solving in dysphoric individuals. *Behaviour Research and Therapy, 48*(8), 747-753.

Santel, S., Baving, L., Krauel, K., Münte, T. F., & Rotte, M. (2006). Hunger and satiety in anorexia nervosa: fMRI during cognitive processing of food pictures. *Brain Research, 1114*(1), 138-148.

Schmidt, U., & Treasure, J. (2006). Anorexia nervosa: Valued and visible. A cognitive-interpersonal maintenance model and its implications for research and practice. *British Journal of Clinical Psychology, 45*, 343-366.

Schultz, W. (2002). Getting formal with dopamine and reward. *Neuron, 36*(2), 241-263.

Schultz, W., Dayan, P., & Montague, P. R. (1997). A neural substrate of prediction and reward. *Science, 275*(5306), 1593-1599.

Segal, Z. V., Williams, J. M. G., & Teasdale, J. D. (2002). *Mindfulness- based cognitive therapy for depression. A new approach for preventing relapse*. New York: Guilford.

Segerstrom, S. C., Stanton, A. L., Alden, L. E., & Shortridge, B. E. (2003). A multidimensional structure for repetitive thought: What's on your mind, and how, and how much? *Journal of Personality and Social Psychology, 85*(5), 909-921.

Seger, C. A., & Cincotta, C. M. (2005). The roles of the caudate nucleus in human classification learning. *The Journal of Neuroscience, 25*(11), 2941-2951.

Selby, E., Connell, L., & Joiner, T. (2010). The pernicious blend of rumination and fearlessness in non-suicidal self-injury. *Cognitive Therapy and Research, 34*(5), 421-428.

Serpell, L., Treasure, J., Teasdale, J., & Sullivan, V. (1999). Anorexia nervosa: Friend or foe? *International Journal of Eating Disorders, 25*(2), 177-186.

Sheline, Y. I., Price, J. L., Yan, Z., & Mintun, M. A. (2010). Resting-state functional MRI in depression unmasks increased connectivity between networks via the dorsal nexus. *Proceedings of the National Academy of Sciences, 107*(24), 11020-11025.

Shulman, G. L., Fiez, J. A., Corbetta, M., Buckner, R. L., Miezin, F. M., Raichle, M. E., et al. (1997). Common blood flow changes across visual tasks: II. Decreases in cerebral cortex. *Journal of Cognitive Neuroscience, 9*(5), 648-663.

Slade, P. (1982). Towards a functional analysis of anorexia nervosa and bulimia nervosa. *British Journal of Clinical Psychology, 21*(3), 167-179.

Small, D. M., Jones-Gotman, M., Zatorre, R. J., Petrides, M., & Evans, A. C. (1997). A Role for the right anterior temporal lobe in taste quality recognition. *Journal of Neuroscience, 17*(13), 5136-5142.

Smith, S. M., & Nichols, T. E. (2009). Threshold-free cluster enhancement: Addressing problems of smoothing, threshold dependence and localisation in cluster inference. *Neuroimage, 44*(1), 83-98.

Speranza, M., Loas, G., Wallier, J., & Corcos, M. (2007). Predictive value of alexithymia in patients with eating disorders: A 3-year prospective study. *Journal of Psychosomatic Research, 63*(4), 365-371.

Spielberger, C., Gorsuch, RC, Lushene, RE, Vagg, PR, Jacobs, GA (1983). *Manual for the state-trait anxiety inventory*. Palo Alto: Consulting Psychologist Press.

Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Lowe, B. (2006). A brief measure for assessing Generalized Anxiety Disorder: The GAD-7. *Archives Internal Medicine, 166*(10), 1092-1097.

Spitzer, R., Williams, J., Gibbon, M., & First, M. (2004). *Structured clinical interview for the DSM-IV (SCID-I/P).* Arlington, VA: American Psychiatric Press.

Stein, M. B., Simmons, A. N., Feinstein, J. S., & Paulus, M. P. (2007). Increased amygdala and insula activation during emotion processing in anxiety-prone subjects. *American Journal of Psychiatry, 164*(2), 318-327.

Steinglass, J. E., Figner, B., Berkowitz, S., Simpson, H. B., Weber, E. U., & Walsh, B. T. (2012). Increased capacity to delay reward in anorexia nervosa. *Journal of the International Neuropsychological Society, 18*, 1-8.

Steinhausen, H.-C. (2009). Outcome of eating disorders. *Child and Adolescent Psychiatric Clinics of North America, 18*(1), 225-242.

Stice, E., Spoor, S., Bohon, C., Veldhuizen, M. G., & Small, D. M. (2008). Relation of reward from food intake and anticipated food intake to obesity: A functional magnetic resonance imaging study. *Journal of Abnormal Psychology, 117*(4), 924-935.

Stice, E., Spoor, S., Ng, J., & Zald, D. H. (2009). Relation of obesity to consummatory and anticipatory food reward. *Physiology & Behavior, 97*(5), 551-560.

Stice, E., Yokum, S., Blum, K., & Bohon, C. (2010). Weight gain is associated with reduced striatal response to palatable food. *The Journal of Neuroscience, 30*(39), 13105-13109.

Stice, E., Yokum, S., Burger, K. S., Epstein, L. H., & Small, D. M. (2011). Youth at risk for obesity show greater activation of striatal and somatosensory regions to food. *The Journal of Neuroscience, 31*(12), 4360-4366.

Strauss, A., & Corbin, J. (1990). *Basics of qualitative research: grounded theory procedures and techniques*. California: Sage Production.

Strober, M., Freeman, R., & Morrell, W. (1997). The long-term course of severe anorexia nervosa in adolescents: Survival analysis of recovery, relapse, and outcome predictors over 10–15 years in a prospective study. *International Journal of Eating Disorders, 22*(4), 339-360.

Surrence, K., Miranda, R., Marroquin, B., & Chan, S. (2009). Brooding and reflective rumination among suicide attempters: Cognitive vulnerability to suicidal ideation. *Behaviour Research and Therapy, 47*(9), 803-808.

Swanson, S. A., Crow, S. J., Le Grange, D., Swendsen, J., & Merikangas, K. R. (2011). Prevalence and correlates of eating disorders in adolescents: Results from the national comorbidity survey replication adolescent supplement. *Archives of General Psychiatry, 68*(7), 714-723.

Swick, D., Ashley, V., & Turken, A. (2008). Left inferior frontal gyrus is critical for response inhibition. *BMC Neuroscience, 9*(1), 102.

Sysko, R., Walsh, B. T., Schebendach, J., & Wilson, G. T. (2005). Eating behavior among women with anorexia nervosa. *The American Journal of Clinical Nutrition, 82*(2), 296-301.

Tchanturia, K., Harrison, A., Davies, H., Roberts, M., Oldershaw, A., Nakazato, M., et al. (2011). Cognitive flexibility and clinical severity in eating disorders. *PLoS ONE, 6*(6), e20462.

Tchanturia, K., Liao, P., Forcano, L., Fernández-Aranda, F., Uher, R., Treasure, J., et al. (2012). Poor decision making in male patients with anorexia nervosa. *European Eating Disorders Review, 20*(2), 169-173.

Tchanturia, K., Liao, P., Uher, R., Lawrence, N., Treasure, J., & Cambell, I. (2007). An investigation of decision making in anorexia nervosa using the Iowa Gambling Task and skin conductance measurements. *Journal of the International Neuropsychological Society, 13*, 635-641.

Teasdale, J. D. (1999). Metacognition, mindfulness and the modification of mood disorders. *Clinical Psychology & Psychotherapy, 6*(2), 146-155.

Teasdale, J. D., & Barnard, P. J. (1993). *Affect, cognition and change*. Hove: Lawrence Erlbaum Associates.

Teasdale, J. D., Segal, Z., & Williams, J. M. G. (1995). How does cognitive therapy prevent depressive relapse and why should attentional control (mindfulness) training help? *Behaviour Research and Therapy, 33*(1), 25-39.

Teasdale, J. D., Segal, Z. V., Williams, J. M. G., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *Journal of Consulting and Clinical Psychology, 68*(4), 615-623.

Treynor, W., Gonzalez, R., & Nolsen-Hoeksema, S. (2003). Rumination reconsidered: a psychometric analysis. *Cognitive Therapy and Research, 27*(3), 247-259.

Troop, N. A., Holbrey, A., & Treasure, J. L. (1998). Stress, coping, and crisis support in eating disorders. *International Journal of Eating Disorders, 24*(2), 157-166.

Uher, R., Brammer, M. J., Murphy, T., Campbell, I. C., Ng, V. W., Williams, S. C. R., et al. (2003). Recovery and chronicity in anorexia nervosa: brain activity associated with differential outcomes. *Biological Psychiatry, 54*(9), 934-942.

Uher, R., Murphy, T., Brammer, M. J., Dalgleish, T., Phillips, M. L., Ng, V. W., et al. (2004). Medial prefrontal cortex activity associated with symptom provocation in eating disorders. *American Journal of Psychiatry, 161*(7), 1238-1246.

Van den Eynde, F., Guillaume, S., Broadbent, H., Campbell, I. C., & Schmidt, U. (2012). Repetitive transcranial magnetic stimulation in anorexia nervosa: A pilot study. *European Psychiatry*. doi:10.1016?j.eurpsy.2011.06.002.

van Kuyck, K., Gérard, N., Laere, K. V., Casteels, C., Pieters, G., Gabriëls, L., et al. (2009). Towards a neurocircuitry in anorexia nervosa: Evidence from functional neuroimaging studies. *Journal of Psychiatric Research, 43*(14), 1133-1145.

van Tol, M. J., van der Wee, N. J. A., van den Heuvel, O. A., Nielen, M. M. A., Demenescu, L. R., Aleman, A., et al. (2010). Regional brain volume in depression and anxiety disorders. *Archives of General Psychiatry, 67*(10), 1002-1011.

Veer, I. M., Beckmann, C., Van Tol, M.-J., Ferrarini, L., Milles, J., Veltman, D., et al. (2010). Whole brain resting-state analysis reveals decreased functional connectivity in major depression. *Frontiers in Systems Neuroscience, 4*(41), 1-10.

Vitousek, K., & Manke, F. (1994). Personality variables and disorders in anorexia nervosa and bulimia nervosa. *Journal of Abnormal Psychology, 103*(1), 137-147.

Vocks, S., Herpertz, S., Rosenberger, C., Senf, W., & Gizewski, E. R. (2011). Effects of gustatory stimulation on brain activity during hunger and satiety in females with restricting-type anorexia nervosa: An fMRI study. *Journal of Psychiatric Research, 45*(3), 395-403.

Vohs, K. D., Heatherton, T. F., & Herrin, M. (2001). Disordered eating and the transition to college: A prospective study. *International Journal of Eating Disorders, 29*(3), 280-288.

Wagner, A., Aizenstein, H., Marzurkewicz, L., Fudge, J., Frank, G. K., Putnam, K., et al. (2008). Altered insula response to taste stimuli in individuals recovered from restricting-type anorexia nervosa. *Neuropsychopharmacology, 33*, 513-523.

Wagner, A., Aizenstein, H., Venkatraman, V. K., Fudge, J., May, J. C., Mazurkewicz, L., et al. (2007). Altered reward processing in women recovered from anorexia nervosa. *American Journal of Psychiatry, 164*(12), 1842-1849.

Wagner, A., Barbarich-Marsteller, N. C., Frank, G. K., Bailer, U. F., Wonderlich, S. A., Crosby, R. D., et al. (2006). Personality traits after recovery from eating disorders: Do subtypes differ? *International Journal of Eating Disorders, 39*(4), 276-284.

Wagner, A., Greer, P., Bailer, U. F., Frank, G. K., Henry, S. E., Putnam, K., et al. (2006). Normal brain tissue volumes after long-term recovery in anorexia and bulimia nervosa. *Biological Psychiatry, 59*(3), 291-293.

Wallis, J. D., & Kennerley, S. W. (2011). Contrasting reward signals in the orbitofrontal cortex and anterior cingulate cortex. *Annals of the New York Academy of Sciences, 1239*(1), 33-42.

Wanden-Berghe, R. G., Sanz-Valero, J., & Wanden-Berghe, C. (2010). The application of mindfulness to eating disorders treatment: A systematic review. *Eating Disorders: The Journal of Treatment & Prevention, 19*(1), 34 - 48.

Wang, L., LaBar, K. S., Smoski, M., Rosenthal, M. Z., Dolcos, F., Lynch, T. R., et al. (2008). Prefrontal mechanisms for executive control over emotional distraction are altered in major depression. *Psychiatry Research: Neuroimaging, 163*(2), 143-155.

Watkins, E. R. (2008). Constructive and unconstructive repetitive thought. *Psychological Bulletin, 134*(2), 163-206.

Watkins, E. R., & Moberly, N. J. (2009). Concreteness training reduces dysphoria: A pilot proof-of-principle study. *Behaviour Research and Therapy, 47*(1), 48-53.

Watkins, E., & Baracaia, S. (2002). Rumination and social problem-solving in depression. *Behaviour Research and Therapy, 40*(10), 1179-1189.

Watkins, E., & Moulds, M. (2005). Distinct modes of ruminative self-focus: Impact of abstract versus concrete rumination on problem solving in depression. *Emotion, 5*(3), 319-328.

Watkins, E., Moulds, M., & Mackintosh, B. (2005). Comparisons between rumination and worry in a non-clinical population. *Behaviour Research and Therapy, 43*(12), 1577-1585.

Watkins, E., & Teasdale, J. D. (2001). Rumination and overgeneral memory in depression: Effects of self-focus and analytic thinking. *Journal of Abnormal Psychology, 110*(2), 353-357.

Watkins, E., & Teasdale, J. D. (2004). Adaptive and maladaptive self-focus in depression. *Journal of Affective Disorders, 82*(1), 1-8.

Watson, D., Clark, L., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063-1070.

Watson, K. K., Werling, D. M., Zucker, N., & Platt, M. (2009). Altered social reward and attention in anorexia nervosa. *Frontiers in Psychology, 1*(36), 1-8.

Wildes, J. E., & Marcus, M. D. (2010). Development of emotion acceptance behavior therapy for anorexia nervosa: A case series. *International Journal of Eating Disorders, 44*(5), 421-427.

Wildes, J. E., Marcus, M. D., Bright, A. C., Dapelo, M. M., & Psychol, M. C. (2012). Emotion and eating disorder symptoms in patients with anorexia nervosa: An experimental study. *International Journal of Eating Disorders*.doi:10.1002/eat.220.20.

Wildes, J. E., Ringham, R. M., & Marcus, M. D. (2010). Emotion avoidance in patients with anorexia nervosa: Initial test of a functional model. *International Journal of Eating Disorders, 43*(5), 398-404.

Williams, J. M. G. (2008). Mindfulness, depression and modes of mind. *Cognitive Therapy and Research, 32*(6), 721-733.

Williams, J. M. G. (2010). Mindfulness and psychological process. *Emotion, 10*(1), 1-7.

Williams, A. D., & Moulds, M. L. (2007). Cognitive avoidance of intrusive memories: Recall vantage perspective and associations with depression. *Behaviour Research and Therapy, 45*(6), 1141-1153.

Wolff, G., & Serpell, L. (1998). A cognitive model and treatment strategies for anorexia nervosa. In H. W. Hoek, J. Treasure & M. Katzman (Eds.), *Neurobiology in the treatment of eating disorders* (Vol. 4, pp. 407-429). New York: John Wiley and Sons.

Wolk, S. L., Loeb, K. L., & Walsh, B. T. (2005). Assessment of patients with anorexia nervosa: Interview versus self-report. *International Journal of Eating Disorders, 37*(2), 92-99.

World Health Organisation (1992). *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10)*. Geneva.

Zastrow, A., Kaiser, Stefan, Stippich, C., Walther, S., Herzog, W., Tchanturia, K., et al. (2009). Neural correlates of impaired cognitive-behavioral flexibility in anorexia nervosa. *American Journal of Psychiatry, 166*(5), 608-616.

Zhou, Y., Wang, K., Liu, Y., Song, M., Song, S., & Jiang, T. (2010). Spontaneous brain activity observed with functional magnetic resonance imaging as a potential biomarker in neuropsychiatric disorders. *Cognitive Neurodynamics, 4*(4), 275-294.

Zhu, X., Wang, X., Xiao, J., Liao, J., Zhong, M., Wang, W., et al. (2011). Evidence of a dissociation pattern in resting-state default mode network connectivity in first-episode, treatment-naive major depression patients. *Biological Psychiatry, 71*(7) 611-617.

Zink, C. F., & Weinberger, D. R. (2010) Cracking the moody brain: The rewards of self starvation. *Nature Medicine, 16*(12), 1382-1383.

Appendices

List for Appendices

Chapter 2 Principle component analysis of a minimally modified Ruminative Response Scale and the association with mindfulness and experiential avoidance

Chapter 3 Rumination and modes of processing around meal times in women with anorexia nervosa

Chapter 4 Neural response to pleasant and aversive food stimuli in recovered anorexia nervosa

Chapter 5 Liking versus wanting for high and low calorie food in anorexia nervosa

Chapter 6 Resting state functional connectivity in recovered anorexia nervosa: Implications for understanding rumination and reward

Appendices 2.1–2.13

University of Oxford

Medical Sciences Office
John Radcliffe Hospital, Headington, Oxford OX3 9DU

From Carol Green

CONFIDENTIAL
Ms F Cowdrey
c/o Dr Rebecca Park
Department of Psychiatry
Warneford Hospital

Ref.MSD/IDREC/C1/2009/122
02 August 2012

CUREC checklist

I am writing to acknowledge receipt of your CUREC/1 form for your project: Rumination in anorexia nervosa: modification of the ruminative response scale.

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/C1/2009/122 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

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

WARNEFORD HOSPITAL
OXFORD
OX3 7JX

TEL: (01865) 226482
FAX: (01865) 793101

PARTICIPANT INFORMATION SHEET

Research title: Preoccupation in Health and Psychopathology

Principal Researcher: Felicity Cowdrey (Dphil student), ***felicity.cowdrey@psych.ox.ac.uk***

Most people find themselves preoccupied with their thoughts and feelings, from time to time. However, for people with certain mental health problems such as depression and anxiety, rumination features as a core symptom and often exacerbates the individual's illness making it harder to treat. We are therefore investigating rumination in health and psychopathology. In order to do this we are looking for healthy volunteers to complete an online questionnaire.

What will I have to do if I take part?
If you agree to take part, you will be asked to complete an online questionnaire. There are not any right or wrong answers. The questionnaires will take no longer than 25 minutes in total. Please note that you may feel that some of the questions are not directly applicable to you. Please do your best to answer all the questions.

Do I have to take part?
No, **taking part is voluntary**. If you don't want to take part, you do not have to give a reason and no pressure will be out on you to try and change your mind. You will not be contacted again after the questionnaire is completed unless you give consent for us to do so.

If I agree to take part what happens to what I say?
All the information you give us **will be confidential** and used for the purposes of this study only. The data will be collected and stored in accordance with the Data Protection Act 1998 and will be disposed of in a secure manner. The information will be used in a way that will not allow you to be identified individually.

What do I do now?
Think about the information on this sheet, and contact the researchers if you are not sure about anything or would like more information. If you agree to take part, follow the web link on this page which will lead you to an electronic consent form. The consent form will not be used to identify you. It will be filed separately from all other information. Once you have given consent, you will be directed to the questionnaire.

If you are interested in participating in this study, please follow this link to access the questionnaire:

http://www.survey.bris.ac.uk/psych-ox/thoughtprocesses

APPROVED BY THE UNIVERSITY OF OXFORD RESEARCH ETHICS COMMITTEE
If you have a concern about any aspect of this project, please speak to the researcher concerned (07523718095) who will do his/her best to answer your query. If you remain unhappy and wish to make a formal complaint, please contact Miss Green [ethics@medsci.ox.ac.uk] who will then direct your complaint to the appropriate body.

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

WARNEFORD HOSPITAL

OXFORD

OX3 7JX

Consent Form

Information Processing in Health and Psychopathology.

Principal researcher: Felicity Cowdrey, Dphil student.

felicity.cowdrey@psych.ox.ac.uk

Please delete as necessary:

- Have you read and understood the participant information sheet? YES/NO
- Have you had the opportunity to ask questions and discuss the study? YES/NO
- Have all your questions been asked satisfactorily? YES/NO
- Have you received adequate information about the study? YES/NO
- Do you understand that this project has received ethics clearance? YES/NO
- Do you understand that you are free to withdraw from the study:
  - At any time YES/NO
  - Without giving any reason YES/NO
- Do you agree to take part in the study? YES/NO

The study has been explained to my satisfaction and I understand that I am free to ask any questions or to withdraw at any time. I agree to take part.

Signature of the participant:………………………Date:…………………………..

Name (in block capitals):……………………………………………..

I have explained the research to the above participant and he/she has agreed to take part

Signature of the researcher: Date:

If you have a concern about any aspect of this project, please speak to the researcher concerned who will do her best to answer your query. If you remain unhappy and wish to make a formal complaint, please contact Miss Green [ethics@medsci.ox.ac.uk] who will then direct your complaint to the appropriate body.

Ruminative Response Scale for Eating Disorder (RRS-ED)

People think and do many different things when they are concerned about controlling their eating, weight and/or shape. Please read each of the items below and indicate whether you almost never, sometimes, often, or almost always think or do each one when you are concerned about controlling your eating, weight and/or shape. Please indicate what you *generally* do, not what you think you should do.

	almost never (1)	**sometimes (2)**	**often (3)**	**almost always (4)**
Think 'why do I always react this way around food' (Brooding)				
Go away by yourself and think about why you try to control your eating, weight and/or shape (Reflection)				
Write down what you think about your eating, weight and/or shape and analyse it (Reflection)				
Think about a recent meal time wishing it had gone better (Brooding)				
Think 'why do I have problems with controlling my eating, weight and/or shape when other people don't' (Brooding)				
Think 'why can't I handle my eating better' (Brooding)				
Consider your personality to understand why you have to try and control your eating, weight and/or shape (Brooding)				
Go someplace alone to think about your feelings concerning your eating, weight and/or shape. (Reflection)				
Think 'why do I have such issues with my eating, weight and/or shape' (Brooding)				

Eating disorder examination (EDE-Q)

Instructions: The following questions are concerned with the past four weeks (28 days) only. Please read each question carefully. Please answer all the questions. Thank you.

Questions 1 to 12: Please circle the appropriate number on the right. Remember that the questions only refer to the past four weeks (28 days) only.

	On how many of the past 28 days….	**No days**	**1-5 days**	**6-12 days**	**13-15 days**	**16-22 days**	**23-27 days**	**Every day**
1	Have you been deliberately trying to limit the amount of food you eat to influence your shape or weight (whether or not you have succeeded)?	0	1	2	3	4	5	6
2	Have you gone for long periods of time (8 waking hours or more) without eating anything at all in order to influence your shape or weight?	0	1	2	3	4	5	6
3	Have you tried to exclude from your diet any foods that you like in order to influence your shape or weight (whether or not you have succeeded)?	0	1	2	3	4	5	6
4	Have you tried to follow definite rules regarding your eating (for example, a calorie limit) in order to influence your shape and weight (whether or not you have succeeded)?	0	1	2	3	4	5	6
5	Have you had a definite desire to have an empty stomach with the aim of influencing your shape or weight?	0	1	2	3	4	5	6
6	Have you had a definite desire to have a totally flat stomach?	0	1	2	3	4	5	6
7	Has thinking about food, eating or calories made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)?	0	1	2	3	4	5	6
8	Has thinking about shape weight made it very difficult to concentrate on things you are interested in (for example, working, following a conversation, or reading)?	0	1	2	3	4	5	6
9	Have you had a definite fear of losing control lover eating?	0	1	2	3	4	5	6
10	Have you had a definite dear that you may gain weight?	0	1	2	3	4	5	6
11	Have you felt fat?	0	1	2	3	4	5	6
12	Have you had a strong desire to lose weight?	0	1	2	3	4	5	6

Questions 13 to 18: Please fill in the appropriate number in the boxes on the right. Remember that the questions only refer to the past four weeks (28 days) only

Over the past four weeks (28 days)

13	Over the past 28 days, how many **times** have you eaten what other people would regard as an unusually large amount of food (given the circumstances)	………
14	…On how many of these times did you have a sense of having lost control over your eating (at the time that you were eating)?	………
15	Over the past 28 days, how many **DAYS** have such episodes of overeating occurred (i.e., you have eaten an unusually large amount of food and have had a sense of loss of control at the time)?	………
16	Over the past 28 days, how many **times** have you made yourself sick (vomit) as a means of controlling your shape or weight?	………
17	Over the past 28 days, how many **times** have you taken laxatives as a means of controlling your shape or weight?	………
18	Over the past 28 days, how many **times** have you exercised in a "driven" or "compulsive" way as a means of controlling your weight, shape or amount of fat, or to burn off calories?	………..

Questions 19 to 21: Please circle the appropriate number. Please note that for these questions the term "binge eating" means eating what others would regard as an unusually large amount of food for the circumstances, accompanied by a sense of having lost control over eating.

19	Over the past 28 days, on how many days have you eaten in secret (ie, furtively)?... do not count episodes of binge eating	No days	1-5 days	6-12 days	13-15 days	16-22 days	23-27 days	Every day
		0	1	2	3	4	5	6
20	On what proportion of the times that you have eaten have you felt guilty (felt that you've done wrong) because of its effect on your shape or weight?...Do not count episodes of binge eating	None of the times	A few of the times	Less than half	Half of the times	More than half	Most of the time	Every time
		0	1	2	3	4	5	6
21	Over the past 28 days, how concerned have you been about other people seeing you eat?...Do not count episodes of binge eating	Not at all		Slightly	Moderately		Markedly	
		0	1	2	3	4	5	6

Questions 22 to 28: Please circle the appropriate number on the right. Remember that the questions only refer to the past four weeks (28 days) only.

	Over the past 28 days….	**Not at all**		**Slightly**		**Moderately**		**Markedly**
22	Has your weight influenced how you think about (judge) yourself as a person?	0	1	2	3	4	5	6
23	Has your shape influenced how you think about (judge) yourself as a person?	0	1	2	3	4	5	6
24	How much would it have upset you if you had been asked to weigh yourself once a week (no more, or less, often) for the next four weeks?	0	1	2	3	4	5	6
25	How dissatisfied have you been with your weight?	0	1	2	3	4	5	6
26	How dissatisfied have you been with your shape?	0	1	2	3	4	5	6
27	How uncomfortable have you felt seeing your body (for example, in the mirror, in a shop window reflection, while undressing or taking a bath or shower)?	0	1	2	3	4	5	6
28	How uncomfortable have you felt about others seeing your shape or figure (for example, in communal changing rooms, when swimming, or wearing tight clothes)?	0	1	2	3	4	5	6

What is your weight at present? (please give your best estimate) ……………………….

What is your height? (please give your best estimate) ………………………

If female: over the past three-to four months have you missed any menstrual periods? ………………………

If so how many? ………………………

Have you been taking the "pill"? ……………………….

Clinical Impairment Assessment (CIA)

INSTRUCTIONS

Please place an ‘X’ in the column which best described how your eating habits, exercising or feelings about your eating, shape or weight have affected your life over the past four weeks (28 days). Thank you.

	Over the past 28 days, to what extent have your eating habit, exercising, or feelings about your eating, shape or weight….	Not at all	A little	Quite a bit	A lot
1	…made it difficult to concentrate?				
2	…made you feel critical of yourself?				
3	…stopped you going out with others?				
4	…affected your work performance (if applicable)?				
5	…made you forgetful?				
6	…affected your ability to make everyday decisions?				
7	…interfered with meals with family or friends?				
8	…made you upset?				
9	…made you feel ashamed of yourself?				
10	…made it difficult to eat out with others?				
11	…made you feel guilty?				
12	…interfered with you doing things you used to enjoy?				
13	…made you absent-minded?				
14	…made you feel like a failure?				
15	…interfered with your relationships with others?				
16	…made you worry?				

Patient Health Questionnaire-9 (PHQ-9)

	Over the <u>last 2 weeks</u>, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1	Little interest or pleasure in doing things	0	1	2	3
2	Feeling down, depressed, or hopeless	0	1	2	3
3	Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4	Feeling tired or having little energy	0	1	2	3
5	Poor appetite or overeating	0	1	2	3
6	Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7	Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8	Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9	Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

Generalised Anxiety Disorder Assessment-7 (GAD-7)

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1 Feeling nervous, anxious or on edge	0	1	2	3
2 Not being able to stop or control worrying	0	1	2	3
3 Worrying too much about different things	0	1	2	3
4 Trouble relaxing	0	1	2	3
5 Being so restless that it is hard to sit still	0	1	2	3
6 Becoming easily annoyed or irritable	0	1	2	3
7 Feeling afraid as if something awful might happen	0	1	2	3

Ruminative Response Scale (RRS)

People think and do many different things when they feel depressed. Please read each of the items below and indicate whether you almost never, sometimes, often, or almost always think or do each one when you feel down, sad, or depressed. Please indicate what you generally do, not what you think you should do.

1 almost never   2 sometimes   3 often   4 almost always

1. think about how alone you feel
2. think "I won't be able to do my job if I don't snap out of this"
3. think about your feelings of fatigue and achiness
4. think about how hard it is to concentrate
5. think "What am I doing to deserve this?"
6. think about how passive and unmotivated you feel.
7. analyze recent events to try to understand why you are depressed
8. think about how you don't seem to feel anything anymore
9. think "Why can't I get going?"
10. think "Why do I always react this way?"
11. go away by yourself and think about why you feel this way
12. write down what you are thinking about and analyze it
13. think about a recent situation, wishing it had gone better
14. think "I won't be able to concentrate if I keep feeling this way."
15. think "Why do I have problems other people don't have?"
16. think "Why can't I handle things better?"
17. think about how sad you feel.

18. think about all your shortcomings, failings, faults, mistakes

19. think about how you don’t feel up to doing anything

20. analyze your personality to try to understand why you are depressed

21.go someplace alone to think about your feelings

22. think about how angry you are with yourself

Five Facet Mindfulness Questionnaire (FFMQ)

Please rate each of the following statements using the scale provided. Write the number in the blank that best describes your own opinion of what is generally true for you.

1	2	3	4	5
Never or very rarely true	Rarely true	Sometimes true	Often true	Very often or always true

_____ 1. When I'm walking, I deliberately notice the sensations of my body moving.
_____ 2. I'm good at finding words to describe my feelings.
_____ 3. I criticize myself for having irrational or inappropriate emotions.
_____ 4. I perceive my feelings and emotions without having to react to them.
_____ 5. When I do things, my mind wanders off and I'm easily distracted.
_____ 6. When I take a shower or bath, I stay alert to the sensations of water on my body.
_____ 7. I can easily put my beliefs, opinions, and expectations into words.
_____ 8. I don't pay attention to what I'm doing because I'm daydreaming, worrying, or otherwise distracted.
_____ 9. I watch my feelings without getting lost in them.
_____ 10. I tell myself I shouldn't be feeling the way I'm feeling.
_____ 11. I notice how foods and drinks affect my thoughts, bodily sensations, and emotions.
_____ 12. It's hard for me to find the words to describe what I'm thinking.
_____ 13. I am easily distracted.
_____ 14. I believe some of my thoughts are abnormal or bad and I shouldn't think that
_____ 15. I pay attention to sensations, such as the wind in my hair or sun on my face.
_____ 16. I have trouble thinking of the right words to express how I feel about things
_____ 17. I make judgments about whether my thoughts are good or bad.
_____ 18. I find it difficult to stay focused on what's happening in the present.
_____ 19. When I have distressing thoughts or images, I "step back" and am aware of the thought or image without getting taken over by it.

_____ 20. I pay attention to sounds, such as clocks ticking, birds chirping, or cars passing.

_____ 21. In difficult situations, I can pause without immediately reacting.

_____ 22. When I have a sensation in my body, it's difficult for me to describe it because I can't find the right words.

_____ 23. It seems I am "running on automatic" without much awareness of what I'm doing.

_____24. When I have distressing thoughts or images, I feel calm soon after.

_____ 25. I tell myself that I shouldn't be thinking the way I'm thinking.

_____ 26. I notice the smells and aromas of things.

_____ 27. Even when I'm feeling terribly upset, I can find a way to put it into words.

_____ 28. I rush through activities without being really attentive to them.

_____ 29. When I have distressing thoughts or images I am able just to notice them without reacting.

_____ 30. I think some of my emotions are bad or inappropriate and I shouldn't feel them.

_____ 31. I notice visual elements in art or nature, such as colors, shapes, textures, or patterns of light and shadow.

_____ 32. My natural tendency is to put my experiences into words.

_____ 33. When I have distressing thoughts or images, I just notice them and let them go.

_____ 34. I do jobs or tasks automatically without being aware of what I'm doing.

_____ 35. When I have distressing thoughts or images, I judge myself as good or bad, depending what the thought/image is about.

_____ 36. I pay attention to how my emotions affect my thoughts and behavior.

_____ 37. I can usually describe how I feel at the moment in considerable detail.

_____ 38. I find myself doing things without paying attention.

_____ 39. I disapprove of myself when I have irrational ideas.

Acceptance and Action Questionnaire II

Please rate how true each statement is for you by circling the below it.

My painful experiences and memories make it difficult to live a life that I would value.

1	2	3	4	5	6	7
Never true	Very seldom true	Seldom true	Sometimes true	Frequently true	Almost always true	Always true

I am afraid of my feelings.

1	2	3	4	5	6	7
Never true	Very seldom true	Seldom true	Sometimes true	Frequently true	Almost always true	Always true

I worry about not being able to control my worries and feelings.

1	2	3	4	5	6	7
Never true	Very seldom true	Seldom true	Sometimes true	Frequently true	Almost always true	Always true

My painful memories prevent me from having a fulfilling life.

1	2	3	4	5	6	7
Never true	Very seldom true	Seldom true	Sometimes true	Frequently true	Almost always true	Always true

Emotions cause problems in my life.

1	2	3	4	5	6	7
Never true	Very seldom true	Seldom true	Sometimes true	Frequently true	Almost always true	Always true

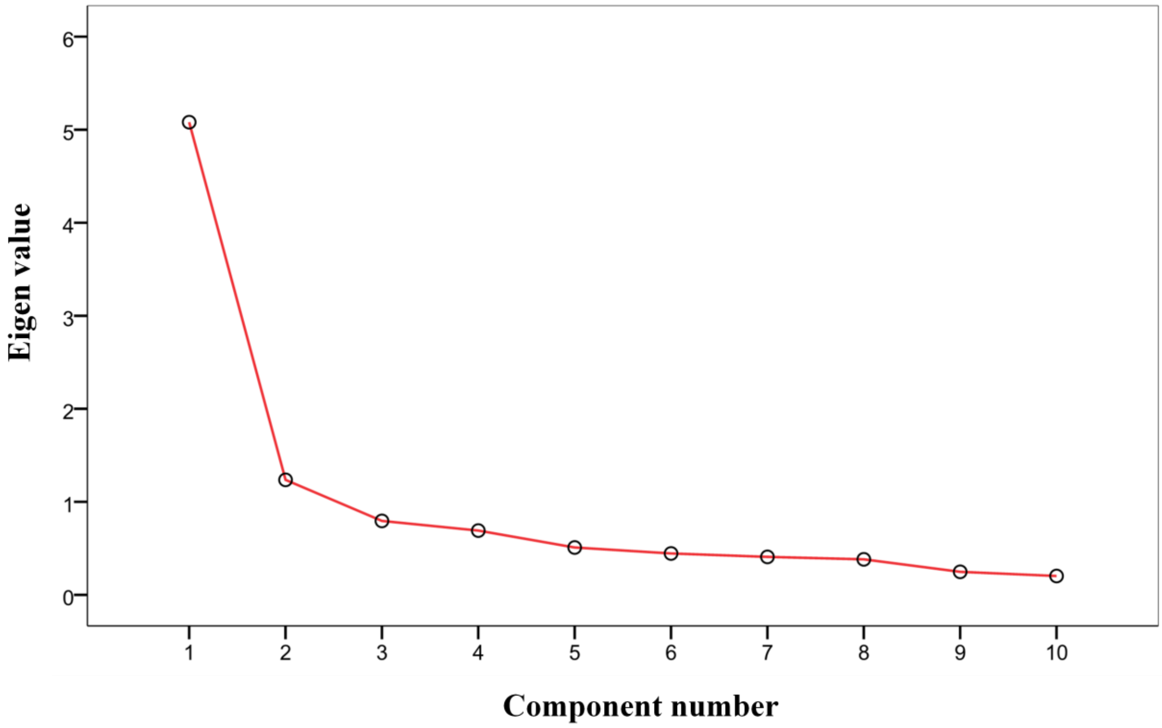
It seems that most people are handling their lives better than I am.

1	2	3	4	5	6	7
Never true	Very seldom true	Seldom true	Sometimes true	Frequently true	Almost always true	Always true

My worries get in the way of my success.

1	2	3	4	5	6	7
Never true	Very seldom true	Seldom true	Sometimes true	Frequently true	Almost always true	Always true

Scree plot showing eigen values for PCA components



Obliquely rotated factor loadings for the 9-item RRS-ED

Items:	Factor 1	Factor 2
Think 'why can't I handle my eating better?'	**.927**	-.134
Think 'why do I have problems with controlling my eating, weight and/or shape when other people don't?'	**.913**	-.100
Think 'why do I have such issues with my eating, weight and/or shape?'	**.899**	-.055
Think 'why do I always react this way around food?'	**.746**	.107
Think about a recent meal time wishing it had gone better.	**.739**	.090
Consider your personality to understand why you have to try and control your eating, weight and/or shape.	**.605**	.264
Go away by yourself and think about why you try to control your eating, weight and/or shape.	-.207	**.866**
Write down what you think about your eating, weight and/or shape and analyse it.	.199	**.643**
Go someplace alone to think about your feelings concerning your eating, weight and/or shape.	.257	**.529**
EIGEN VALUES	5.08	1.24
% OF VARIANCE	50.8	12.4
CRONBACH'S ALPHA	.90	.61

Note. Factor loadings that are greater or equal to 0.4 are displayed in bold type

Appendices 3.1-3.11

Outer West London REC
Level 7 Maternity, Room 019
Northwick Park Hospital
Watford Road
Harrow
HA1 3UJ

Telephone: 020 8869 3928
Facsimile: 020 8869 5222

29 March 2010

Miss Felicity Cowdrey
Department of Psychiatry
Warneford Hospital
Oxford
OX3 7JX

Dear Miss Cowdrey

Study Title:	**The experience of using CD- guided exercises before meal times in patients with Eating Disorders.**
REC reference number:	**10/H0709/20**
Protocol number:	**1.1**

Thank you for your e-mail dated 25th March 2010 responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk. *Where the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.*

Sponsors are not required to notify the Committee of approvals from host organisations.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*	
REC application		02 February 2010	
Protocol	1.1	31 January 2010	
Investigator CV		02 February 2010	
GP/Consultant Information Sheets	1.1	02 February 2010	
Statement of indemnity arrangements		03 February 2010	
CV for Rebecca Jane Park (Academic Supervisor)		23 February 2010	
Participant Information Sheet: adolescent	1.2	23 March 2010	
Participant Information Sheet: adult	1.2	23 March 2010	
Participant Consent Form	1.2	19 March 2010	
Letter of invitation to participant – adult	1.1	23 March 2010	
Evidence of insurance or indemnity			
letter of invitation to participant – adolescent	1.1	23 March 2010	
Response to Request for Further Information			

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

10/H0709/20	**Please quote this number on all correspondence**

Yours sincerely

Dr Jan Downer
Chair

Email: alison.okane@nwlh.nhs.uk

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Ms Heather House*
[R&D office for NHS care organisation at lead site]

Our Ref: OBMH 788

1 April 2010

Miss Felicity Cowdrey
Dept of Psychiatry
Warneford Hospital
Oxford
OX3 7JX

Dear Felicity

Re: The experience of using CD-guided exercises before meal times in patients with eating disorders
REC No: 10/H0709/20

The above research study has been reviewed by the Trust's Research and Development Committee and I can confirm that Oxfordshire and Buckinghamshire Mental Health NHS Foundation Trust will provide management approval for this study, as described in your application to the National Research Ethics Service. This confirmation is dependent on the formal approval of the National Research Ethics Service.

I must remind you of the declaration that was signed in the Site-Specific Information form. This explains your responsibilities as a researcher including adherence to the principles of the Research Governance Framework, Good Clinical Practice and the Data Protection Act.

Trust Management approval is on-going and dependent upon completion of satisfactory annual reports when requested. It is a condition of management approval that you inform the Trust R&D department of any amendments to the protocol, changes to the project end date and that you submit a final report on completion of the study.

I wish you every success with the study

Yours sincerely

Professor Tom Burns
Research & Development Lead Director
Oxfordshire and Buckinghamshire Mental Health NHS Foundation Trust

DEPARTMENT OF PSYCHIATRY

UNIVERSITY OF OXFORD

Felicity Cowdrey
Department of psychiatry
University of oxford
Warneford hospital
OX37JX
01865223918

PARTICIPANT INFORMATION SHEET

The experience of using audio-guided exercises before meal times in individuals who have experienced an eating disorder

Principal Researcher*: Felicity Cowdrey (DPhil student), felicity.cowdrey@psych.ox.ac.uk / 01865 223918*

Part 1 tells you the purpose of this study and what will happen if you agree to take part.
Part 2 gives you more detailed information about the conduct of the study

Part 1 of the information sheet:

You are being invited to take part in a research project. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read this information carefully. We encourage you to share and discuss the study with your family, friends and/ or health care professionals if you wish. If there is anything you do not understand, or if you would like more information, please contact the researcher named above. Take time to decide whether you wish to take part.

What is the purpose of the study?

Meal times are difficult for people who have an eating disorder and often evoke negative thoughts, feelings and behaviours. We are interested in exploring whether short exercises practiced before meal times could help alleviate some of these negative thoughts, feelings and behaviours. We are also interested in whether such exercises could be of use to people with different severity of eating disorder and also for those who have recovered.

What will I have to do if I take part?

If you agree to take part, you will be enrolled into the study for 3 days. You will be asked to use 3 audio- guided exercises before a meal time- just one on each day. You will also be asked to complete some short scales on each of these days in the practice diary. Therefore in total, the study will run for 3 days. One of the researchers may make contact with you by phone or text to answer any questions or concerns that may have arisen.

In addition, before the study commences you will be invited to meet one of the researchers who will introduce the study and practice the audio-guided exercises with you. However, if you prefer we have instructions written out which we can send to you, in conjunction with phone or email support from one of the named researchers. You will also receive some questionnaires to complete before the study commences, as well as the three audio-guided exercises on separate CDs and a practice diary. You will have the opportunity to feedback to the researchers your views of the audio-guided exercises. We will encourage you to copy the exercises from the CDs onto an MP3 player. The researchers will be able to help with this and there will be an option to borrow MP3 players from the researchers if needed.

Do I have to take part?

No, **taking part is voluntary**. If you don't want to take part, you do not have to give a reason and no pressure will be out on you to try and change your mind.
If you do consent to participate, you remain free to withdraw from the study at any time without giving a reason and without any consequences to the care or treatment you may otherwise be receiving.
You will not be contacted again after the study unless you give consent for us to do so.

Why have I been chosen?

You are being invited because we have ethical permission to recruit participants from Cotswold House.

If I agree to take part what happens to what I say and do?

All the information you give us **will be confidential** and used for the purposes of this study only. The data will be collected and stored in accordance with the Data Protection Act 1998 and will be disposed of in a secure manner. Relevant sections of the records and data collected during the study may be looked at by responsible individuals from the University of Oxford and other regulatory bodies, where it is relevant to your taking part in this research.
The information collected during the study will be used in a way that will not allow you to be identified individually. The study will contribute to the principal researcher's doctoral thesis and we plan to publish the findings in scientific journals - you will **not** be identified personally in these. We will make the results available to you, if you wish.

<u>Part 2 of the information sheet:</u>

Benefits and risks:

We cannot promise the study will help you but the information we get from this study may help our understanding of eating disorders and may lead to improvements in the treatment of people with eating disorders and the prevention of relapse.
In recognition of your time and help you will receive a gift voucher at the end of the study valued at £10. In addition you will be given the CDs to keep- you can therefore continue to use them if you have found them helpful. We will also cover any reasonable travel expenses.
There are not thought to be any significant risks in this study.

Other Important Information:

If you agree to take part in this study and you are happy for us to do so, your GP and / or individual therapist / clinician will be sent a letter informing them of your decision to take part.

What is something goes wrong?

Indemnity:

The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor. NHS indemnity operates in respect of the clinical treatment with which you are provided.

Complaints:

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the researcher (Felicity Cowdrey) or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 857939 or the head of CTRG, email heather.house@admin.ox.ac.uk

Funding:

This work is funded by the Sir Jules Thorn Charitable Trust.

What do I do now?

Think about the information on this sheet, and contact the researchers if you are not sure about anything or would like more information. If you agree to take part, please sign the consent form and contact details sheet. The consent form will not be used to identify you. It will be filed separately from all other information. Please post or email the completed forms back to the named researcher.

Contact Details:
Miss Felicity Cowdrey (Principal Researcher)
Warneford Hospital,
Oxford,
OX3 7DX
felicity.cowdrey@psych.ox.ac.uk
01865 223918

THANK YOU FOR TAKING TIME TO READ THIS INFORMATION SHEET

Dr Rebecca Park Felicity Cowdrey Dr Anne Stewart Jill Roberts

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

CONSENT TO RESEARCH FORM

The experience of using CD- guided exercises before meal times in individuals with eating disorders.

INVESTIGATORS: Felicity Cowdrey, Dr Rebecca Park, Dr Anne Stewart, Jill Roberts

Signing this form does not commit you to completing this study. You remain free to leave the study at any time and without having to give any reason for doing so.

Please initial

I have read the information sheet dated………………. (version…...). I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily ☐

I understand that relevant sections of any of my records and data collected during the study may be looked at by responsible individuals from the University of Oxford and other regulatory bodies, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. ☐

I agree to take part in the study ☐

Name of participant: Date:

Signature:

Please tick the box if you agree for your details to be kept on record and if you agree to be contacted regarding future studies ☐

Name of researcher taking consent

Date:

Signature:

UNIVERSITY OF OXFORD

Oxfordshire and Buckinghamshire Mental Health NHS
NHS Foundation Trust

PRACTICE DIARY

Participant Code:

INTRODUCTION:

Welcome and thank you for agreeing to participate in this study.

Please read the following information explaining why the research is being done and what it will involve.

If you have any questions about the study please contact me at any point by email [felicity.cowdrey@psych.ox.ac.uk] or telephone [01865 223918].

General Information:

Many people who have an eating disorder find meal times distressing.

We want to investigate whether practicing different exercises before meal times can reduce distressing thoughts, feelings and behaviours.

This study will involve listening to one of three short audio-guided exercises before one meal time daily for 3 consecutive days and completing a practice diary.

You will also be asked to give your feedback on the exercises at the end of the study.

Overview of the study

Day 1: Complete questionnaire pack

↓

Yellow Phase: 'First CD'- Day 2

- **Listen to the first audio-guided exercise before a meal.**

↓

Purple Phase: 'Second CD'- Day 3

- **Listen to the second audio-guided exercise before a meal.**

↓

Pink Phase: 'Third CD' –Day 4

- **Listen to the third audio-guided exercise before a meal.**

↓

Return practice diary

Pre practice questions	
Please rate the following scales by placing an 'X' on the line	
At the moment my thoughts are concerned with trying to understand, explain or make sense of things	Not at all Extremely 0 100
At the moment I am focusing on the experience of the moment, noticing my sensory experiences and feelings	Not at all Extremely 0 100
At the moment I feel fat	Not at all Extremely 0 100

Post- practice questions	
Please rate the following scales by placing an 'X' on the line	
At the moment my thoughts are concerned with trying to understand, explain or make sense of things	Not at all Extremely 0 100
At the moment I am focusing on the experience of the moment, noticing my sensory experiences and feelings	Not at all Extremely 0 100
At the moment I feel fat	Not at all Extremely 0 100

Post- meal questions	
Please rate the following scales by placing an 'X' on the line	
At the moment my thoughts are concerned with trying to understand, explain or make sense of things	Not at all Extremely 0 ……………………………………………………………………………100
At the moment I am focusing on the experience of the moment, noticing my sensory experiences and feelings	Not at all Extremely 0 ……………………………………………………………………………100
At the moment I feel fat	Not at all Extremely 0 ……………………………………………………………………………100
I felt that the exercise helped me manage the meal	Not at all Extremely 0 ……………………………………………………………………………100

End of Purple Phase:

Please comment on the second exercise.

(Continue on a separate sheet if necessary)

You will now be moving on to the 'pink phase' of the study.

Script for mindful breathing exercise

(Modified from Segal, Williams and Teasdale, 2002).

Finding a place to sit and making a definite change in your posture, so that this embodies a sense of alertness and dignity. Starting by bringing your awareness to just how things are for you right now. Having your eyes closed if you wish, but if you care to have them open then letting your gaze fall and focus in front of you on the floor. This a brief practice so really bringing to it the intention to be fully present and fully in each moment.

For the **first step** bringing awareness to your posture and how you are sitting, being aware of any sensations in the body and also being aware of any thoughts or emotions that are around for you right now. As best you can just allowing whatever you find to be just as it is. So having stepped away from being on automatic pilot, being fully in the here and now.

Now for the **second step**, choosing to focus and narrow awareness to rest on the breath. Being fully aware of the physical sensations of breathing, not believing that you have to alter or change the breath in any way, but just really narrowing the focus of the awareness to the single breath, to wherever you may feel it most vividly, to the in breath and the out breath as they very naturally follow one after the other.

And now for the **final step** of this practice, expanding awareness round the breath and broadening out the focus. Seeing as you do if you can bring some openness and spaciousness to this, flooding the body with awareness as you breath and coming back to an awareness of posture, how you are sitting. Coming back to the feet meeting the ground, and to your facial expression. So being fully present as you sit here breathing, fully in the here and now. And perhaps bringing this sense of spaciousness into the next moments of your day.

Script for rumination induction

(Minimally modified from Watkins and Teasdale, 2004)

Please find a place to sit comfortably.

For the next few minutes, try your best to think about each of the following items. As you listen to the items, use your imagination and concentration to think about the causes, meanings and consequences of the items. Spend a few moments visualising and concentrating on each item, attempting to make sense of and understand the issues raised by each item.

Think about the physical sensations in your body.
Think about the degree of clarity in your thinking right now.
Think about the way you feel inside.
Think about the way you react.
Think about the experience of your present feelings lasting.
Think about your feelings.
Think about how tired or awake you are.
Think about the amount of tension in your muscles.
Think about the amount of stress in your body.
Think about your present feelings of fatigue and energy.
Think about the amount of certainty you feel.
Think about how hopeful or hopeless you are feeling.
Think about your physical sensations.
Think about the level of motivation you feel right now.
Think about the degree of helplessness you feel right now.
Think about the degree of calmness or restlessness you feel.
Think about the way you feel.
Think about the experience of your feelings.
Think about how happy or sad you are feeling.
Think about the way your body feels right now.
Think about how passive or active you feel.
Think about how optimistic or pessimistic you feel about the future.
Think about how weak or strong your body feels right now.
Think about how relaxed or agitated you feel.
Think about the degree of control you feel right now.
Think about your current physical state lasting.
Think about how quick or slow your thinking is right now.
Think about the degree of decisiveness you feel.

Script for the music distraction exercise

(Modified from Holmes, James, Coode-Bate and Deeprose, 2009)

"Please sit down and listen. For the next few minutes, you will hear several short extracts of music. These extracts have been selected because it is thought that they are fairly pleasant to listen to. As you listen to the music extracts, think carefully about how pleasant you find each one. It will be easy to tell when one extract ends and another begins as at the end of each extract of music you will be asked to mentally rate how pleasant you found it on a scale of 1 to 9, where 1 corresponds to '*extremely unpleasant*' and 9 corresponds to '*extremely pleasant*'. Remember to sit down during the course of this exercise and stay focused on the music. The first extract will commence in a few moments."

Clip 1 (40 Seconds)
Please rate in your mind how pleasant you found the music extract on a scale of 1 to 9, where
(1 = extremely unpleasant) (5 = midway) (9 = extremely pleasant)
[PAUSE]

Clip 2 (40 seconds)
Again, please rate how pleasant you found the music extract on a scale of 1 to 9, where
(1 = extremely unpleasant) (5 = midway) (9 = extremely pleasant)
[PAUSE]

Clip 3 (40 seconds)
Again, please rate how pleasant you found the music extract on a scale of 1 to 9, where
(1 = extremely unpleasant) (5 = midway) (9 = extremely pleasant)
[PAUSE]

This is the end of the exercise.

Beck Depression Inventory-II

Instructions

This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the one statement in each group that best describes the way you have been feeling during the past two weeks, including today. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness
0 I do not feel sad.
1 I feel sad much of the time.
2 I am sad all of the time.
3 I am so sad or unhappy that I can't stand it.

2. Pessimism
0 I am not discouraged about my future.
1 I feel more discouraged about my future than I used to be.
2 I do not expect things to work out for me.
3 I feel my future is hopeless and will only get worse.

3. Past Failure
0 I do not feel like a failure.
1 I have failed more than I should have.
2 As I look back, I see a lot of failures.
3 I feel I am a total failure as a person.

4. Loss of Pleasure
0 I get as much pleasure as I ever did from the things I enjoy.
1 I don't enjoy things as much as I used to.
2 I get very little pleasure from the things I used to enjoy.
3 I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings
0 I don't feel particularly guilty.
1 I feel guilty over many things I have done or should have done.
2 I feel quite guilty most of the time.
3 I feel guilty all of the time.

6. Punishment Feelings
0 I don't feel I am being punished.
1 I feel I may be punished.
2 I expect to be punished.
3 I feel I am being punished.

7. Self-Dislike
0 I feel the same about myself as ever.
1 I have lost confidence in myself.
2 I am disappointed in myself.
3 I dislike myself.

8. Self-Criticalness
0 I don't criticize or blame myself more than usual.
1 I am more critical of myself than I used to be.
2 I criticize myself for all of my faults.
3 I blame myself for everything bad that happens.

9. Suicidal thoughts or Wishes
0 I don't have any thoughts of killing myself.
1 I have thoughts of killing myself, but I would not carry them out.
2 I would like to kill myself.
3 I would kill myself if I had the chance.

10. Crying
0 I don't cry anymore than I used to.
1 I cry more than I used to.
2 I cry over every little thing.
3 I feel like crying, but I can't.

11. Agitation

0 I am no more restless or wound up than usual.
1 I feel more restless or wound up than usual.
2 I am so restless or agitated that it's hard to stay still.
3 I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0 I have not lost interest in other people or activities.
1 I am less interested in other people or things than before.
2 I have lost most of my interest in other people or things.
3 It's hard to get interested in anything.

13. Indecisiveness

0 I make decisions about as well as ever.
1 I find it more difficult to make decisions than usual.
2 I have much greater difficulty in making decisions than I used to.
3 I have trouble making any decisions.

14. Worthlessness

0 I do not feel I am worthless.
1 I don't consider myself as worthwhile and useful as I used to.
2 I feel more worthless as compared to other people.
3 I feel utterly worthless.

15. Loss of Energy

0 I have as much energy as ever.
1 I have less energy than I used to have.
2 I don't have enough energy to do very much.
3 I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0 I have not experienced any change in my sleeping pattern

1a I sleep somewhat more than usual
1b I sleep somewhat less than usual.

2a I sleep a lot more than usual.
2b I sleep a lot less than usual.

3a I sleep most of the day.
3b I wake up 1-2 hours early and can't get back to sleep.

17. Irritability

0 I am no more irritable than usual.
1 I am more irritable than usual.
2 I am much more irritable than usual.
3 I am irritable all the time.

18. Changes in Appetite

0 I have not experienced any change in my appetite.

1a My appetite is somewhat less than usual.
1b My appetite is somewhat greater than usual.

2a My appetite is much less than before.
2b My appetite is much greater than usual.

3a I have no appetite at all.
3b I crave food all the time.

19. Concentration Difficulty

0 I can concentrate as well as ever.
1 I can't concentrate as well as usual.
2 It's hard to keep my mind on anything for very long.
3 I find I can't concentrate on anything.

20. Tiredness or Fatigue

0 I am no more tired or fatigued than usual.
1 I get more tired or fatigued more easily than usual.
2 I am too tired or fatigued to do a lot of the things I used to do.
3 I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I am much less interested in sex now.
3 I have lost interest in sex completely.

State-Trait Anxiety Inventory

[State subscale]

<u>INSTRUCTIONS</u>: A number of statements which people have used to describe themselves are given below. Read each statement and circle an answer to indicate how you feel *right now*, that is, at this moment. There are no right or wrong answers. Do not spend too much time on any one statement, but give the answer which seems to describe your present feelings best.

		Not at all	***Somewhat***	***Moderately so***	***Very Much so***
1.	I feel calm	0	1	2	3
2.	I feel secure	0	1	2	3
3.	I am tense	0	1	2	3
4.	I feel strained	0	1	2	3
5.	I feel at ease	0	1	2	3
6.	I feel upset	0	1	2	3
7.	I am presently worrying over possible misfortunes	0	1	2	3
8.	I feel satisfied	0	1	2	3
9.	I feel frightened	0	1	2	3
10.	I feel comfortable	0	1	2	3
11.	I feel self-confident	0	1	2	3
12.	I feel nervous	0	1	2	3
13.	I am jittery	0	1	2	3
14.	I feel indecisive	0	1	2	3
15.	I am relaxed	0	1	2	3
16.	I feel content	0	1	2	3
17.	I am worried	0	1	2	3
18.	I feel confused	0	1	2	3
19.	I feel steady	0	1	2	3
20.	I feel pleasant	0	1	2	3

State-Trait Anxiety Inventory

[Trait scale]

<u>INSTRUCTIONS</u>: A number of statements which people have used to describe themselves are given below. Read each statement and then circle an answer to indicate how you <u>generally</u> feel. here are no right or wrong answers. Do not spend too much time on any one statement, but give the answer which seems to describe how you generally feel.

		Almost Never	*Sometimes*	*Often*	*Almost Always*
1.	I feel pleasant	0	1	2	3
2.	I feel nervous and restless	0	1	2	3
3.	I feel satisfied with myself	0	1	2	3
4.	I wish I could be as happy as others seem to be	0	1	2	3
5.	I feel like a failure	0	1	2	3
6.	I feel rested	0	1	2	3
7.	I am "calm, cool, and collected"	0	1	2	3
8.	I feel that difficulties are piling up so that I cannot overcome them	0	1	2	3
9.	I worry too much over something that really doesn't matter	0	1	2	3
10.	I am happy	0	1	2	3
11.	I have disturbing thoughts	0	1	2	3
12.	I lack self-confidence	0	1	2	3
13.	I feel secure	0	1	2	3
14.	I make decisions easily	0	1	2	3
15.	I feel inadequate	0	1	2	3
16.	I am content	0	1	2	3
17.	Some unimportant thought runs through my mind and bothers me	0	1	2	3
18.	I take disappointments so keenly that I can't put them out of my mind	0	1	2	3
19.	I am a steady person	0	1	2	3
20.	I get in a state of tension or turmoil as I think about my recent concerns and interests	0	1	2	3

Overview of thematic analysis using a modified grounded theory approach

Following the transcription of each diary, Glaser and Strauss' (1967) process of open coding was applied. In this approach, the data is broken down into smaller units (sentences, individual words) and the researcher (in this case FC) examines each unit and notes down as many codes as necessary to describe the content. The codes aim to explain the substance of the data and thus often codes incorporate words or phrases used by the participants. Each code is then compared to every other code (referred to as constant comparison) and those which overlap in content are assigned to categories (for example, the code of "anxiety before the meal" may be put in the same category as "increased stress before the meal"). A preliminary category name is also derived based on the common themes of each category (for example, "negative emotions around the meal time"). The next stage of the qualitative analysis involves the development of a tentative framework. This is achieved by comparing each category with all others and those which pertain to a similar phenomena form higher order categories which describe the data. This approach to qualitative data analysis is therefore a data- driven rather than theory-driven approach as categories are derived directly from the data rather than devised a priori (hence why it is described as a modified grounded theory analysis method). The flexibility this method provides is particularly helpful for new areas of research as in the presented in this thesis and can be used to generate novel formulations and hypotheses.

Appendices 4.1-4.12

National Research Ethics Service

Central London REC 1

Level 7N019 Maternity Block
Northwick Park Hospital
Watford Road
Harrow
Middx
HA13UJ
Telephone: 02088693775
Facsimile: 02088695222

14 May 2010

Miss Felicity Cowdrey
DPhil student
Department of Psychiatry, University of
Oxford Department of Psychiatry
Warneford Hospital
Oxford
OX3 7,1X

Dear Miss Cowdrey

Study title: Reward processing in individuals recovered from anorexia nervosa.
REC reference: 10/H0718/15
Protocol number: 1.3

Thank you for your letter of 12 April 2010, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered in correspondence by a sub-committee of the REC at a meeting held on 14th May 2010. A list of the sub-committee members is attached.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

The favourable opinion applied to the following research site(s):

Research site	**PI / Local Collaborator**
Warneford Hospital, University of Oxford	Miss Felicity Cowdrey

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

<u>Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.</u>

For NHS research sites only, m*anagement permission ("R&D approval") should be sought from* all *NHS organizations involved in the study in accordance with NHS research governance arrangements.* Guidance on applying for NI-IS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs,uk. Where the only involvement of the NHS organization is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

DOCUMENT	*VERSION*	*DATE*
REC application		15 FEB 2010
Protocol	1.3	
Investigator CV		10 FEB 2010
Participant consent form	1.2	08 FEB 2010
Letter from sponsor		12 FEB 2010
Advertisement		
Participant Information sheet: AN recovered	1.3	13 APRIL 2010
Participant information sheet: healthy control	1.3	13 APRIL 2010
Referees or other scientific critique report		16 APRIL 2010
Questionnaires		
Rest procedure overview		
Response to request for further information		12 APRIL 2010

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *'After ethical review — guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

10/H0711/50315 **Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

Dr John Keen
Chair
Email: Julie.kidd@nwlh.nhs.uk

Copy to:

Heather House, Research and Development Heatherhouse@admin.ox.ac.uk

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

Felicity Cowdrey
Department of Psychiatry
University of Oxford
Warneford Hospital
Headington
Oxford
OX37JX
Felicity.cowdrey@psych.ox.ac.uk

INFORMATION FOR VOLUNTEERS

Reward processing in individuals recovered from Anorexia Nervosa.

Part 1 tells you the purpose of this study and what will happen if you take part.
Part 2 gives you more detailed information about the conduct of the study.

Part 1:

You are being invited to take part in a research project. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read this information carefully and discuss it with friends, relatives and others if you wish. If there is anything you do not understand, or if you would like more information, please ask us. Take time to decide whether you wish to take part.

What is the purpose of the study?

To investigate the neural response to reward in individuals who have recovered from Anorexia Nervosa (AN) is the aim of our study**.** ***AN*** is an eating disorder characterized by extremely low body weight, distorted body image and an obsessive fear of gaining weight. It is difficult to treat and current psychological and medical treatments for AN are only modestly helpful. Long term outcome therefore remains poor. One feature which presents a particular challenge in treatment and remains poorly understood is that individuals with AN find aspects of their disorder rewarding at the expense of normal pleasures. This in part may reflect a lack of understanding of how brain systems are altered in people affected by the illness.

A key aim of the present proposal is to see how participants with a history of AN respond to rewarding stimuli such as pictures and tastes of chocolate in the scanner. Thus we are investigating reward processing in individuals who have recovered from Anorexia Nervosa. To investigate this, we will use magnetic resonance imaging (MRI) to look at brain responses to pleasurable sensations including pictures of chocolate and positive facial expressions as well as actual chocolate in the mouth.

There are no known risks of MRI for most people. MRI scans use a combination of strong magnetic fields and radio waves to identify areas of the brain that are active when people perform simple cognitive tasks.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason.

Why have I been chosen?

We are interested in how the brain processes rewarding information and how a history of AN might affect this system. To do this, we would like to scan 2 groups of people, those who have who have recovered from AN (you) and second group who have never experienced AN.

You have received information about this study because either you registered with the Oxford Research Database for Anorexia Nervosa (ORDA, orda@nexus.ox.ac.uk) or you have responded to an email or poster advertisement recruiting individuals recovered from AN.

What will happen if I take part?

The study will involve coming for an initial screening visit. During this visit you will have an interview to ask about current and past psychological symptoms. We would also like you to fill out some questionnaires on the screening day and have a practice run of the actual experiment i.e. tasting chocolate and rating the stimuli. This screening visit will take no more than 2 hrs. Also on the screening day you will be given some questionnaires to take home and fill out and bring back in with you for the scan day.

On the experimental day we will arrange for you to come in for your scan. You will first come to the John Radcliffe Hospital (OCMR) where you will have an MRI scan. The whole test day will last under 2 hours in total.

What will I have to do?

fMRI scan: The fMRI technique identifies changes in blood flow in different parts of the brain that are active when people perform simple cognitive or taste tasks designed to measure the way the brain deals with emotional/sensory information. fMRI uses the same methods that are used for MRI brain scanning which provides detailed pictures of the brain.

The scanner is a large cube shape and has a tube running through the middle, which is open at both ends. You will enter the scanner head first and your feet/lower legs will remain outside the tube. During the scan you will hear some loud noises (earplugs are provided). The radiographer and researcher will be able to see you throughout the scan and we will provide you with a call button which you can press at any time.

When in the scanner you will receive some trials in which liquid chocolate is delivered in 0.5ml aliquots in your mouth and in some trials there will be pictures of chocolate as well. In some trials there will be a less pleasant strawberry taste delivered to your mouth and in some trials this will be paired with a strawberry picture. We will ask you to rate all the stimuli via a button box in the scanner. You will also be asked to respond to pictures of faces whilst in the scanner using the button box.

The tests will take about 60 minutes. We will also ask you to complete some simple questionnaires about mood before and after you go in the scanner. After the fMRI scan you will be able to go home.

What will happen to the results of the study?

We can give you up to a week to decide if you would like to take part in the study and, of course, you might wish to discuss it with relatives or friends. All personal data will be treated in strict confidence and you will not be identified personally in any subsequent publication. This is a research project and you are perfectly free to withdraw from it at any time without giving any reason for doing so. The study will contribute to the principal researcher's doctoral thesis and we plan to publish the findings in scientific journals - you will **not** be identified personally in these. We will make the results available to you, if you wish. We plan to study up to 32 people.

You will be able to contact the researchers during or after the study if you have any questions. You will be given a copy of this information sheet and the signed consent sheet to keep. Please contact us if you would any like any further information to help you decide.

Part 2:

What will happen if I don't want to carry on with the study?

If you do decide to take part in this study, you can withdraw at any time without giving a reason for doing so. Further, if you want to stop the study at any time you are free to do so. Information collected may still be used.

Risks and benefits

There are no known risks of MRI for most people. However, the use of magnets means that the scan procedure is not suitable for people with pacemakers, mechanical heart valves, hip replacements or with other metal implants in their body. Also, if you have ever sustained an eye injury involving metal or have any history of seizures you should not take part. If you are pregnant you should also not take part. Women who are at risk of pregnancy may be asked to have a pregnancy test before taking part. If you suffer from claustrophobia or if you have suffered previously from anxiety in confined spaces, you may find sitting or lying still in the scanner unpleasant and it may be better not to take part.

In the unlikely event of us seeing any abnormalities on your scan, a member of our research team will discuss the implications with you and, with your permission, your GP may be notified. However, it is important to note that we do not carry out our scans for diagnostic purposes, and therefore these scans are not a substitute for a clinical appointment. Rather, our scans are intended for research purposes only.

There will be no direct benefit to the participant by taking part. However, you will be reimbursed for your time and may also benefit from gaining insight into how studies are run and the reasons for the study which can be discussed with the researcher if you so wish after the study.

Exclusion Criteria

General exclusion criteria include being male, left handedness, any current or past psychological problems (other than past Anorexia Nervosa) or any medical condition such as epilepsy. You will also not be able to take part if you are on any regular medication as we need to exclude drug effects (except the contraceptive pill), or if you are claustrophobic as the MRI scanner is a confined space.

fMRI scanning should not be performed if you have a heart pacemaker, mechanical heart valve, mechanical implant such as an aneurysm clip, hip replacement, or if you carry pieces of metal that have accidentally entered your body. This is to ensure that we do not take the risk of metal being in your body when you go into the scanner. You should not take part in the study if you are pregnant. Also, it is not possible to wear normal glasses in the scanner. However, we can provide scanner-safe glasses for most prescriptions. Before going into each scanner the operator radiographer will go through the procedure with you and ensure that you are safe to go into the scanner (i.e. make sure you do not have a pacemaker etc). When recruited, participants will be asked if they have taken any regular medication over the last three months (other than the contraceptive pill) and if so they will be excluded.

What if there is a problem?

You will be given the phone number of one of the researchers for the duration of your involvement in the study. You will be able to contact them if you have any concerns. In addition, if you are concerned about any aspects of the research, you can seek general advice from the research information website ‘Involve’ – http://www.invo.org.uk/.

The University has arrangements in place to provide for harm arising from participation in the study for which the University is the research sponsor. Any complaints before, during or after the study can be directed to the Clinical Trials and Research Governance (CTRG) office on 01865857939 or the head of CTRG, email: heather.house@admin.ox.ac.uk.

Expenses and payments

In recognition of your time and help you will paid £10 for the initial screening and an additional £25 if you complete the study. You will also be reimbursed reasonable travel expenses (e.g. bus fares, parking expenses/ mileage).

Will my taking part in the study be kept confidential?

All the information about your participation in this study will be kept confidential. Your results will be coded with a participant number and no personal information will be attached to the data. This anonymisation will occur at the point of data collection. Data will be stored on a university computer for up to three years. Only the named researchers will have access to this data. The overall results of the study may be published in scientific journals. However, all personal data will remain confidential. Some parts of the data collected for the study may be looked at by authorised persons from the University of Oxford and those from regulatory authorities (i.e. Research Ethics Service) to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site.

Who has reviewed this study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed by the London Research Ethics Committee.

Sponsorship and Funding

The University of Oxford is the sponsor for this study. This work is funded by the Sir Jules Thorn Charitable Trust.

Contact details

If you would like further information on this study, please contact either Ciara McCabe or Felicity Cowdrey :

Tel.: (01865) 223778 / (01865) 223918.

Email: ciara.mccabe@psych.ox.ac.uk

felicity.cowdrey@psych.ox.ac.uk

Thank you for taking the time to read this information sheet

Dr Ciara McCabe   Felicity Cowdrey   Dr Catherine Harmer   Dr Rebecca Park

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

Warneford Hospital
Oxford
OX3 7JX
TEL: 01865 223778 /01865 223 918
ciara.mccabe@psych.ox.ac.uk
felicity.cowdrey@psych.ox.ac.uk

INFORMATION FOR VOLUNTEERS

Reward processing in individuals recovered from Anorexia Nervosa.

**Part 1 tells you the purpose of this study and what will happen if you take part.
Part 2 gives you more detailed information about the conduct of the study.**

Part 1:

You are being invited to take part in a research project. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read this information carefully and discuss it with friends, relatives and others if you wish. If there is anything you do not understand, or if you would like more information, please ask us. Take time to decide whether you wish to take part.

What is the purpose of the study?

To investigate the neural response to reward in individuals who have recovered from Anorexia Nervosa (AN) compared to those with no history of AN is the aim of our study**.** ***AN*** is an eating disorder characterized by extremely low body weight, distorted body image and an obsessive fear of gaining weight. It is difficult to treat and current psychological and medical treatments for AN are only modestly helpful. Long term outcome therefore remains poor. One feature which presents a particular challenge in treatment and remains poorly understood is that individuals with AN find aspects of their disorder rewarding at the expense of normal pleasures. This in part may reflect a lack of understanding of how brain systems are altered in people affected by the illness.

A key aim of the present proposal is to see how participants with a history of AN, compared to those who have never experienced AN, respond to rewarding stimuli such as pictures and tastes of chocolate in the scanner. Thus we are investigating reward processing in individuals who have recovered from AN compared to individuals who have never experienced AN. To investigate this, we will use magnetic resonance imaging (MRI) to look at brain responses to pleasurable sensations including pictures of chocolate and facial stimuli as well as actual chocolate in the mouth.

There are no known risks of MRI for most people. MRI scans use a combination of strong magnetic fields and radio waves to identify areas of the brain that are active when people perform simple cognitive tasks.

Do I have to take part?

It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason.

Why have I been chosen?

We are interested in how the brain processes rewarding information and how a history of Anorexia Nervosa might affect this system. To do this, we would like to scan 2 groups of people, those who have never experienced Anorexia Nervosa (you) and another group of people who have recovered from Anorexia Nervosa.

You have received information about this study because either you registered with our department's volunteer database or you have responded to an email or poster advertisement recruiting healthy participants.

What will happen if I take part?

The study will involve coming for an initial screening visit. During this visit you will have an interview to ask about current and past psychological symptoms. We would also like you to fill out some questionnaires on the screening day and have a practice run of the actual experiment i.e. tasting chocolate and rating the stimuli. This screening visit will take no more than 2 hrs. Also on the screening day you will be given some questionnaires to take home and fill out and bring back in with you for the scan day.

On the experimental day we will arrange for you to come in for your scan. You will first come to the John Radcliffe Hospital (OCMR) where you will have an MRI scan. The whole test day will last under 2 hours in total.

What will I have to do?

fMRI scan: The fMRI technique identifies changes in blood flow in different parts of the brain that are active when people perform simple cognitive or taste tasks designed to measure the way the brain deals with emotional/sensory information. fMRI uses the same methods that are used for MRI brain scanning which provides detailed pictures of the brain.

The scanner is a large cube shape and has a tube running through the middle, which is open at both ends. You will enter the scanner headfirst and your feet/lower legs will remain outside the tube. During the scan you will hear some loud noises (earplugs are provided). The radiographer and researcher will be able to see you throughout the scan and we will provide you with a call button which you can press at any time.

When in the scanner you will receive some trials in which liquid chocolate is delivered in 0.5ml aliquots in your mouth and in some trials there will be pictures of chocolate as well. In some trials there will be a less pleasant strawberry taste delivered to your mouth and in some trials this will be paired with a strawberry picture. We will ask you to rate all the stimuli via a button box in the scanner. You will also be asked to respond to pictures of faces whilst in the scanner using the button box.

The tests will take about 60 minutes. We will also ask you to complete some simple questionnaires about mood before and after you go in the scanner. After the fMRI scan you will be able to go home.

What will happen to the results of the study?

We can give you up to a week to decide if you would like to take part in the study and, of course, you might wish to discuss it with relatives or friends. All personal data will be treated in strict confidence and you will not be identified personally in any subsequent publication. This is a research project and you are perfectly free to withdraw from it at any time without giving any reason for doing so. The study will contribute to the principal researcher's doctoral thesis and we plan to publish the findings in scientific journals - you will **not** be identified personally in these. We will make the results available to you, if you wish. We plan to study up to 32 people.

You will be able to contact the researchers during or after the study if you have any questions. You will be given a copy of this information sheet and the signed consent sheet to keep. Please contact us if you would any like any further information to help you decide.

Part 2:

What will happen if I don't want to carry on with the study?

If you do decide to take part in this study, you can withdraw at any time without giving a reason for doing so. Further, if you want to stop the study at any time you are free to do so. Information collected may still be used.

Risks and benefits

There are no known risks of MRI for most people. However, the use of magnets means that the scan procedure is not suitable for people with pacemakers, mechanical heart valves, hip replacements or with other metal implants in their body. Also, if you have ever sustained an eye injury involving metal or have any history of seizures you should not take part. If you are pregnant you should also not take part. Women who are at risk of pregnancy may be asked to have a pregnancy test before taking part. If you suffer from claustrophobia or if you have suffered previously from anxiety in confined spaces, you may find sitting or lying still in the scanner unpleasant and it may be better not to take part.

In the unlikely event of us seeing any abnormalities on your MRI scan, a member of our research team will discuss the implications with you and, with your permission, your GP may be notified. However, it is important to note that we do not carry out our scans for diagnostic purposes, and therefore these scans are not a substitute for a clinical appointment. Rather, our scans are intended for research purposes only.

There will be no direct benefit to the participant by taking part. However, You will be reimbursed for your time and may also benefit from gaining insight into how studies are run and the reasons for the study which can be discussed with the researcher if you so wish after the study.

Exclusion Criteria

General exclusion criteria include being male, left handedness, any past or current psychological problems or any serious medical conditions such as epilepsy. You will also not be able to take part if you are on any regular medication as we need to exclude drug effects (except the contraceptive pill) or if you are claustrophobic as the MRI scanner is a confined space.

fMRI scanning should not be performed if you have a heart pacemaker, mechanical heart valve, mechanical implant such as an aneurysm clip, hip replacement, or if you carry pieces of metal that have accidentally entered your body. This is to ensure that we do not take the risk of metal being in your body when you go into the scanner. You should not take part in the study if you are pregnant. Also, it is not possible to wear normal glasses in the scanner. However, we can provide scanner-safe glasses for most prescriptions. Before going into each scanner the operator radiographer will go through the procedure with you and ensure that you are safe to go into the scanner (i.e. make sure you do not have a pacemaker etc). When recruited, participants will be asked if they have taken any regular medication over the last three months (other than the contraceptive pill) and if so they will be excluded.

What if there is a problem?

You will be given the phone number of one of the researchers for the duration of your involvement in the study. You will be able to contact them if you have any concerns. In addition, if you are concerned about any aspects of the research, you can seek general advice from the research information website 'Involve' – http://www.invo.org.uk/.

The University has arrangements in place to provide for harm arising from participation in the study for which the University is the research sponsor. Any complaints before, during or after the study can be directed to the Clinical Trials and Research Governance (CTRG) office on 01865857939 or the head of CTRG, email: heather.house@admin.ox.ac.uk

Expenses and payments

In recognition of your time and help you will paid £10 for the initial screening and an additional £25 if you complete the study. You will also be reimbursed for reasonable travel expenses (e.g. bus fares, parking expenses, mileage).

Will my taking part in the study be kept confidential?

All the information about your participation in this study will be kept confidential. Your results will be coded with a participant number and no personal information will be attached to the data. This anonymisation will occur at the point of data collection. Data will be stored on a university computer for up to 3 years, while personal details will be stored separately in a locked filing cabinet. Only the named researchers will have access to this data. The overall results of the study may be published in scientific journals. However, all personal data will remain confidential. Some parts of the data collected for the study may be looked at by authorised persons from the University of Oxford and those from regulatory authorities (i.e. Research Ethics Service) to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site.

Sponsorship and Funding

The University of Oxford is the sponsor for this study. This work is funded by the Sir Jules Thorn Charitable Trust.

Who has reviewed this study?

All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed by London Research Ethics Committee.

Contact details

If you would like further information on this study, please contact either Ciara McCabe or Felicity Cowdrey :

Tel.: (01865) 223778 / (01865) 223918

Email: ciara.mccabe@psych.ox.ac.uk
felicity.cowdrey@psych.ox.ac.uk

Thank you for taking the time to read this information sheet

Dr Ciara McCabe Felicity Cowdrey Dr Catherine Harmer Dr Rebecca Park

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

Warneford Hospital
Oxford
OX3 7JX
TEL direct line: 01865 223 778 / 01865 223918
E-MAIL:Ciara.Mccabe @psych.ox.ac.uk/ felicity.cowdrey@psych.ox.ac.uk

CONSENT TO RESEARCH FORM

<u>Reward processing in individuals recovered from Anorexia Nervosa .</u>

INVESTIGATORS: Dr Ciara McCabe, Felicity Cowdrey, Dr Catherine Harmer, Dr Rebecca Park

Signing this form does not commit you to completing this study; you remain free to leave the study at any time and without having to give any reason for doing so.

Please initial

I have read the information sheet dated………………. (version…..). I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. However, I understand that any anonymised data already collected may be retained and used.

I understand that relevant sections of any of my records and data collected during the study may be looked at by responsible individuals from the University of Oxford and other regulatory bodies, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

I agree to take part in the study.

Name of participant Date

Signature

Name of researcher taking consent Date

Signature

NART (2nd edition)

Verbal IQ = 129 – (No. of Incorrect * 0.919)

CHORD	SIMILE
ACHE	BANAL
DEPOT	QUADRUPED
AISLE	CELLIST
BOUQUET	FACADE
PSALM	ZEALOT
CAPON	GAUCHE
DENY	TOPIARY
NAUSEA	LEVIATHAN
DEBT	BEATIFY
COURTEOUS	PRELATE
RAREFY	SIDEREAL
DRACHM	EQUIVOCAL
AEON	NAIVE
PLACEBO	CATACOMB
ABSTEMIOUS	GAOLED
DÉTENTE	THYME
IDYLL	HEIR
PUERPERAL	RADIX
AVER	ASSIGNATE
HIATUS	DEMESNE
SUBTLE	SYNCOPE
PROCREATE	LABILE
GIST	CAMPANILE
SUPERFLUOUS	
GOUGE	

Fawcett-Clark Pleasure Capacity Scale

What follows is a list of situations that might influence how a person feels. Please read each one carefully and decide how much the situation would give you pleasure **right now** in your present mood. Then circle the number that best describes your response.

Rate a situation as pleasurable if:

- you would enjoy the situation
- the situation would lift your spirits, or
- the situation would be fun for you

Circle only one number for each situation and do not skip any items. If a situation does not apply to you, try and imagine that it does anyway.

1 = No pleasure at all
2 = Mild pleasure
3 = Moderate pleasure
4 = Great pleasure
5 = Extreme and lasting pleasure

At the end of this test add up all the numbers to your answers creating a total score.
Try and take this test several times before our next meeting.
Keep track of all of your total scores on each test taken

1.	You sit watching a beautiful sunset in an isolated, untouched part of the world	1	2	3	4	5
2.	When you leave the house wearing new and attractive clothes several people give you compliments on how great you look	1	2	3	4	5
3.	You accidentally overhear your child boasting to playmates about what a terrific parent you are	1	2	3	4	5
4.	You are listening to beautiful music in peaceful surroundings	1	2	3	4	5
5.	While fishing, you feel a tug on your line and watch a 6-pound fish jump out of the water with your bait in its mouth	1	2	3	4	5
6.	You reach full sexual climax with someone you love very much	1	2	3	4	5
7.	You come to the end of a job that you find meaningful because of its immediate results	1	2	3	4	5
8.	Several years after your youngest child has moved out of the house, you realize that all your children have made happy and successful lives for themselves	1	2	3	4	5
9.	Your spouse surprises you with a tender hug and tell you that "no one could have a better companion or lover."	1	2	3	4	5
10.	After much concentration and hard work you finally master a new skill on your own.	1	2	3	4	5
11.	After some vigorous physical exercise, you pause to catch your breath and relax your muscles	1	2	3	4	5
12.	You discover in the newspaper that your lottery ticket is worth £5000	1	2	3	4	5
13.	Your supervisor gives you an unexpected merit pay increase in recognition for outstanding work.	1	2	3	4	5

14.	You are skiing down a mountain very fast while still in good control of yourself	1	2	3	4	5
15.	While raking leaves on a beautiful autumn day, you pause to watch your children playing in the leaf piles.	1	2	3	4	5
16.	A group of your neighbors selects you to receive an award for your work in the community.	1	2	3	4	5
17.	You lie soaking in a warm bath.	1	2	3	4	5
18.	You are skillfully flying an airplane by yourself on a clear day.	1	2	3	4	5
19.	You lie basking in the sun on a relaxed week-end.	1	2	3	4	5
20.	During a quiet early-morning walk along the seashore, you feel very much at peace and at one with the universe.	1	2	3	4	5
21.	You sit savoring a good meal of well-prepared food.	1	2	3	4	5
22.	Someone whose career you have taken an interest in and encouraged begins to become very successful.	1	2	3	4	5
23.	You come to the end of a difficult and complicated task without having made a single mistake.	1	2	3	4	5
24.	You win a very large bet you have made on a football game.	1	2	3	4	5
25.	Your work on a physical fitness program results in many compliments on how healthy and trim you are looking.	1	2	3	4	5
26.	Someone gently begins to scratch your back.	1	2	3	4	5
27.	Your neighbors rave about the way you keep up your house and yard.	1	2	3	4	5
28.	You take off on a trip to China, scheduled to visit all the places you've read and heard about.	1	2	3	4	5
29.	You find yourself at a lively party with many fascinating people.	1	2	3	4	5
30.	Someone who makes you feel loved wraps you in his/her arms and holds you closely.	1	2	3	4	5
31.	You sit with good friends, huddled close to a warm bonfire and roasting marshmallows on a chilly night.	1	2	3	4	5
32.	You spend a low and gentle period of time in sexual foreplay with someone you love very much.	1	2	3	4	5
33.	Someone calls on you for help during an emergency, and your help sees him/her through a difficult situation.	1	2	3	4	5
34.	You come to the end of a difficult work project that has taken much of your energy and many weeks of time.	1	2	3	4	5
35.	You find that one of your close friends is someone you can talk to about almost anything.	1	2	3	4	5
36.	A member of the opposite sex takes a special interest in you.	1	2	3	4	5

Screening for chocolate liking / frequency of eating

(As used is McCabe, Cowen and Harmer, 2009)

1. **On a scale from 1-10** *(10 is the highest)* **how much would you say that you sometimes crave chocolate?**

2. **On a scale from 1-10** *(10 is the highest)* **how much would you say that you like chocolate?**

3. **On a scale from 1-10** *(10 is the highest)* **how much would you say that you like milk?**

4. **How frequently do you eat chocolate?**

5. **How much chocolate do you eat at a time? (To estimate this, please use as units a regular bar of chocolate)**

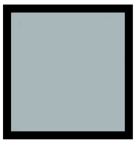
Positive and Negative Affective Schedule (PANAS)

This scale consists of a number of words that describe different feelings and emotions. Please read each item and mark the appropriate answer in the space next to the word. Indicate to what extent you have felt this way IN THE LAST HOUR.

1. **Very slightly or not at all**
2. **A little**
3. **Moderately**
4. **Quite a bit**
5. **Extremely**

Interested	____	**Irritable**	____
Distressed	____	**Alert**	____
Excited	____	**Ashamed**	____
Upset	____	**Inspired**	____
Strong	____	**Nervous**	____
Guilty	____	**Determined**	____
Scared	____	**Attentive**	____
Hostile	____	**Jittery**	____
Enthusiastic	____	**Active**	____
Proud	____	**Afraid**	____

Stimuli combinations used in the reward paradigm

Condition 1	chocolate in the mouth + grey visual stimulus	 
Condition 2	picture of chocolate	
Condition 3	chocolate in the mouth + a picture of chocolate	 
Condition 4	strawberry in the mouth + grey visual stimulus	 
Condition 5	picture of mouldy strawberries	
Condition 6	strawberry in the mouth + a picture of mouldy strawberries	 
Rinse condition	tasteless rinse control solution + grey visual stimulus	

Contrast 1: (chocolate in the mouth + grey visual stimulus) – (rinse + grey visual stimulus)
Contrast 2: (picture of chocolate) – (grey visual picture)
Contrast 3: (chocolate in the mouth + a picture of chocolate) – (rinse + grey visual stimulus)
Contrast 4: (strawberry in the mouth + grey visual stimulus) – (rinse + grey visual stimulus)
Contrast 5: (picture of strawberry) – (grey visual picture)
Contrast 6: (strawberry in the mouth + a picture of strawberry) – (rinse + grey visual stimulus)

Note. The term 'chocolate in the mouth' refers to the intra-oral delivery through a teflon tube of 0.5 ml of a fine liquid chocolate, which was identical for all such trials, and which could not be seen by the subject. The term 'strawberry in the mouth' refers to the intra-oral delivery of 0.5 ml of an unpleasant strawberry flavoured drink through a tube that also could not be seen by the subject. The term 'picture of chocolate' refers to a picture of a bar of brown i.e. milk chocolate shown on the display screen, and the term 'picture of mouldy strawberries' to a picture of mouldy strawberries.

Brief overview of FMRI

Functional neuroimaging techniques

Functional neuroimaging encompasses several different techniques including positron emotion tomography (PET), single photon emission computed tomography (SPECT) and functional magnetic resonance imaging (FMRI). These techniques map local physiological or metabolic signals from the brain and thus all have the ultimate aim of visualising cerebral activity. The next section will provide a brief overview of FMRI as this is the neuroimaging technique that is employed in Chapters 4 and 6.

FMRI and MRI

Both FMRI and MRI take advantage of the same basic principle, namely that of nuclear magnetic resonance. Most human tissue is water (H_2O) based, although the amount of water in each type of tissue varies. The single protons that are found in water molecules (the hydrogen nuclei in H_2O) have a net positive charge and therefore act as microscopic magnets. Before stimulation, the nuclei are oriented randomly but when the body is exposed to a strong static magnetic field (for example, when entered into the bore of a MRI scanner), the nuclei of the hydrogen atoms will align with the magnetic field. Although aligned, the protons from different atoms continue to spin (or precess) out of phase with each other until they are subjected to electromagnetic radiation in the form of radio waves. When subjected to radio waves at the right frequency (RF pulse), the energy content of the protons change and they are knocked by 90 degrees from their original orientation. As the protons spin in the new state they produce a detectable change in the magnetic field. After the RF pulse is switched off, the protons return to their previous state (or relax). The protons in tissues will return back to their original positions at different rates depending on the density of the hydrogen molecules and the way they are bonded together. The signal recorded as hydrogen molecules relax back to their original spinning orientations has two components: (1) a component along the direction of the static magnetic field (B_0) which decays over time (T_1) until it is back to its original position and spin phase and, (2) a component which decays over time due to the local interaction with other nearby molecules (T_2). The signals which are emitted as the protons return back to their original positions is used to create MR images (for example, it is the T_1 component which forms the basis of MR structural images as different tissues have different relaxation times and can be identified separately). The process of stimulation and relaxation is repeated as the scanner sends radio waves to different slices of the brain.

The fundamental assumption of FMRI is that active brain areas have higher energy demands and there is an increase in blood flow to this area to meet the demand. The blood oxygen level dependent (BOLD) signal of FMRI depends on the magnetic properties of haemoglobin and the changes in blood flow and metabolism that are related to neuronal activity. Neuronal activity requires oxygen supplied by haemoglobin and the magnetic properties of haemoglobin depend on the amount of oxygen it carries. When a region of the brain is activated by a stimulus (for example the ventral striatum may become stimulated by a monetary reward) there is a significant increase in regional cerebral blood flow carrying oxyhaemoglobin. Despite the large increase of oxyhaemoglobin to the specific brain region, there is only a modest increase in actual oxygen consumption from the blood. Therefore, the overall effect of neural activity is a regional increase in oxyhaemoglobin and a relative decrease in deoxyhaemoglobin.

As oxygenated haemoglobin is diamagnetic, it has little effect on the magnetic field of a MR scanner. However, deoxyhaemoglobin is paramagnetic relative to the brain tissues, meaning that is will disturb the local magnetic field (B_0) and thus will produce distortions in the T_2 component. Localised distortions caused by the magnetic components of deoxyhaemoglobin mean that the actual time taken for the signal emitted by relaxing hydrogen molecules is quicker than the theoretical T_2 time and is denoted as T_2*. The T_2* decay times form the basis of images collected using FMRI as the presence of deoxyhaemoglobin in the blood vessels causes a darkening of the image in those voxels.

In summary, when neural activity increases there is a relative decrease in paramagnetic deoxyhaemoglobin and this results in an increased BOLD signal. The T_2* weighted images used in FMRI display the contrast between areas with relatively more and relatively less oxygenated blood. Areas showing a higher BOLD signal are therefore interpreted as having increased functional activity.

Strengths and limitations of FMRI

The main advantage of FMRI is that is non-invasive and does not require a contrast agent to be administered (unlike PET). In addition, structural brain images can be collected in the same session meaning that sources of activation can be accurately mapped. However, FMRI is an indirect measure of neural activity which relies on the delivery of increased oxygenated blood to active brain areas. Therefore the temporal resolution (i.e., the smallest time period that can be separated) is limited by the delay between increased neural activation and the peak BOLD signal, (known as the heamodynamic response function). Lastly, it is not possible to directly map neuroreceptors using FMRI (unlike PET).

Neuroimaging software

Whilst a full evaluation of software used to analyse neuroimaging data is beyond the scope of this thesis, brief consideration will be given to the two packages which have been used in Chapters 4 and 6.

Two popular software choices for FMRI analysis are Statistical Parametric Mapping (SPM, Wellcome Department of Cognitive Neurology, London, UK; http://www.fil.ion.ucl.ac.uk/spm/software/) and the FMRIB Software Library (FSL, http://www.FMRIB.ox.ac.uk/fsl). More information on using these programmes is provided in Chapters 4 and 6. There is a significant amount of overlap between these software packages in terms of what kind of data can be analysed. Therefore, choice of software is usually based more on the platform needed to run it, the software cost (although both these programmes are free, SPM is coded as a Matlab tool box which means a Matlab licence is necessary) and the local expertise. FSL is particularly useful for running model-free analysis methods, such as Independent Component Analysis (ICA). This method was essential for analysing the resting state FMRI data reported in Chapter 6.

Subjective ratings of the picture and taste stimuli used in the reward paradigm

	Group											
	Pleasantness				**Intensity**				**Wanting**			
	Recovered AN (*n* = 15)		HC (*n* = 16)		Recovered AN (*n* = 15)		HC (*n* = 16)		Recovered AN (*n* = 15)		HC (*n* = 16)	
Condition	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Chocolate in the mouth + grey visual stimulus	1.05	.47	1.14	.46	1.62	.54	1.94	.63	0.92	.55	1.05	.98
Picture of chocolate	0.74	.29	0.85	.39	1.10	.44	1.44	.65	0.52	.41	.76	.30
Chocolate in the mouth + picture of chocolate	1.17	.51	1.31	.42	1.98	.60	2.22	.64	.99	.60	1.18	.54
Strawberry in the mouth + grey visual stimulus	-0.94	.82	-0.36	.90	2.17	.69	2.04	.60	-1.09	.73	-0.54	92
Picture of mouldy strawberries	-1.02	.44	-1.15	.32	1.30	.47	1.79	.76	-1.25	.50	-1.32	.36
Strawberry in the mouth + picture of mouldy	-1.26	.44	-0.99	.72	2.30	.81	2.45	.74	-1.40	.39	-1.20	.72

4.11

Regions showing main effects of task irrespective of group

Brain region	Montreal Neurological Institute (MNI) Coordinates			*Z* score	Significance (*p* value)
	X	Y	Z		
Chocolate in the mouth:					
Anterior insula	-32	20	2	5.08	<.001
	36	18	2	4.61	<.001
Ventral striatum	10	8	-4	5.04	<.001
Anterior cingulate	-2	34	20	3.97	<.001
Frontal lobe	18	20	-14	3.22	SVC
Sight of chocolate:					
Occipital cortex	14	-96	-4	INF.	<.001
	-26	-92	-6	INF.	<.001
Ventral striatum	10	6	-4	5.71	<.001
Anterior cingulate/ Cingulate gyrus	8	18	38	5.21	<.001
Superior frontal gyrus	40	44	34	5.01	<.001
Middle frontal gyrus	32	48	18	4.2	<.001
Strawberry in the mouth:					
Orbitofrontal cortex/ Insula	30	24	-2	4.79	<.001
Anterior insula	-32	20	8	4.85	<.001
Putamen	16	12	-2	4.78	<.001

Regions showing main effect of task irrespective of group (continued).

Sight of mouldy strawberries:					
Occipital cortex	10	-96	-2	INF.	<.001
	-18	-90	-8	INF.	<.001
Anterior insula	-30	20	8	6.24	<.001
	38	-4	10	6.47	<.001
Lateral orbitofrontal cortex	38	22	-16	5.37	=.003

Note.

INF, infinity
p values, clusters whole brain fully corrected (FWE). Threshold p = .05.

Appendices 5.1-5.9

National Research Ethics Service

NRES Committee South Central - Oxford A

South West Research Ethics Committee Centre
Whitefriars
Level 3 Block B
Lewins Mead
Bristol
BSI 2NT

Telephone: 01173421331
Facsimile: 01173420445

18 August 2011

Miss Felicity Cowdrey
DPhil student
Department of Psychiatry, University of Oxford
Department of Psychiatry
Warneford Hospital
Oxford
OX3 71X

Dear Miss Cowdrey

Study title: Reward and rumination in women recovered from anorexia nervosa.
REC reference: 11SC10315
Protocol number: N/A

Thank you for your letter of 17 August 2011, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice-Chair.
Confirmation of ethical opinion
On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all *NHS organisations involved in the study in accordance with NHS research governance arrangements*. Guidance on applying for NI-IS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs,uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation. Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Advertisement	1	12 July 2011
Advertisement	1	12 July 2011
Covering Letter		11 July 2011
Evidence of insurance or indemnity		12 July 2011
Investigator CV		12 July 2011
Investigator CV		07 November 2011
Other: Non NHS SSI		12 July 2011
Other: Risk Management Course Booking		
Other: Example Images		
Other: Oxford Research Database for Anorexia Nervosa (ORDA) Leaflet		
Participant Consent Form: Consent Form	1.1	22 June 2011
Participant Information Sheet: Reward processing in women recovered from Anorexia Nervosa	1.2	05 August 2011
Participant Information Sheet: Reward processing in women recovered from Anorexia Nervosa Healthy Controls	1.2	05 August 2011
Protocol	1.2	12 July 2011
Questionnaire: STA-Y		
Questionnaire: TAI-Y		
Questionnaire: RRS-ED		
Questionnaire: FCPS		
Questionnaire: Beck Depression Inventory		
Questionnaire: Eating Questionnaire		
Questionnaire: Manipulation Checks		

Questionnaire: Mood and hunger ratings		
Questionnaire: NART		
REC application		12 July 2011
Referees or other scientific critique report		08 July 2011

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *'After ethical review — guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

111SC/0315	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

Sara Owen Vice-Chair
Email: scsha.oxfordreca@nhs.net

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

WARNEFORD HOSPITAL
OXFORD
OX3 7JX

Direct line: (01865) 223918
FAX: (01865) 793101

PARTICIPANT INFORMATION SHEET

Reward processing in women with anorexia nervosa.

***Principal Researcher**: Felicity Cowdrey (DPhil student), felicity.cowdrey@psych.ox.ac.uk / 01865 223918*
Co –investigators/ collaborators: Dr Rebecca Park, Professor Catherine Harmer, Dr Graham Finlayson

Part 1 tells you the purpose of this study and what will happen if you agree to take part.
Part 2 gives you more detailed information about the conduct of the study

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. One of our team will go through the information sheet with you and answer any questions you have. Talk to others about the study if you wish. Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study. Ask us if there is anything that is not clear.

Part 1:

What is the purpose of the study?
Anorexia nervosa is an eating disorder characterized by extremely low body weight, distorted body image and an obsessive fear of gaining weight. There are two features which present as a particular challenge in treatment and remain poorly understood: (1) individuals with anorexia nervosa are preoccupied with repetitive *thoughts about* their body, and eating control (2) individuals with anorexia nervosa find aspects of their disorder rewarding. This study will investigate these two features using a range of computerised and pen and paper tasks.

We aim to recruit a sample of **women with anorexia nervosa**, women recovered from anorexia nervosa as well as women who have never had anorexia nervosa. All participants must be willing to attend the Department of Psychiatry (Warneford Hospital).

What will I have to do if I take part?
If you agree to take part you will be invited to attend the Department of Psychiatry on one occasion.

The session will last around one and a half hours. You will be invited to answer some general questions about your psychological well being and complete a questionnaire pack. If you are happy for us to do so, your height and weight will be taken (fully clothed).

You will be invited to complete two computerized tasks; one involving food pictures and the other involving decision making. You will also take part in a touch task, during which three different touch stimuli will be applied briefly to the underside of your left arm - these are not painful. You will be blindfolded for the touch task and asked to make a series of judgements about the stimuli. You will perform the touch task for a second time after reading and concentration on a series of verbal statements.

An inconvenience allowance will be provided at the end of the session (£15) and reasonable travel expenses will be reimbursed.

Why have I been chosen?

You have received information about this study because either you have responded to an email or poster advertisement recruiting individuals with personal experiences of anorexia nervosa or because you registered for the Oxford Research Database for Anorexia Nervosa (ORDA) and gave permission for us to contact you about our research studies.

Exclusion Criteria:

You will not be eligible to take part in this study if you are current receiving inpatient treatment for a psychological/ psychiatric problem. In addition, people under the age of 16 years will not be able to take part and those who are not sufficiently fluent in English.

This is an experimental study and we are unable to offer treatment as part of this study.

Do I have to take part?

No, **taking part is voluntary**. If you don't want to take part, you do not have to give a reason and no pressure will be out on you to try and change your mind. Not taking part in the study or withdrawing from the study will not affect any future health care you may seek. You will not be contacted again after the study unless you give consent for us to do so.

If I agree to take part what happens to what I say and do?

All the information you give us **will be confidential** and used for the purposes of this study only. The information collected during the study will be used in a way that will not allow you to be identified individually. The data will be collected and stored in accordance with the Data Protection Act 1998. Personal identifiers will be destroyed. Anonymised data will be stored on a password protected computer and any paper records will be stored in a locked filing cabinet.

Relevant sections of the records and data collected during the study may be looked at by responsible individuals from the University of Oxford and other regulatory bodies, where it is relevant to your taking part in this research.

What will happen to the study results?
We will make the results available to you, if you wish, and we plan to publish our findings in scientific journals but you will not be identified personally. The results will also form part of the chief investigators PhD thesis.

Part 2 of the information sheet:

Benefits and risks:
The information we get from this study may help improve our understanding of eating disorders.

In recognition of your time and help you will receive an inconvenience allowance of (£15). You will also gain insight into the running of an experimental study and can be kept up to date with the research as it develops. We will also cover any reasonable travel expenses, e.g. bus fares, parking costs.

There is a risk that the psychiatric screening may reveal significant eating related or other psychiatric symptoms. If this is the case, you will be signposted to appropriate services. We are however unable to offer treatment as part of this research study.

What will happen if I don't want to carry on?
Participation is voluntary and you are free to withdraw at any time without giving any reason and without any medical care or legal rights being affected. However, data collected prior to withdrawal will be kept and may be included in the data analysis.

What if there is a problem?
If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact Felicity Cowdrey (01865223918, felicity.cowdrey@psych.ox.ac.uk) or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865572224 or the head of CTRG, email: heather.house@admin.ox.ac.uk. The University has arrangements in place to provide for harm arising from participation in the study for which the University is the Research Sponsor

Who has reviewed this study?
All research in the NHS is looked at by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed by the South Central Oxford A Research Ethics Committee.

Funding:

This work is funded by the Sir Jules Thorn Charitable Trust.

What do I do now?

Think about the information on this sheet, and contact the researchers if you are not sure about anything or would like more information. If you are interested in taking part, either contact the named researcher directly by email, post or telephone, or complete the reply-slip below and post / email to the researcher.

You will be asked to sign a consent form after you have had the opportunity to have any questions answered. The consent form will not be used to identify you. It will be filed separately from all other information.

For further information:

Felicity Cowdrey (Chief Researcher)
Warneford Hospital,
Oxford,
OX3 7DX
Felicity.cowdrey@psych.ox.ac.uk
01865 223918 (office hours only)

You can also seek independent general advice from the research information website 'Involve' – http://www.invo.org.uk/.

THANKYOU FOR TAKING TIME TO READ THE INFORMATION SHEET

REPLY SLIP

Reward processing in women with anorexia nervosa

I am interested in taking part in the study entitled '**Reward processing in women with anorexia nervosa'**

Name:

Postal address:

Email address:

Telephone number:

Best method of contact:

Best time of contact:

I am happy for the named researcher (Felicity Cowdrey) to contact me about the study entitled **'Reward processing in women with anorexia nervosa'** Yes / No

Please return to Felicity Cowdrey (Chief Researcher). Warneford Hospital, Oxford, OX3 7JX. Felicity.cowdrey@psych.ox.ac.uk Tel. 01865 223918 (office hours only).

UNIVERSITY OF OXFORD

DEPARTMENT OF PSYCHIATRY

WARNEFORD HOSPITAL
OXFORD
OX3 7JX

TEL: (01865) 226482
FAX: (01865) 793101

Consent Form

Reward processing in recovered anorexia nervosa.

Principal researcher: Felicity Cowdrey, Dphil Student.
felicity.cowdrey@psych.ox.ac.uk/ 01865223918

Please initial box

- I confirm that I have read and understand the information sheet dated................ (*version*............) for the above study.
- I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.
- I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. I agree that any data collected prior to withdrawal will be kept.
- I understand that data collected during the study may be looked at by authorized individuals from the University of Oxford where it is relevant to my taking part in this research. I permit these individuals to access my research records
- I agree to take part in the above study.

Name of participant *(in block capitals)*:........……………………

Signature of the participant:…………….………… Date:…………………………..

Please initial the box if you agree for your contact details to be kept on record and if you agree to be contacted regarding future studies

---

Name of person taking consent:....................................

Signature of person taking consent:................................. Date:………………………

Mood and hunger visual analogue scales

[Please mark an 'X 'on each line]

At the moment I feel.......

Happy	Not at all Extremely 0 100
Despondent (disheartened, hopeless)	Not at all Extremely 0 100
Anxious	Not at all Extremely 0 100
Hungry	Not at all Extremely 0 100
Thirsty	Not at all Extremely 0 100

[Please mark an 'X 'on each line]

Please rate your….

…..level of fullness at the moment	Not at all Extremely 0 100
…..desire to eat at the moment	Not at all Extremely 0 100

Categories of photographic food stimuli used in the LO-FPQ computer task and example images

HCaSW	HCaSA	LCaSW	LCaSA
Muffin	Samosa	Apple	Carrot
Profiteroles	Garlic bread	Orange	Tomatoes
Ice cream	Pizza	Grapes	Lettuce
Chocolate	Chips	Raisins	Mange tout

HCaSA Muffin

HCaSA Pizza

LCaSW Orange

LCaSW Lettuce

Scoring algorithm for implicit 'wanting' task (D-RT)

Greenwald, Nosek and Banaji (2003) developed and validated a new scoring algorithm for the Implicit Association Test which aims to provide a measure of strengths of automatic associations. It is calculated from performance speeds during the task. The authors argued that the new algorithm outperforms the original algorithm on a number of levels (Greenwald, Nosek, & Banaji, 2003).

A number of studies have applied this algorithm to calculate implicit 'wanting' in the LFPQ (for example, Finlayson et al., 2012). Thus in these studies, the reaction times from the implicit 'wanting' task, in which participants are asked to select between two foods based on which one they would want to eat more, are transformed into a standardized '*d*-score' (D-RT) using the validated algorithm described by Greenwald, Nosek and Banaji (2003). Using the algorithm aims to improve statistical reliability and reduce contamination by individual variability in total average response speed.

The algorithm was also applied to the implicit 'wanting' data collected in Study 4 (Chapter 5). In line with previous studies, D-RT was calculated as follows: (1) overall *SD* from pooled response trials were calculated; (2) average reaction times (RT) for each category (for example, HCSA) were computed; (3) average RT for relevant comparison categories (for example, LCSA, HCSW, LCSW, HCSA) were computed; (4) the difference between category mean and comparison mean was calculated; (5) the difference was divided by the pooled *SD*.

Final scores were inverted for ease of interpretation and therefore the higher the D-RT, the greater the implicit 'wanting' for that food category relative to other categories in the task.

Self-reported clinical variables for anorexia nervosa participants

	AN-C		AN-W		AN-R		
	M	*SD*	*M*	*SD*	*M*	*SD*	*p*
Age of onset (years)	15.45	2.74	15.91	4.08	15.27	2.60	.798
Lowest ever BMI	13.85	1.65	14.13	4.78	14.46	2.85	.842
Duration of illness (months)	116.45	111.59	45.64	32.84	47.14	53.01	.003
Time in treatment (months)	29.9	34.33	22.86	25.45	19.55	21.19	.463
Duration of recovery (months)	--	--	--	--	39.05	35.45	--

Note. AN-R = Recovered anorexia nervosa; AN-W = Weight restored anorexia nervosa; AN-C = Current anorexia nervosa.

VAS ratings of mood and appetite-related variables before and after the task

VAS	Group	Time	*M*	*SD*	*p*
VAS-happy	AN-C	Pre	49.95	25.01	.276
		Post	54.40	25.13	
	AN-W	Pre	55.73	19.60	.846
		Post	55.23	21.27	
	AN-R	Pre	65.45	10.68	.064
		Post	72.09	13.26	
	HC	Pre	71.98	10.68	.126
		Post	73.56	13.26	
VAS-despondent	AN-C	Pre	21.70	25.13	.641
		Post	22.95	25.93	
	AN-W	Pre	19.09	14.43	.358
		Post	21.77	17.06	
	AN-R	Pre	16.64	6.66	.312
		Post	12.91	12.11	
	HC	Pre	6.85	6.66	.569
		Post	7.78	12.11	
VAS-anxious	AN-C	Pre	34.60	27.23	.008
		Post	28.45	26.14	
	AN-W	Pre	24.09	22.09	.914
		Post	24.46	20.76	
	AN-R	Pre	16.55	12.46	.059
		Post	13.74	8.85	
	HC	Pre	9.46	12.46	.323
		Post	8.17	8.85	
VAS-hungry	AN-C	Pre	24.95	19.36	.975
		Post	25.10	20.17	
	AN-W	Pre	25.36	22.93	<.001
		Post	43.46	26.77	
	AN-R	Pre	30.77	24.05	<.001
		Post	43.86	23.81	
	HC	Pre	34.54	24.05	<.001
		Post	48.73	23.81	

VAS ratings of mood and appetite-related variables before and after the task (continued)

VAS-thirsty	AN-C	Pre	38.55	26.74	.529
		Post	37.00	27.04	
	AN-W	Pre	28.77	26.10	.175
		Post	32.82	23.54	
	AN-R	Pre	25.91	22.33	.267
		Post	30.18	24.45	
	HC	Pre	35.27	24.45	.002
		Post	49.32	22.08	
VAS-feeling full	AN-C	Pre	60.60	19.10	.235
		Post	57.05	20.42	
	AN-W	Pre	46.05	20.65	.058
		Post	41.23	19.83	
	AN-R	Pre	53.55	22.08	.286
		Post	50.18	20.51	
	HC	Pre	49.32	22.08	.371
		Post	47.42	20.51	
VAS-desire to eat	AN-C	Pre	27.6	20.54	.337
		Post	32.15	30.32	
	AN-W	Pre	31.64	21.16	.019
		Post	40.05	25.24	
	AN-R	Pre	33.77	25.56	.003
		Post	46.68	24.12	
	HC	Pre	39.27	25.56	<.001
		Post	48/83	24.12	

Note. VAS = Visual analogue scale; HC = Healthy control; AN-R = Recovered anorexia nervosa; AN-W = Weight restored anorexia nervosa; AN-C = Current anorexia nervosa.

Explicit wanting and liking and implicit ‘wanting’ ratings across the groups

	Explicit wanting (0-100)				Explicit liking (0-100)				‘Implicit wanting’ D-RT			
	High calorie		Low calorie		High calorie		Low calorie		High calorie		Low calorie	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
HC	50.4	3.7	43.8	3.2	54.6	3.5	49.1	2.9	.16	.07	-.13	.07
AN-R	41.2	5.0	45.3	4.3	48.9	4.7	49.4	4.0	-.02	.10	.02	.10
AN-W	34.3	5.0	48.7	4.3	38.3	4.7	51.1	4.0	-.35	.09	.35	.09
AN-C	23.5	5.2	37.8	4.5	29.4	4.9	41.0	4.2	-.49	.10	.54	.10

Note. HC = Healthy control; AN-R = Recovered anorexia nervosa; AN-W = Weight restored anorexia nervosa; AN-C = Current anorexia nervosa.
Implicit ‘wanting’ scores (D-RT) have been inverted for interpretation ease.

Appendices 6.1-6.2

Group demographics and questionnaire scores for the recovered anorexia nervosa and healthy control participants

	Group			
	Recovered AN (*n* = 16)		**HCs** (*n* =14)	
Measure	***M***	***SD***	***M***	***SD***
Age (years)	23.06	3.55	24.11	2.85
BMI	21.33	2.17	21.01	1.56
IQ	115.93	4.7	114.65	4.26
EDE-Q	.99	1.46	.36	.33
BDI-II	5.44	6.36	1.17	1.38
STAI-T	15.75	9.79	14.21	8.07
STAI-S	12.67	7.31	9.93	4.27
PANAS-positive	24.81	5.05	25.71	7.3
PANAS-negative	12.75	4.45	12.0	4.98
RRS-ED	16.5	7.03	10.15	1.52*

Note. BDI-II = Beck Depression Inventory-II; STAI-T = State Trait Anxiety Inventory- trait subscale; STAI-S = State Trait Anxiety Inventory- state subscale; EDE-Q = Eating Disorder Examination questionnaire; PANAS = Positive and Negative Affect Scale; BMI = Body Mass Index; RRS-ED = Ruminative Response Scale for Eating Disorders.

* $p < .05$ Mann-Whitney *U*

Between-group correlations between self-report measures and the precuneus and DLPFC dual regression output

Recovered anorexia nervosa participants

Spearman's rho (*alpha in brackets*)	DLPFC	Precuneus	RRS-ED	EDE-Q	BDI-II
DLPFC	1.00				
Precuneus	-.21 (.43)	1.00			
RRS-ED	.36 (.18)	.11 (.68)	1.00		
EDE-Q	.49 (.06)	.26 (.34)	.81 (.001)	1.00	
BDI-II	.31 (.25)	.11 (.70)	.57 (.02)	.81 (.001)	1.00

Note. DLPFC = Dorsolateral prefrontal cortex; RRS-ED = Ruminative Response Scale for Eating Disorders; EDE-Q = Eating Disorder Examination Questionnaires; BDI-II = Beck Depression Inventory-II

Healthy control participants

Spearman's rho (*alpha in brackets*)	DLPFC	Precuneus	RRS-ED	EDE-Q	BDI-II
DLPFC	1.00				
Precuneus	-.05 (.88)	1.00			
RRS-ED	-.04 (.89)	-.27 (.37)	1.00		
EDE-Q	.8 (.78)	-.07 (.82)	.32 (.28)	1.00	
BDI-II	.18 (.54)	.01 (.98)	.14 (.65)	.70 (.006)	1.00

Note. DLPFC = Dorsolateral prefrontal cortex; RRS-ED = Ruminative Response Scale for Eating Disorders; EDE-Q = Eating Disorder Examination Questionnaires; BDI-II = Beck Depression Inventory-II