A Clinical Neuroscience Investigation into Flashbacks and Involuntary Autobiographical Memories

Ian Alexander Clark

St Hilda's College

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Department of Psychiatry

University of Oxford

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Abstract

Recurrent and intrusive distressing recollections of trauma are a hallmark symptom of Posttraumatic Stress Disorder (PTSD). The term 'flashback' is used in this thesis to refer to vivid, sensory perceptual (predominantly visual images), emotional memories from a traumatic event that intrude involuntarily into consciousness. Furthermore, intrusive image based memories occur in a number of other psychological disorders, for example, bipolar disorder and depression. Clinically, the presence and occurrence of flashbacks and flashback type memories are well documented. However, in terms of the neural underpinnings there is limited understanding of how such flashback memories are formed or later involuntarily recalled. An experimental psychopathology approach is taken whereby flashbacks are viewed on a continuum with other involuntary autobiographical memories and are studied using analogue emotional events in the laboratory.

An initial review develops a heuristic clinical neuroscience framework for understanding flashback memories. It is proposed that flashbacks consistent of five component parts – mental imagery, autobiographical memory, involuntary recall, attention hijacking and negative emotion. Combining knowledge of the component parts helped provide a guiding framework, at both a neural and behavioural level, into how flashback memories may be formed and how they return to mind unbidden.

Four studies (1 neuroimaging, 3 behavioural) using emotional film paradigms were conducted. In the first study, the trauma film paradigm was combined with neuroimaging (n = 35) to investigate the neural basis of both the *encoding* and the *involuntary recall* of flashback memories. Results provided a first replication of a specific pattern of brain activation at the *encoding* of memories that later returned as flashbacks. This included elevation in the rostral anterior cingulate cortex, insula, thalamus, ventral occipital cortex and left inferior frontal gyrus (during just the encoding of scenes that returned as flashbacks) alongside suppressed activation in the left inferior frontal gyrus (during the encoding of scenes that returned as flashbacks in other participants, but not that individual). Critically, this is also the first study to show the brain activation at the moment of *flashback involuntary recall* in the scanner. Activation in the middle and superior frontal gyri and the left inferior frontal gyrus was found to be associated with flashback involuntary recall.

In the second study, control conditions from 16 behavioural trauma film paradigm experiments were combined (n = 458) to investigate commonly studied factors that may be protective against flashback development. Results indicated that low emotional response to the traumatic film footage was associated with an absence of flashbacks over the following week. The third study used a positive film to consider the emotional valence of the emotion component of the framework. Positive emotional response at the time of viewing the footage was associated with positive involuntary memories over the following week. The fourth study aimed to replicate and extend this finding, comparing the impact of engaging in two cognitive tasks after film viewing (equated for general load). Predictions were not supported and methodological considerations are discussed.

Results may have implications for understanding flashbacks and involuntary autobiographical memories occurring in everyday life and across psychological disorders. Further understanding of the proposed components of the clinical neuroscience framework may even help inform targeted treatments to prevent, or lessen, the formation and frequency of distressing involuntary memories.

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List of Abbreviations

ANOVA	Analysis of Variance
APA	American Psychiatric Association
BDI-II	Beck Depression Inventory, 2nd edition
BOLD	Blood Oxygen Level Dependent
CBM	Cognitive Bias Modification
CBT	Cognitive Behavioural Therapy
DSM IV (TR)	Diagnostic and Statistical Manual, 4th Edition (text revision)
DSM-5	Diagnostic and Statistical Manual, 5th Edition
EMDR	Eye Movement Desensitisation and Reprocessing
EPI	Echo Planner Image
FEAT	FMRI Expert Analysis Tool
fMRI	functional Magnetic Resonance Imaging
IAM	Involuntary Autobiographical Memory
IFG	Inferior Frontal Gyrus
MDQ	Mood Disorders Questionnaire
MEG	Magnetoencephalography
MTG	Middle Temporal Gyrus
NICE	National Institute for Health and Care Excellence
PANAS	Positive and Negative Affect Schedule
PET	Positron Emission Spectroscopy
PTSD	Posttraumatic Stress Disorder
R	R statistical package
ROI	Region of Interest
rACC	rostral Anterior Cingulate Cortex
SPSS	Statistical Package for the Social Sciences
SPECT	Single-Photon Emission Computed Tomography
STAI-T	State Trait anxiety Inventory – Trait version
TEQ	Traumatic Experiences Questionnaire

Chapter 1: Introduction

Posttraumatic stress disorder (PTSD) is an anxiety disorder that can occur after a variety of traumatic events (Diagnositic and Statistical Manual IV-TR (DSM-IV-TR), American Psychiatric Association, 2000). A traumatic event is one in which an individual experiences or witnesses serious injury or threat to the physical integrity to the self or others, and their response involves intense fear, helplessness or horror (Criteria A1 & A2 of the American Psychiatric Association (APA) DSM-IV-TR). The lifetime prevalence of PTSD is estimated at around 10-20% (Breslau et al., 1998), with personal traumas (e.g. sexual assault) leading to higher rates of PTSD.

For a diagnosis of PTSD, patients must also have three types of symptoms; re-experiencing, avoidance, and hyper-arousal, all present for at least 1 month. The work described in this thesis focuses on the re-experiencing criteria, specifically on the hallmark symptom of "flashbacks". The term "flashback" is used throughout this thesis to refer to "vivid, sensory-perceptual (predominantly visual images), emotional memories from a traumatic event that intrude involuntarily into consciousness" (Bourne, Mackay, & Holmes, 2013). The term flashback is also sometimes used to describe only the intense periods of re-experiencing associated with dissociation, for example, when an individual loses contact with their surroundings and believes that they are back at the time of the traumatic event. Such experiences in clinical practice, however, are relatively rare. The broader definition used in this thesis is therefore designed to cover the more common feature reported in the clinic and aid translation with analogue studies of trauma.

Clinically, the experience of a flashback is well documented (see Chapter 2 section *The Patient Experience of Flashbacks*), and they occur in around 50-97% of individuals after

a traumatic event (Ehlers & Steil, 1995). Additionally, flashback type memories occur in everyday life, known as involuntary (autobiographical) memories (Berntsen, 1996), and in other psychological disorders, for example bipolar disorder (Holmes, Geddes, Colom, & Goodwin, 2008) and depression (Williams & Moulds, 2007). However, an understanding of flashbacks and flashback type memories from a cognitive neuroscience perspective is lacking. PTSD is one of the few disorders requiring an index event for diagnosis. Ethical and practical reasons make it difficult to study traumatic events as they occur. Experimental designs using analogue trauma allow for prospective investigations in controlled laboratory settings, offering an opportunity to investigate how a traumatic event leads to the formation of flashbacks and subsequently how these memories are involuntarily recalled.

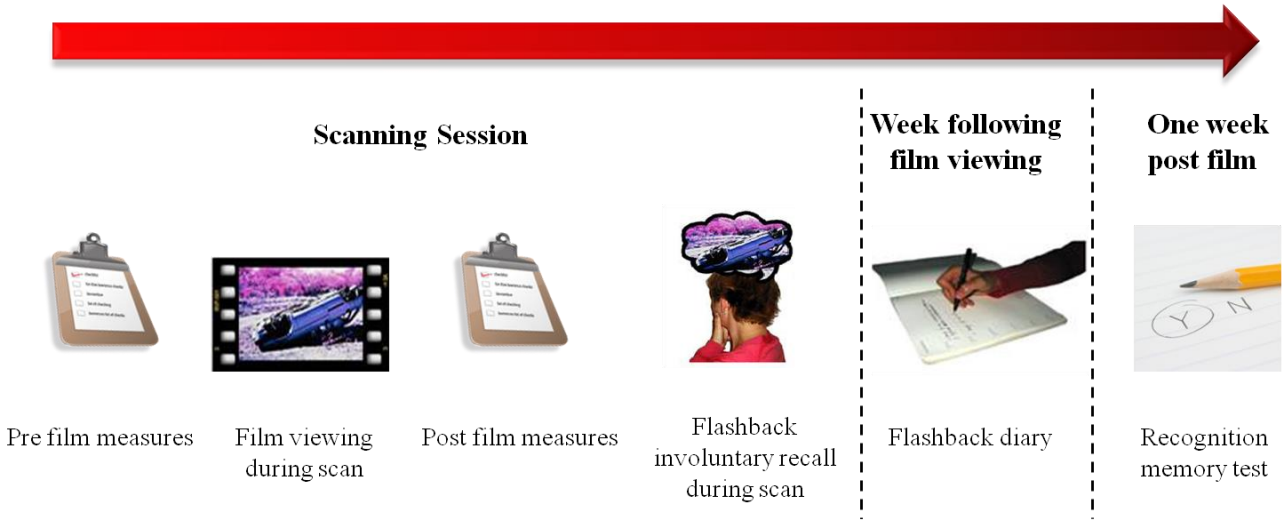
Throughout this thesis flashbacks are taken to be on a continuum of normal functioning, ranging from involuntary autobiographical memories in everyday life to intrusive memories in depression and bipolar disorder and recurrent flashbacks in PTSD. A pragmatic clinical neuroscience framework is proposed in Chapter 2, suggesting that a flashback compromises five component parts; autobiographical (trauma) memory, involuntary recall, negative emotions, mental imagery and attention hijacking. Flashbacks are poorly understood at a neuroscientific level, but more is known about each of the proposed component parts. The proposed framework is used as a guide for the work presented in this thesis. A brief overview of each of the chapters is presented below.

In Chapter 2, the clinical neuroscience framework of flashbacks is proposed. The chapter reviews the current clinical understanding of flashbacks, an experimental method for studying flashbacks in the laboratory (the trauma film paradigm) and the neuroimaging research that has been conducted with PTSD patients. A brief overview of the patient

experience of flashbacks from the component parts of the framework and how this can be mapped onto the brain is presented.

In Chapter 3, a neuroimaging study using the trauma film paradigm is described, designed to investigate the neural basis of the encoding and recall of analogue flashbacks. Only one previous neuroimaging study has investigated the neural basis of the encoding of flashback memories (Bourne, et al., 2013), and none have identified the exact mechanisms involved in flashback involuntary recall during scanning. The experiment has four aims. 1) To replicate the findings of Bourne et al. (2013) hypothesising that a distinct widespread pattern of activity is involved in the encoding of a flashback, including the amygdala, rostral anterior cingulate cortex, thalamus, ventral occipital cortex, left inferior frontal gyrus and middle temporal gyrus. 2) To extended the paradigm by dividing the trauma film according to whether or not moments of the film (stills) could be identified on a recognition memory test at one week – analysing only those stills which were successfully identified on the recognition memory test. It is hypothesised that there would be minimal encoding differences in comparison to using both non-identified and identified stills. 3) To compare flashback events with potential events using identified and non-identified stills from the recognition memory test. As low numbers of events were expected, this analysis was exploratory and no hypotheses were made. 4) The paradigm was further extended to capture the brain activation involved at the moment of flashback involuntary recall in the scanner soon after trauma film viewing, hypothesising that flashback involuntary recall would involve brain regions associated with the components of the proposed clinical neuroscience framework. The experimental procedure can be seen in Figure 1.1.

Figure 1.1. The experimental procedure used in the neuroimaging study presented in Chapter 3.



Although flashbacks are common after trauma, not all individuals experience them. Understanding psychological factors that are protective against flashback formation may help develop interventions to reduce involuntary flashback recall. However, to my knowledge, prospective experimental work investigating psychological factors that may be associated with an absence of flashbacks has been lacking. As in real trauma, not all participants experience flashbacks after viewing the traumatic footage. A study is presented in Chapter 4 that performed an individual participants data meta analysis on data from the control conditions of 16 behavioural trauma film paradigm studies (n = 458) with the aim of investigating commonly studied psychological factors that may be protective against flashback development.

Chapter 5 considers an aspect of the proposed clinical neuroscience framework by exploring the importance of emotional valance for the formation of 'flashback type' memories. Flashback type memories (i.e. involuntary autobiographical memories that hijack attention) can also be positive and in everyday life these 'positive flashbacks' are in fact more frequent than their negative counterparts (Berntsen & Rubin, 2002). However, 'positive

flashbacks', referred to in this thesis as positive involuntary autobiographical memories (IAMs), have received little attention. The proposed clinical neuroscience framework of flashbacks would suggest that these positive IAMs should be similar to flashbacks, differing only in their emotional valence. Adapting the trauma film paradigm for positive footage allows for investigation into the formation of positive IAMs, and subsequent comparison to the formation of flashback memories, investigating whether the flashback framework can also improve understanding of other flashback type memories. The experiment presented in Chapter 5 investigates whether emotional response to a positive film, recognition memory of the positive film or participant baseline characteristics are associated with the frequency of positive IAMs.

The final experiments, described in Chapter 6, continues the exploration of positive IAMs, aiming to replicate and extend the findings presented in the previous chapter. Research into modulating flashback frequency has demonstrated that playing the visuospatial computer game Tetris reduces the frequency of flashbacks to traumatic footage, while the verbal computer game PubQuiz does not (Holmes, James, Kilford, & Deeprose, 2010). Whether the difference in impact of Tetris and Pub Quiz is due to the modality of the tasks (visuospatial or verbal) or general working memory taxation is currently unknown. Additionally, preliminary work suggests that playing Tetris can also reduce the frequency of IAMs arising from a positive film (Davies, Malik, Pictet, Blackwell, & Holmes, 2012). However, the emotional valence of the IAMs were not reported, and the study was limited by the lack of an active control condition. Two experiments are presented designed to address these limitations and to replicate the findings reported in Chapter 5. Experiment 1 presents a pilot study to compare the level of general working memory required for Tetris and Pub Quiz game play. Experiment

2 aims to replicate the association of positive emotional response and IAM frequency, and to investigate the impact of playing Tetris and Pub Quiz, compared to No Task, on positive IAM frequency.

The final chapter, Chapter 7, will present a general discussion of the overall findings, with conclusions and recommendations for future work.

Chapter 2: Intrusive imagery and Posttraumatic Stress Disorder - An experimental psychopathology approach to flashbacks

Abstract

This chapter presents a brief review of the patient experience and neuroimaging findings of Posttraumatic Stress Disorder (PTSD), focusing on flashbacks. It starts by describing the patient experience of PTSD and flashbacks. The current evidence-based treatments are briefly reviewed. Next, one mechanism of how to model the flashback experience in the laboratory, the trauma film paradigm, is examined. The relatively few neuroimaging studies investigating flashbacks are reviewed. A pragmatic framework to help bridge the clinical presentation and neuroscience of flashbacks is proposed. An experimental psychopathology approach is taken, yielding a framework in which a flashback comprises five component parts; autobiographical (trauma) memory, involuntary recall, negative emotions, mental imagery and attention hijacking. Each component is considered in turn, both behaviourally and from a brain imaging perspective. The components of the framework are examined in relation to potential use in laboratory experiments. A mapping of these five components of a flashback onto our understanding of the brain is described. Unanswered questions that exist in the understanding of flashbacks are considered using the proposed framework. It is suggested that the clinical neuroscience framework may aid the development of a firmer bridge between theory and clinic and possibly help develop preventative treatments against flashback development.

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The Patient Experience of Flashbacks

"I was in the car outside my house. The mugger put a knife to my neck; he said 'give me your money'. I was scared he would realise that I live here; I was worried for my daughter. He then checked my pockets and asked for my purse to check it and rummaged through it. I was feeling helpless; I was worried I had forgotten some money and he would find it and say I was lying to him. He then ran off and I looked back to my house to see my daughter crying and banging at the door. I felt guilty that she may have seen what happened and that she would be traumatised by it."

A patient's description of a traumatic event, taken from Holmes et al. (2005)

Posttraumatic Stress Disorder (PTSD) can occur after a variety of traumatic events. Breslau et al. investigated rates of PTSD after a range of psychologically traumatic events using a sample of over 2000 people (Breslau, et al., 1998). Events categorised as "held captive/ tortured/ kidnapped", "rape" and "badly beaten up" were those events most likely to lead to PTSD (53.4%, 49% and 31.9% conditional risk respectively). Other types of trauma such as "sudden unexpected death of a close friend or relative", "child's life-threatening illness" or "natural disaster" can also lead to PTSD but at varying degrees of risk (14.3%, 10.4%, 3.8% conditional risk respectively).

Trauma is defined not merely as a very stressful event but specifically as experiencing or witnessing serious injury or threat to the physical integrity to the self or others - Criterion A1 (see Figure 2.1a) of the American Psychiatric Association (APA), Diagnostic and Statistical Manual IV-TR (DSM-IV-TR; American Psychiatric Association, 2000). Additionally, the DSM-IV-TR requires that the person's response to the index trauma must involve intense fear, helplessness or horror (Criterion A2, see Figure 2.1a). These diagnostic criteria are particularly interesting as PTSD is one of the few disorders in the DSM-IV-TR that requires an index event to have occurred for diagnosis. This opens up an area of investigation for clinical research to try to understand how PTSD arises from a specific event.

Changes to the new Diagnostic and Statistical Manual - DSM-5 - published at the time of submission (see Appendix XVI for a summary of the changes; American Psychiatric Association, 2013) has refined criterion A of the PTSD diagnosis (see Figure 2.1b). The DSM-IV-TR criterion A2 has been removed as it has "no utility" in predicting the onset of PTSD. For example, research has demonstrated that many more negative emotions than the three mentioned in DSM-IV-TR are involved in traumatic events, including guilt, anger, sadness and disgust (Grey & Holmes, 2008; Grey, Holmes, & Brewin, 2001; Lee, Scragg, & Turner, 2001).

A diagnosis of PTSD in the DSM-IV-TR also requires patients to have three other types of symptoms. These are the hallmark symptom of re-experiencing, including 'flashbacks' (Criteria B1, B2, B3, see Figure 2.1a), persistent avoidance of trauma related stimuli (Criterion C) and persistent symptoms of increased arousal (Criterion D), all present for at least 1 month (Criterion E). The DSM-5 also includes an additional Criterion of negative cognitions and mood (American Psychiatric Association, 2013).

This thesis focuses on the re-experiencing criterion of PTSD, specifically 'flashbacks'. Trauma can be re-experienced in a number of different ways (see Figure 2.1a, Criterion B) all of which are highly distressing experiences. Within this thesis, the term flashback is used to describe "vivid, sensory–perceptual (predominantly visual images), emotional memories from a traumatic event that intrude involuntarily into consciousness" (Bourne, et al., 2013), encompassing criteria B1, B2 and B3. It is noted that this definition is broad. The term flashback is also sometimes used to describe only those intense periods of re-experiencing associated with profound dissociation (Criterion B3); "acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions,

Figure 2.1a. The exposure criteria (Criterion A) and a summary of the re-experiencing criteria (Criterion B) required for a diagnosis of PTSD in DSM-IV-TR.

Criterion A
The person has been exposed to a traumatic event in which both the following were present:
A1. The person experienced, witnessed or was confronted with serious injury or a threat to physical integrity of self or others
A2. The persons response involved intense fear, helplessness or horror.
Criterion B
The traumatic event is persistently re-experienced in one (or more) of the following ways:
B1. Recurrent and intrusive distressing recollections of the event, including images, thoughts or perceptions.
B2. Recurrent distressing dreams of the event.
B3. Acting or feeling as if the traumatic event were recurring.
B4. Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the trauma
B5. Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the trauma.

Figure 2.1b. The exposure criteria (Criterion A) required for a diagnosis of PTSD in DSM-5.

The person was exposed to one or more of the following event(s): death or threatened death, actual or threatened serious injury, or actual or threatened sexual violation, in one or more of the following ways:
1. Experiencing the event(s) him/herself
2. Witnessing, in person, the event(s) as they occurred to others
3. Learning that the event(s) occurred to a close relative or close friend; in such cases, the actual or threatened death must have been violent or accidental
4. Experiencing repeated or extreme exposure to aversive details of the event(s) (e.g., first responders collecting body parts; police officers repeatedly exposed to details of child abuse); this does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related.

hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated)". An example of a patient experience of B3 might be when a person loses contact with their surroundings and believes that they are back at the time of the traumatic event. While commonly portrayed in films, such experiences in clinical practice are rather rare. It has therefore been chosen to use the term flashback to cover the more common clinical feature that patients (at least in British English) refer to as "their flashbacks". An example related to the patient description of a traumatic event described earlier (from Holmes, et al., 2005) would be (1) the sudden image of the moment a mugger raised a knife,

accompanied by an intense feeling of fear and (2) a separate image of her daughter's crying face, with the feeling of guilt.

Flashbacks are rarely a replay of the entire traumatic event from beginning to end. Patients often recall one hotspot of the traumatic event at a time. Hotspots are defined as those moments reported by patients as one of their "worst moments" within a traumatic event and cause the greatest level of emotional distress (Ehlers & Clark, 2000; Foa & Rothbaum, 1998). The events in Figure 2.2 are the hotspots of another patient who was physically assaulted during a mugging. The hotspots depict a range of negative emotions, in this case fear, humiliation, sadness and degradation. On average, patients experience 3-4 hotspots per trauma, with associated emotions ranging from fear and helplessness to anger, guilt and shame (Grey & Holmes, 2008; Holmes, et al., 2005). It is these hotspots in the memory that define which images return as a flashback to the mind of the patient.

Figure 2.2. Hotspots from one PTSD patient during a mugging. Each is associated with specific emotions and meanings which are present when the images flashback, taken from Holmes et al. (2005)

Event within trauma	**Emotional reaction**
Hands pulling at bag	They're trying to pull me over; Fear
Fallen down on the ground	I've lost, they've won, I'm stupid; Humiliation
Kicked in stomach	They're taking away my chance to have children; Sadness
Assailants walking away slowly	They can't even be bothered to run; Degraded

Not all experiences of trauma result in the persistent experience of flashbacks and a diagnosis of PTSD. The question therefore arises as to why some experiences give rise to flashbacks. This is not a straightforward question to answer, particularly as traumatic events are difficult to study. A number of possible predictors have been investigated. The strongest predictors of the development of PTSD are peritraumatic psychological processes (Ozer, Best, Lipsey, & Weiss, 2003). The term peritraumatic refers to the individual's experience during

and immediately after the traumatic event. Additionally, cognitive behavioural clinical models of PTSD suggest that the cognitive processing during the traumatic event has a large impact on the nature of the trauma memory (Brewin, 2001; Ehlers & Clark, 2000). Furthermore, the development of PTSD 12 months post trauma can be predicted by the level of re-experiencing symptoms 8 days after the traumatic event (O'Donnell, Elltiot, Lau, & Creamer, 2007). Hence, the experience of the individual at the time of the trauma and the symptoms shortly afterwards seem to be highly important for predicting whether a traumatic event will lead to the experience of flashbacks and PTSD.

Evidence-Based Treatment

Current guidelines for PTSD do not recommend treatment until one month after trauma when a diagnosis can be established. The National Institute for Health and Clinical Excellence (NICE; National Institue for Health and Clinical Excellence, 2005), the American Psychiatric Association (2004) and the International Society for Traumatic Stress Studies (Foa, Keane, Friedman, & Chohen, 2008) guidelines all recommend that individuals meeting the criteria for PTSD should be offered psychological treatment following one month of symptoms. Psychological treatment can either be eye movement desensitisation and reprocessing (EMDR; Shapiro, 1995) or trauma focused cognitive behavioural therapy (CBT; Ehlers & Clark, 2000; Foa & Rothbaum, 1998).

In contrast, medication recommendations are limited as a treatment method for PTSD. The NICE guidelines advise that medication is not used as a routine first line treatment, and should only be used when patients express a wish not to undergo psychological treatment, or cannot start psychological treatment (National Institue for Health and Clinical Excellence, 2005). The 2004 APA guidelines suggest that SSRI treatment is an acceptable first line

treatment. However, the APA Guideline Watch published a review in 2009 suggesting that SSRI treatment will be recommended at a lower level in the next treatment guidelines.

EMDR is a psychological treatment that is thought to work with the memory networks to create associations with the traumatic memory and information contained in other memories. The aim is to form more positive and less distressing connections. EMDR works by the patient briefly attending (15-30 seconds) to their trauma memory, while simultaneously focusing on therapist directed eye movement. This continues over subsequent sessions until the patient is no longer distressed by the memory. Performing eye movements while thinking about the traumatic images reduces their vividness and emotional intensity, decreasing the impact of a flashback (Engelhard, van den Hout, Janssen, & van der Beek, 2010). The exact mechanisms as to why EMDR is effective are currently unclear, although it is thought that eye movements during memory recall create a competition for working memory resources, blurring the trauma memory (e.g. van den Hout et al., 2011; van den Hout et al., 2010; van den Hout et al., 2012).

CBT is predominantly a talking therapy. CBT is tailored to different disorders, and there are even variations of CBT protocols for the same disorder. CBT for PTSD focuses on exposure based treatment (Foa & Rothbaum, 1998). Exposure therapy has been refined using cognitive models of PTSD (Ehlers & Clark, 2000), focusing on the hotspots of the trauma memory and treating a broad range of negative emotions (Bisson et al., 2007; Ehlers et al., 2010; Ehlers & Clark, 2008; Ehlers, Clark, Hackmann, McManus, & Fennell, 2005). The patient first "relives" the trauma in the therapy session by describing it in detail, including their thoughts and emotions as well as the basic actions and facts. This allows for the identification of the most distressing parts of the memory. Initially these aspects may be

challenging and upsetting. However, identification of the problematic flashback memories can facilitate emotional processing of these moments. It is possible to target these hotspots using a technique known as restructuring. This involves the patient holding the hotspot in mind while rehearsing reappraisals of the situation, transforming the meaning of the hotspot and reducing the associated distress (Grey, Young, & Holmes, 2002). A detailed example, taken from Grey et al. (2002) can be seen in Figure 2.3

Figure 2.3 An example of cognitive restructuring of a hotspot associated with shame taken from Grey et al. (2002)

NE was a 26-year-old woman who was assaulted in an office over a period of 20 minutes. She had many re-experiencing symptoms and four peritraumatic hotspots were identified. The worst of these was a moment when the attacker stood over her just before he stabbed her again. This image was also her most frequent intrusive memory. At this moment NE reported overwhelming feelings of shame and humiliation. She reported that she felt these emotions at the time of the trauma itself (i.e. peritraumatically). Further questioning elicited the meaning of this moment for NE, which was ‘‘I’m the lowest of the low, I’m bad. Repeated reliving (i.e. traditional prolonged exposure) during the sessions and for homework helped reduce distress surrounding the fearful aspects of the assault but NE continued to experience distress with the hotspot associated with humiliation/shame. After other attempts, cognitive restructuring was employed. NE rehearsed the coping statement “I’m a good OK person and have done hundreds of things that show this’’. During the reliving, she held the hotspot vividly in her mind and was guided by the therapist to introduce the new corrective information, which was more consistent with her being a good OK person, at the point at which she felt ashamed. In the session, NE’s self reported distress rating reduced from ten to six. On further regular listening to the therapy tape, this reduced to three. The frequency of the intrusive memory reduced from once per day to once every two weeks.

Modelling the Patient Experience of Flashbacks in the Laboratory

Real life traumatic events and the subsequent development of flashbacks are clearly difficult to study in laboratory settings due to both ethical and practical reasons. The trauma film paradigm (Figure 2.4) is a well-established method to provide an analogue model of psychological trauma in a controlled experimental setting (Halligan, Clark, & Ehlers, 2002; Holmes & Bourne, 2008; Holmes, Brewin, & Hennessy, 2004; Woud, Holmes, Postma, Dalgleish, & Mackintosh, 2012). In the paradigm, healthy participants watch a film depicting traumatic events such as car crashes and surgery, based on the definition of trauma as defined

in DSM-IV-TR (see criterion A, Figure 2.1a). Participants typically experience several analogue flashbacks of events in the film during the following week, defined as memories of the trauma film returning to mind involuntarily. These flashbacks are recorded in a diary, similar to diaries given to PTSD patients undergoing CBT. Information recorded in the diary allows for features of the involuntary memory (e.g. number, vividness, emotional rating) to be recorded as well as identification of the film scene (analogue hotspot) which the memory originated from.

Figure 2.4. Diagram of the general procedure of the trauma film paradigm. Participants view a distressing film as an analogue of a traumatic event. Over the following week they record any flashbacks of the film in a diary. This allows for investigation of baseline differences affecting flashback development, or tasks that might increase / decrease later flashbacks.

Recent work using the trauma film paradigm has examined the development of flashbacks and factors that worsen or ameliorate flashback development. The computer game Tetris (a highly visuospatial game where the player manipulates coloured shapes) is an example of a task that when played during trauma memory consolidation reduces analogue flashbacks (Holmes, James, Coode-Bate, & Deeprose, 2009; Holmes, et al., 2010). Why might

playing Tetris help? Cognitive models of PTSD propose that two types of memory are involved in the formation of flashbacks: one involving meaning and context, the other sensory visuospatial inputs (Brewin, 2001; Brewin, Dalgleish, & Joseph, 1996; Brewin, Gregory, Lipton, & Burgess, 2010; Ehlers & Clark, 2000). Flashbacks are predominantly sensory images (Ehlers et al., 2002; Ehlers & Steil, 1995) and playing Tetris is thought to compete for resources during the consolidation of image-based memories, preventing the formation of flashbacks.

Summary

A flashback is a vivid, sensory–perceptual (predominantly visual images), emotional memory from a traumatic event that intrudes involuntarily into consciousness. The peritraumatic experience of the individual has been found to be highly important in the development of PTSD (Ozer, et al., 2003). Psychological therapies, such as trauma-focused CBT and EMDR focus on flashbacks, attempting to reduce the negative and distressing effect that they have on the patient. Experimental psychopathology models, for example the trauma film paradigm, can be used as analogues of real life trauma. Using analogue models, we can investigate the experience and development of flashbacks in a controlled manner. While we have treatments for the full-blown disorder, increasing our understanding of flashbacks at the cognitive neuroscience level will be beneficial in the development of preventative treatments designed to reduce the build up of flashbacks and possibly prevent full-blown PTSD.

Clinical Neuroscience of Flashbacks and PTSD

The brain is a highly complex system. Neuroimaging techniques have allowed researchers to begin to understand more about how the brain functions in living people. The

more we understand, however, the more complex descriptions of the brain become. Box 2.1 presents two diagrams of the main brain areas mentioned in this chapter, and throughout this thesis, to help visualise the areas involved in flashbacks.

Neuroimaging of the patient experience

The symptom provocation paradigm has been widely used in neuroimaging studies to examine the brain activation which occurs during the patient's experience of PTSD symptoms such as flashbacks. In the symptom provocation paradigm, PTSD patients are exposed to stimuli designed to trigger their symptoms. This is done by using images and sounds, for example visual images of combat situations (e.g. Shin et al., 1997) or verbal autobiographical scripts (i.e. playing back a trauma script written by the patient describing their traumatic experience). Stimuli are presented while the patient is in a brain scanner, most recently using functional magnetic resonance imaging (fMRI), and previously positron emission spectroscopy (PET) and single-photon emission computed tomography (SPECT). Several reviews have been conducted in this area, notably Lanius et al. (2006), Francati et al. (2007), and most recently Hughes and Shin (2011). Overall, these reviews have concluded that PTSD patients' symptoms experience involves decreased anterior cingulate cortex, medial prefrontal cortex, parahippocampal and thalamic activity, and, generally, increased amygdala activity. However, the symptom provocation paradigm does not always cause patients to experience flashbacks. Symptom provocation serves as a reminder of the trauma, encouraging patients to remember the traumatic event. This brings the trauma memories to mind, causing, for example, heighted emotional responses and avoidance, but not necessarily flashbacks. To my knowledge, only four neuroimaging studies of PTSD have reported patients who experienced a flashback while undergoing symptom provocation. Rauch et al. (1996) reported that all eight

Box 2.1. The diagrams below are of the main areas of the outer surface of the brain (Figure 2.5a) and the deeper structures of the brain (Figure 2.5b). These figures are to help visualise the structures referred to in this chapter. The terms of reference used to navigate around the brain are also included in Figure 2.5b. The colours used match with those of Figure 2.7.

Figure 2.5a The main areas of the brain mentioned in the chapter, pictured from a lateral perspective (the outer areas of the brain).

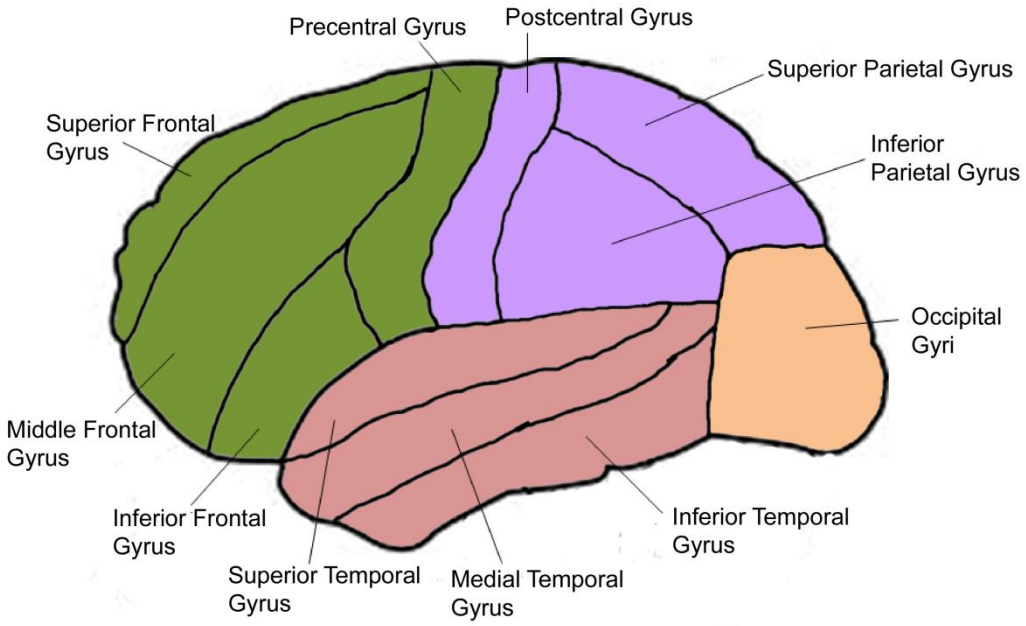
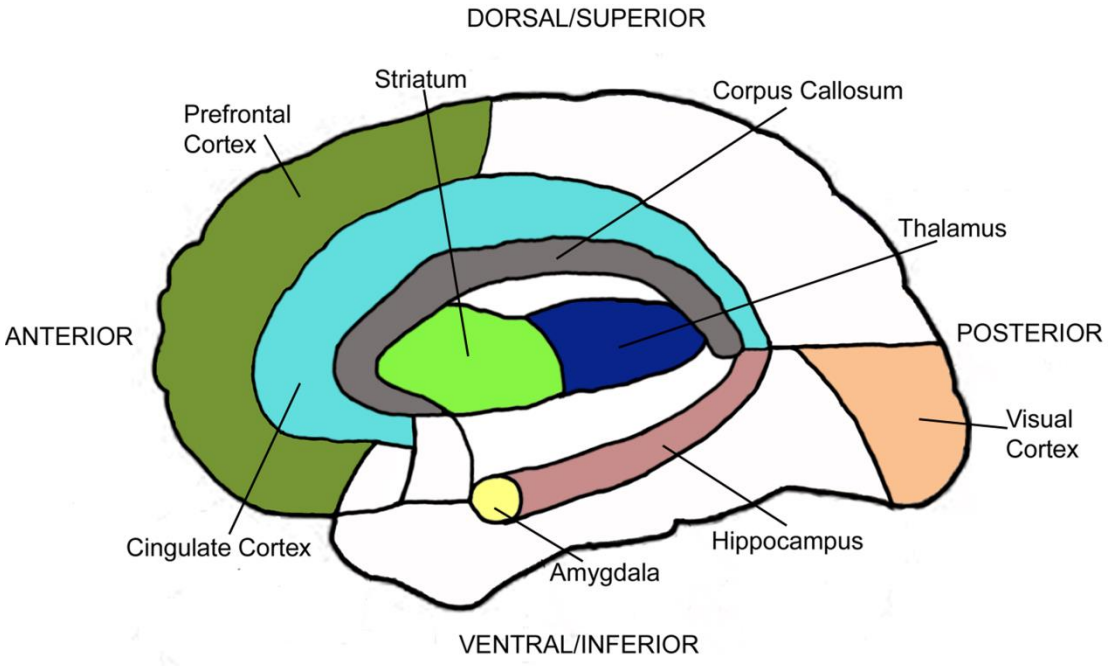


Figure 2.5b The main areas of the brain mentioned in the chapter from a medial perspective (the deeper structures of the brain). NB. The hippocampus is surrounded by the parahippocampal gyrus (not shown in the diagram). The terms of reference (dorsal/ventral and anterior/posterior) are also included.



of their PTSD patients experienced at least one flashback, Shin et al. (1999) that one of their eight PTSD patients experienced a flashback, and Osuch et al. (2001) that 8 of 11 PTSD patients experienced a flashback during script driven symptom provocation. Finally, Liberzon et al. (1997) reported a single patient who experienced a flashback while exposed to combat sounds. These studies suggest increased activity in limbic and paralimbic areas including the insula, anterior cingulate cortex, thalamus and amygdala, and decreased activation in inferior frontal areas.

A further study recently attempted to compare the neural activation of 10 PTSD patients' flashback memories with their episodic memories for the same content (Whalley et al., 2013). Patients were asked to write a narrative account of their traumatic event, highlighting any sections that caused a flashback while they were writing the narrative. Approximately one week later participants performed an autobiographical memory task while undergoing fMRI, stating whether presented narratives were from their own trauma or another, similar, narrative. Narratives that caused a flashback at the initial writing, or in the scanner, were defined as "flashbacks". Greater activation for "flashback" vs. "own episodic" was identified in left anterior cingulate cortex, middle occipital cortex, right supplementary motor area, right medial prefrontal cortex, bilateral precentral areas , inferior parietal (supramarginal) cortex and insula. However, as flashbacks could also occur one week before the scan, and not in the scanner itself, the activation identified may not be specific to that of flashback recall at that present moment, but more general increased emotional content of that specific memory.

The majority of neuroimaging studies concerning PTSD have therefore not directly examined the phenomena of flashbacks. Even for those studies which include reports of

flashbacks, the question arises as to what exactly is being measured? A typical flashback may last for only a few seconds. Kossyln (1994) reports that mental imagery rapidly decays, lasting on average for only 250ms. Even if active maintenance is performed to keep the mental image in mind, the image often only lasts for a few seconds (Cocude, Charlot, & Denis, 1997; Cocude & Denis, 1988; Pazzaglia & Cornoldi, 1999). Scanning sessions, on the other hand, will last for much longer. It is therefore likely that the data reported is more general than the specific experience of a flashback, perhaps representing increased arousal brought about by the symptom provocation.

Furthermore, these studies examine brain activation in patients once symptoms are already established. Key questions, including those involving aetiology nevertheless remain. For example, why do some people experience flashbacks and not others? Why are certain moments of the original trauma re-experienced as flashbacks and not others? It is not possible to investigate the brain mechanisms behind the development of real trauma. Therefore, analogue models such as the trauma film paradigm (see Figure 2.4) may be used.

Neuroimaging the encoding of analogue flashbacks

To my knowledge, only one recent study has used neuroimaging to investigate the encoding of images during a trauma film to which participants later experience flashbacks (Bourne, et al., 2013). Four other studies have examined the encoding of involuntary memories for verbal stimuli and concrete objects, which are discussed later in this chapter (see *Involuntary Recall* section). However, these phenomena are not the same as flashbacks.

Bourne et al. (2013) utilised the trauma film paradigm to examine the differences in brain activations when viewing "Flashback scenes" (unpleasant scenes that retuned as flashbacks over the following week), "Control scenes" (scenes that have been found to never

cause flashbacks), and "Potential scenes" (unpleasant scenes that have previously elicited flashbacks in other participants but not in that individual). The authors reported a 'flashback signature' for the encoding of memories that were later experienced as flashbacks. This signature included increased activations in the amygdala, thalamus, rostral anterior cingulate cortex, striatum and ventral occipital cortex, which was observed when viewing those images that would be re-experienced as flashbacks in comparison to both Control and Potential scenes. Additionally, the left inferior frontal gyrus and middle temporal gyrus showed suppressed activation for Potential scenes compared to both Flashback and Control scenes, suggesting a possible protective effect of these areas.

The authors were able to conclude that at the time of trauma the brain is responding differently for those scenes which later return as flashbacks, compared to those scenes which do not cause flashbacks for that individual. The latter scenes were considered equally traumatic because they led to flashbacks in other participants viewing the same footage. This demonstrates the possibility of using neuroimaging techniques to study development of flashbacks at a neural level using an analogue of trauma. This allows understanding of the neural context implicated in the formation of flashbacks, and in doing so, provide insights as to how to clinically treat flashbacks and reduce flashback formation.

Interim Summary

This section of the chapter has focused on functional neuroimaging studies using the symptom provocation paradigm to examine the neuroscience behind the patient experience of PTSD. This has highlighted multiple gaps in understanding the neuroscience of flashbacks. Flashbacks are the hallmark symptom of PTSD and by focusing on the patient experience of flashbacks a specific, debilitating part of PTSD can be targeted. Investigating the clinical-

neuroscience of flashbacks can help guide the development of treatments. Understanding the brain processes that lead to the formation of a flashback may help to develop targeted treatments to prevent their formation.

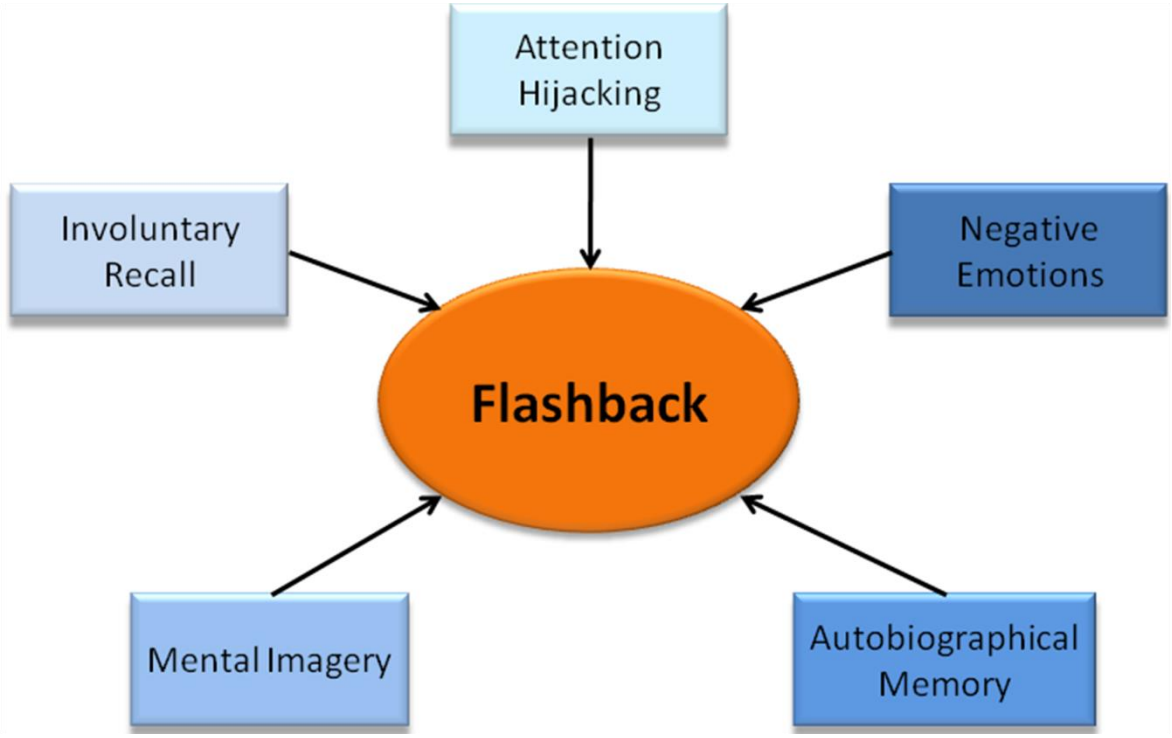
A Clinical-Neuroscience Flashback Framework

A pragmatic clinical neuroscience flashback framework is proposed. This framework takes flashbacks as part of a continuum of normal functioning. By looking at flashbacks as a combination of events that take place in everyday life, knowledge concerning these individual areas can be combined to help inform the understanding of flashbacks. Flashbacks are defined as comprising five component parts; autobiographical memory, involuntary recall, negative emotions, mental imagery and attention hijacking (Figure 2.6). It is hypothesised that for a flashback to be encoded and experienced, all of these components must be present. The following sections set out how each of these components are involved in a flashback and briefly summarises the neural components behind them. The experience of a flashback is mapped onto the brain, culminating in Figure 2.7, with the components of the clinical neuroscience framework in the centre, surrounded by the different brain areas involved.

Autobiographical (trauma) Memory

Autobiographical memory is the area of memory related to the recollection of past personal events and can either correspond to a particular episode in life, or to a more general experience that has particular personal relevance (Conway & Pleydell-Pearce, 2000). The autobiographical component of a flashback, therefore, corresponds to the experiencing (Criterion A) and subsequent re-experiencing (Criterion B) of the traumatic event, as set out in the DSM-IV-TR (American Psychiatric Association, 2000 - see Figure 2.1).

Figure 2.6. A proposed pragmatic clinical-neuroscience framework of flashbacks. All five components should be present for a flashback to be experienced.



The literature surrounding autobiographical memory is vast and for recent reviews on the neuroimaging of memory see Cabeza and Nyberg (2000) and Spaniol et al. (2009). Overall, these reviews conclude that autobiographical memory is normally associated with activity in the right anterior and lateral prefrontal gyri, the medial temporal gyrus, the lateral and medial parietal regions and the posterior cingulate cortex. Specifically, the ventrolateral prefrontal gyrus and medial temporal gyrus are thought to be involved in encoding, while the left superior parietal gyrus and the dorsolateral and anterior prefrontal gyri are thought to play an important role in recall (Dobbins, Foley, Schacter, & Wagner, 2002; Dobbins & Wagner, 2005; Spaniol, et al., 2009). Additionally, it is thought that the full encoding of a memory takes place in a six hour window (McGaugh, 2000; Walker, Brakefield, Hobson, & Stickgold, 2003), a process known as consolidation. Research has implicated the involvement of the

hippocampus in particular, but other cortical areas including the nucleus accumbens and ventral striatum are also implicated in memory consolidation (Bermudez-Rattoni, 2010).

Involuntary Recall

Flashbacks are image based sensory memories that come to mind spontaneously and unbidden, and, therefore, *involuntarily*. The term involuntary memory recall, however, has been used by multiple authors to mean different things. Involuntary memory is defined here consistent with Ebbinghaus: "often, even after years, mental states once present in consciousness return to it with apparent spontaneity and without any act of the will, that is they are produced involuntarily" (Ebbinghaus, 1964; Mace, 2007). More recently, Berntsen (1996) similarly defined involuntary memory as a memory spontaneously brought to consciousness without previous attempts at retrieval.

In a review of the literature [search terms; neuroimaging, fMRI, functional magnetic resonance imaging, MRI, magnetic resonance imaging, PET, SPECT, combined with flashback, involuntary memory, incidental memory and unintentional memory] only five neuroimaging studies were found that had directly compared voluntary and involuntary recall (Hall, Gjedde, & Kupers, 2008; Kompus, Eichele, Hugdahl, & Nyberg, 2011; Ramponi, Barnard, Kherif, & Henson, 2011; Rugg, Fletcher, Frith, Frackowiak, & Dolan, 1997; Whalley, et al., 2013). Of these studies, only one (Whalley, et al., 2013) investigated flashbacks and autobiographical memory – the others using memory for verbal stimuli and concrete objects.

As mentioned earlier in the chapter, Whalley et al. (2013) used an autobiographical memory task to compare the neural activation of flashback memories with episodic memories for the same content (see *Neuroimaging the Patient Experience*). Results suggested

involvement of the left anterior cingulate cortex, middle occipital cortex, inferior parietal cortex and insula in flashback recall. The main limitation however resides in the flashback memory category – defined as any memory that lead to a flashback either in the scanner or at the time of writing the narrative. Thus, differences in activation reported can not be uniquely associated with involuntary recall.

The remaining four studies investigating involuntary and voluntary recall for non-autobiographical stimuli highlight a potential difference in brain activation between voluntary and involuntary recall. One study showed increased activation during involuntary compared to voluntary recall – in the left middle frontal gyrus and left superior frontal gyrus (Hall, et al., 2008). On the other hand, greater activation for voluntary versus involuntary recall has been found in the right dorsolateral frontal gyrus and parietal cortex (Kompus, et al., 2011; Rugg, et al., 1997), and in the right middle frontal gyrus (Hall, et al., 2008). Additionally, greater hippocampus and amygdala activity has also been reported for voluntary recall (Ramponi, et al., 2011). However, the evidence is limited and mixed, and it remains to be established whether these findings can also be generalised to autobiographical memory.

Negative Emotions

The patient experience of flashbacks is characterised by strong negative emotions. This is important when investigating flashbacks experimentally as involuntary memories are not always negative. Research has found that involuntary memories are not limited to negative experiences or indeed to clinical populations - a telephone survey of 1500 Danes identified that approximately 60% of involuntary memories reported were positive in nature (Berntsen & Rubin, 2008). It is important, therefore, to model flashbacks as negative emotional events.

Research into emotion often implicates the anterior cingulate cortex (ACC), prefrontal cortex (PFC) and the amygdala (Dalgleish, 2004; Davidson, Jackson, & Kalin, 2000; Phelps, 2006). The traditional view was that the amygdala was involved in negative emotions, especially that of fear (Phelps, 2004, 2006). However, more recent work suggests that the amygdala is also involved in positive emotions (Murray, 2007) and that the amygdala may respond to emotional salience rather than whether the emotion is positive or negative (Phan et al., 2004). Additionally, the ACC is often implicated in threat detection, and the prefrontal cortex is thought of as being involved in emotion regulation – allowing top down control in emotional situations (Bishop, Duncan, Brett, & Lawrence, 2004; Davidson, et al., 2000).

When looking at the brain activation of emotional memory the story is also complex. With memory recall, the ability to remember events from a negative encoding context has been associated with amygdala activity at the time of encoding. The ability to remember events from a positive encoding context, on the other hand, is associated with activation of the right anterior parahippocampal gyrus (Erk et al., 2003). However, in other studies, the level of amygdala activation during the encoding of emotional stimuli has been found to correlate with the success of recall regardless of emotion (Cahill, Uncapher, Kilpatrick, Alkire, & Turner, 2004; McGaugh, 2004).

In the proposed clinical neuroscience framework, emotional memory is negative as this corresponds to the patient experience of flashbacks. In the context of understanding the neural signature of a flashback it will be important to establish whether positive and negative valence influence the brain activation patterns associated with involuntary memories.

Mental Imagery

Flashback memories tend to occur as sensory based images (Ehlers, et al., 2002; Ehlers & Steil, 1995). Mental imagery is defined as occurring when perceptual information is accessed from memory, compared to perceptual information that is directly registered from the senses (Kosslyn, Ganis, & Thompson, 2001). Mental imagery can create the same emotional and physiological reactivity as seeing an object or event itself (Holmes & Mathews, 2010). Furthermore, mental imagery has a similar effect on the body as actually seeing the object or event in question. Skin conductance, heart and breathing rate all increase when visualising threatening objects (P. J. Lang, Greenwald, Bradley, & Hamm, 1993).

Widespread activation across the brain implicating both visual and memory areas has been observed when participants use mental imagery. Neuroimaging studies have consistently reported activation of the visual cortex during mental imagery (Thompson & Kosslyn, 2000). Additionally, visual mental imagery has been found to activate the middle frontal gyrus, the superior frontal gyrus, the middle occipital cortex, right anterior cingulate cortex and the left inferior parietal cortex (Belardinelli et al., 2009), along with the hippocampus, amygdala, entorhinal cortex, parahippocampal cortex and the anterior insula (Kosslyn et al., 1996; Kreiman, Koch, & Fried, 2000). Mental imagery may therefore bridge the experience, memory and recollection of the traumatic event during a flashback.

Attention Hijacking

A final proposed requirement for a flashback is that it hijacks attention to some degree. Sensory information in the world around us is abundant, and attention is used to select the information that is relevant at a given time (Wolfe & Horowitz, 2004). Flashbacks appear to

override selective attention geared towards current goals, directing attention to the internal mental representation of the trauma.

How might a flashback override selective attention? Research using a word stem completion task has suggested that PTSD patients demonstrate enhanced priming for trauma related words (Michael, Ehlers, & Halligan, 2005). Further, measurement of enhanced priming just after trauma were found to be associated with symptom severity at three, six and nine months post trauma. Additionally, PTSD patients have been reported as having poorer emotional working memory performance compared to healthy controls, suggesting an inability in PTSD patients to ignore emotional trauma related stimuli (Schweizer & Dalgleish, 2011). Comparison of PTSD patients and trauma exposed controls suggests that this is an inability of patients to move their attention away from trauma related stimuli, and not an increase of facilitated attention to trauma related stimuli (Pineles, Shipherd, Mostoufi, Abramovitz, & Yovel, 2009; Pineles, Shipherd, Welch, & Yovel, 2007). A poor ability to remove information that is no longer relevant from mind, measured in non clinical participants before viewing traumatic footage, has also been associated with flashback frequency in the subsequent week (Verwoerd, Wessel, de Jong, Nieuwenhuis, & Huntjens, 2011). This suggests that this inability to move attention away from non relevant stimuli may be a vulnerability factor for flashback development.

To my knowledge, no research has yet investigated the neuroimaging of attention in PTSD patients. In healthy individuals, visual selective attention has been associated with activity in widespread brain regions, including the parietal, temporal and prefrontal cortices (Nobre, Coull, Walsh, & Frith, 2003). It has been proposed that the frontal regions deal with specifying, consolidating and selecting targets, while the posterior parietal, occipital and

temporal regions filter out distracting stimuli (Akyurek, Vallines, Lin, & Schubo, 2010; Friedman-Hill, Robertson, Desimone, & Ungerleider, 2003; Wojciulik & Kanwisher, 1999). Specifically, the left inferior frontal gyrus is thought to be involved in the selection of competing memory representations and interference resolution, in particular, for verbal stimuli (Jonides & Nee, 2006; Nelson, Reuter-Lorenz, Persson, Sylvester, & Jonides, 2009), with the addition of the anterior insula for emotional words (Levens & Phelps, 2010). Whether these regions are involved in the development and experience of flashbacks, predominantly image based memories, is currently unknown.

The Clinical-Neuroscience Framework and the Laboratory

Experimental research across disciplines (e.g. genetics, psychopharmacology) requires the use of models to examine specific effects (e.g. genes, medication). Experimental psychopathology is no exception. The trauma film paradigm is a well-used method to create analogue flashbacks (Holmes & Bourne, 2008). Are analogue flashbacks experienced after watching the trauma film comparable to flashbacks experienced by patients? Table 2.1 demonstrates how each of the components of the proposed clinical-neuroscience framework is described to participants in the laboratory when the flashback diary is explained to them. As can be seen, each component of the analogue experience is matched to a proposed component of the flashback framework.

Table 2.1. Table illustrating the descriptions given to participants to describe the experience of a flashback and how this description matches the proposed components of the flashback framework.

Flashback Component	Involuntary Memory Diary Instructions
Autobiographical Memory	It may be that over the next week **images from the film** pop into mind
Involuntary Recall	Images from the film may **pop into your mind involuntarily and spontaneously.**
Negative Emotion	These involuntary images may be **negative**
Mental Imagery	Mental images are sensory based; **pictures that can be accompanied by sounds and bodily sensations**
Attention Hijacking	Involuntary memories **pop into mind without you expecting it.**

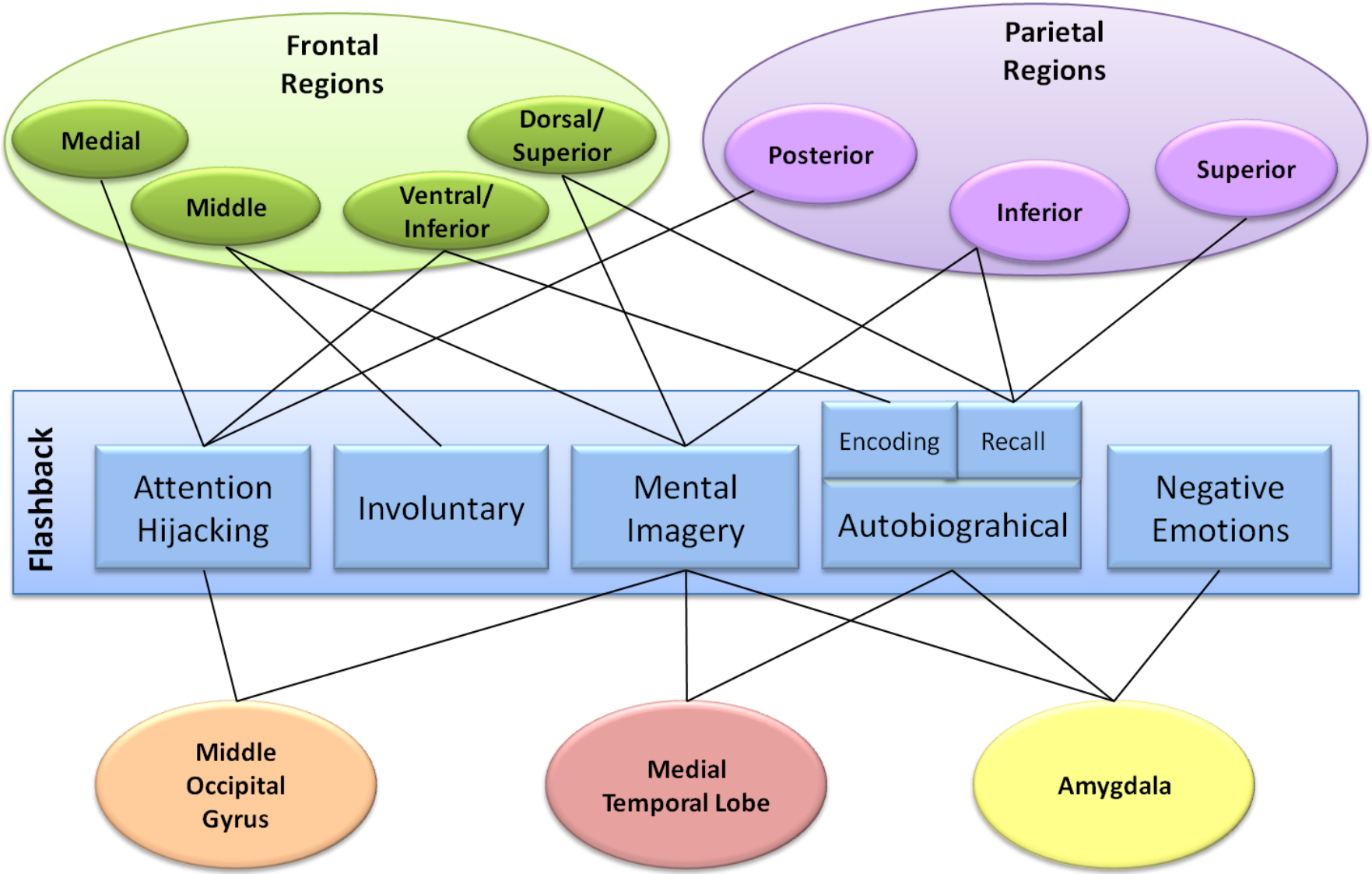
Mapping the Patient Experience of a Flashback onto the Brain

Using the proposed clinical neuroscience framework, it is hypothesised that a series of events happen simultaneously to create a flashback (Figure 2.6). Involuntary autobiographical memory recall hijacks attention, which, when coupled with negative emotional activity and mental imagery brings the past trauma memory to life, in the most extreme cases mentally placing the patient back into the time of the traumatic event.

Figure 2.7 maps the proposed clinical neuroscience framework onto the brain. The centre of the diagram shows the different components that make up a flashback. Surrounding this are the brain areas, linked by respective colours, which correspond to the diagrams in Box 2.1. As can be seen, flashbacks are a whole brain phenomenon, with many areas being involved in multiple components of the framework.

What, therefore, can be seen by mapping the hypothesised flashback components onto the brain? Interestingly, the brain areas involved in mental imagery are also involved in the other components listed above. This suggests that mental imagery may be a key overarching component in flashbacks.

Figure 2.7. Diagram mapping the clinical neuroscience flashback framework onto the brain. The components of the proposed clinical neuroscience framework are in the centre, surrounded by the different brain areas involved. The colours correspond to those used in Figures 2.5a and 2.5b..



In addition to mental imagery, the frontal areas of the brain are involved in attention hijacking and involuntary recall, suggesting that the frontal regions may be involved in the spontaneous recollection of mental images. Furthermore, areas associated with autobiographical memory (predominantly the medial temporal lobe, but also parietal and frontal regions) have been found to be involved in mental imagery, demonstrating a possible connection between the traumatic memory and mental imagery. Moreover, the parietal regions and the left inferior frontal gyrus are also involved in attention hijacking, suggesting a link between the traumatic memory and an overriding of attention. Finally, amygdala activation is predominantly associated with emotional processing. However, the amygdala is also activated by mental imagery and autobiographical memory. The emotion of the traumatic memory may therefore also be associated with the mental imagery of the event. Connections between all five components of our hypothesised flashback framework, predominantly linking back to mental imagery, therefore exist. Combining each of these individual components, which on their own are required for normal functioning, may lead to the experience of a flashback.

What is gained by looking at flashbacks in this way? Much more work is needed to understand flashbacks, especially in terms of neuroscience (Mace, 2007). Breaking flashbacks into the proposed components suggests a framework for developing and testing hypotheses. Understanding how each component individually contributes to flashbacks, and the neuroscience behind it, increases the knowledge of an otherwise incredibly complex phenomenon. While the understanding of the neuroscience behind flashbacks per se is limited, much more is known about the neuroscience of attention, autobiographical memory, emotion, mental imagery and involuntary recall. By tailoring research and hypotheses in these areas towards flashbacks and PTSD a better clinical neuroscience understanding of the patient experience of flashbacks can be developed.

Some Unanswered Questions

Using the proposed flashback framework, hypotheses can be guided to increase our neuroscientifc understanding of flashbacks, aiding the bridging of the clinic and clinical neuroscience. This thesis attempts to answer some of these questions.

First, the encoding of flashbacks is an area that has only recently received attention. Replication of this finding is essential to understand the differences between flashback encoding and normal "healthy" autobiographical memory encoding. Second, it will be important to establish whether there is a neural difference between voluntary and involuntary autobiographical memory recall. Understanding differences in autobiographical memory recall will help to pinpoint areas of memory that are distinct to flashbacks, possibly suggesting ways to decrease flashback frequency, while keeping the memory of the trauma intact. Third, the neural basis of flashback involuntary recall and the subsequent attention hijacking of the memory has received limited attention. Understanding the neural basis of involuntary recall may suggest ways to prevent flashback recall, and understanding how a flashback memory overrides selective attention may present clues as to how to reduce flashback impact at recall. Fourth, not all individuals develop flashbacks after witnessing traumatic events. Understanding the factors associated with an absence of flashbacks could therefore suggest areas of the clinical neuroscience framework that may be important for the reduction of flashback memories. Fifth, as involuntary memories can also be positive, it will be important to investigate similarities between flashbacks and positive involuntary autobiographical memories to see if the clinical neuroscience flashback framework can also improve understanding of flashback type memories not arising from trauma.

Additionally, beyond the scope of this thesis, cognitive research has identified that an existing inability to shift attention away from irrelevant information may be a

predisposing factor as to whether individuals are likely to develop flashbacks (Verwoerd, et al., 2011). By understanding this in more detail, it may be possible to improve patients' emotional working memory to be better equipped to shift attention away from trauma related stimuli and subsequent memories (e.g. Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish, 2013).

Discussion and Conclusion

Studying real life trauma experimentally is particularly challenging. Experimental psychopathology therefore uses analogue models. The changes to DSM-5 (American Psychiatric Association, 2013, see Figure 2.1b) suggest that the use of the trauma film paradigm as an experimental tool for researching flashbacks is pertinent. One of the changes to the experiencing criteria (Criterion A) of PTSD is "Experiencing repeated or extreme exposure to aversive details of the event(s); this does not apply to exposure through electronic media, television, movies, or pictures, unless this exposure is work related". Hence, exposure to trauma through electronic media under certain circumstances may cause flashbacks.

Additionally, neuroimaging offers considerable potential as demonstrated in the recent work using the trauma film paradigm to investigate the encoding of flashbacks (Bourne, et al., 2013). Combining knowledge and techniques from the clinic, behavioural research and neuroscience, we can begin to gain a better understanding of the patient experience of flashbacks.

The proposed clinical neuroscience framework sets out experimental hypotheses for mapping the brain processes that contribute to the experience of flashbacks. Using the framework, research can be guided to increase the current knowledge of the patient experience of flashbacks. Hopefully, understanding the individual components of a flashback will lead to greater insight into both the recall and encoding of flashbacks. From

there, preventative treatments to lessen and prevent the intense emotional reaction of flashbacks after traumatic events can be developed. Using a clinical neuroscience approach to flashbacks and mapping the subjective experience of the patient onto the brain, the gap between patients' experiences as seen in the clinic and the clinical neuroscience behind them can be bridged.

The following chapter presents a neuroimaging study investigating both the encoding and involuntary recall of flashbacks.

Chapter 3: Neuroimaging the encoding and recall of flashbacks

Abstract

A common symptom after witnessing or experiencing trauma is the experience of 'flashbacks' – image based emotional memories of the trauma that intrude involuntarily into consciousness. However, the neural basis of both the encoding and the involuntary recall of flashbacks is poorly understood; only one study has reported the brain activity at flashback encoding, and no studies have observed the brain activity at the moment of flashback involuntary recall in the scanner. The current experiment combined the trauma film paradigm with neuroimaging to observe the brain activation at both the encoding and the involuntary recall of flashback memories. Comparisons were made between "Flashback scenes" (unpleasant scenes that were recalled involuntarily over the following week), "Control scenes" (neutral scenes that were never recalled involuntarily) and "Potential scenes" (unpleasant scenes that were recalled involuntarily in other participants, but not that individual). Results are in line with the proposed components of the framework in Chapter 2. Critically, the results support the existence of a distinct pattern of activity during the encoding of Flashback scenes compared to Potential and Control scenes. This pattern could not simply be explained by a subsequent memory effect. Further, the study provides the first preliminary indication, to my knowledge, that there are possible differences for the encoding of identified versus non-identified Flashback stills, but not for identified versus non-identified Potential stills. Flashback involuntary recall was characterised by activity in middle and superior frontal regions, and in the left inferior frontal gyrus and brain regions associated with emotional processing. Understanding the neural basis of both flashback encoding and involuntary recall may aid in the development of future treatments.

Introduction

The previous chapter proposed a clinical neuroscience framework for understanding flashbacks – used here to describe "vivid, sensory–perceptual (predominantly visual images), emotional memories from a traumatic event that intrude involuntarily into consciousness" (Bourne, et al., 2013). As mentioned, although a large body of neuroimaging research has been conducted in trauma victims with posttraumatic stress disorder (PTSD) once symptoms have been established, there is a lack of research that has been conducted investigating the neural basis of the *encoding* of flashback memories. The trauma film paradigm offers an experimental analogue of trauma that can be used to prospectively study the encoding of flashback memories. Only one previous neuroimaging study has used the trauma film paradigm to investigate flashback encoding (Bourne, et al., 2013). The current study aimed to replicate the findings of Bourne et al. (2013), and extend findings by incorporating a recognition memory test of the film and to examine the brain activation at the moment of flashback involuntary recall in the scanner.

There is increasing evidence that flashback type memories are not unique to PTSD, occurring across disorders and in everyday life (Berntsen, 2010; Bryant, O'Donnell, Creamer, McFarlane, & Silove, 2011). A continuum perspective suggests that flashback type involuntary memories may range from distressing intrusive memories to full blown dissociative flashbacks reported (rarely) by some PTSD patients (Berntsen, 2001; Rubin, Berntsen, & Bohni, 2008). Viewing flashbacks as a continuum offers an opportunity to study the aetiology and formation of flashback memories using experimental paradigms. As mentioned in Chapter 2, psychological processing at the time of trauma (peritraumatic processing), in particular an individual's emotional response, has been highlighted as important for the development of PTSD in clinical research (American Psychiatric Association, 2000; Ehlers & Clark, 2000; Ozer, et al., 2003). Understanding the neural

basis of flashback encoding may help increase our knowledge of how flashbacks are formed, and help probe what makes certain moments return as flashbacks while other traumatic moments do not.

Studying real life trauma and the subsequent development of flashbacks is difficult for both ethical and practical reasons. The trauma film paradigm is a widely used analogue of trauma (see Chapter 2). Recently, the trauma film paradigm was adapted for use with functional magnetic resonance imaging (fMRI) to investigate the neural basis of flashback encoding (Bourne, et al., 2013). Traumatic footage was combined from previous experiments identifying *Potential scenes* in the film – scenes that had previously caused flashbacks, and *Control scenes* – scenes that had never caused flashbacks. Participants watched the traumatic footage while undergoing fMRI. A flashback diary was then kept in daily life for the following week, allowing for identification of idiosyncratic *Flashback scenes* – scenes that were recalled as flashbacks for that individual. Comparisons of the brain activation at the time of encoding between Flashback and both Potential and Control scenes were performed, finding increases in activation in the amygdala, rostral anterior cingulate cortex, thalamus and ventral occipital cortex for scenes that returned as flashbacks compared to those that did not. Suppressed activation in the left inferior frontal gyrus and middle temporal gyrus was found for Potential scenes compared to both Flashback and Control scenes. Results were obtained despite modelling only a mean of 3.5 Flashback scenes per person.

The brain areas identified in the analogue experimental study by Bourne et al. (2013) as being involved in flashback encoding are predominantly in line with those brain areas identified as being important in PTSD patients once symptoms are established. A well supported neurocircuitry model of PTSD suggests that PTSD is characterised by enhanced amygdala (and other limbic) activation and reduced ventromedial prefrontal

region activation (Rauch, Shin, & Phelps, 2006). These findings highlight the possibility of an increased fear response, with diminished capacity to move attention away from trauma related stimuli. Further, neuroimaging research has used symptom provocation paradigms with PTSD patients to try to understand the neural basis of symptom occurrence (see Chapter 2). Recent reviews of neuroimaging studies using symptom provocation suggest that PTSD patients' symptom experience involves increased amygdala activity and decreased medial prefrontal cortex activity (Francati, et al., 2007; Hughes & Shin, 2011; Lanius, et al., 2006), similar areas as highlighted by the neurocircuitry model of PTSD (Rauch, et al., 2006). However both the neurocircuitry model of PTSD and symptom provocation paradigms focus on symptom occurrence (i.e. memory *recall*) not *encoding*, thus caution should be taken in making direct comparisons with the encoding findings.

As mentioned in Chapter 2, the symptom provocation paradigm does not always cause the involuntary recall of flashbacks. The paradigm serves to act as a reminder of the trauma, bringing trauma memories to mind while the patient undergoes neuroimaging and causing, for example, heightened emotional arousal and avoidance, but not necessarily involuntary flashback memories. Only four symptom provocation studies have reported at least one patient experiencing an involuntary flashback while undergoing fMRI (Liberzon, et al., 1997; Osuch, et al., 2001; Rauch, et al., 1996; Shin, et al., 1999). These studies found that flashback recall was associated with increased activity in limbic and paralimbic areas - including the insula, anterior cingulate cortex, thalamus and amygdala - and decreased activation in the left inferior frontal gyrus. However, none of the studies were able to identify the precise moment of the flashback during scanning. Results are based on whole scan activation compared to baseline activation, making it difficult to separate activity specific to the involuntary recall of a flashback from general symptom experience (e.g. heightened arousal).

One recent study attempted to more precisely identify the brain activation involved in involuntary flashback recall, and to compare this activation with the patients' deliberate episodic memory for the same content using narratives of the patients trauma (Whalley, et al., 2013). Greater activation was identified for "flashback memory" compared to "episodic memory" in the left anterior cingulate cortex, middle occipital cortex, right supplementary motor area, right medial prefrontal cortex, bilateral precentral areas, inferior parietal cortex and the insula. These results show overlap with those identified by more general symptom provocation paradigms in relation to flashback recall. Additionally, reverse inference (which should therefore be interpreted with caution) suggests that the brain regions identified are associated with three of the five categories suggested by the clinical neuroscience flashback framework in Chapter 2 - mental imagery, autobiographical memory recall and negative emotions - but not the category of involuntary recall and only partly with attention hijacking. This may be explained by the category definition for "flashback memory" used by Whally et al. (2013). A "flashback memory" was any part of the narrative that caused a flashback during the scan itself *and* any part of the narrative that caused a flashback when the patients originally wrote their narrative (approximately 1-week prior to scanning). As not all events were actual flashbacks while the patients underwent fMRI, it remains difficult to separate the brain regions involved in flashback involuntary recall from those involved in more deliberate remembering of the event.

As mentioned in Chapter 2, in addition to Whalley et al. (2013) there have only been a limited number of neuroimaging studies that have compared flashback (or involuntary/incidental) memory recall with deliberate memory recall, all of which have used verbal stimuli or concrete objects. Further, only one study found greater activation for involuntary recall compared to voluntary recall – highlighting the left middle frontal and

left superior frontal gyri (Hall, et al., 2008). This provides preliminary insight into the involuntary recall of flashbacks, however, whether results from verbal and concrete objects can be extrapolated to autobiographical memory is unknown. Additionally, the left inferior frontal gyrus (IFG) has been implicated in the selection of competing memory representations for verbal stimuli (Jonides & Nee, 2006; Nelson, et al., 2009), with the addition of the insula for emotional words (Levens & Phelps, 2010), and these brain regions may represent the attention hijacking component thought to be involved in flashback involuntary recall. However, previous neuroimaging findings concerning PTSD symptom experience have found a decrease in left IFG activity (e.g. Rauch et al., 1996; Shin et al., 1999). The direction of the possible involvement of the left IFG therefore remains unclear.

The Bourne et al. (2013) study indicated promising results for differences in encoding for traumatic events that later returned as flashbacks, compared to traumatic events that did not. However, replication of these results is essential before firm conclusions can be made about flashback encoding. As acknowledged by the authors, the number of events modelled was low for an fMRI event based design (Jezzard, Matthews, & Smith, 2001), creating possible uncertainties about the reliability of the results.

Additionally, no comparison was made between flashback memory encoding and successful episodic memory encoding of items that could later be recalled voluntarily. The widespread increase in activation observed may therefore, at least in part, be due to a subsequent memory effect (Paller & Wagner, 2002). The subsequent memory effect is the difference in activation for events that are later remembered compared to events that are later forgotten. Greater activity during neutral film viewing for scenes later remembered compared to scenes later forgotten (as reported by cued recall and a recognition memory test at 3 weeks) has been reported in the parahippocampus, superior temporal gyrus,

anterior temporal poles and the temporal parietal junction (Hasson, Furman, Clark, Dudai, & Davachi, 2008). Further, greater activity between the amygdala and medial temporal lobe memory systems has been found for the successful encoding of emotionally arousing events (see Kensinger & Corkin, 2004; LaBar & Cabeza, 2006). Teasing apart differences at encoding between subsequent successful remembering and the later involuntary recall of a flashback is important for understanding the distinct nature of the formation of a flashback memory. As a first step, the current study therefore included a recognition memory test at one week.

The current experiment had four aims. 1) To replicate previous findings (Bourne et al., 2013), hypothesising that a distinct pattern of brain activity at the encoding of memories that later returned as flashbacks would be identified. 2) To extend the paradigm by dividing the trauma film according to whether or not moments of the film (stills) could be identified on a recognition memory test at one week – analysing only those stills which were successfully identified on the recognition memory test. It was hypothesised that there would be minimal encoding differences in comparison to using both non-identified and identified stills. 3) To compare flashback events with potential events using identified and non-identified stills from the recognition memory test. As low numbers of events were expected, this analysis was exploratory and no hypotheses were made. 4) The paradigm was further extended, to capture the brain activation involved at the moment of flashback involuntary recall in the scanner, hypothesising that involuntary recall would involve brain regions associated with the components of the proposed clinical neuroscience framework.

Method

Ethical approval was obtained from the University of Oxford Central University Research Ethic Committee (MSD/IDREC/C1/2012/31; Appendix I).

Participants

Previous work (Bourne et al., 2013) suggested a large effect size for Flashback scenes compared to Potential scenes and Control scenes. This would suggest that a sample size of 26 participants would be adequate to detect any differences between scene types (Cohen, 1992). As the number of different Flashback events expected is low however, for an fMRI based design, a larger number of participants were recruited to consider this. Subsequently, 41 participants were recruited from the local community. Six participants were not included in the final analysis: two reported no flashbacks of the trauma film, one participant stopped the scan during the film, one failed to return to follow up at one week, for one participant the scan stopped before film completion and one participant performed below chance on the recognition memory test suggesting low attention to the film and experimental compliance. The final analysis therefore included 35 participants (mean age = 22.43 years, *SD* = 7.52; 29 female, 6 male; 30 white British or white other). The 6 excluded participants did not differ on age [mean age = 21.0 years, *SD* = 2.53; t(39) = .46, $p = .65$], gender [3 female, 3 male; $\chi^2 = 3.23$, $p = .072$] or ethnicity [4 white British or white other, $\chi^2 = 1.31$, $p = .25$]. All participants reported no current or previous psychiatric history. Due to ethical considerations, the nature of the traumatic film material was declared on the recruitment information sheets.

Nine additional participants were recruited to act as controls for the flashback involuntary recall analysis. The 9 participants did not differ from those that took part the main experiment on age [mean age = 24.22 years, *SD* = 3.46; t(42) = .69, $p = .49$], gender [5 female, 4 male; $\chi^2 = 3.04$, $p = .081$] or ethnicity [6 white British or white other, $\chi^2 = 1.75$, $p = .19$].

Behavioural Measures

Baseline measures

History of hypomania was assessed using the Mood Disorders Questionnaire (MDQ; Hirschfield et al., 2000). The self-report questionnaire is split into three sections; section one consists of 13 yes/no items investigating lifetime (hypo)manic symptoms, section two investigating symptom co-occurrence, and section three symptom severity on a four point scale (no problem, minor problem, moderate problem, serious problem). Total scores range from 0-17, with severity scored from 0-3 respectively. Higher scores represent higher levels of hypomanic history. The MDQ has good internal validity with an alpha coefficient of .84 (Hirschfeld et al., 2003).

Current depression levels were measured using the Beck Depression Inventory Second Edition (BDI-II; Beck, Steer, & Brown, 1996). Participants responded to 21 questions on a scale of 0-3, asking about their mood over the last two weeks. Higher total scores represent higher levels of current depression. The BDI-II has good internal validity with an alpha coefficient of .81 (Beck, Steer, & Garbin, 1988)

Trait anxiety was measured using the State-Trait Anxiety Inventory-Trait version (STAI-T; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). The STAI-T contains 20 anxiety related items which participants rate on a four point scale as to how they generally feel. Higher total scores represent higher levels of trait anxiety. The STAI-T has good internal validity with an alpha coefficient of .9 (Spielberger, Reheiser, Owen, & Sydeman, 2004).

Emotional response to the film

Participants rated their current mood before and after film viewing using 10cm visual analogue scales (VAS) for ‘sad’, ‘hopeless’ and ‘depressed’. A composite negative mood response was calculated from the mean of the three VAS (Holmes, et al., 2010).

Trauma film

The trauma film lasted for 21 minutes and 19 seconds and was presented using Presentation v16 software (www.neurobs.com). The trauma film contained 15 short video clips, each introduced with a short written script to provide context for the following images. The 15 clips comprised 20 Potential scenes – scenes previously shown to be recalled as flashbacks (mean length = 22.5s; range 5-37s) and 16 control scenes - scenes that never returned as flashbacks (mean length = 16.4s; range 5-36s). Potential and control scenes were matched as closely as possible and were approximately the same length ($t(34) = 1.94$, N.S). Scenes were selected to be easily discriminated from each other and scene order was arranged so that no more than four of the same scene type occurred in a row with at least six seconds between any Potential and Control scene to allow the BOLD response to return to baseline between scenes (see Appendix IV). The film used was identical to that of Bourne et al. apart from one video clip, compromising three control scenes, which was shortened to allow for more time to be allocated to later scene introductions without overly lengthening the film. The three control scenes in the shortened video clip were kept the same length to ensure that the average control scene length was not altered.

Flashback involuntary recall

To investigate the neural basis of flashback involuntary recall, after film viewing participants were asked to lie in the scanner for 6 minutes and to press a button if they experienced a flashback of the film. Flashbacks were described to participants as mental images of the film contents that spontaneously and involuntarily came to mind. Participants were told that the purpose of the scan was to collect data to help with analysis and it was made clear to the participants that they may or may not experience any flashbacks during the scan (see Appendix XI for the verbatim instructions). Participants were told that they could think about anything they wished to during the scan and to not

press the button if they voluntarily (deliberately) thought about the film. After the scan, participants wrote a description of the flashback events they experienced in the flashback diary in sufficient detail that they could be identified as matching a scene in the film.

Flashback diary

In the week following film viewing participants used a pen and paper flashback diary (Appendix X) to record any further flashbacks they experienced in daily life (Bourne, et al., 2013; Holmes, et al., 2004). Participants were asked to write descriptions of the flashbacks' content so that each flashback could be matched to a specific scene in the film for later analysis.

Recognition memory test at 1-week

To investigate participants' recognition memory of the film contents participants returned 1-week after film viewing and performed a visual recognition memory test (see Appendix VII). The visual recognition memory test comprised 201 stills, of which 102 were from the film and 99 were from unused sections of the film clips that had been edited out or were from similar situations (Clark, Mackay, & Holmes, 2013; Wegner, Quillian, & Houston, 1996). The 102 stills from the film were selected to be at least 6 seconds apart and could be identified as unique to all other points in the film. Fifty-one of the stills were from possible flashback scenes and 51were from control scenes. The stills were defined for each individual as Flashback, Potential or Control, and then by identified or non-identified, creating six possible event types.

The recognition memory test was presented using Presentation v16 software (www.neurobs.com). Each still was presented on the screen for a maximum of 3 seconds, after which the still was replaced by a black screen for up to a further 7 seconds. Participants were asked to respond at any point after the still was presented, pressing "1" if they thought the picture was in the film and "2" if the picture was not in the film. Upon participants' response a text screen appeared asking participants to rate how confident they

were in their answer; *High Confidence, Low Confidence or Guessing* (button press of "1", "2" or "3" respectively). Participants had up to 10 seconds to answer. Upon participants confidence response the next still was presented. Any correct answers that were rated by the participant as *Guessing* were excluded from the subsequent analysis (Hasson, et al., 2008).

Scene emotional response

To understand participants' subjective emotional response to the film, participants individually rated each of the 20 Potential scenes and 16 Control scenes at follow up. Written descriptions of each of the scenes were provided and participants were asked to think back to when they watched the film the week before and rate how emotional they found each scene at the time they were viewing it on an 11 point scale anchored at 0*, not at all,* and 10, *very emotional*.

Procedure

The experimental protocol containing all the verbatim instructions given to participants can be seen in Appendix XI.

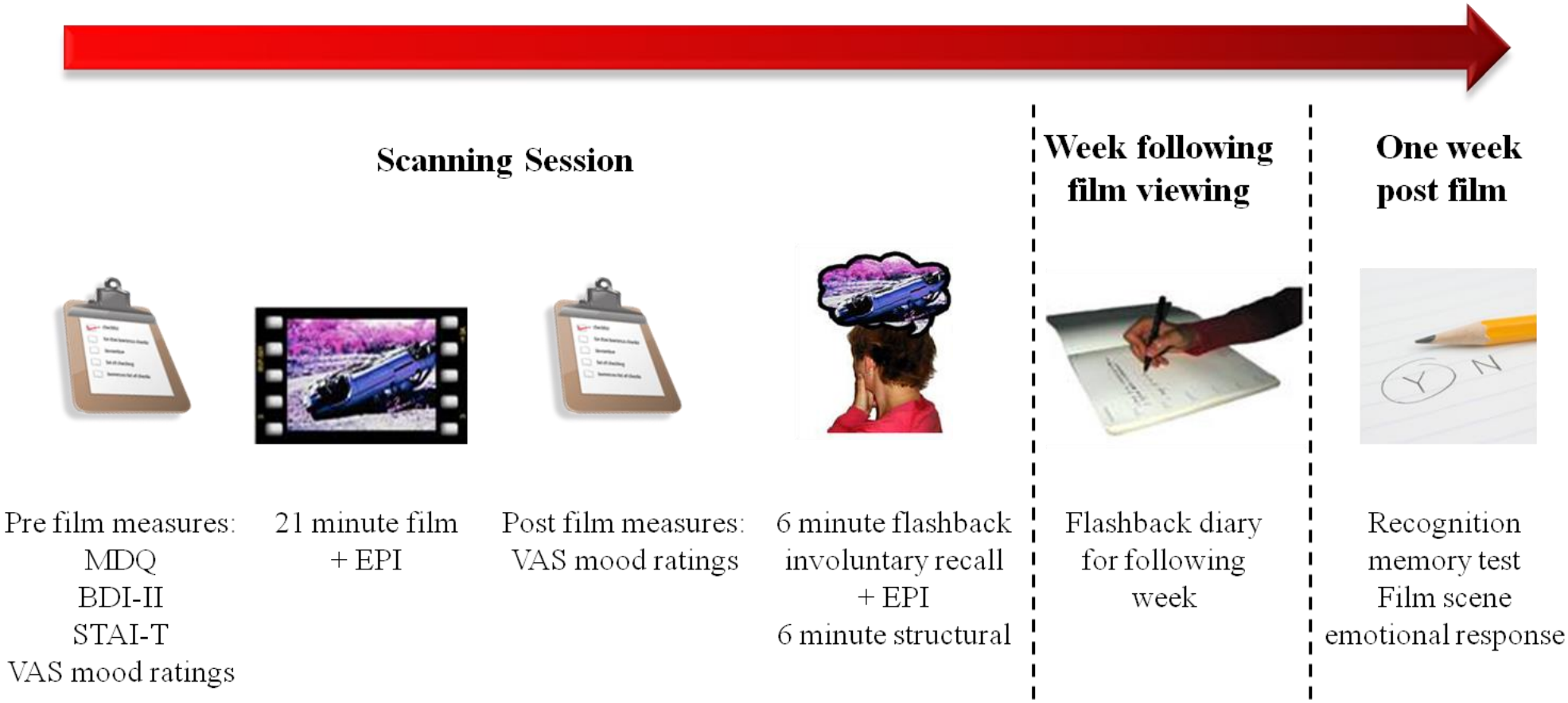
At initial contact participants were informed about the traumatic nature of the film footage and participants were pre-screened to ensure they were MRI safe. On arrival to the laboratory all participants gave written informed consent and filled out the MRI safety screening form. Participants were then asked to complete baseline measures concerning their history of hypomania, current depression and trait anxiety and rate their current mood. On completion, participants were placed into the fMRI scanner with a 12 channel head coil and a viewing mirror in order to see the projector screen behind them. Participants were asked to watch the film as if the events being depicted were happening to them or around them right now. On film completion the participant was taken out of the scanner and mood questionnaires were re-administered giving participants a short break

from the scanner. Participants were then returned into the scanner and underwent a 6-minute functional scan, indicating with a button press if they experienced a flashback of the film footage. Over the following week participants recorded any further flashbacks they experienced of the footage, returning a week later to perform a surprise recognition memory test (Figure 3.1).

Statistical analysis

Throughout the thesis a similar exploratory data analysis was performed on all data based on Tabachnick and Fidell (1996). Data were examined for any missing cases. Any participants who had not completed the whole study were excluded from analysis (i.e. did not complete both sessions 1 and 2). All participants who completed the whole study completed all measures, so there was no missing data. The presence of univariate outliers, defined as three standard deviations above or below the mean, was examined. None were found in the key dependent variable – flashbacks. Normality of dependent variables and predictive variables was assessed graphically. When data were highly skewed scores were square or cube rooted to return to normality. As flashbacks are count data and not normally distributed, appropriate (non-parametric) statistical tests were used (e.g. Mann Witney, Kruskal Wallace and negative binomial regressions). The use of these tests are indicated when appropriate. Homogeneity was assessed using statistical tests across groups (reported where appropriate) to investigate similarity between groups. Violations of sphericity for normally distributed data were assessed using Mauchly's test of sphericity. If sphericity could not be assumed Greenhouse Geisser correction was employed and the degrees of freedom were altered accordingly.

Figure 3.1. The experimental procedure.



fMRI analysis

Image acquisition and analysis

Echo planar imaging data were acquired on a 3-T Siemens TIM Trio System with a 12-chanel head coil [voxel resolution = 3 x 3 x 3 mm^3; repetition time (TR) = 3s, echo time (TE) = 30ms]. T1-weighted structural images were acquired for subject registration using a magnetisation prepared rapid gradient echo (MPRAGE) sequence (voxel resolution = 1 x 1 x 1 mm^3; TR = 2040ms; TE = 4.7ms].

All analyses were performed using FEAT (FMRI Expert Analysis Tool) version 6.0 [part of the Functional Magnetic Resonance Imaging of the Brain (fMRIB)'s Software Library, www.fmrib.ox.ac.uk/fsl]. Data were pre-processed using FEAT default options: motion correction was applied using McFlirt and fieldmaps with an echo planar imaging (EPI) echo spacing of .49ms and TE of 22ms; Gaussian spatial smoothing was applied with a full width half maximum of 5mm; brain matter was separated from non brain using a mesh deformation approach; high pass temporal filtering was applied with a cut off of 100s.

Flashback encoding analysis

Events for the flashback encoding analysis were modelled in the "scenes space". Scenes in the film were predetermined to be either Potential scenes or Control scenes. For each individual, 'n' of the Potential scenes were recalled as flashbacks and became Flashback scenes leaving '20 – n' Potential scenes. Flashback scenes were defined on an individual basis, using descriptions in the flashback diary and the written descriptions from the flashback involuntary recall in the scanner. None of the 16 Control scenes became a flashback event in any individual.

The three event types were specified for each individual in the general linear model along with the duration of each event. Events were modelled by convolving with a γ

hemodynamic response function. A fourth variable was also entered to model the time periods when participants were reading information slides. All four event types were included in a general linear model applied voxel wise to the pre-processed imaging data. Analysis was performed on an individual participant basis using FILM (FMRIB's Improved Linear Model), with contrasts of interest registered to the Montreal Neurological Institute (MNI) 152 template. Voxel wise group analysis was performed in MNI standard space using FLAME (FMRIB's Local Analysis of Mixed Effects) stage 1 (Beckmann, Jenkinson, & Smith, 2003; Woolrich, 2008; Woolrich, Behrens, Beckmann, Jenkinson, & Smith, 2004). *z* statistic images were thresholded at $z > 2.3$ and a family wise error corrected cluster significance threshold of $p < .05$ (Forman et al., 1995).

BOLD signal change was extracted from predefined regions of interest (ROI) to present a clearer picture of the signal change for each scene type. The predefined regions were those identified by Bourne et al. (2013) – the amygdala, accumbens, putamen, rostral anterior cingulate cortex (rACC), thalamus, ventral occipital cortex, left inferior frontal gyrus (left IFG), middle temporal gyrus (MTG) and hippocampus – and two additional ROIs, the insula and parahippocampus. The insula was included due to its association with pain related networks and emotional awareness (e.g. Craig, 2009), and the parahippocampus was included to further understand the involvement of more basic memory areas (e.g. Squire & Zola-Morgan, 1991). Apart from the left IFG and MTG, ROIs were created from the Oxford-Harvard cortical and sub-cortical probabilistic anatomical atlases, thresholded at a minimum probability of 20%. The left IFG and MTG were defined according to Bourne et al. (2013) – areas that were significantly activated on a whole brain basis in the flashback versus potential contrast, but not for the flashback versus control contrast.

Recognition memory analysis

Events for the recognition analysis were modelled in the "stills space". As with the flashback encoding analysis, stills used in the recognition memory test were predetermined to be either Emotional (51 stills) or Control (51 stills). All Emotional stills were taken from the predetermined Potential scenes in the film. Emotional stills that were taken from Potential scenes that returned as flashbacks were defined as Flashback stills for that individual. Emotional stills from potential scenes that did not return as flashbacks were defined as Potential stills.

The three event types were then further defined by whether they were identified or not identified by the participant, creating six event types: Flashback identified, Flashback non-identified, Potential identified, Potential non-identified, Control identified and Control non-identified. As with the flashback encoding analysis, the six event types were entered into the general linear model (each still modelled for 0.5 seconds) and applied to the pre-processed data in FILM for each participant. Group wise analysis was performed in MNI standard space using FLAME with *z* statistic images thresholded at $z > 2.3$ and a family wise error corrected cluster significance threshold of $p < .05$.

BOLD signal change was extracted from the same predefined regions as described in the flashback encoding analysis section.

Flashback involuntary recall analysis

Events in the flashback involuntary recall analysis were modelled around the button press. To my knowledge, no previous research investigating flashbacks has reported the moment of flashback involuntary recall during neuroimaging. Analysis was therefore based on previous work investigating the neural basis of hallucinations, where hallucination occurrence was signalled by the participant during scanning (Diederen et al., 2010). As the time of flashback recall in relation to the button press was unknown, finite impulse response (FIR) basis functions were used to detect brain activation surrounding

the button press. The hemodynamic response functions used more commonly, and in the previous analyses, reflect the slow increases and decrease in BOLD function after activation in the brain. However, to correctly model the hemodynamic response, clear timing information about the event of interest is required (see Diederen, et al., 2010; Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001, for further details). FIR on the other hand makes no assumptions about the fMRI response. Five consecutive 'time bins' were created, each modelling a single time point of three second duration (the TR) surrounding the button press. To take into account the approximate six second delay in hemodynamic response function the five time bins modelled from -3 seconds to +12 seconds (in relation to the button press). The five time bins were entered into a single general linear model and applied to the pre-processed data in FILM for each participant. The FIR basis function was modelled as a single basis function, with a 0 second phase shift and 3 second time window.

To compare the brain activation associated with a random button press alone with that observed during button press to indicate flashback involuntary recall, 9 additional participants (who did not take part in the rest of the experiment) were recruited. Participants underwent a six minute scan, as per the flashback involuntary recall procedure, during which they were asked to randomly press a button between approximately 5 and 10 times. This was to match the mean number of flashbacks recalled in the trauma film participants. The same FIR analysis was performed on the button press alone sample as with the flashback involuntary recall sample. Group wise analysis between the flashback involuntary recall group and the button press group was performed in MNI standard space using FLAME with *z* statistic images thresholded at $z > 1.7$ and a family wise error corrected cluster significance threshold of $p < .05$.

Percentage BOLD signal change was extracted from ROIs significantly activated in the flashback involuntary recall versus button press alone analyses, and in the precentral gyrus to measure motor activity. The precentral gyrus was created from the Oxford-Harvard cortical and sub-cortical probabilistic anatomical atlases, thresholded at a minimum probability of 20%.

Results

Behavioural Measures

Baseline Measures

Across the 35 participants, the mean MDQ score was 3.74 (*SD* = 3.84), the mean BDI-II score was 4.26 (*SD* = 5.19) and the mean STAI-T score was 38.66 (*SD* = 9.63). Scores were within the non clinical range on all measures. A score of 7 or more is required on the MDQ for a clinical classification (Hirschfield, et al., 2000) and a student population survey reported a mean score of 3.6 with a standard deviation of 3.3 (Chandler, Wang, Ketter, & Goodwin, 2008). A score of below 10 on the BDI-II is classified as an absence of depression (Beck, Steer, & Brown, 1996) and a mean score of 35.55 (SD = 9.76) is reported for a healthy population on the STAI-T (Spielberger, et al., 1983).

Emotional response to the film

A repeated measures ANOVA was performed to investigate the effect of the film on participants' mood, finding that, as predicted, ratings of negative mood significantly increased from baseline (mean = 1.05, *SD* = 1.26) to post film viewing (mean = 3.14, *SD* = 1.94) [$F(1,34) = 56.10$, $p < .001$, $\eta^2_p = .62$].

Flashback involuntary recall

In the scanner, soon after film viewing, 25 of the 35 participants reported experiencing flashbacks of the film. In total, 148 flashbacks were reported in the scanner (mean = 5.92, *SD* = 4.08). Some events were experienced as flashbacks more than once; the mean number of different Flashback scenes per person was 2.36 (*SD* = 1.37).

Flashback diary

Thirty three of the thirty five participants reported at least one flashback in the 1-week diary. In the diaries, 144 flashbacks were reported (mean = 4.36, *SD* = 4.36). The mean number of different scenes was 2.42 (*SD* = 1.28).

Total flashbacks to the trauma film

All 35 participants reported at least 1 flashback either during the flashback involuntary recall scan or in the flashback dairy. Across the 35 participants there was a total of 303 flashbacks reported during the flashback involuntary recall scan and the 1-week flashback diary (mean = 8.66, *SD* = 7.15). The mean number of different scenes per person was 3.08 (*SD* = 1.46).

Recognition memory test

Across the 35 participants, 9 participants were able to identify all their corresponding Flashback stills as from the film. Subsequently, non identified Flashback stills could not be modelled for those participants and they were removed from further analysis.

Within the 26 participants reporting at least 1 forgotten Flashback still, the mean hit rate (correctly identifying stills from the film) was .67 (*SD*= .089) and the mean false alarm rate (identifying foils as from the film) was .32 (*SD* = .11). Signal detection theory was used to calculate participants' discriminabiliy between stills from the film and foils (*d'*) and a measure of bias (*C*). *d'* and bias scores were calculated using http://memory.psych.mun.ca/models/recognition, accessed September 2013. A larger *d'* corresponds to a better ability to discriminate between film stills and foils and values of *C* above 0 correspond to a bias less willing to choose film stills, while a value below 0 corresponds to a bias more willing to choose film stills. The mean d' was .94 (SD = .27) and the mean C was .0067 (SD = .25) suggesting a reasonable ability to discriminate between film stills and foils but no bias towards choosing either.

Examination of individual scores found that the range of false alarm rates was from .15 to .52. Low false alarm rates (< .25, n = 8) were characterised by a response bias for not choosing film stills (mean C = .25). As low false alarm rates could not be explained by a response bias for choosing film stills over foils no further participants were excluded from the analysis.

Classification by the six event types gave a mean number of events of: 7.88 (*SD* = 4.0) in the Flashback identified; 2.12 (*SD* = 1.28) Flashback non-identified; 24.0 (*SD* = 6.54) Potential identified; 14.73 (*SD* = 5.37) Potential non-identified; 32.92 (*SD* = 5.21) Control identified; 16.85 (*SD* = 4.78) Control non-identified.

Participants' subjective emotional response to the film

The mean emotionality rating for Flashback scenes was 7.61 (*SD* = 1.79), for Control scenes was 2.73 (*SD* = 1.22) and Potential scenes was 5.67 (*SD* = 1.48). Repeated measures ANOVA showed that emotionality ratings were different between the scene types [$F(2, 68) = 148.49$, $p < .001$, $\eta^2_p = .81$]. Paired samples t-tests, corrected for multiple comparisons, found a significant difference in emotionality between Flashback and Potential scenes [$t(34) = 5.89$, $p < .001$, $d = 1.18$], Flashback and Control scenes [$t(34) = 15.68$, $p < .001$, $d = 3.19$], and Potential and Control scenes [$t(34) = 14.89$, $p < .001$, $d = 3.60$].

The correlation between subjective emotional response and flashbacks was assessed to further understand the effect of emotional response to individual flashback scenes and the likelihood of the scene becoming a flashback. The mean emotionality rating across participants for flashback scenes was significantly correlated with the number of participants reporting that scene as a flashback ($r = .48$, $p = .033$).

fMRI analysis

Hypothesis 1: Flashback encoding analysis[1]

Whole brain analysis

A whole brain analysis was performed to investigate differences in activation at the encoding of Flashback, Potential and Control scenes. Results for the three contrasts of interest (Flashback vs. Potential; Flashback vs. Control; Potential vs. Control) can be seen in Figure 3.2. As predicted, Flashback scenes compared to Potential scenes (Figure 3.2, top row) revealed widespread increases in activation across the brain, including the thalamus, striatum, rACC, MTG, left IFG and ventral occipital cortex. Increased activation in the amygdala approached significance. The reverse contrast found no areas of activation.

Analysis of Flashback scenes compared to Control scenes (Figure 3.2, middle row) also found widespread increases in activation, including the thalamus, striatum, rACC and ventral occipital cortex. Increased activation in the amygdala approached significance, but no increase in activity was seen in the MTG and left IFG. The reverse contrast found no areas of activation. The final analysis compared Potential scenes to Control scenes (Figure 3.2, bottom row). Less activation was observed than in the previous contrasts, but increased activation included the thalamus and ventral occipital cortex as before. Decreased activation in Potential scenes compared to Control scenes was observed in the MTG and left IFG. Peak voxel coordinates are provided in Table 3.1

To further understand the difference in activation between Flashback, Potential and Control scenes, the mean percentage BOLD signal change was plotted for each ROI for Flashback and Potential scenes relative to Control scenes (Figure 3.3).

[1]Inital analysis was also performed using emotion as a covariate. The examiners are thanked for informative discussion suggesting that emotion is not a variable of 'no interest' (i.e. it did have an effect between scene types), as demonstrated by the subjective participant emotion ratings, and therefore it is inappropriate to covary emotion (Miller & Chapman, 2001). Subsequently analyses using emotion as a covariate were removed.

Figure 3.2. Whole brain analysis of Flashback vs. Potential vs. Control film scenes. Areas of increased blood oxygen level-dependent (BOLD) response are shown in colour. The top row shows areas with greater activation when viewing Flashback scenes compared to Potential scenes (orange), the middle row shows areas with greater activation when viewing Flashback scenes compared to Control scenes (yellow) and the bottom row shows areas with greater activation when viewing Potential scenes compared to Control scenes (blue). The underlying image is the Montreal Neurological Institute (MNI) 152 template, *z* statistic images are thresholded at $z > 2.3$ with a family wise error corrected cluster significance threshold of $p < .05$

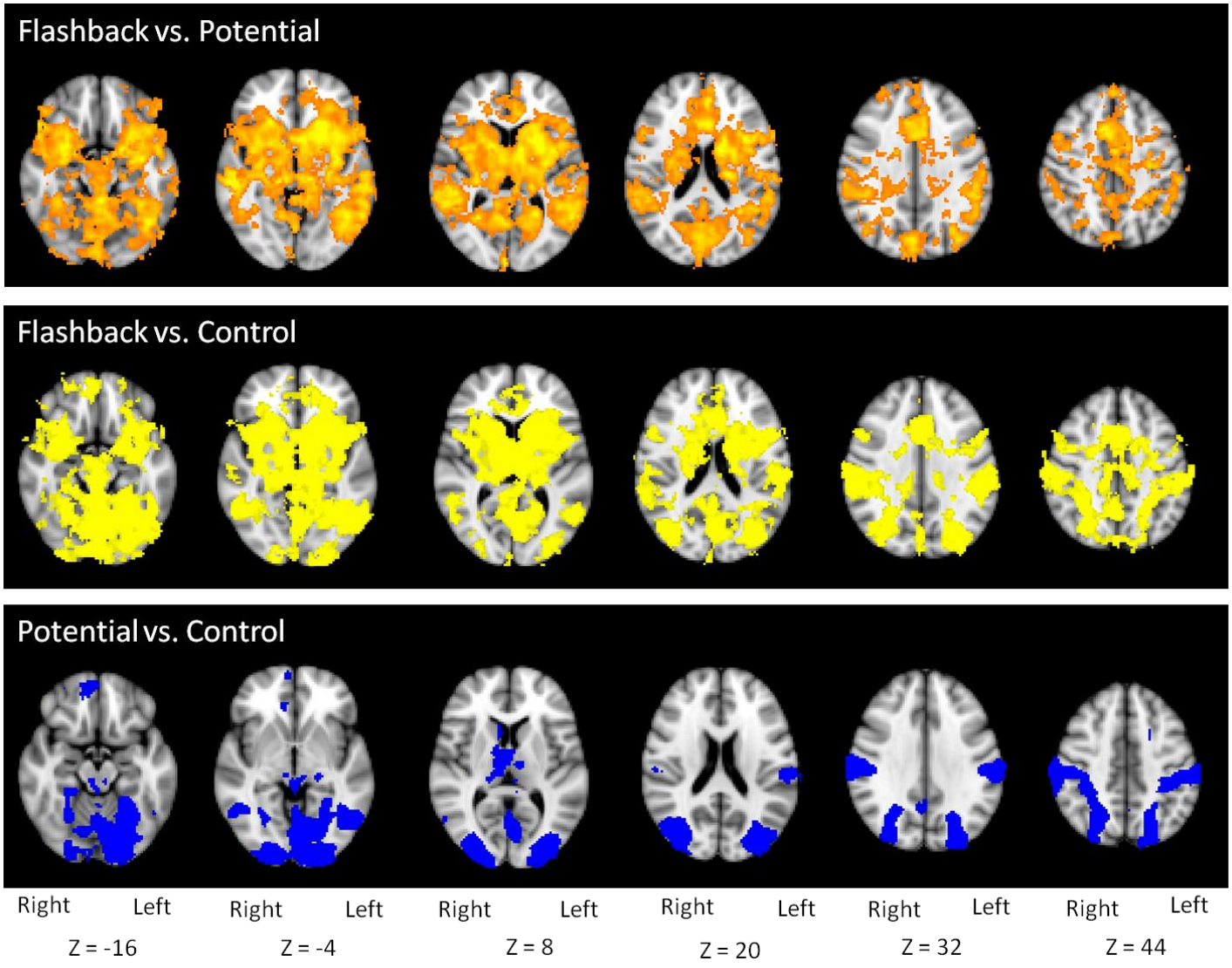
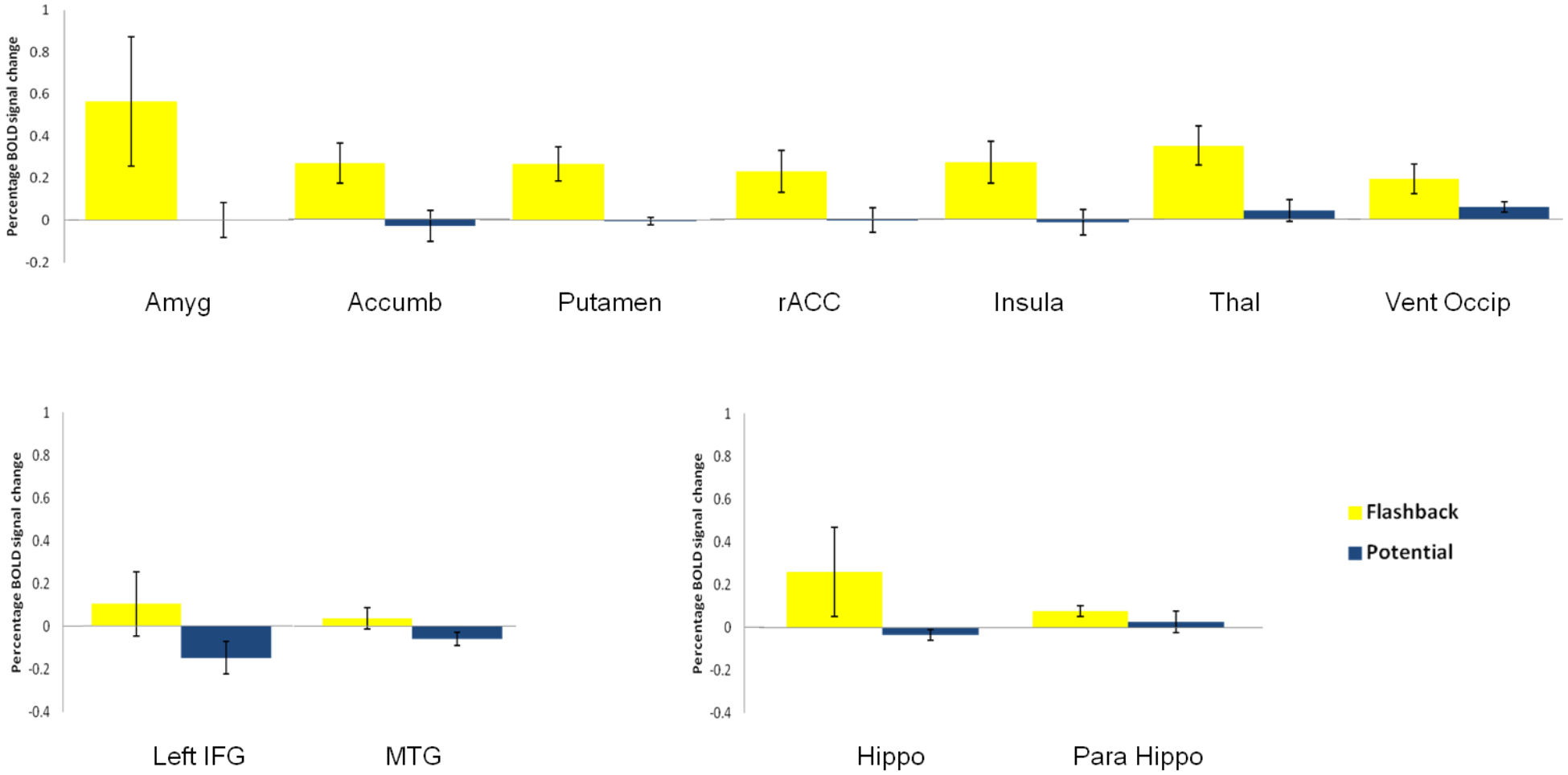


Table 3.1; Peak voxel coordinates identified in the whole brain flashback encoding analysis. Brain regions identified using the Oxford-Harvard cortical and subcortical anatomical atlas.

Analysis	Location	Cluster size	x	y	z	z-stat
Flashback>Potential	Left Putamen	80991	-14	8	2	6.08
	Left Precuneous		-22	-54	6	5.94
	Left Insular		-36	12	-6	5.83
	Left Middle Temporal Gyrus		-56	-56	10	5.82
	Left Caudate		-12	14	0	5.81
Flashback>Control	Left Inferior Temporal gyrus	85347	-44	-58	-6	6.37
	Left Supramarginal		-60	-26	30	6.27
	Left Caudate		-14	10	2	6.25
	Right Thalamus		10	-20	10	6.18
Potential>Control	Left Occipital fusiform gyrus	30148	-20	-70	-14	6.51
	Right Supramarginal		60	-22	36	6.48
	Left Lingual Gyrus		-8	-72	-6	6.45
	Left Temporal Occipital Fusiform Cortex		-26	-62	-12	6.44
	Right Superior Parietal		22	-50	74	6.2
	Right Thalamus	939	8	-16	12	5.18
	Left Thalamus		-8	-14	12	4.14
	Right Caudate		12	0	12	4.09
	Right Superior Frontal	769	24	-6	62	5.28
	Right Middle Frontal		26	-2	54	4.71
	Left Superior Frontal	625	-26	-4	62	4.33
	Left Precentral		-22	-10	66	3.48
	Right Frontal Pole	572	14	56	-14	4.43
	Right Frontal Orbital		22	34	-12	3.81
	Brain Stem	528	0	-34	-4	4.51
	Left Thalamus		-22	-26	-4	3.44
	Posterior Cingulate		-2	-38	4	3.42
	Hippocampus		-6	-38	6	3.25

Figure 3.3. ROI showing pattern of BOLD signal change for Flashback and Potential scenes relative to Control scenes.



Hypothesis 2: Recognition memory

Whole brain analysis

First, comparisons were made to investigate the three contrasts of interest as for the Flashback encoding analysis (Flashback vs. Potential; Flashback vs. Control; Potential vs. Control) to determine that analyses in the stills plain with fewer participants produced comparable results. For as high a level of similarity as possible both identified and non-identified stills were included in the analysis. As expected, the same pattern of results was found with decreased spatial extent (Figure 3.4). Peak voxel coordinates can be seen in Table 3.2.

Second, comparisons of activation were performed with only the identified stills. Activation in Flashback identified stills was compared with Potential identified stills to model the Flashback scenes vs. Potential scenes contrast (Figure 3.5, top row). The mean percentage BOLD signal change for Flashback identified vs. Potential identified is shown in Figure 3.6. Due to the low number of Flashback events in comparison to control events, Emotional identified stills (combined Flashback identified and Potential identified) were compared with Control identified stills to model the Flashback vs. Control contrast (Figure 3.5, bottom row). Results of the contrasts showed a similar pattern of activation as to Flashback vs. Potential and the Flashback vs. Control respectively. BOLD signal change for ROIs can be seen in Figure 3.7. Peak voxel coordinates can be seen in Table 3.2.

Hypothesis 3: Flashback vs. Potential: Identified vs. Non Identified

Third, an interaction between Flashback identified and Flashback non-identified vs. Potential identified and Potential non-identified stills was performed. Due to the low number of Flashback forgotten events (mean 2.12, *SD* = 1.28) and the short time period each event was modelled for (0.5 seconds) this analysis was exploratory and a z threshold of 1.7 was used. Results showed increases in activation in the insula, hippocampus and parahippocampus for Flashback identified vs. non-identified stills compared to Potential

identified vs. non-identified stills (Figure 3.8). Peak voxel coordinates can be seen in Table 3.2. BOLD signal change was plotted from activated areas to better understand the interaction between Flashback identified vs. non-identified and Potential identified vs. non identified. Three ROIs were taken from the areas showing activation in the whole brain analysis; the first corresponding to all areas with activation above the z threshold of 1.7 (the interaction), the second corresponding to activity in the insula and the third corresponding to activity in the hippocampus and parahippocampus (Figure 3.9).

Figure 3.4. Whole brain analysis of Flashback vs. Potential vs. Control stills. A similar pattern of activation can be seen but to a decreased spatial extent as for the whole brain flashback encoding analysis. Underlying image is the Montreal Neurological Institute (MNI) 152 template, *z* statistic images are thresholded at $z > 2.3$ with a family wise error corrected cluster significance threshold of $p < .05$.

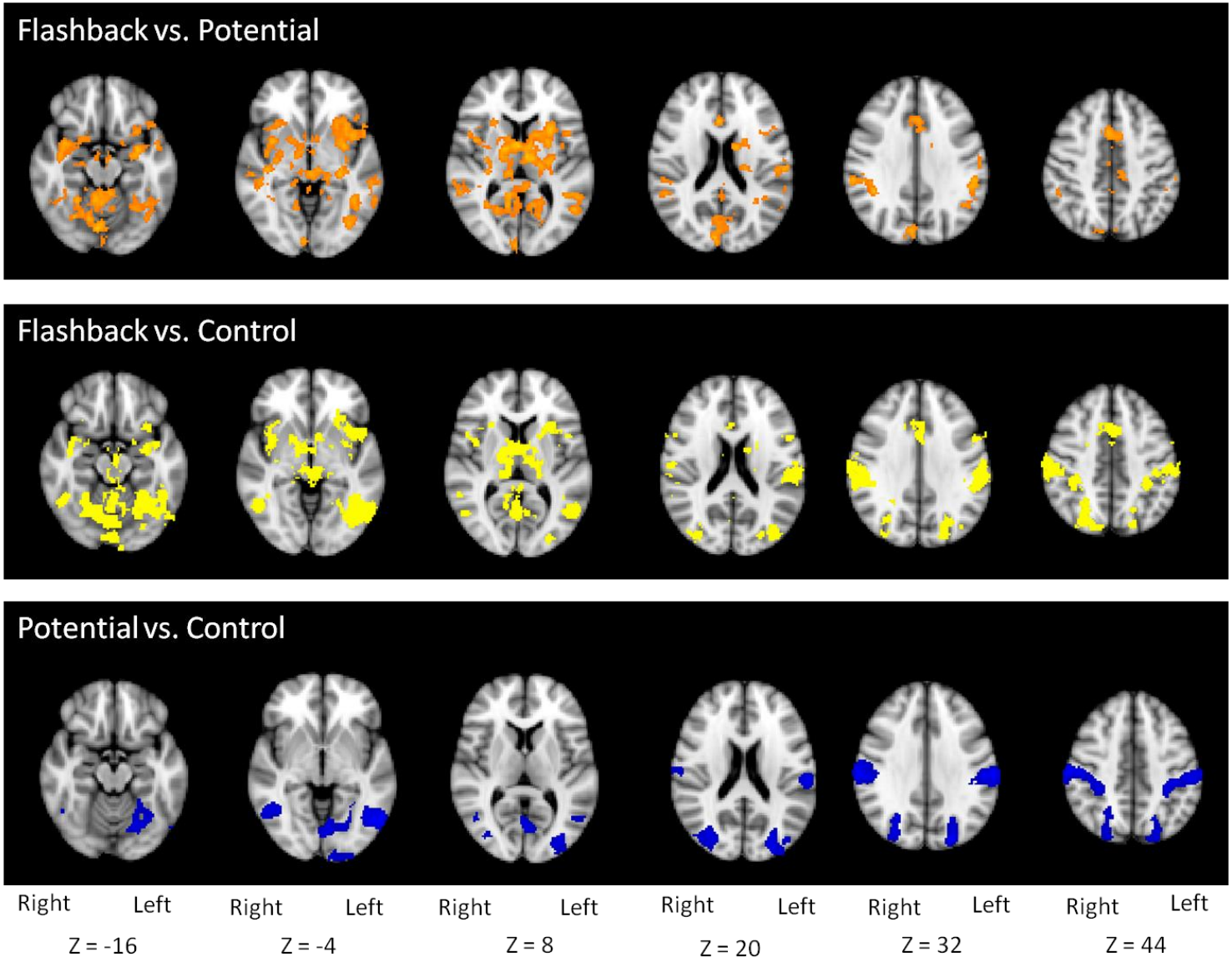


Figure 3.5. Whole brain analysis of Flashback identified vs. Potential identified stills (top row) and Emotional identified vs. Control identified stills (bottom row). Results show similar patterns of activation as for Flashback vs. Potential scenes and Flashback vs. Control scenes respectively. Underlying image is the Montreal Neurological Institute (MNI) 152 template, *z* statistic images are thresholded at $z > 2.3$ with a family wise error corrected cluster significance threshold of $p < .05$.

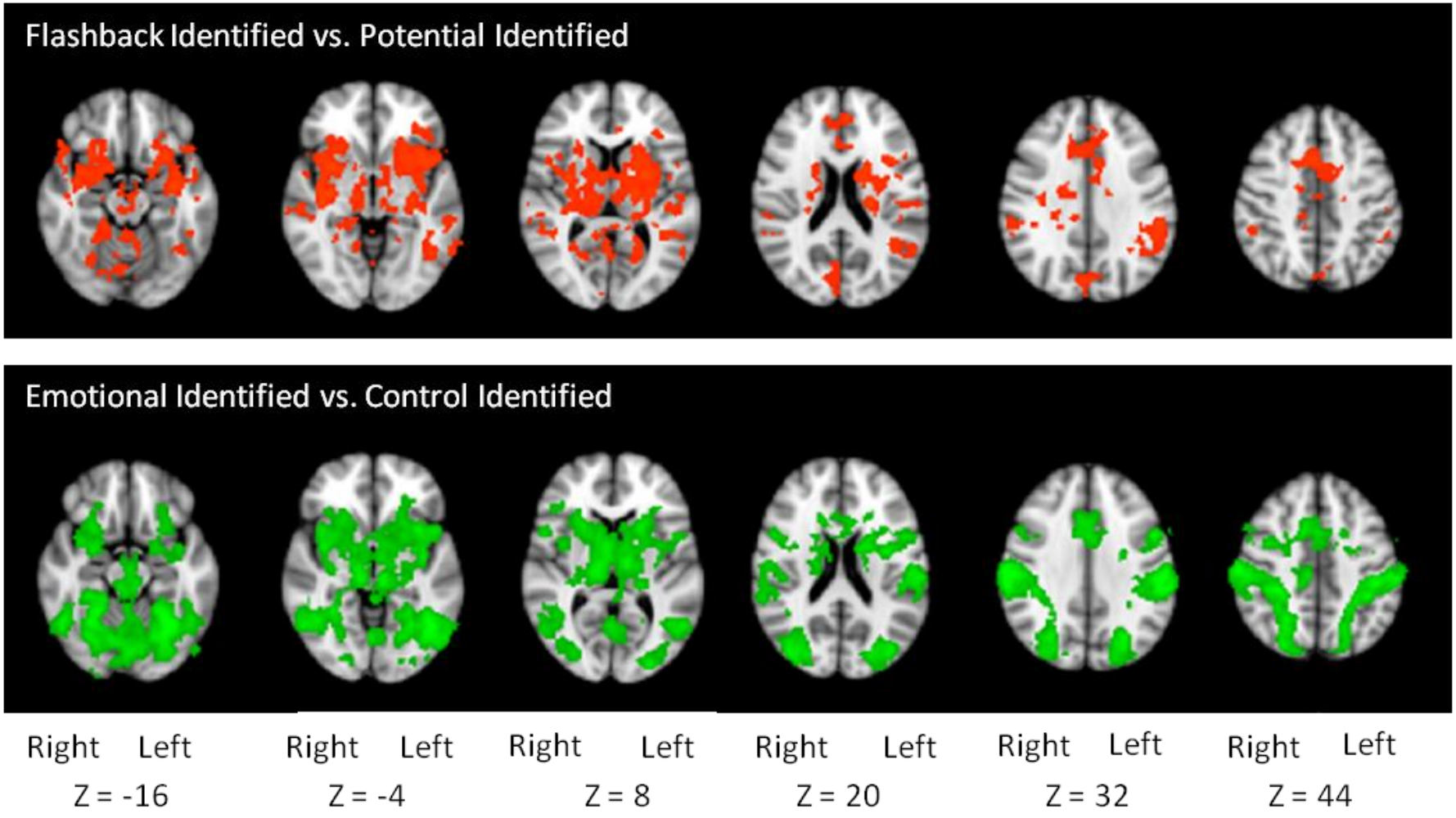


Figure 3.6. ROI showing pattern of BOLD signal change for Flashback identified stills (green) and Potential identified stills (purple) relative to baseline.

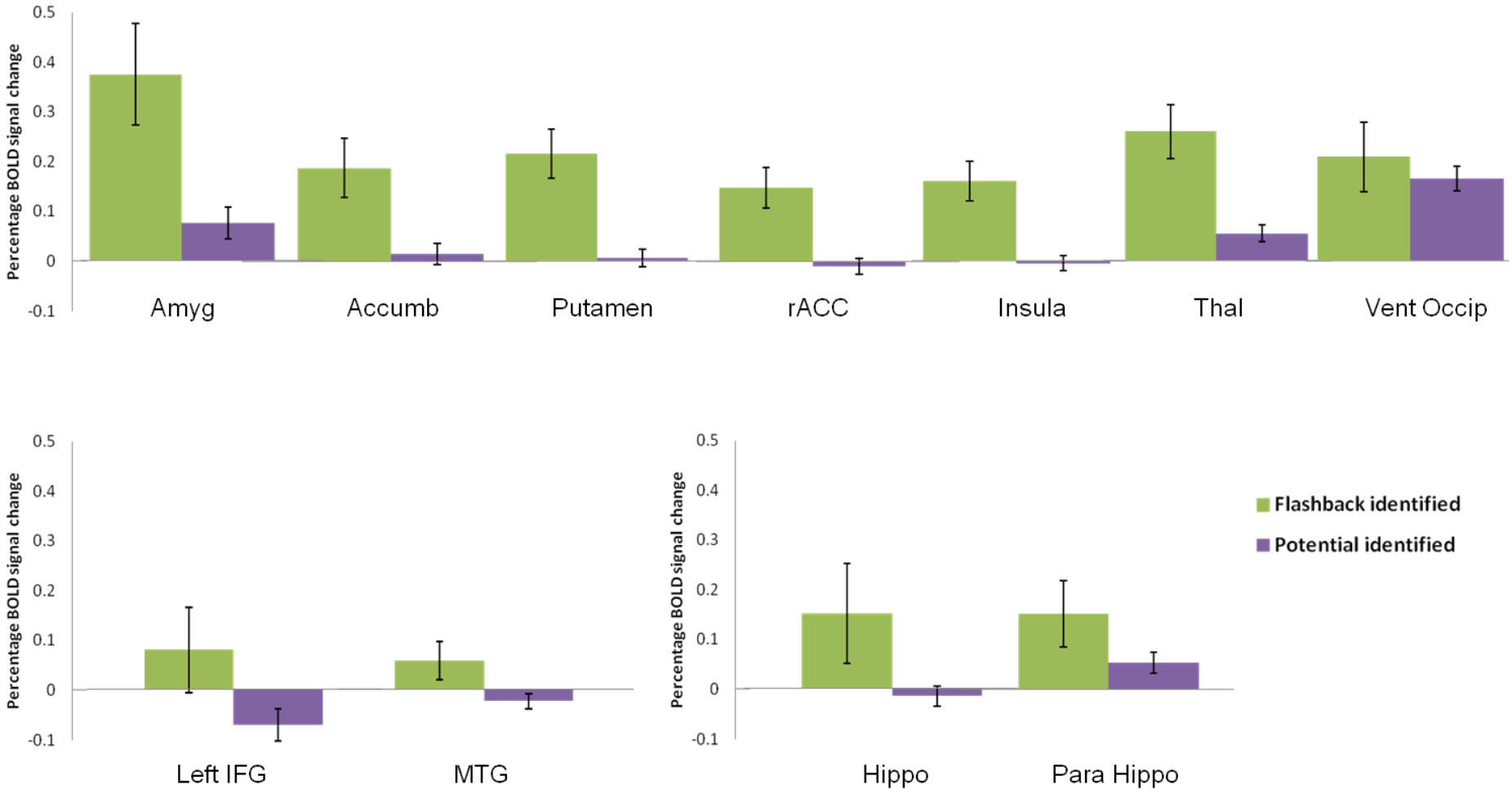


Figure 3.7. ROI showing pattern of BOLD signal change for Emotional identified stills and Control identified stills relative to baseline.

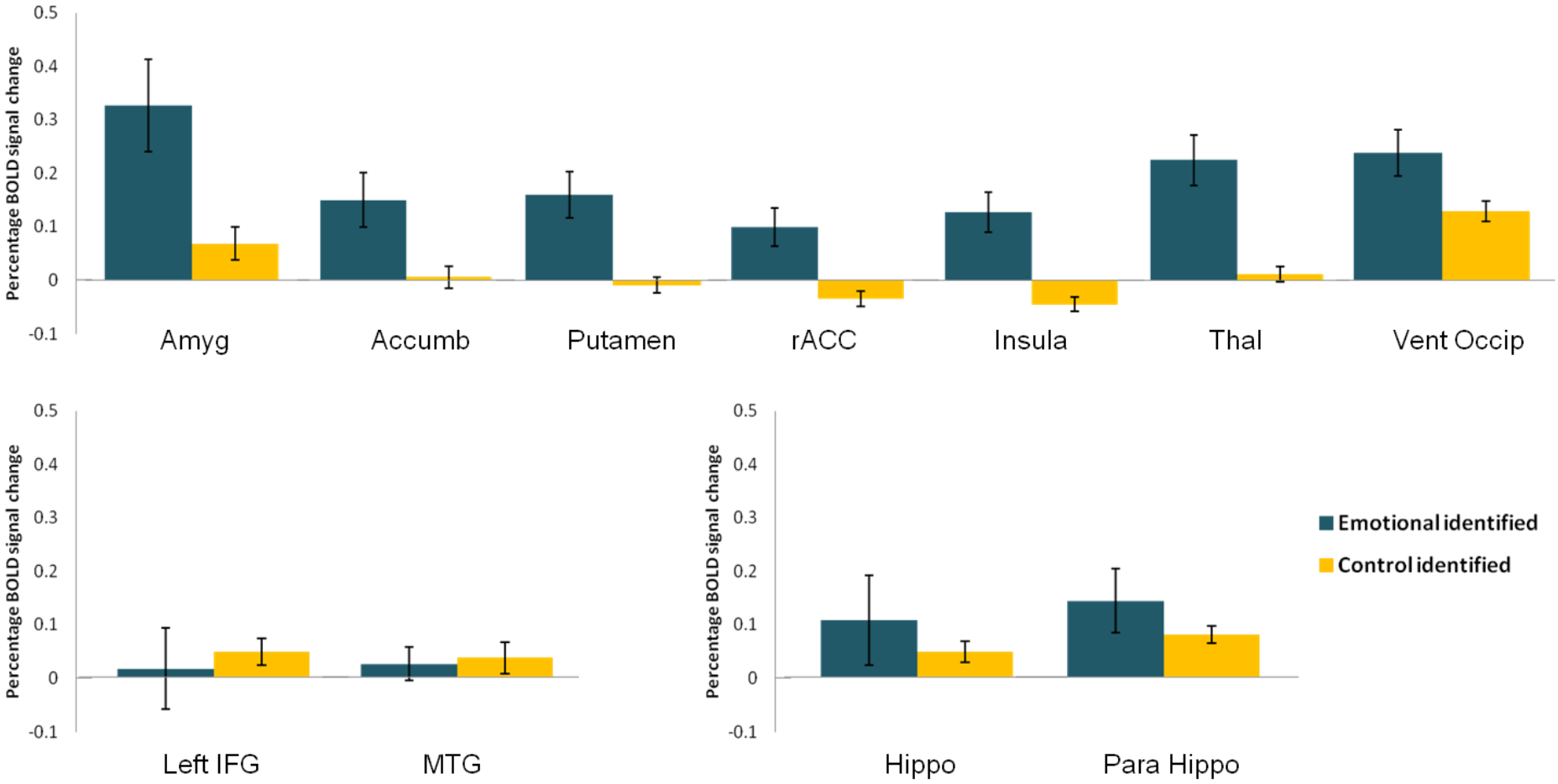


Figure 3.8. Whole brain analysis showing interaction between Flashback identified and Flashback non identified vs. Potential identified and Potential non-identified at z threshold of 1.7. Underlying image is the Montreal Neurological Institute (MNI) 152 template, *z* statistic images are thresholded at $z > 1.7$ with a family wise error corrected cluster significance threshold of $p < .05$.

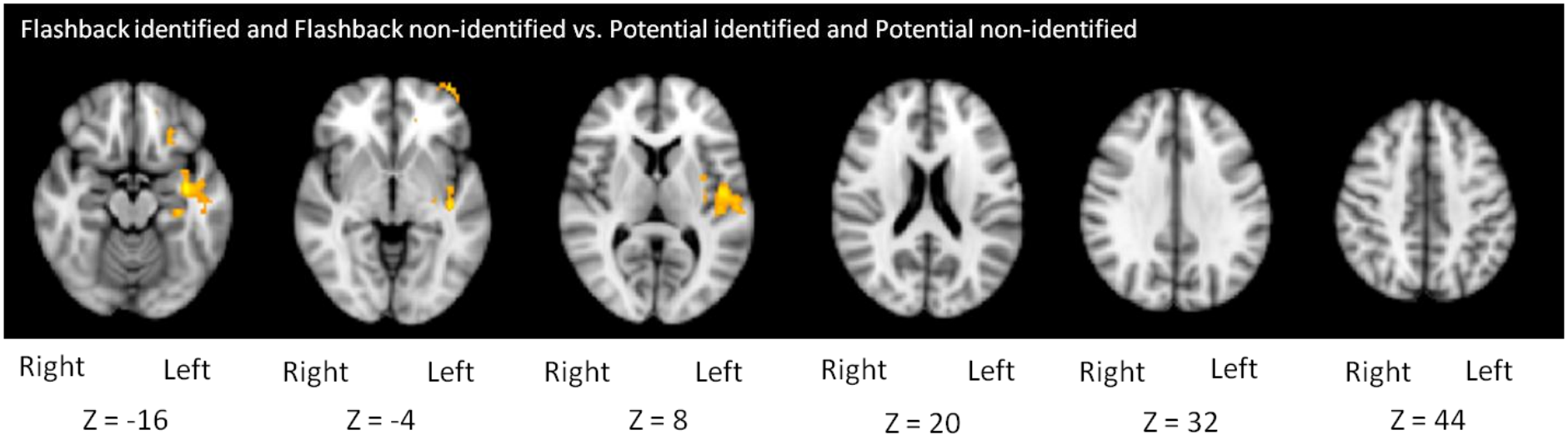


Figure 3.9. ROIs from the whole brain analysis at z threshold of 1.7 showing pattern of BOLD signal change for Flashback identified stills (dark green), Flashback non-identified stills (light green), Potential identified stills (dark purple) and Potential non-identified stills (light purple) relative to baseline.

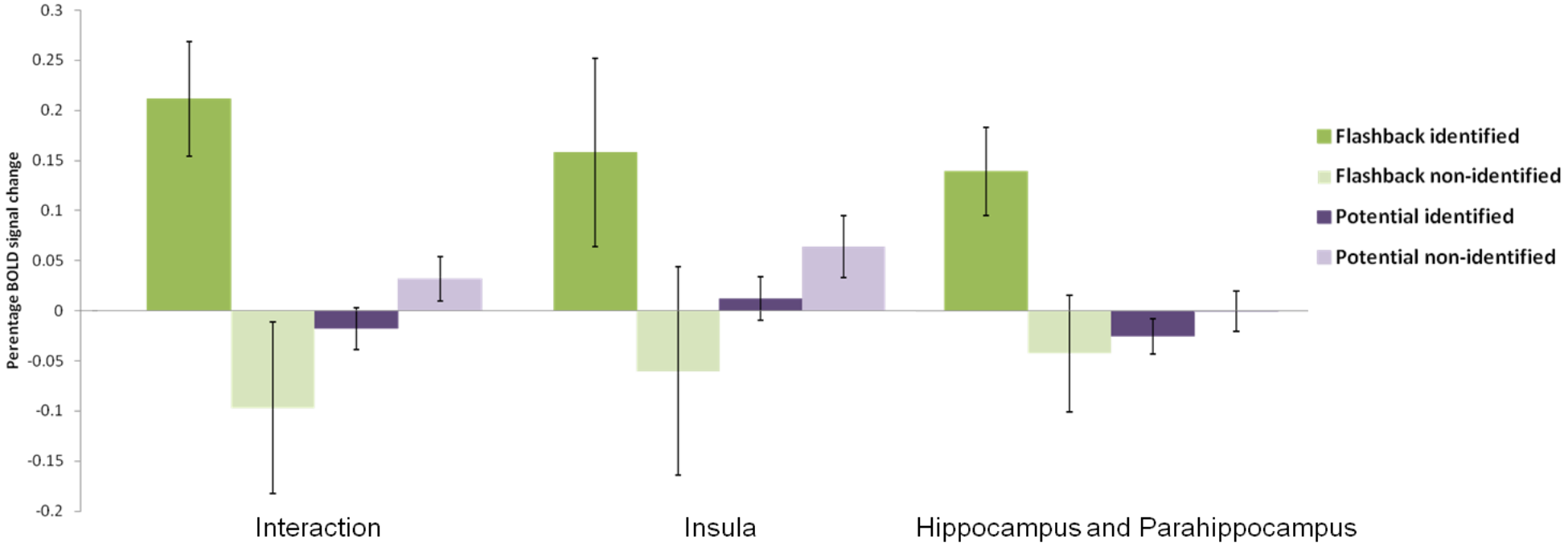


Table 3.2; Peak voxel coordinates identified in the whole brain stills encoding analysis. Brain regions identified using the Oxford-Harvard cortical and subcortical anatomical atlas and Cerebellar Atlas in MNI152 space after normalisation with FLIRT.

Analysis	Location	Cluster size	x	y	z	z-stat
Flashback>Potential	Left Amgydala	15601	-28	-8	-12	4.42
	Right Thalamus		16	-4	8	4.01
	Right Insular		36	6	0	4.01
	Left Insular		-28	14	6	3.99
	Left Supplementary Motor	2032	-2	-2	66	4.52
	Right Precentral		12	-16	54	3.53
	Anterior Cingulate		4	20	22	3.53
	Left Precueneous		-4	-44	62	3.51
	Right Supramarginal Gyrus	962	58	-36	38	3.65
	Right Middle Temporal Gyrus		46	-44	12	3.57
	Right Supramarginal		60	-34	34	3.49
	Parietal Operculum Cortex		60	-34	30	3.44
Flashback>Control	Left Middle Temporal Gyrus	14937	-52	-62	4	4.77
	Cerebellum. Right VIIb		18	-68	-48	4.74
	Left Temporal Occipital Fusiform Cortex		-30	-60	-22	4.62
	Cerebellum		-32	-46	-32	4.54
	Left Lateral Occipital Cortex		-40	-66	-2	4.41
	Left Inferior Temproal Gyrus		-42	-54	-6	4.41
	Left Supramarginal	8384	-58	-52	20	4.89
	Right Supramarginal		62	-20	42	4.81
	Left Superior Parietal Lobule		-36	-42	52	4.57
	Left Superior Frontal	2691	-24	-4	66	4.3
	Anterior Cingulate		-2	10	40	4.22
	Left Supplementary Motor		-2	4	54	4.13
	Right Middle Frontal		26	0	54	4.11
	Right Superior Frontal		18	4	80	4.02
Potential>Control	Right Superior Parietal	5738	18	-52	70	5.36
	Right Postcentral		62	-18	38	5.01
	Left Superior Parietal	5298	-34	-42	56	5.03
	Left Postcentral		-52	-24	38	4.96
	Left Supramarginal		-62	-24	34	4.9
	Left Lingual Gyrus	1362	-2	-74	0	4.7
	Left Occipital Fusiform		-20	-72	-8	3.81
	Left Temporal Occipital Fusiform Cortex		-24	-52	-14	3.56
	Left Lateral Occipital gyrus	852	-48	-66	0	5.14
	Right Superior Frontal	771	28	-4	56	4.83
	Right Middle Frontal		34	0	54	4.07
	Cerebellum	713	16	-72	-46	4.47
	Left Superior Frontal	586	-24	-6	58	4.28
	Left Precentral		-34	-4	68	3.4
	Right Lateral Occipital	516	52	-62	-10	4.94
	Right Inferior Temporal		48	-54	-6	4.03
Flashback identified >Potential identified	Right Putamen	27101	32	6	0	4.69
	Right Insular		38	-6	-12	4.68
	Left Putamen		-16	8	2	4.54
	Left Amgydala		-32	-4	-12	4.48
Emotional identified > Control identified	Left Supramarginal	57171	-56	-24	34	5.94
	Right Supramarginal		60	-20	36	5.74

	Left Temporal Occipital Fusiform Cortex		-28	-58	-14	5.73
	Left Inferior Temproal Gyrus		-44	-60	-4	5.69
	Left Middle Temporal Gyrus		-44	-60	0	5.66
	Right Thalamus		14	-20	12	5.42
Flashback vs.	Left Parahippocampus	1945	-28	6	-28	3.7
Potential; Identified vs.	Left Heschls gyrus		-48	-12	6	3.25
Non Identified	Left Insular		-38	-10	-14	3.22
Interaction (z = 1.7)	Left Frontal Orbital		-24	10	-22	3.19
	Left Middle Temporal Gyrus		-52	-8	-28	3.19

Hypothesis 4: Flashback involuntary recall

The control participants had a mean button press of 7.89 (*SD* = 2.15), which did not significantly differ from the frequency of flashbacks involuntarily recalled [mean flashbacks = 5.92, *SD* = 4.08; *t*(27.08) = 1.81, *p* = .081].

Whole brain analysis

Whole brain analyses using the five time bins were compared between the flashback involuntary recall group (i.e. flashback involuntary recall in the scanner soon after film viewing) and the button press alone group. No above threshold activation was found between -3 and 0, and 9 to 12 seconds. Increased activation was seen for the flashback involuntary recall in the middle and superior frontal regions between 0 and 3 seconds, and in the left inferior frontal gyrus and bilateral frontal and central operculum between 3 and 6 seconds. Increased activation for the button press alone group was seen between 6 and 9 seconds in the right insula and frontal pole. The whole brain analysis for the three time bins between 0 and 9 seconds can be seen in Figure 3.10. Peak voxel coordinates can be seen in Table 3.3.

ROI analysis

ROIs were created for the four areas found to show significant differences between flashback involuntary recall and the button press - the middle frontal gyrus, the superior frontal gyrus, the operculum (encompassing both frontal and central) and left inferior frontal gyrus. Additionally, ROIs were created for the precentral gyrus (to compare motor activation) and the areas associated with significant activation observed for button press alone compared to flashback. Profile plots of the change in BOLD signal activation over the time bins in each ROI for flashback involuntary recall in relation to the button press alone can be seen in Figure 3.11.

Figure 3.10. Whole brain analysis showing the pattern of brain activation when contrasting the flashback involuntary recall and button press alone at the three time bins showing significant differences in activation (0 to 3 seconds, 3 to 6 seconds and 6 to 9 seconds in relation to the button press). Underlying image is the Montreal Neurological Institute (MNI) 152 template, *z* statistic images are thresholded at $z > 1.7$ with a family wise error corrected cluster significance threshold of $p < .05$.

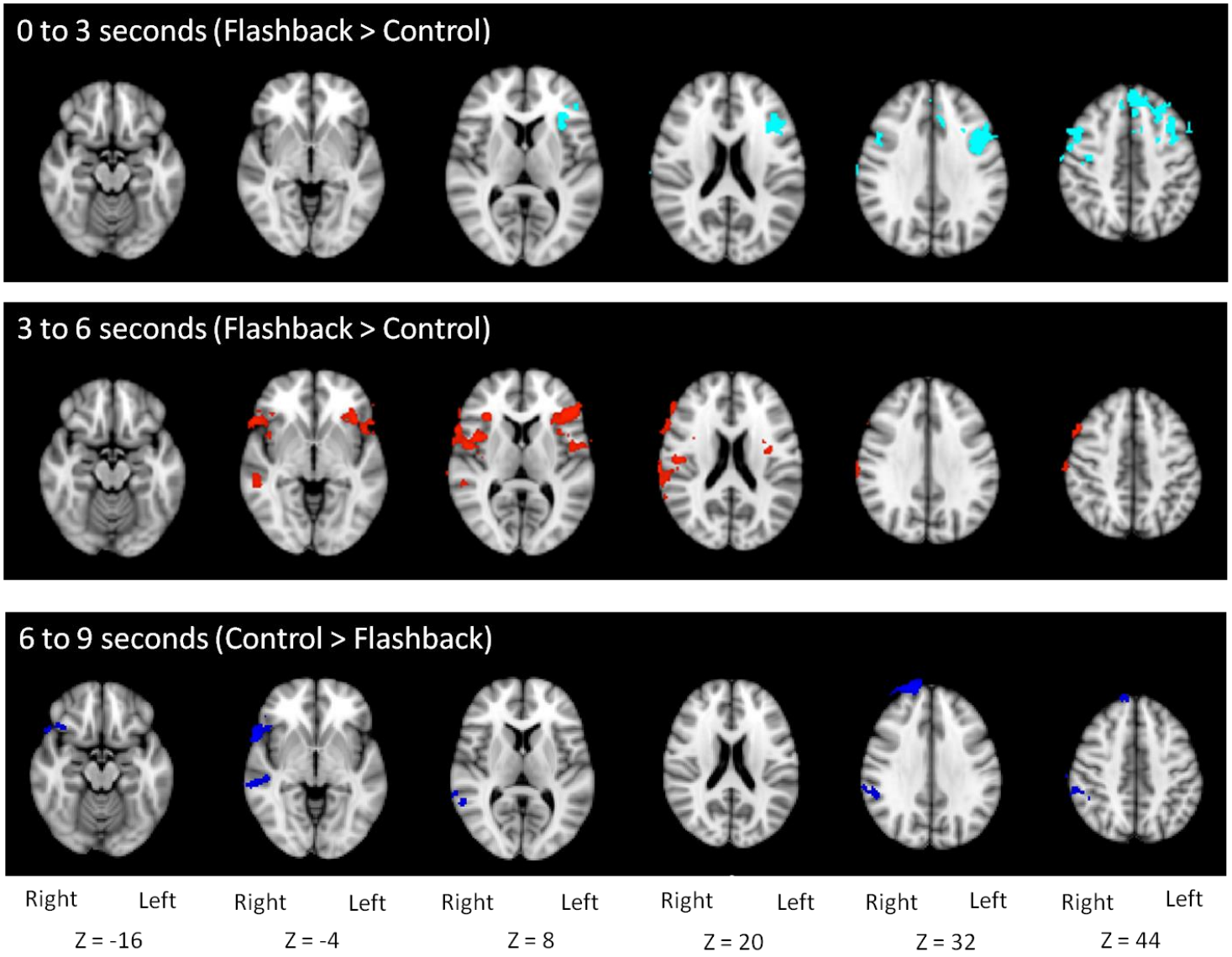


Figure 3.11. Profile plots of the signal change observed across each time bin from -3 to +12 seconds in relation to the button press in both conditions for the ROIs associated with flashback involuntary recall over the button press alone, the precentral gyrus and regions associated with the button press alone condition over the flashback condition. Flashback signal change activation is shown in pink, button press alone signal change activation in light blue.

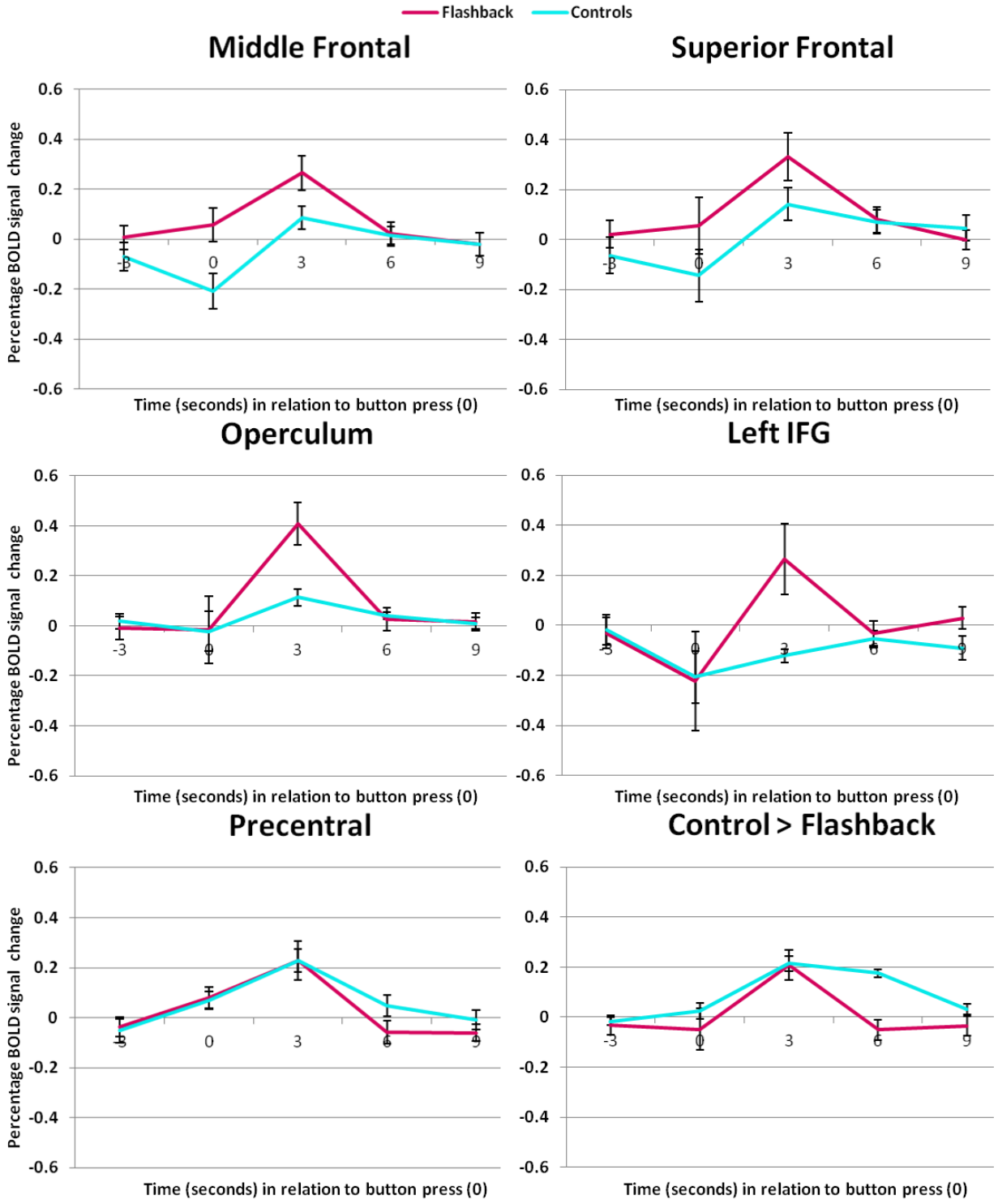


Table 3.3; Peak voxel coordinates identified in the whole brain flashback involuntary recall analysis. Brain regions identified using the Oxford-Harvard cortical and subcortical anatomical atlas.

Analysis	Location	Cluster size	x	y	z	z-stat
Flashback > Control; 0-3 sec	Left Middle Frontal gyrus	4312	-48	14	32	3.39
	Right Postcentral		54	-10	54	3.12
	Superior Frontal		0	10	60	3.09
	Right Precentral		44	-12	68	3.06
Flashback > Control; 3-6 sec	Right Inferior Frontal gyrus	2997	60	14	2	3.4
	Right Postcentral		58	-12	54	3.21
	Right Middle Frontal		54	18	42	3.05
	Right Central Opercular		36	6	16	2.96
	Left Frontal Operculum	1205	-32	22	10	3.12
	Left Inferior Frontal		-48	30	8	2.78
	Left Central Opercular		-46	-2	14	2.74
	Left Frontal Orbital		-40	22	-4	2.68
	Left Inferior Frontal		-52	36	6	2.68
Control > Flashback; 6-9 sec	Right Middle Frontal gyrus	8180	42	34	28	3.24
	Right Frontal Pole		30	42	10	2.92
	Right Postcentral		26	-30	64	2.87
	Left Lingual Gyrus	2324	-6	-86	-6	2.71
	Right Supracalcarine cortex		6	-78	16	2.66
	Right Superior Parietal		20	-56	72	2.6
	Right Lateral Occipital		32	-66	52	2.55
	Right Intracalcarine cortex		14	-82	12	2.53

Discussion

To my knowledge, this is only the second study to investigate the neural basis of the encoding of flashback memories, and the first to investigate differences between identified and non-identified Flashback stills compared to unpleasant scenes that did not cause flashbacks (Potential scenes). Additionally, this is the first study to capture brain activation involved at the moment of flashback involuntary recall in the scanner. Participants watched traumatic footage while undergoing fMRI. After a short break, participants spent six minutes in the scanner, responding with a button press if they experienced a flashback to the film. Over the following week participants recorded any further flashbacks in a diary, returning to perform a surprise recognition memory test of the film content.

Overall, results are in line with the proposed clinical neuroscience framework of flashbacks, with the possible addition of a more language based component due to the predominant involvement of the left inferior frontal gyrus in both flashback encoding and flashback involuntary recall. In regards to the four aims of the study, first, the previous findings (Bourne et al., 2013) of a distinct pattern of activity associated with the encoding of flashback memories were replicated. Second, the flashback encoding activation persisted when using only identified moments of the film (determined by a recognition memory test), as compared to the first hypothesis using all moments of the film regardless of whether they could be identified. Third, differences in the insula, hippocampus and parahippocampus were observed at the time of film viewing for identified versus non-identified Flashback stills but not for Potential identified versus non-identified stills. Fourth, flashback involuntary recall was characterised by brain regions previously found to be associated with involuntary recall for verbal stimuli and objects – the middle and superior frontal cortices – and in areas previously found to be associated with attention

hijacking, emotional processing and autobiographical memory – the frontal operculum and left IFG.

The current study successfully replicated the finding of Bourne et al. (2013) suggesting that a distinct widespread pattern of activity including increased activity in the amygdala, accumbens, putamen, rACC, insula, thalamus, ventral occipital cortex, left IFG and MTG can be associated with the encoding of an analogue flashback. Reverse inferences suggests that there are increases in activation for Flashback scenes in brain areas previously found to be associated with emotional processing (e.g. amgydala - Phelps, 2004), pain and the perception of others pain (e.g. insula, anterior cingulate, thalamus - Jackson, Meltzoff, & Decety, 2005; Leknes & Tracey, 2008), threat, in particular surprise to threat (e.g rACC - Bishop, et al., 2004; Browning & Harmer, 2012), visual processing and mental imagery (e.g. ventral occipital cortex - Kosslyn, et al., 2001) and attentional salience (e.g. ACC and insula - Seeley et al., 2007; Sridharan, Levitin, & Menon, 2008). However, as these associations are made with reverse inference, comparisons should be made with caution. Additionally, the left IFG and bilateral MTG showed suppressed levels of activation for Potential scenes compared to both Flashback and Control scenes, suggesting possible protective effects of these areas. The left IFG and MTG have been previously associated with successful autobiographical memory encoding (Cabeza & Nyberg, 2000; Spaniol, et al., 2009), language processing (e.g. Binder et al., 1997; Vigneau et al., 2006) and the selection of competing inputs for verbal stimuli (Jonides & Nee, 2006; Levens & Phelps, 2010; Nelson, et al., 2009). Reverse inference suggests that the functions of the identified regions are potentially similar to some the categories proposed in the clinical neuroscience flashback framework developed in Chapter 2 (Clark, Holmes, & Mackay, in press) with the exception of language processing (which is not a category in the framework). Further, some of the brain areas identified are comparable to

those highlighted in patient studies, in particular, increased activity in amygdala and emotional processing areas (Francati, et al., 2007; Rauch, et al., 2006).

Participants' subjective emotion ratings at one week suggested that scenes that became Flashbacks were more emotional at the time of viewing, compared to both Potential scenes and Control scenes. Additionally, subjective emotional response correlated with the number of participants reporting that scene as a flashback. This is consistent with cognitive models of flashback and PTSD development (e.g. Brewin, et al., 1996; Ehlers & Clark, 2000) suggesting that high levels of peritraumatic distress predict later intrusive memories.

However, there are a number of limitations of this measure. First, scene descriptions were given using written narratives, while previously they had been viewed by participants as film images. Second, as ratings were taken at one week after film viewing, there is an underlying assumption that participants could remember the scenes in enough detail to rate their emotional intensity one week previously when viewing the film. As identified by the recognition memory test this assumption may not be valid. However, though non-ideal this approach was taken in line with Bourne et al. (2013) since performing the emotionality ratings soon after film viewing could have provided an active manipulation that would likely have reduced the overall number of flashbacks then experienced, in line with data from Krans et al (2009). Third, Flashback scenes may have been recalled more frequently than Potential and Control scenes possibly inflating emotionality ratings due to better memory for those scenes due to their very nature. Finally, many other measures other than emotionality, for example, vividness, surprise and relevance to self, may also contribute to flashback formation. Further consideration of psychological factors during film viewing is an important area for understanding how flashback memories are formed and for interpretation of the neuroimaging results.

Flashback encoding activation persisted when using only identified moments of the film on the recognition memory test, i.e. removing any items that were not correctly identified as being from the film. This preliminarily suggests that the increases in activation observed for flashback encoding may not simply be due to Flashback events being better remembered than Potential events. fMRI paradigms using non traumatic movie footage have highlighted a subsequent memory effect in the parahippocampus, superior temporal gyrus, anterior temporal poles and temporal parietal junction (Hasson, et al., 2008), and successful encoding of emotional stimuli has been associated with amygdala and medial temporal lobe activity (LaBar & Cabeza, 2006). The results of the current study, however, suggest wider increases in activation in additional areas previously associated with emotion, pain and threat for identified Flashback events compared to identified Potential events, and identified Emotional events (combined Flashback and Potential) compared to identified Control events.

Further, increased activation in the insula, parahippocampus and hippocampus was observed for Flashback identified vs. Flashback non identified stills, but not for Potential identified vs. Potential non-identified stills. Previous work, predominantly for verbal stimuli and concrete objects (not autobiographical memory), suggests possible differences in involuntary and voluntary memory recall (Hall, et al., 2008; Kompus, et al., 2011; Ramponi, et al., 2011; Rugg, et al., 1997), however there has been no work comparing involuntary and voluntary autobiographical memory encoding. The current results raise the tentative possibility of neural differences at the time of viewing Flashback stills that were later identified versus non-identified. Equally tentatively, there did not appear to be a difference between viewing Potential stills that were later identified versus non-identified. However, results should be interpreted with caution. First, the number of events modelled, in particular ‘flashback non-identified’ events, was low. Second, the memory test at one

week only investigated recognition memory which in hindsight is not the best choice for the topic of interest (what could be deliberately recalled from the film). Future work should also use a cued recall test (as in Holmes, et al., 2004) or develop better measure of free recall. Third, some stills defined as Flashback may not have been the exact flashback moment for that individual. Within the recognition memory analysis film stills were classified as per the whole film scene (range 6-36 seconds), however, flashbacks may be short events, perhaps encompassing only part of the defined Flashback scene. It is possible that some stills defined as Flashback may therefore not have returned as part of the flashback for that individual. As yet there is no methodology available within the current paradigm to test the actual duration of a flashback, nor how to match it with second (or millisecond) accuracy. Ideally, more detailed timing information would allow for identification of just those specific flashback moments. However, this would likely result in a very low number of events that could be modelled from the current experimental design, in particular given that the duration of an event for neuroimaging purposes should be a minimum of 6 seconds duration

Additionally, the foil stimuli used in the recognition memory test have not yet been validated in comparison to the still picture stimuli taken from the trauma film. Ideally for a recognition memory test, two matched sets of items (e.g. stills taken from two film sets) would be used, with participants counterbalanced across the two sets so that stills are both foils and previously seen for different participants. As only one film set was used, foils were sourced from alternative footage. The plausibility of these foil stills in relation to the previously seen film stills therefore needs to be determined, otherwise memory effects may simply be due to participants easily identifying foil stills. This seems unlikely in the current results since the hit rate for film stills was not at ceiling but .67. Future work

should compare the foil stimuli with the picture stills from the film on multiple dimensions, for example, emotionality, visual complexity and content, to address this.

Hypothesis four investigated the neural basis of flashback involuntary recall. Due to limited research identifying the moment of flashback involuntary recall during scanning, different analysis methodology from the previous analyses were used to best model flashback involuntary recall. FIR basis functions were chosen due to their ability to model specific periods of time, referred to as time bins. This allowed for detailed examination of the activation occurring surrounding the button press. To control for activation specific to the button press, activation from control participants asked to press a button while in the scanner was also included in the analysis. The pattern of activation shown in the precentral gyrus, peaking at the time bin modelling 3 to 6 seconds after the button press, the expected peak due to the delay in BOLD signal response, suggests successful modelling of changes in activation. Additionally, the high level of similarity between the flashback condition and the control condition outside of the two significant time bins suggests strong support for the differences found between flashback and control activation.

It is noted that statistical correction for multiple comparisons across the time bins was not conducted. Ideally, repeated measures ANOVA would have been performed and if significant, subsequent individual t contrasts as post hoc tests to investigate differences between time bins. However, this technique is not supported by the current FSL software and is under development. The alternative of performing Bonferroni corrections would have been too conservative as the time bins are not independent. Results should be interpreted with this in consideration.

Increased activation for the flashback condition compared to button press alone was found in two time bins. In the first time bin (0 – 3 seconds in relation to the button press), increased activity was found in the middle and superior frontal cortices. These

findings are in line with previous research using non autobiographical stimuli, suggesting that involuntary memory recall is associated with the middle and superior frontal cortices (Hall, et al., 2008). The current results therefore extend this work, suggesting that the middle and superior frontal cortices may also be involved in the involuntary recall of autobiographical events. In the second time bin (3 – 6 seconds after the button press), increases in activation were found in the operculum (encompassing frontal and central) and the left inferior frontal gyrus. Previous research has associated activation in the frontal operculum with the attentional control of cognitive processes and task selection (e.g. Eckert et al., 2009; Higo, Mars, Boorman, Buch, & Rushworth, 2011), and the left IFG with the selection of competing memory representations for emotional verbal stimuli (Levens & Phelps, 2010). It has also been suggested that the frontal operculum and left IFG are associated with the self referencing and experience of emotions due to connections with the neighbouring insula (Craig, 2009). Reverse inference also suggests involvement of these areas in language; the left IFG has been associated with selecting and interpreting the meaning of ambiguous sentences (Rodd, Johnsrude, & Davis, 2012) and selecting semantic information (Moss et al., 2005) and the central operculum with language processing (Vigneau, et al., 2006). One possibility is that these areas are, in colloquial terms, processing the "worst thought" – reliving the "I am going die" moment during flashback recall – the left IFG 'flags' this and selects this input as being the most relevant at the time, overriding current goals and attention.

Unexpectedly, increased activation was also found for the button press alone condition (compared to the flashback condition) in a third time bin (6 – 9 seconds after the button press) in the right insular and frontal pole. This may be due to limitations of the control condition. Performing a task at random is cognitively complex (e.g. Baddeley, 1998) and is thought to involve multiple brain regions, including, but not limited to,

superior frontal regions (Jahanshahi, Dirnberger, Fuller, & Frith, 2000). On the other hand, participants in the flashback condition were asked to respond, with a button press, to an internally generated stimulus – the experience of a flashback. Although increases in activation for the button press alone condition compared to the flashback condition were only observed during the 6 - 9 second time bin, it remains unknown exactly what psychological and neural processes may have been involved. Differences in processing between random generation and stimulus generation should therefore be considered when interpreting the current results. Future research may be able to address this by using an internally generated stimulus, for example whenever participants think about their upcoming week, instead of a random button press.

Of note in the current findings is the involvement of the left IFG in both the encoding of flashbacks and flashback involuntary recall. These results are surprising in terms of the belief that flashbacks are image based memories (see Chapter 2), and previous research suggesting decreases in left IFG activation during PTSD symptom experience (e.g. Rauch et al., 1996; Shin et al., 1997). Hypothetically, it may be that the left IFG reflects the individual's 'conscious' processing of the traumatic event in terms of the degree of emotional severity. Decreased activation at emotional moments in comparison to neutral moments may protect the individual and allow them to function. However, when the event becomes too emotionally severe the left IFG no longer acts protectively, instead 'flagging' the event as being important to the individual. It is then this "worst thought" that can be seen at flashback encoding, returning to be relived and hijack attention at flashback involuntary recall. The involvement of the left IFG may have not previously been observed due to the previous studies not capturing the exact moment of flashback involuntary recall, but rather a more general PTSD symptom experience. It may therefore be that for the

majority of the symptom experience the left IFG is acting protectively, and only at the exact moment of flashback involuntary recall there is an increase in left IFG activation.

A particular strength of the current study is the high degree of similarity between the results reported here and those reported in Bourne et al. (2013). As in Bourne et al. (2013) the number of events modelled in the current study was low compared to more traditional fMRI designs. A low number of events increases noise in fMRI data, normally making it difficult to find meaningful results. Finding a nearly identical pattern of activation for flashback events as Bourne et al. (2013) suggests high reliability for this activation in the encoding of flashback memories with this paradigm.

In terms of relating the current results to the wider context of flashbacks in PTSD, the validity of the film as an analogue of trauma should be considered. The traumatic film used depicted images of real death and injury, and caused a negative emotional response in participants – in line with criteria for a traumatic event, though to a lesser extent, as defined in the Diagnostic and Statistical Manual fourth edition (DSM-IV, American Psychiatric Association, 2000). Further, viewing traumatic events on television (for example the September 11th terrorist attack news footage) has been associated with PTSD symptoms (Silver, Holman, McIntosh, Poulin, & Gil-Rivas, 2002). Thus, the use of traumatic footage as an analogue for trauma has utility and suggests that results, at least in part, may be generalisable to real life trauma.

Future work could more explicitly examine the neural differences between the encoding of autobiographical memories later recalled involuntarily and voluntarily using a free recall test. Additionally, better understanding of psychological and psychometric factors that contribute to flashback encoding will be important to interpret the brain activation occurring during flashback encoding. Ratings of, for example, emotionality, vividness, perception of pain, surprise, brightness and specific content (e.g.

people/vehicles/animals) may also help highlight why some scenes are more likely to return as flashbacks compared to others, as well as highlight possible central requirements for flashback formation. Further, the current study provides the most precise analysis of flashback involuntary recall to date. Advances in neuroimaging techniques, for example the ability to perform rapid whole brain scans using multiband fMRI (aprox. 0.5 sec for a whole brain scan - Neggers, Hermans, & Ramsey, 2008), and the increasing availability of MEG provide further opportunities to try and pinpoint the exact mechanisms involved in flashback involuntary recall.

In conclusion, the results of the current study support the existence of a distinct pattern of brain activation at flashback *encoding*. Additionally, this activation suggests a possible protective role of the left IFG, with decreased activation for Potential scenes compared to both Control scenes and Flashback scenes. Comparison of identified versus non-identified flashback and potential scenes further suggests differences in brain activity at the time of film viewing for Flashback stills compared to Potential stills.

Additionally, the results suggest a predominant role for the middle and dorsolateral frontal cortices for the initial involuntary *recall* of flashback memories, with attentional hijacking of the flashback possibly associated with left IFG activity, along with activation in areas associated with emotion processing and autobiographical memory.

Finally, the involvement of the left IFG, in both flashback *encoding* and *involuntary recall* may represent the inability of the brain to act protectively when an individual experiences, and at recall re-experiences, their worst moment, representing the overarching selective attention towards, for example when viewing the film, the "(s)he's about to die" moment in the brain.

The next chapter investigates the possibility of protective factors against flashback formation in behavioural data. Not all individuals experience flashbacks after trauma.

Better understanding of factors associated with an absence of flashbacks to the trauma film paradigm may help to provide suggestions for further research developing preventative treatments against flashback development.

Chapter 4: Low emotional response to traumatic footage is associated with an absence of flashbacks: An individual participant data meta-analysis of 16 trauma film paradigm studies

Abstract

Most people will experience or witness a traumatic event during their lifetime. A substantial number of trauma survivors will develop involuntary, sensory perceptual, emotional memories of the event, here referred to as flashbacks. Some individuals, however, have no flashbacks. Prospective work investigating psychological factors associated with an absence of flashbacks is lacking. The current study performed an individual participant data meta-analysis on 16 experiments (n = 458) using the trauma film paradigm to investigate the association of baseline characteristics and emotional response to the film footage with an absence of flashbacks. An absence of flashbacks was associated with low trait anxiety and current depression levels, and a low emotional response to the traumatic film footage. Trauma history and recognition memory for the film content were not significantly associated with an absence of flashbacks. Understanding why some individuals report an absence of flashbacks may aid preventative treatments against flashback development.

Introduction

In the previous chapter, a neuroimaging experiment was described that was designed to investigate the neural basis of the encoding and recall of flashbacks. However, not everyone develops flashbacks after trauma. The experiment presented in the current chapter uses the trauma film paradigm to investigate the association between some commonly studied psychological factors and an absence of flashbacks.

As mentioned, the majority of people will experience a traumatic event during their lifetime, with a lifetime prevalence of posttraumatic stress disorder (PTSD) of 10-20% (Breslau, et al., 1998). Flashbacks are experienced by 50-97% of individuals, with higher rates reported for interpersonal traumas, e.g. sexual assault (Ehlers & Steil, 1995). Although some individuals do not develop flashbacks after trauma, to my knowledge, experimental prospective work, investigating psychological factors that may be associated with an *absence* of flashback has been lacking. Factors protective against the development of PTSD are becoming increasing researched (e.g. Bonanno, 2005; Bonanno, Westphal, & Mancini, 2011).

Psychological models of PTSD emphasise that cognitive processing at the time of trauma is associated with the formation of flashbacks and PTSD itself (Brewin, et al., 1996; Ehlers & Clark, 2000). Further, one of the strongest predictors of PTSD development is an individual's emotional response at the time of the traumatic event (Ozer, et al., 2003). Additionally, some pre-existing risk factors have been associated with PTSD development, including baseline characteristics at the time of the trauma, e.g. psychiatric history prior to trauma (e.g. anxiety and depression) and past trauma history predicts PTSD development to a small but significant extent (Ozer, et al., 2003). However, although current models and research can provide suggestions about risk factors for PTSD,

it remains to be tested whether such aspects are also involved in protection against flashback development.

A limitation of clinical research studies is that data is often collected retrospectively which can be prone to errors. Experimental designs using analogue trauma offer an opportunity to prospectively investigate flashbacks in controlled laboratory settings (Holmes & Bourne, 2008). Participants watch traumatic film footage, designed to match diagnostic criteria for PTSD (e.g. scenes of real life car crashes, close ups of surgical procedures) and then keep a diary of any subsequent flashbacks of the film over the following week (Holmes, et al., 2004). The majority of participants report at least one flashback after viewing the traumatic film footage, however, as in real life, some participants report an absence of flashbacks. This offers an opportunity to prospectively investigate psychological factors that may be associated with an absence of flashbacks.

The current study conducted an individual participant data meta-analysis (Riley, Lambert, & Abo-Zaid, 2010) using 16 experiments that shared a similar trauma film paradigm protocol. The main aim of the meta-analysis was to investigate the association of commonly collected psychological measures with an absence of flashbacks. Individually, these separate studies are limited by small sample sizes, however, conducting an individual participant data meta-analysis from the combined control conditions creates a large dataset of participants, some of whom reported an absence of flashbacks (note; all active experimental conditions were discarded).

A one stage binary logistic regression independent participant data meta-analysis was used to compare those participants who reported no flashbacks vs. those participants who reported flashback occurrence in the week following film viewing on common measures shared across the experiments (Debray, Moons, Abo-Zaid, Koffijberg, & Riley, 2013) . Traditional meta-analysis techniques combine effect sizes across studies, creating a

large pool of participants, but require a research question to have been previously assessed. Performing an independent participant data meta-analysis kept the advantage of a large dataset from previously performed experiments while also being able to assess a novel research question. Additionally, performing a one-stage IPD meta-analysis allows for data from individual experiments to be combined while preserving the clustering and controlling for any effect of individual studies.

It was hypothesised that an absence of flashbacks would be associated with those participants who scored low on baseline measures of trait anxiety, current depression and trauma history, and with those participants who had a low emotional response to the film footage. Recognition memory of the film content was also investigated to test whether scores would be associated with an absence of flashbacks to the film.

Method

Database

A database was created combining experiments which followed a similar trauma film paradigm protocol (see section *study protocols*). Sixteen individual experiments were identified compromising 14 published experiments in 9 publications, and 2 unpublished experiments, 1 currently under review and 1 in preparation (see Table 4.1).

The majority of experiments (12 published, 1 in preparation) investigated manipulations to reduce flashback frequency (Bourne, Frasquilho, Roth, & Holmes, 2010 - two experiments; Deeprose, Zhang, Bossward, Dalgleish, & Holmes, 2011 - two experiments; Hagenaars, van Minnen, Holmes, Brewin, & Hoogduin, 2008; Holmes, et al., 2004 - three experiments; Holmes, et al., 2009; Holmes, et al., 2010 - two experiments; James & Holmes, in prep; Krans, Naring, Holmes, & Becker, 2010). Of the remaining three experiments, one used the trauma film paradigm to simulate the emotional effects of trauma exposure with no manipulation (Brown, Danquah, Miles, Holmes, & Poliakoff,

2010), one investigated the neural substrates of flashback encoding in fMRI (Bourne et al., 2013) and one investigated a possible trait vulnerability factor to the development of flashbacks (Malik, Goodwin, & Holmes, under review). Combining the control conditions (i.e. no experimental manipulation) of these 16 experiments yielded a total of 458 participants.

Sample size

A sample size calculation was performed based on the number of independent variables included in the analysis. A large effect size with an alpha of .05 and a power of 0.8 requires a minimum of 102 participants for seven independent variables (Cohen, 1992).

Measures

Table 4.1 provides details of the measures in each of the individual experiments.

Baseline measures

Trait anxiety was assessed using the State-Trait Anxiety Inventory-Trait version (STAI-T, Spielberger, et al., 1983) in 11 of the 16 experiments (n = 361). The STAI-T contained 20 anxiety related items which participants rated on a four point scale as to how they generally feel. The STAI-T is widely used and has good reliability and validity with an alpha coefficient of .9 (Spielberger, et al., 1983).

Trauma history was assessed using the Traumatic Experiences Questionnaire (TEQ, adapted from Foa, 1995) in 11 of the 16 experiments (n = 314). Participants indicated whether they had experienced or witnessed each of the 12 traumatic events listed. The total number of events endorsed was summed to create a total score.

Current depression levels were assessed using the Beck Depression Inventory Second Edition (BDI-II, Beck, Steer, & Brown, 1996) in 9 of the 16 experiments (n = 288). Participants responded to 21 questions on a four point scale asking about their mood

Table 4.1. Measures included in each of the 16 experiments in the dataset

Experiment	n	Outcome	Emotional Response															Participant Characteristics					Recognition Memory
		Flashbacks	Fearful*	Anxious*	Depressed^	Sad^	Happy^	Horrified	Helpless	Calm	Disgust	Hopeless	Irritable	Ashamed	Guilty	Angry	Age	Gender	STAI-T	TEQ	BDI	Written Recognition Test
Holmes et al. (2004) Experiment 1	17	✓		✓	✓		✓									✓	✓	✓		✓		
Holmes et al. (2004) Experiment 2	20	✓	✓	✓	✓		✓	✓	✓		✓			✓	✓	✓	✓	✓		✓		✓
Holmes et al. (2004) Experiment 3	19	✓	✓	✓	✓		✓	✓	✓		✓			✓	✓	✓	✓	✓		✓		✓
Hagenars et al. (2008)	27	✓		✓		✓	✓	✓								✓	✓	✓				✓
Holmes et al. (2009)	20	✓	✓		✓	✓	✓			✓		✓				✓	✓	✓	✓		✓	✓
Bourne et al. (2010) Experiment 1	14	✓	✓	✓	✓		✓	✓	✓		✓			✓	✓	✓	✓	✓		✓		✓
Bourne et al. (2010) Experiment 2	19	✓	✓			✓	✓	✓		✓		✓				✓	✓	✓	✓	✓	✓	✓
Brown et al. (2010)	55	✓		✓	✓		✓									✓	✓	✓	✓			
Holmes et al. (2010) Experiment 1	20	✓		✓	✓	✓	✓			✓		✓				✓	✓	✓	✓	✓	✓	✓
Holmes et al. (2010) Experiment 2	26	✓		✓	✓	✓	✓			✓		✓				✓	✓	✓	✓	✓	✓	✓
Krans et al. (2010)	18	✓	✓			✓	✓	✓								✓	✓	✓	✓			✓
Deeprose et al. (2011) Experiment 1	20	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓			✓	✓	✓	✓	✓	✓	
Deeprose et al. (2011) Experiment 2	23	✓		✓	✓	✓	✓			✓		✓				✓	✓	✓	✓	✓	✓	✓
Bourne et al. (2013)	22	✓	✓			✓	✓	✓		✓		✓				✓	✓	✓	✓		✓	✓(n-1)
Malik et al. (under review)	110	✓	✓	✓	✓	✓							✓				✓	✓	✓	✓	✓	✓
James et al. (in prep)	26	✓	✓	✓	✓	✓	✓	✓		✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓

Note. n is of experiment control condition Composite negative mood change is the mean of all available emotional responses (happy and calm reversed scored); * = Fear emotional response; ^ = Depressive emotional response

over the last two weeks. The BDI-II has high internal consistency, alpha level .9 (Beck, Steer, Ball, & Ranieri, 1996).

Emotional response to the traumatic film footage

Participants rated their mood before and after film viewing using 10cm visual analogue scales or 11 point likert scales anchored at 0 (not at all) and 10 (extremely). As the film contains negative footage, it was expected that the predominant mood response would be negative. A composite negative mood change score was therefore calculated from the available mood change scores (post – pre film) for each experiment (see Table 1).

To investigate whether specific types of emotions had different effects on an absence of flashbacks two further variables were created; fear emotional response (mean change score of *fearful* and *anxious*) and depressive emotional response (mean change score of *depressed*, *sad* and *happy* - reversed scored).

Recognition memory of the traumatic film footage

Recognition memory for the film contents was assessed in 13 of the 16 experiments (n = 360) using a written forced choice recognition memory test one week after viewing the traumatic footage. The recognition memory test compromised a series of statements regarding the film that participants answered either true or false.

Study Protocols

The included experiments all shared a similar protocol derived from Holmes, Brewin and Hennesey (2004). On arrival to the laboratory the experiment was explained and participants gave informed consent. Participants were then asked to complete baseline questionnaires (e.g. trait anxiety) and ratings of their current mood. Participants then viewed the traumatic footage, being asked to immerse themselves in the footage and to try and imagine that the events being depicted where happening to them, or around them, right at that present moment. After viewing the footage, mood assessments were repeated. Over the following week, participants were asked to keep a record of any flashbacks of the film

in a simple diary divided into three sections; morning, afternoon and evening. In one of the experiments (Malik, et al., under review) participants responded to thrice daily Short Messenger Service (SMS) prompts reporting by SMS if they had had any flashbacks of the film since the last prompt. One week later, participants returned the diary and in 13 of the 16 experiments completed a recognition memory test of the film contents.

Statistical Analysis

One stage individual participant data meta-analyses using binary logistic regression models (no flashbacks vs. flashbacks) were used. A one stage approach allows for all the data to be modelled simultaneously (keeping the advantage of combining data across studies) while controlling for the clustering across the different studies (see Debray, et al., 2013; Riley, et al., 2010). The regression analyses were performed in R (R Development Core Team, v. 3.01). Odds ratios were calculated as a measure of effect size.

Results

Flashbacks

In total, the 458 participants reported 2532 flashbacks in the diaries in the week after viewing the trauma film. The mean number of flashbacks per person was 5.53 (*SD* = 6.52). An absence of flashbacks (i.e. 0) was reported by 71 participants (15.5%).

Baseline measures

Across the whole sample, 175 of the participants were male (38.21%) and the mean age was 24.45 years (*SD* = 7.86 years). The mean score on the STAI-T was 37.91 (*SD* = 9.50), the mean score on the TEQ was 1.66 (*SD* = 1.59), and the mean BDI-II score was 5.61 (*SD* = 5.61). Scores were within the non clinical range for a normal population (see Chapter 3).

Emotional response to the traumatic film footage

In terms of participants' emotional response to the film, the mean negative mood increase across the film was 1.76 (*SD* = 1.77), the mean fear emotional increase was 1.45 (*SD* = 2.53) and the mean depressive emotional increase was 2.02 (*SD* = 1.93).

Recognition memory of the traumatic film footage

Across the 13 studies that involved a memory test, the mean percentage correct on the recognition memory test was 64.49% (*SD* = 12.01).

Individual participant data meta-analysis; Binary Logistic Regression

Results of the regression analyses can be seen in Table 4.2. A single binary regression was first performed with experiment (of which there were 16) as a random factor. This model was used to provide a statistical comparison for the mixed models of interest – likelihood ratio tests (LRT) were performed to assess for differences in model fitting. An absence of flashbacks was defined as 0, and the occurrence of flashbacks was defined as 1. The distributions of Age, TEQ and BDI scores were skewed and were square rooted to return to normality.

As a measure of effect size, odds ratios are reported: an odds ratio close to 1 suggests a small effect of the measure on the absence of flashbacks. An odds ratio less than 1 suggests that a higher score on the measure is associated with an absence of flashbacks, while an odds ratio greater than 1 suggests that a lower score on the measure is associated with an absence of flashbacks.

Baseline measures

Age (square rooted) and gender were collected in all of the experiments and were entered into a regression analysis together with experiment as a random factor (n = 458). Comparison to experiment alone suggested that the addition of age and gender did not

significantly improve model fit (χ^2 = 3.21, *df* = 2, *p* = .20). Neither age nor gender were significantly associated with an absence of flashbacks.

STAI-T scores were entered into a separate regression with experiment as a random factor (n = 361). Comparison to experiment alone suggested that the addition of STAI-T significantly improved model fit (χ^2 = 124.3, *df* = 1, *p* < .001)**.** STAI-T had a small association with an absence of flashbacks with an odds ratio of 1.05.

TEQ (square rooted) was entered into a separate regression model with experiment as a random factor (n = 314). Comparison to experiment alone suggested that the addition of TEQ (square rooted) significantly improved model fit (χ^2 = 118.58, *df* = 1, *p* < .001). TEQ, however, was not significantly associated with an absence of flashbacks.

BDI-II score (square rooted) was entered into a separate regression model with experiment as a random factor (n = 288). Comparison to experiment alone suggested that the addition of BDI-II (square rooted) significantly improved model fit (χ^2 = 190.84, *df* = 1, *p* < .001). BDI-II score (square rooted) was associated with an absence of flashbacks with an odds ratio of 1.62.

Emotional response to the traumatic film footage

Composite negative mood change was entered into the first regression analysis investigating participants' emotional response to the film, with experiment as a random factor (n = 458). Comparison to experiment alone suggested that the addition of composite negative mood change significantly improved model fit (χ^2 = 27.02, *df* = 1, *p* < .001). In the model, low scores on composite negative mood change were associated with an absence of flashbacks with an odds ratio of 1.72.

A second regression analysis was performed to better understand the relationship between different types of emotional response. The variables fear emotional response and depressive emotional response were entered into a single model, with experiment as a random factor (n = 458). Comparison to experiment alone suggested that the addition of

fear emotional response and depressive emotional response significantly improved model fit (χ^2 = 28.72, *df* = 2, *p* < .001). In the model, both fear emotional response and depressive emotional response were associated with an absence of flashbacks, with odds ratios of 1.24 and 1.32 respectively.

Recognition memory of the traumatic film footage

Percentage correct on the recognition memory was entered into a final regression model, with experiment as a random factor (n = 358). Comparison to experiment alone suggested that the addition of recognition memory significantly improved model fit (χ^2 = 84.58, *df* = 1, *p* < .001). No significant relationship between recognition memory and an absence of flashbacks was found.

Table 4.2. Binary logistic regression analyses showing an absence of IAMs was associated with participants' emotional response to the film, trait anxiety and current depression

Variable	*B*	*SE*	OR	95% CI
Baseline Measures				
Age (SQRT) and Gender (n = 458)				
Intercept	2.20	1.01	9.07*	[1.24, 66.12]
Age (SQRT)	-.097	.19	.91	[.62, 1.32]
Gender [Male = 1]	.49	.29	1.64	[.93, 2.87]
STAI-T as single variable (n = 361)				
Intercept	.51	.79	1.66	[.35, 7.79]
STAI-T	.050	.021	1.05*	[1.00, 1.09]
TEQ (SQRT) as single variable (n=314)				
Intercept	2.07	.42	7.90***	[3.44, 18.16]
TEQ (SQRT)	-.039	.24	.96	[.60, 1.54]
BDI-II (SQRT) as single variable (n = 288)				
Intercept	1.73	.46	5.65***	[2.29, 13.97]
BDI-II (SQRT)	.48	.17	1.62**	[1.16, 2.28]
Emotional Response				
Composite Negative Mood Change (n= 458)				
Intercept	1.21	.33	3.36***	[1.77, 6.39]
Composite Negative Mood Change	.54	.12	1.72***	[1.37, 2.16]
Fear and Depressive Emotions (n = 458)				
Intercept	1.34	.31	3.80***	[2.07, 7.00]
Fear Emotional Response	.21	.074	1.24**	[1.07, 1.43]
Depressive Emotional Response	.28	.096	1.32**	[1.10, 1.60]
Recognition Memory				
Recognition Memory (n = 360)				
Intercept	1.46	.91	4.29	[.72, 25.51]
Recognition Memory	.001	.013	1.01	[.99, 1.04]

Note. OR = Odds Ratios; CI = Confidence Intervals; SQRT = Square Root; Composite negative mood change = mean of all available emotional responses; Fear emotional response = mean of *fearful* and anxious; Depressive emotional response = mean of *depressed*, *sad* and *happy* (reversed scored); STAI-T = State Trait Anxiety Inventory Trait version; TEQ = Traumatic Experiences Questionnaire; BDI-II = Beck Depression Inventory Second Edition.

*** = $p < .001$; ** = $p < .01$; * = $p < .05$.

Discussion

To my knowledge, this is the first experimental prospective meta-analysis to investigate psychological factors associated with an absence of flashbacks after viewing traumatic film footage. An individual participant data meta-analysis approach was taken (Debray et al., 2013; Riley et al., 2010). Data was combined from the no manipulation conditions of 16 experimental studies. A one step approach was used, taking into account the possible effect of the individual studies. Results suggested that, as predicted, an absence of flashbacks was associated with low trait anxiety, low current depression levels and a low emotional response to the traumatic film footage. Contrary to predictions, previous trauma history was not associated with an absence of flashbacks. Recognition memory for the film content was not significantly associated with an absence of flashbacks, suggesting that poor memory of the traumatic footage was unlikely to explain an absence of flashbacks.

Odds ratios were calculated as a measure of effect size for all possible predictors. Here, an odds ratio greater than 1 suggests that lower scores on that measure were associated with an absence of flashbacks. The further away from 1 the larger the effect size. Emotional response to the film footage had the largest effect size in predicting an absence of flashbacks (OR = 1.72). Although an individual's emotional response to trauma has been widely associated with PTSD (American Psychiatric Association, 2000; Ozer, et al., 2003), this is the first experimental study to show a association with low emotional response and an absence of flashback symptoms.

Additionally, due to the range of different types of emotional response measured, the current study was able to investigate depressive as well as fear emotional responses. Both depressive and fear emotional responses had a significant association with an absence of flashbacks (OR of 1.32 and 1.24 respectively). Some studies suggest that the A2

criterion of PTSD, requiring the trauma to elicit "intense fear, helplessness or horror" are too narrow, with other negative emotions (e.g. sadness and disgust) being associated with PTSD (e.g. Adler, Wright, Bliese, Eckford, & Hoge, 2008; Engelhard, Olatunji, & de Jong, 2011). Depressive emotional reactions are not currently included in PTSD diagnostic criteria (American Psychiatric Association, 2000), and the changes to DSM-5 have removed the need for a specific emotional response (American Psychiatric Association, 2013). It is noted that in the current study changes in depressive mood alone over film viewing were significantly associated with an absence of flashbacks.

Participants' baseline measures of current depression and trait anxiety revealed significant associations with an absence of flashbacks (OR of 1.62 and 1.05 respectively). For the significant finding in regards to BDI-II scores it should be noted that depression scores were square rooted to ensure normality, thus interpretation of the odds ratio should be made with caution. The odds ratio suggests that for each 1 point decrease in BDI *square rooted*, the odds of an absence of flashbacks increases by 1.62. This is in comparison to anxiety, where the odds ratio suggests that for each 1 point decrease in STAI-T, the odds of an absence of flashbacks increases by 1.05. As a rough approximation, an increase in 1 point on a square root scale is approximately 6 points on the original scale; therefore for each 6 point decrease in BDI score the odds of an absence of flashbacks increase by 1.62. Both low current depression levels and low scores on trait anxiety have previously been associated with low flashback frequency following an analogue trauma (Laposa & Alden, 2008). Low levels of current depression have also been found to increase the likelihood of following a "resilience trajectory" (individuals may experience transient perturbations in normal functioning, but generally exhibit a stable trajectory of healthy functioning) following trauma in soldiers (Dickstein, Suvak, Litz, & Adler, 2010). Thus, low scores on these measures may be protective against flashback development.

There are a number of limitations to the current study. Viewing traumatic events as a film in a laboratory is not the same as witnessing the events in real life. However, it should be noted that the traumatic footage used depicted real life images of death and injury; comparable to diagnostic criteria for a traumatic event (American Psychiatric Association, 2000). Future studies investigating real life trauma may provide additional possible explanations as to why some individuals report an absence of flashbacks. The pen and paper diary methodology used in the trauma film paradigm allows for measurement of flashbacks in everyday life, but is not without its weaknesses. Future work should therefore seek to use complementary laboratory based methods for inducing flashbacks to investigate an absence of flashback memories (e.g. Berntsen, Staugaard, & Sørensen, 2012; Schlagman & Kvavilashvili, 2008). Of note, convergent findings to the current study in terms of the frequency of an absence of flashbacks have been reported by two laboratory word association experiments designed to induce flashbacks, finding a similar number of participants (14% and 10%) reporting an absence of flashbacks (Bradley, Moulin, & Kvavilashvli, 2013).

The results of the current study have possible implications for future research aimed at reducing flashback symptoms after traumatic events. The current work highlights the importance of a low emotional response for an absence of flashback symptoms, suggesting an important role for the 'negative emotion' component of the proposed clinical neuroscience flashback framework in the reduction of flashback involuntary recall as well as their formation. Relatedly, a higher proportion of participants told to "suppress" their internal and external emotions while viewing traumatic film footage were found to report an absence of flashbacks over the following week compared to both a control group, who watched the film normally, and an acceptance group, who were told to accept their emotions and immerse themselves in any emotions caused by the film (Dunn, Billotti,

Murphy, & Dalgleish, 2009). Future research designed towards better understanding of emotional response at the time of trauma may help in developing preventative treatments against the formation of flashback memories and possible later PTSD – an area where interventions are currently lacking.

The current study therefore highlights the importance of emotional response at the time of trauma film viewing in flashback development. The next chapter aims to further examine the emotion component of the proposed flashback framework (Chapter 2), investigating a positive film. Is positive emotional response at the time of viewing positive footage associated with the frequency of positive flashback type memories?

Chapter 5: Predicting the Frequency of Positive Involuntary Autobiographical Memories: A behavioural study

Abstract

Involuntary autobiographical memories (IAMs) are typically discussed in the context of negative memories such as trauma 'flashbacks'. However, IAMs occur frequently in everyday life and are predominantly *positive*. In spite of this, surprisingly little is known about how such positive IAMs arise. The trauma film paradigm is often used to generate negative IAMs. Recently an equivalent positive film was developed inducing positive IAMs (Davies, et al., 2012). The current study is the first to investigate which variables (emotional response to film; recognition memory of the film; participant characteristics) would best predict the frequency of positive IAMs. Higher levels of positive mood change to the film were significantly associated with the number of positive IAMs recorded in the subsequent week. Results demonstrate the importance of positive emotional response at the time of an event for subsequent positive IAMs.

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Introduction

The previous chapters have focused on negative flashback memories arising from traumatic footage. Further, the previous chapter found an association with emotional response to traumatic film footage and an absence of flashbacks. The experiment outlined in this chapter considers the negative emotion component of the flashback framework, exploring the importance of emotional valence for the formation of flashback type memories. The experiment presented adapts the trauma film paradigm for positive footage, investigating whether emotional response to positive film footage is associated with positive involuntary memories of the footage.

As mentioned, autobiographical memory is the area of memory related to the recollection of past personal events (Conway & Pleydell-Pearce, 2000). In some cases autobiographical memory occurs via a voluntary or deliberate process – actively recalling past events to remember a particular detail or to relive an experience. In contrast, involuntary memories are those which are spontaneously brought to consciousness without preceding attempts to retrieve them (Berntsen, 1996; Mace, 2007). A recent study using a mechanical counter found that involuntary autobiographical memories (IAMs) occurred three times as frequently as voluntary autobiographical memories over the course of a normal day in everyday life (Rasmussen & Berntsen, 2011). Additionally, a telephone survey of 1500 Danes identified that approximately 60% of IAMs reported were positive in nature (Berntsen & Rubin, 2008).

Surprisingly little is known about how or why such positive IAMs arise. Flashbacks, as defined in the previous chapters, are similar to positive IAMs, differing only in their emotional valence; both flashbacks and positive IAMs are image based, involuntary, autobiographical memories which hijack attention. Can the clinical

neuroscience framework of flashbacks therefore also improve understanding of positive IAMs?

To my knowledge, there has only been one previous study examining involuntary memories of potentially positive rather than negative film material. This study from 1973 compared stressful films with 'erotic' films and studied participants 'mental content' while performing a signal detection task (Horowitz & Becker, 1973). They reported no difference in the frequency of intrusive mental content (partially related to IAMs) between the two films, and this frequency was inversely correlated with negative, but not positive, emotional reactions to the erotic film. Thus, it is not clear whether the intrusive mental content of the erotic film was emotionally positive for participants. It would therefore be of interest to test a film with overtly positive material and to measure positive IAMs directly.

Potential similarities between positive IAMs and flashbacks as according to the proposed framework suggests that research into flashback development may be able to inform our understanding of positive IAMs. Emerging research suggests that flashback processes are similar to general memory formation (Berntsen & Rubin, 2008; Krans, Näring, & Becker, 2009). An individual's emotional response during and immediately after a traumatic event is one of the strongest predictors of PTSD (Ozer, et al., 2003). Individual characteristics, (e.g. gender, history of depression, anxiety) have also been found to predict PTSD but to a lesser extent (Brewin, Andrews, & Valentine, 2000; Ozer, et al., 2003). Additionally, patients with bipolar disorder frequently report flashback type memories (Gregory, Brewin, Mansell, & Donaldson, 2010). Emotional reaction during an event and some participant characteristics may therefore also be important for the formation of positive IAMs.

As described, a commonly used methodology to investigate flashback development is the trauma film paradigm (Holmes & Bourne, 2008). Positive emotional films have also

been used in experimental studies to increase positive affect (e.g. Gruber, Johnson, Oveis, & Kellner, 2008). Recently, an equivalent 'positive' version of the trauma film paradigm was developed, successfully eliciting IAMs of positive footage (Davies, et al., 2012). The current study extended the positive film of Davies et al. (2012) and included a measurement of participant's emotional valence of their IAMs was included to investigate whether the IAMs were emotionally positive.

The current experiment investigated the influence of state and trait variables on the frequency of positive IAMs, predicting that, in line with flashback development, film viewing variables (emotional response to the film, recognition memory), would have a greater effect than participant characteristics (age, gender, history of hypomania, depression, anxiety).

Method

Ethical approval was obtained from the University of Oxford Central University Research Ethic Committee (MSD/IDREC/C1/2011/2; Appendix II).

Participants

A sample size calculation was performed based on the number of independent variables included in the analysis. A large effect size with an alpha of .05 and a power of 0.8 requires a minimum of 91 participants for five independent variables (Cohen, 1992).

The sample consisted of 95 participants (53 female) with a mean age of 23.45 years (*SD* = 7.0). Participants were recruited from the local area and universities using advertisements in online newspapers and the community and were paid £10 for their time and travel expenses.

Measures

Participant Characteristics

History of hypomania was assessed using the Mood Disorders Questionnaire (MDQ; Hirschfield, et al., 2000). The self-report questionnaire is split into three sections; section one consists of 13 yes/no items investigating lifetime (hypo)manic symptoms, section two investigating symptom co-occurrence, and section three symptom severity on a four point scale (no problem, minor problem, moderate problem, serious problem). Total scores range from 0-17, with severity scored from 0-3 respectively. Higher scores represent higher levels of hypomanic history. The MDQ has good internal validity with an alpha coefficient of .84 (Hirschfeld, et al., 2003).

Current depression levels were measured using the Beck Depression Inventory Second Edition (BDI-II; Beck, Steer, & Brown, 1996). Participants responded to 21 questions on a scale of 0-3, asking about their mood over the last two weeks. Higher total scores represent higher levels of current depression. The BDI-II has good internal validity with an alpha coefficient of .81 (Beck, et al., 1988)

Trait anxiety was measured using the State-Trait Anxiety Inventory-Trait version (STAI-T; Spielberger, et al., 1983). The STAI-T contains 20 anxiety related items which participants rate on a four point scale as to how they generally feel. Higher total scores represent higher levels of trait anxiety. The STAI-T has good internal validity with an alpha coefficient of .9 (Spielberger, et al., 2004).

Film Viewing Variables

Emotional reaction to the film was assessed by the positive subscale of the Positive and Negative Affect Schedule 10 (PANAS-10; Watson, Clark, & Tellegen, 1988) before and after film viewing. Scores on the positive subscale can range from 10 to 50, with higher scores representing higher positive affect. Emotional response to the film (residual

PANAS mood change) was determined from the standardised residuals of the PANAS-10 change scores to take into account mood before the film (as in Laposa & Alden, 2008).

Recognition memory of the film was assessed one week after film viewing using a 38-item forced choice visual recognition memory test. The recognition memory test comprised 19 stills from the film and 19 stills from unused sections of clips that had been edited out of the film or were from similar situations (Wegner, et al., 1996).

Positive Film

The positive film was developed by the author over for the current experiment. The film was extended to include an additional 12 clips to the 7 included in the Davies et al., (2012) study. The flashback diaries of Davies et al., (2012) were used to identify the moments of the included clips that returned as flashbacks. These were kept in the current film, non flashback moments that were not required for context were discarded. The additional clips were selected to be positive for a young adult student audience. Example clips include, the the jubilation of being enthusiastically greeted after finishing university final exams, the excitement of a rollercoaster ride and extreme sports, the pride of graduating, the thrill of gambling, and the intensity of a live performance at Glastonbury (see Appendix V for details).

Involuntary Memory Diary

IAMs of the film were recorded in an involuntary memory diary (Holmes, et al., 2004). For each IAM, participants wrote a brief description and rated the emotion on a 5-point scale from *very negative* to *very positive* (Berntsen, 2001). A rating of 4 or 5 was classed as a positive IAM and 3 as a neutral IAM.

Statistical analysis

As IAMs are count data, negative binomial regression was used (Gardner, Mulvey, & Shaw, 1995; Venables & Ripley, 1999). The regression analyses were performed in R

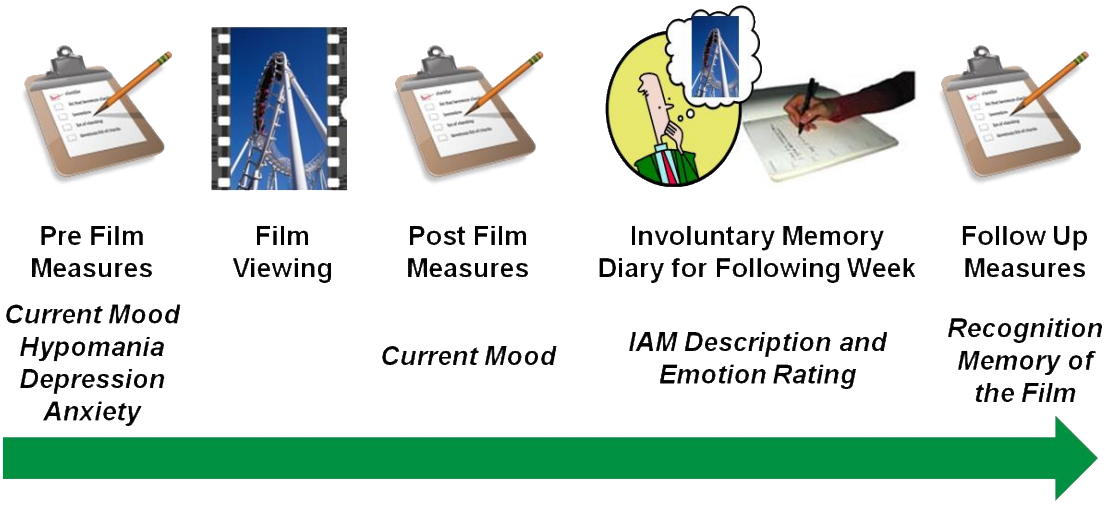
(R Development CoreTeam, 2011). Pearson statistics for general linear models were calculated for each of the regression analyses.

Procedure

The protocol, containing all the verbal instructions given to participants, can be seen in Appendix XI.

In brief, on arrival to the laboratory all participants gave informed consent. Participants were then asked to complete questionnaires concerning their current mood and baseline characteristics. Participants then watched the positive film, imagining that the events being depicted were happening to them right now. After film viewing, participants' mood was reassessed and they were asked to record any IAMs of the film in a 1-week diary (Holmes, et al., 2004). Participants returned after one week and completed a recognition memory test of the film (Figure 5.1).

Figure 5.1 Diagram showing the experimental procedure of the positive film paradigm**.** Participants filled out questionnaires concerning their current mood and baseline characteristics before watching the positive film. After film viewing mood was reassessed and participants were asked to record any involuntary memories of the film over the following week. Participants returned a week later and completed a recognition memory test of the film.



Results

The mean MDQ score was 6.11 (SD = 4.55), the mean BDI score was 5.62 (SD = 5.81) and the mean STAI-T score was 38.19 (SD = 10.86). Scores on the BDI and STAI-T were within normal non-clinical range, scores on the MDQ are higher than reported norms, but still within non clinical range (as reported in Chapter 3). The mean change score over the film on the PANAS 10 positive subscale was 4.05 (SD = 6.76). The mean percentage correct on the recognition memory test at one week was 74.96 (SD = 8.92).

In the involuntary memory diaries, 186 positive IAMs of the film were reported (mean = 1.96, *SD* = 2.34; range 0-11), with 65% of participants reporting at least one positive IAM. IAMs could be of the same or different scenes per participant; the mean number of different scenes was 1.39 (*SD* = 1.48).

Prediction of positive IAM frequency was assessed using separate regression analyses for film viewing variables and participant characteristics. Depression scores were skewed and cube-rooted (BDI-IIcr). As IAMs are count data, negative binomial regression was used to fit the models (Gardner, et al., 1995).

The regression models fitted the data well [Pearson statistic for general linear models: film viewing: $\chi^2 = 85.33$ ($df = 92$, $p = .40$); participant characteristics: $\chi^2 = 83.70$ ($df = 89$, $p = .14$)]. Within the film viewing variables, residual PANAS mood change (i.e. the change in score on the positive subscale, with participants' mood before film viewing taken into account) significantly predicted the frequency of positive IAMs. That is, all else being equal, the odds of a positive IAM occurring increased by 1.6 for each 1 point increase in residual PANAS mood change. Thus, as positive mood change increases, so does the likelihood of a positive IAM (Table 1).

Neither recognition memory nor any participant characteristic was found to be significantly associated with positive IAMs (Table 3.1).

To understand better the relationship between positive mood change and positive IAMs, further analyses were performed to see whether emotional response to the film was also associated with neutral IAM frequency. In addition to the positive IAMs, participants reported 148 neutral IAMs (mean = 1.56, *SD* = 1.75; range 0-8). A weak but significant correlation was found between positive and neutral IAM frequency (r = 0.25, *p* = .015). Association with neutral IAM frequency was also assessed using a negative binomial regression model. As the only significant predictor of positive IAMs residual PANAS mood change was the only variable entered into the model. The regression model fitted the data well (χ^2 = 73.23, *df* = 93, *p* = .62). Residual PANAS mood change was significantly associated with the frequency of neutral IAMS; all else being equal, the odds of a positive IAM increased by 1.32 for each 1 point increase in residual PANAS mood change (Table 5.1).

Table 5.1 Negative binomial regression models showing that residual PANAS mood change over the film was associated with the frequency of positive and neutral IAMs over one week

Variable	*B*	*SE*	OR	95% CI
Positive IAMs Film Viewing Model				
Intercept	0.70	1.09	2.01	[0.24,16.93]
Residual PANAS Mood Change	0.47	0.13	1.60***	[1.23, 2.06]
Recognition Memory of the Film	-0.0015	0.014	1.00	[0.97, 1.03]
Positive IAMs Participant Characteristics Model				
Intercept	0.71	0.73	2.03	[0.48, 8.52]
Age	0.0039	0.018	1.00	[0.97, 1.04]
Gender [Male coded as 1]	0.14	0.25	1.15	[0.70, 1.90]
MDQ	0.023	0.031	1.02	[0.96, 1.09]
BDI-IIcr	-0.22	0.20	0.81	[0.55, 1.19]
STAI-T	-0.00066	0.013	1.00	[0.97, 1.03]
Neutral IAMs Mood Change Model				
Intercept	0.41	0.12	1.51***	[1.20, 1.91]
Residual PANAS Mood Change	0.28	0.12	1.32*	[1.04, 1.67]

Note. OR = Odds Ratios; CI = Confidence Intervals; MDQ = Mood Disorders Questionnaire; STAI-T = State Trait Anxiety Inventory Trait version; BDI-IIcr = Beck Depression Inventory Second Edition, cube rooted.
***= p<0.001; **=p<0.01; *=p<0.05

Discussion

To the best of my knowledge, this is the first study to investigate in detail the formation of positive IAMs from overtly positive stimuli. The results highlight the importance of emotional reaction at the time of a positive event for the formation of positive and neutral IAMs. Interestingly, the extent of the increase in IAM frequency seems to be valence dependent – the odds ratio associated with the occurrence of positive IAMs was higher than for neutral IAMs. Additionally, the results support the notion that flashback type memories also occur for positive information (Berntsen, 2001; Berntsen & Rubin, 2008; Krans, Näring, et al., 2009), and that these positive IAMs may develop due to similar cognitive processes, in particular due to high levels of emotional processing at the time of the event.

The current study found no relationship between positive IAMs (involuntary memories) and recognition memory for the film. That is, these types of memory may behave independently. Recent work suggests that involuntary and voluntary autobiographical memories share the same episodic memory encoding systems, but differ in their retrieval (Berntsen, 2010). The current study is consistent with this view point. In the current study, positive emotional reaction at the time of film viewing was associated with both positive and neutral IAMs. Related to this - emotional intensity at the time of encoding has been found to be important for the successful recall of voluntary autobiographical memories (Talarico, LaBar, & Rubin, 2004).

None of the participant characteristics included were associated with positive IAMs. The lack of an association between history of hypomania and positive IAMs from the film may be for several reasons. Bipolar patients experience involuntary images during periods of elevated mood, but these are often of future events rather than past events (Gregory, et al., 2010; Ivins, Di Simplicio, Close, Goodwin, & Holmes, under review).

There may therefore be important differences in the formation of involuntary future images and IAMs. However, fundamentally, it is still a question whether 'positive' is a genuine link to hypomania; positive biases in cognition are not associated with bipolar disorder, while negative biases are (Kelly et al., 2011). History of hypomania may therefore not be enough to predict positive IAMs. In terms of depression and anxiety, the non significant finding may be due to high levels of depression and anxiety being associated with a bias for negative and fearful stimuli (Mathews & MacLeod, 2005). This bias enhances processing of negative events, for example trauma, but may not also enhance processing for positive events.

The current results may also have relevance for the treatment of emotional disorders. Positive autobiographical memories are lacking in depression (Werner-Seidler & Moulds, 2011) and understanding how positive IAMs are formed may have implications for increasing positive memories. On the other hand, positive involuntary images may be involved in the maintenance of manic episodes in bipolar disorder (Holmes, et al., 2008; McCarthy-Jones, Knowles, & Rowse, 2012). Understanding the mechanisms of IAMs may lead to the development of treatments that aim to manipulate the frequency of IAMs relevant to the specific nature of the disorder.

Future work investigating positive IAMs should include a free recall test to explore whether there is a difference between various measures of involuntary and voluntary autobiographical memory retrieval. Additionally, it would be interesting to include convergent measures to the diary of IAMs to address possible limitations of the diary methodology.

In conclusion, the current study found that positive emotional response at the time of experiencing a positive event was best associated with the frequency of later positive IAMs. This suggests a similarity between positive IAMs and flashbacks in terms of the

impact of emotional response. The experiments outlined in the next chapter aim to test replication of this effect and extend it by investigating whether cognitive tasks shown to modulate flashback frequency also modulate positive IAM frequency.

Chapter 6: The impact of cognitive tasks on positive involuntary autobiographical memories: Tetris vs. Pub Quiz

Abstract

Involuntary imagery that is overtly positive in affect, such as in bipolar disorder, may offer a possible therapeutic target. Two experiments are described in the current chapter investigating the impact of cognitive tasks on positive involuntary autobiographical memories (IAMs). Playing the visuospatial computer game after viewing traumatic footage has been found to reduce subsequent flashback frequency, while the verbal computer game Pub Quiz does not. However, whether these effects are due to task modality of general working memory taxation is unknown.

Experiment 1 piloted a visual reaction time task to assess general working memory taxation in each of three conditions; the task alone, as a dual task with Tetris game play, and as a dual task with Pub Quiz game play. Task performance was slowed and less accurate in both dual task conditions, but not differentially so. Results tentatively suggest that the previous effects of playing Tetris and Pub Quiz may not be due to differences in general working memory taxation.

Preliminary results also suggest that Tetris can reduce IAM frequency after viewing positive footage. Experiment 2 aimed to a) replicate the association between positive IAMs and positive emotional response at the time of film viewing. b) Replicate previous results that Tetris reduces IAM frequency after positive footage compared to No Task. c) Investigate the impact of playing Pub Quiz on positive IAM frequency. Results did not replicate the association of higher positive emotional response and positive IAM frequency. Additionally, no significant difference was found between the three groups on IAM frequency. Findings and potential methodological limitations are discussed.

Introduction

As discussed in the previous chapter, involuntary autobiographical memories (IAMs) are memories of personal events that appear to spontaneously return to mind without previous attempt to deliberately retrieve them (Berntsen, 1996). IAMs may therefore be similar to flashbacks as defined by the proposed clinical neuroscience framework. The results of the experiment presented in Chapter 5 suggested one similarity between flashbacks and IAMs finding that emotional response at the time of viewing positive footage was associated with positive IAM frequency over the subsequent week. The experiments described in the current chapter aim to replicate and extend the findings of similar mechanisms involved in the formation of flashbacks and positive IAMs, investigating whether cognitive tasks shown to reduce flashback frequency also reduce positive IAM frequency.

Why modulate the frequency of positive IAMs?

Involuntary positive imagery and affect are increasingly being thought of as possible therapeutic targets in psychological disorders (for a recent review see Carl, Soskin, Kerns, & Barlow, 2013). Although traditional wisdom suggests that positive emotions are beneficial, positive emotions and memories in bipolar disorder may not always be favourable. Research into bipolar disorder suggests that positive involuntary images, particularly of future events, may be involved in the mood instability characterised in bipolar patients (Holmes et al., 2011). Mania is often described as being related to higher accomplishment and highly ambitious goal setting (Johnson, 2005). Positive imagery, both as IAMs and involuntary future events (flashforwards), may amplify these goals by strengthening the feeling of wanting to act upon an event (see Holmes, et al., 2008). Further, suicidal imagery in bipolar disorder is often rated as positive by bipolar patients and can be highly compelling (Hales, Deeprose, Goodwin, & Holmes, 2011).

Imagining future events is thought to be cognitively and neuraly similar to remembering past events (Rasmussen & Berntsen, 2013; Schacter, Addis, & Buckner, 2008) - understanding possible ways to reduce positive IAM frequency may also help to reduce the frequency of positive images of the future.

In contrast, a number of studies have highlighted the *lack* of positive emotions and memories in depressed patients. One of the main symptoms of depression is the inability to generate positive emotions (e.g. anhedonia; American Psychiatric Association, 2000). Compared to healthy controls, depressed patients report experiencing a lower increase in positive affect in response to positive films (Rottenberg, Kasch, Gross, & Gotlib, 2002) and pictures (Dunn, Dalgleish, Lawrence, Cusack, & Ogilvie, 2004). Additionally, depressed patients report a poor ability to imagine prospective future positive events, but not future negative events (Morina, Deeprose, Pusowski, Schmid, & Holmes, 2011), as well as reporting fewer positive memories (Werner-Seidler & Moulds, 2011). Even when recalling positive memories, remitted depressed patients do not show an increase in positive affect (Joorman, Siemer, & Gotlib, 2007). Increasing positive emotions may present a distinct treatment target for depressed patients.

Recent work suggests possible methods for increasing positive affect in depressed patients. Two small-scale studies have been conducted promoting positive imagery using a computerised Cognitive Bias Modification (CBM) technique (Blackwell & Holmes, 2010; T. J. Lang, Blackwell, Harmer, Davison, & Holmes, 2012). In the active condition, depressed patients are asked to imagine a series of ambiguous scenarios which are resolved positively. Performing CBM over a one week period increased participants' positive interpretation bias and mood. Of note, some participants spontaneously reported experiencing positive IAMs of the scenarios during the week. This is particularly interesting in light of recent work investigating the effect of emotional control, memories

and affect change. As mentioned, in depressed patients, recall of positive memories can lead to mood deterioration (Joorman, et al., 2007). However, when depressed patients were asked to recall a memory in which they had no control over their positive emotions, the patients reported an increase in positive affect compared to when they recalled a memory in which they had full control over their emotions (Kang & Gruber, 2013). This suggests that uncontrollable positive events (e.g. positive IAMs) may be able to increase positive affect in depressed populations.

Modulating IAMs

Investigations using the trauma film paradigm have found a bidirectional effect of different cognitive tasks on IAM frequency. Visuospatial tasks (e.g. Tetris) have been found to decrease IAMs of the traumatic footage, while verbal tasks (e.g. Pub Quiz) do not (e.g. Holmes, et al., 2009; Holmes, et al., 2010). This suggests potential for simple cognitive tasks to also modulate positive IAM frequency.

There are two hypotheses as to how cognitive tasks may modulate IAM frequency. Models of memory suggest different working memory systems in the brain; the visuospatial sketchpad and phonological loop, governed by a central executive (Baddeley, 2003). These systems are thought to have limited capacity to processes information (Marois & Ivanoff, 2005). Visuospatial tasks may therefore compete for resources involved in sensory perceptual IAM generation resulting in fewer IAMs, while verbal based tasks do not compete and may encourage IAM development. Contrary to this hypothesis, there is also evidence that any task that sufficiently taxes general working memory, regardless of modality, can reduce IAMs (e.g. Gunter & Bodner, 2008), and that more complex tasks are more efficient at reducing emotionality and vividness of both positive and negative memories (Engelhard, van den Hout, & Smeets, 2011; Engelhard, van Uijen, & van den Hout, 2010).

The experiment described in the previous chapter found that positive IAM frequency was associated with increased positive mood at encoding (Clark, et al., 2013). Additionally, playing the computer game Tetris after viewing positive footage has been found to decrease IAM frequency compared to a No Task control (Davies, et al., 2012). The latter study suggests that positive IAMs may be modulated in a similar manner to negative IAMs, but was limited by the lack of an active control condition (e.g. Pub Quiz, as used in Holmes et al. 2010) and the emotional valence of the IAMs was not reported. The current study aimed to replicated and extend this previous work.

A general working memory taxation hypothesis would predict that any two cognitive tasks that require equivalent general working memory resources would similarly decrease positive IAM frequency. On the other hand, a modality specific hypothesis would predict that regardless of levels of general working memory taxation, a visuospatial task would reduce positive IAMs, while a verbal task would not – the suggested explanation for the results found for participants playing Tetris and Pub Quiz after negative footage (Holmes, et al., 2010). No study, however, has yet compared the level of general working memory taxation required for playing Tetris and Pub Quiz – playing Tetris and Pub Quiz may therefore tax general working memory to differing extents.

Aims and Hypotheses

The current study consists of two experiments:

In Experiment 1, a visual reaction time task was piloted to assess general working memory taxation. Three conditions were compared; task alone, as a dual task with Tetris game play, and a dual task with Pub Quiz game play. It was hypothesised that compared to the visual reaction time task alone, the dual task computer game conditions would show an increase in reaction times and decreased accuracy, but that this would not be differential between the dual task conditions. As no previous research has investigated the similarities

of Tetris and Pub Quiz in regards to general working memory taxation this study was a pilot study designed to generate estimates of effect size to enable power calculations for a full null hypothesis study.

The aim of experiment 2 was to replicate and extend the previous findings of Chapter 5 and Davies et al. (2012) investigating the association of positive emotional response to the film footage, and the impact of playing Tetris and Pub Quiz after viewing the footage on positive IAM frequency. It was hypothesised that a) positive emotional response to the film footage would be associated with positive IAM frequency; b) playing Tetris after viewing the positive film would decrease positive IAMs frequency compared to a No Task condition and c) playing Pub Quiz after viewing the positive film would increase positive IAM frequency compared to a No Task condition.

Experiment 1; General working memory taxation during computer game play

Method

Ethical approval was obtained from the University of Oxford Central University Research Ethic Committee (MSD/IDREC/C1/2011/85; Appendix III).

Design

A within subjects design was used with all participants taking part in all three conditions.

Participants

As this was a pilot study to calculate the appropriate sample size, twelve participants (9 female, mean age 27.17 years, *SD* = 5.04) were recruited from the local universities using online advertisements and word of mouth. Seven of the participants were current students, four were employed and one unemployed. All participants were educated to degree level or higher (mean years of education 17.75, *SD* = 2.05).

Materials

Visual reaction time task

Previous work has used the visual reaction time task to test whether a dose related response is apparent between the degree of general working memory taxation and reductions of vividness and emotionality of distressing memories (Engelhard, van den Hout, et al., 2011; van den Hout, et al., 2010). Reaction time is thought to be positively associated with the depth of processing. Worsening of performance of the visual reaction time task therefore provides a measure of the level of general working memory taxation required to play Tetris and Pub Quiz (see van den Hout, et al., 2010).

The visual reaction time task used was a computer based task requiring participants to respond with a button press as quickly and accurately as possible to presented stimuli. Participants were instructed to press the "H" key on the keyboard when a green circle appeared and the "F" key when a yellow circle appeared using their non dominant hand Seventy circles (35 yellow, 35 green) were presented for 500ms in a random order, with an inter-stimulus interval ranging from 2.2 to 3 seconds (mean = 2.6s). Reaction time (time from the presentation of the stimulus to button response), accuracy (correct response) and number of non responses (missed button press to presented stimuli) were recorded for each participant.

Tetris

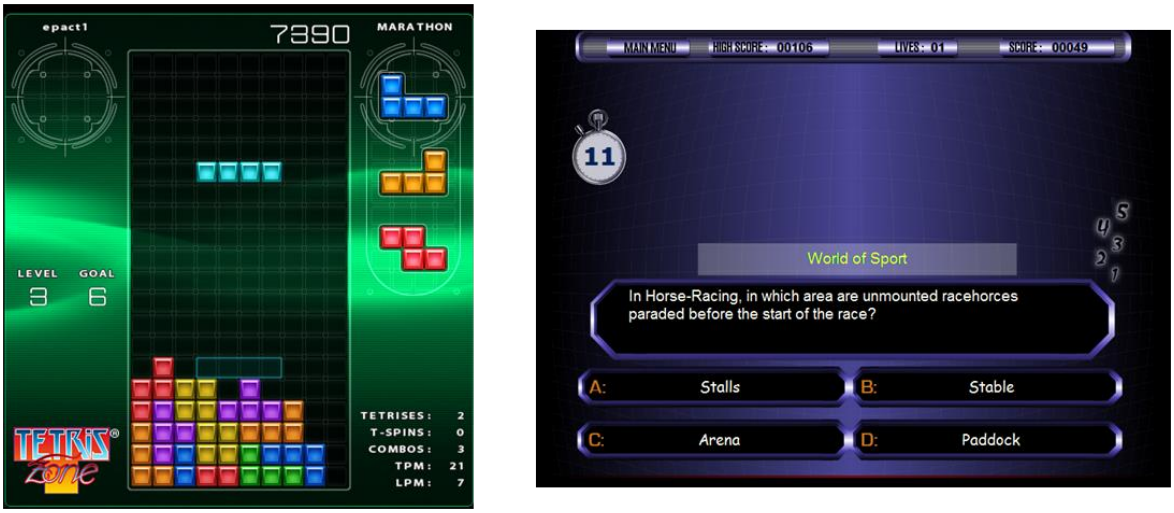
Tetris ("Tetris Zone," 2007) is a visuospatial computer game (Green & Bavelier, 2003) requiring participants to rotate and move falling blocks to complete horizontal lines on the game screen. Participants use the arrow keys on the keyboard with their dominant hand to move the blocks. For each complete horizontal line participants are awarded points, and the line disappears. As the player progresses the game speed is increased. Participants are asked to focus on both the block that is falling and the three blocks shown on the right hand side of the screen that will be the next to fall (Figure 6.1). The game ends

when the blocks reach the top of the screen. Participants are instructed to try and get as many complete lines as possible before the blocks reach the top of the screen.

Pub Quiz

The Pub Quiz computer game (Rorschach, 2007) requires participants to use the mouse with their dominant hand to select the correct answer to the presented question from four choices (Figure 6.1). Topics vary, including general knowledge, science and technology, sport and music. Participants have 15 seconds to answer each question. A correct answer awards participants points, while a wrong answer costs players one of three lives. Participants are instructed to try and get as many points before losing all their lives.

Figure 6.1. Screen shots of the Tetris and Pub Quiz computer games. Tetris is shown on the left; participants are asked to move and rotate the falling block to make as many complete horizontal lines as possible before the blocks fill the screen. Pub Quiz is shown on the right; participants are asked to try to answer as many questions correctly as possible before losing all their lives.



Procedure

All participants were tested singularly and gave informed consent to take part. On arrival to the laboratory participants initially performed 10 practice trials of the visual reaction time task with their non dominant hand, after which all participants were able to perform the task. Following the practice trials they then carried out the visual reaction time task under three conditions; as a single task with no dual task, a dual task while playing

Tetris, and a dual task while playing Pub Quiz. The order of conditions was counterbalanced across participants. Each condition lasted for approximately 3 minutes depending on the reaction times of the participant. If during the dual tasks computer game play ended a new game was started immediately. The tasks were presented on 19" computer screens. Tetris and Pub Quiz were presented on a separate computer screen to the visual reaction time task.

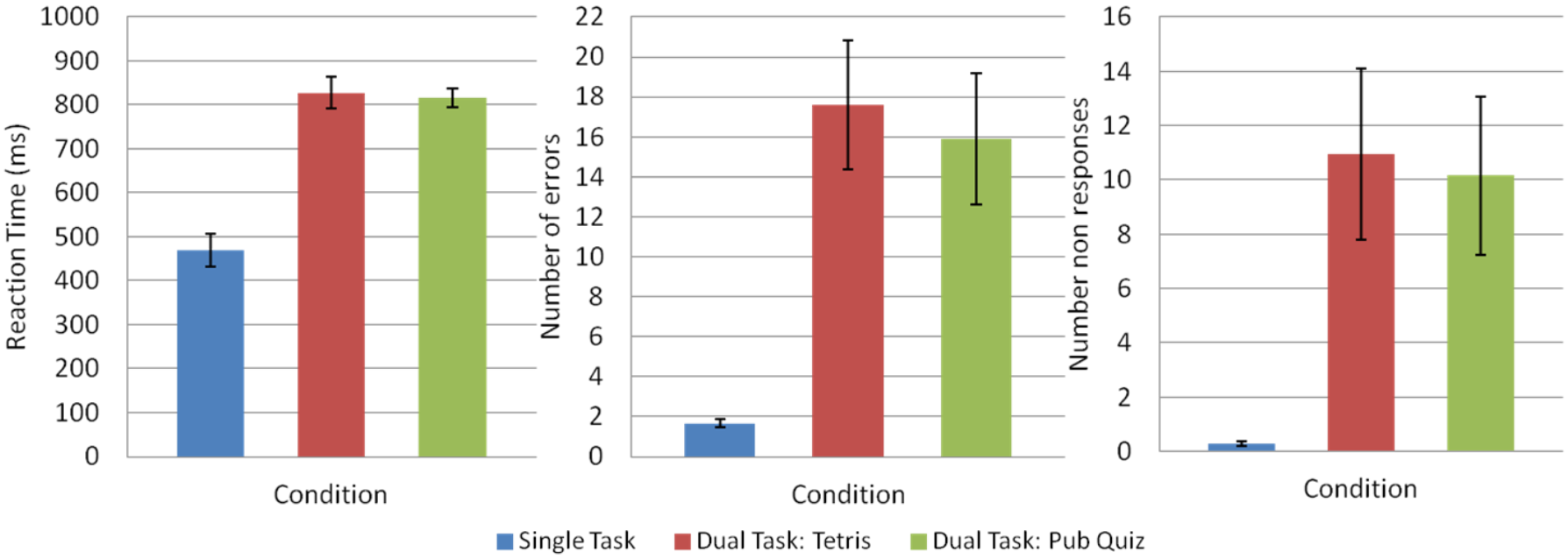
Results and Discussion

Results were non normally distributed; non parametric analyses were performed for all contrasts. Effect sizes are reported for all results. Confidence intervals of the effect sizes for non significant results are also included to observe how close to significance the differences between Tetris and Pub Quiz were. Figure 6.2 shows the mean reaction times, accuracy (number of errors) and number of non responses for each of the three conditions. All three measures of performance (reaction time, accuracy and non responses) differed between the conditions [$\chi^2(2) = 644.8$, $p < .001$; $\chi^2(2) = 18.57$, $p < .001$; $\chi^2(2) = 18.17$, $p < .001$ respectively].

Planned comparisons of the mean reaction time in each condition using Wilcoxon signed ranks revealed a difference between the single task and Tetris dual task (z = -21.11, $p < .001$, $d = 3.34$) and the single task and Pub Quiz dual task (z = -21.91, $p < .001$, $d = 3.28$). No significant difference between Tetris dual task and Pub Quiz dual task was found (z = -.65, $p = .51$, d = 0.09, CI = -.71, .89). Mean reaction times were higher in both the Tetris and Pub Quiz dual task conditions than the single task condition.

A similar pattern of results was found for both accuracy and non responses. Planned comparisons found a poorer accuracy and higher numbers of non responders between the single task and Tetris dual task (z = -3.06, $p = .002$, $d = 2.01$; z = -2.94, $p =$

Figure 6.2. Reaction times, number of errors and number of non responses on the visual reaction time task when performed as a single task (condition 1), as a dual task while playing Tetris (condition 2) and as a dual task while playing Pub Quiz (condition 3). Error bars represent the standard error of the mean.



.003, *d* = 1.38) and the single task and Pub Quiz dual task (z = -2.94, *p* = .003, *d* = 1.77; z = -3.07, *p* = .002, *d* = 1.18). No significant difference was found in accuracy scores and the number of non responders between the Tetris Dual Task and Pub Quiz dual task (z = -1.16, *p* = .25, *d* = .15, CI = -.66, .94; z = -1.34, *p* = .18, *d* = .21, CI = -.6, 1).

As hypothesised, the results of Experiment 1 found an increase in reaction time and a decrease in accuracy on the visual reaction time task performed as a dual task with both Tetris and Pub Quiz, compared to the visual reaction time task performed alone. Additionally, as hypothesised performance on the Tetris dual task did not significantly differ to performance on the Pub Quiz dual task. These results tentatively suggest that any differences in IAM frequency after playing Tetris or Pub Quiz in previous studies (e.g. Davies, et al., 2012; Holmes, et al., 2009; Holmes, et al., 2010) may not be due to the general working memory demands of playing the tasks. An alternate possibility is that any differences are due to the modality, i.e. visuospatial or verbal, of the tasks (Holmes, et al., 2010).

However, the sample size of the current experiment, in particular for a null hypothesis test, was small as it was a pilot study from which to calculate the required sample size for a null hypothesis test. Sample size calculations were performed with a beta of .95 and alpha of .05. To accept the null hypothesis (that there is no difference between Tetris and Pub Quiz) with a probability of .05 for reaction time a sample of 1338 is required, for accuracy 483 and non responses 247. As the current sample size is only 12, any conclusions made from the current results should be done so with extreme caution.

There are a number of limitations that should be considered. Although the conditions were counterbalanced across the participants, the effect of the order of the conditions is unknown due to the low number of participants in each counterbalance (n = 2). Performance may still be altered by the position of the task. Additionally, the influence

of the reaction time task on Tetris and Pub Quiz performance is not known – some participants may have performed better on the reaction time task at the cost of Tetris and Pub Quiz or vice versa. Obtaining individual performance norms (i.e. playing Tetris and Pub Quiz with no other task) and comparison of these scores to dual task performance would allow for assessment of the bidirectional effects of dual task performance. Finally, the visual nature of the reaction time task potentially makes the task more similar to Tetris than Pub Quiz in terms of the cognitive processing required. Results may therefore not represent a pure comparison of general working memory between Tetris and Pub Quiz. Additional comparison using a more verbal based reaction time task (e.g. responding to a button press whenever a certain category of word is heard) may provide further understanding of similarities and differences for the required general working memory resources required for both Tetris and Pub Quiz.

Experiment 2; The impact of playing Tetris and Pub Quiz on positive IAM frequency

Aim and Hypotheses

As stated previously, the aim of Experiment 2 was to replicate and extend the previous findings of Chapter 5 and Davies et al. (2012) investigating the association of positive emotional response to the film footage, and the impact of playing two computer games after viewing the footage on positive IAM frequency. It was hypothesised that a) positive emotional response to the film footage would be associated with positive IAM frequency; b) playing Tetris after viewing the positive film would decrease positive IAMs frequency compared to a No Task condition and c) playing Pub Quiz after viewing the positive film would increase positive IAM frequency compared to a No Task condition. Additionally, to more directly replicate the results of Davies et al. (2012), the impact of

playing Tetris versus Pub Quiz versus No Task on the frequency of all IAMs arising from the positive film (regardless of valence) was assessed.

Method

Ethical approval was obtained from the University of Oxford Central University Research Ethic Committee (MSD/IDREC/C1/2011/85; Appendix III).

Design

A between subjects design with three conditions (Tetris, Pub Quiz or No Task) was used.

Participants

A sample size calculation was performed based on a large effect size, $d > .8$ (as shown in Davies et al. 2012 and Holmes et al. 2010). A large effect size with an alpha of .05 and a power of 0.8 requires a minimum of 26 participants per group for a two group comparison (Cohen, 1992).

Seventy eight participants took part in the experiment (n = 26 per group). Participants were recruited from the local area and universities using advertisements in online newspapers and the community and were paid £15 for their time and travel expenses. Participants were allocated to condition after film viewing using a minimisation scheme (Altman & Bland, 2005; Scott, McPherson, Ramsay, & Campbell, 2002) – the first 38 participants were randomly allocated to condition. The remaining participants were allocated to group depending on their scores on baseline measures (history of hypomania, current depression levels, trait anxiety) and their emotional response to the film, measured using self report measures before and after film viewing.

Measures

Baseline measures

History of hypomania was assessed using the Mood Disorders Questionnaire (MDQ; Hirschfield, et al., 2000). The self-report questionnaire is split into three sections; section one consists of 13 yes/no items investigating lifetime (hypo)manic symptoms, section two investigating symptom co-occurrence, and section three symptom severity on a four point scale (no problem, minor problem, moderate problem, serious problem). Total scores range from 0-17, with severity scored from 0-3 respectively. Higher scores represent higher levels of hypomanic history. The MDQ has good internal validity with an alpha coefficient of .84 (Hirschfeld, et al., 2003).

Current depression levels were measured using the Beck Depression Inventory Second Edition (BDI-II; Beck, Steer, & Brown, 1996). Participants responded to 21 questions on a scale of 0-3, asking about their mood over the last two weeks. Higher total scores represent higher levels of current depression. The BDI-II has good internal validity with an alpha coefficient of .81 (Beck, et al., 1988)

Trait anxiety was measured using the State-Trait Anxiety Inventory-Trait version (STAI-T; Spielberger, et al., 1983). The STAI-T contains 20 anxiety related items which participants rate on a four point scale as to how they generally feel. Higher total scores represent higher levels of trait anxiety. The STAI-T has good internal validity with an alpha coefficient of .9 (Spielberger, et al., 2004).

Emotional response

Participants' mood was assessed using the positive subscale of the Positive and Negative Affect Schedule 10 (PANAS-10; Watson, et al., 1988). Scores on the positive subscale can range from 10 to 50, with higher scores representing higher positive affect.

Positive film

The positive film was based upon the film used in Chapter 5 to induce positive IAMs (Clark, et al., 2013, see Appendix IV for details). The film contained scenes depicting the excitement of a rollercoaster ride and extreme sports, the pride of graduating and finishing university final exams, and the thrill of gambling. The positive film was adapted based on the findings of Chapter 5 to pilot suitability for use with fMRI. As in Chapter 3, scene order was arranged so that there was at least six seconds between any Potential and Control scenes.

Tetris Task

The Tetris task was similar to that used in Experiment 1. All participants were asked to play for 3 minutes before film viewing as practice, and those in the Tetris condition played for 10 minutes after film viewing.

Pub Quiz Task

The Pub Quiz task was similar to that used in Experiment 1. All participants were asked to play for 3 minutes before film viewing as practice, and those in the Pub Quiz condition played for 10 minutes after film viewing.

No Task

Participants in the No Task condition were asked to sit quietly for 10 minutes after film viewing. Participants were told that they could think about anything that they wanted to, but were not allowed to interact with the experimenter or use any electronic devices.

Computer game task compliance, enjoyment and difficulty

Participants in the Tetris and Pub Quiz conditions were asked to rate their task compliance (to what extent they had followed instructions over the last 10 minutes) on a 10cm visual analogue scale (VAS) anchored from 0 *"not at all"* to 10 *"extremely"*. Additionally, they were asked to rate how enjoyable they found the task (anchored from 0 *"not at all"* to 10 *"extremely"*) and how difficult they found the task (anchored from 0 *"not at all difficult"* to 10 *"extremely difficult"*).

Involuntary memory diary

IAMs of the film were recorded in an involuntary memory diary. For each IAM participants were asked to write a brief description to ensure that the content of the IAM could be matched to the film, and rated the emotion of the IAM on a 5-point scale anchored at 1 "*very negative*", 3 "*neutral*" and 5 "*very positive*" (Berntsen, 2001). As in chapter 5, a rating of 4 or 5 was classed as a positive IAM (Clark, et al., 2013).

Diary accuracy

Participants were asked to rate how accurate they thought they had been in completing the diary (diary accuracy) from 1 *"not at all accurate"* to 10 *"extremely accurate"*.

Predicted effect of task

Participants in the Tetris and Pub Quiz conditions were also asked to rate how much they thought that playing the task after viewing the footage would increase or decrease their IAMs of the film, anchored at -10 *"extreme decrease"* 0 *"no effect"* and 10 *"extreme increase"* (predicted effect of task; Stuart, Holmes, & Brewin, 2006).

Visual recognition memory

As in chapter 5, recognition memory of the film was assessed using a 32-item forced choice visual recognition memory test. The recognition memory test comprised 16 randomly chosen stills from the film, designed to capture a range of different moments from throughout the film, and 16 foils - stills from unused sections of clips that had been edited out of the film and were not seen by the participants or were from similar situations. Each still was presented for 5 seconds in a fixed order, deigned to differ from the sequence when they viewed the film. Each clip was represented by two pictures: either two stills from the film, two foils, or one still and one foil (Clark, et al., 2013; Wegner, et al., 1996). Appendix IX shows the still pictures used in the visual recognition memory test.

Emotional experience ratings of film scenes

Subjective emotional experience was measured at follow up using short written descriptions for individual scenes in the film (based upon Bourne et al., 2013). Emotional experience was retrospectively assessed at one week as previous research would suggest that performing the emotional experience ratings immediately post film viewing would disrupt the memory processes, altering IAM frequency reported in the diaries (Krans, Naring, et al., 2009)**.** Participants rated each scene for how emotional they found it at the time of viewing the week before, from 0 *"not at all"* to 10 *"very emotional"*. Each scene was defined as "IAM", "Control", or "Potential", for each participant. An IAM scene was one that returned as an IAM for that individual, a Control scene was one that never returned as an IAM for any participant (including participants in Chapter 5, total n = 173), and a Potential scene was a scene that returned as an IAM for other participants but not in that individual.

Statistical analysis

Statistical analysis was performed in IBM SPSS statistical package v20 and R (R Development Core Team, v. 2.14). When scores were normally distributed ANOVA were used to compare means between all the three conditions, Kruskal Wallis was used when the data violated normality. Independent samples *t*-tests were used to compare means between the two task conditions. ANOVA and paired samples *t*-tests, corrected for multiple comparisons, were used to compare mean emotional experience scores between Control, Potential and IAM scenes. Negative binomial regression was used to investigate the association between emotional response to the film and positive IAM frequency.

Procedure

The protocol, containing all the verbal instructions given to participants, can be seen in Appendix XIII.

In brief, on arrival to the laboratory all participants gave informed consent. Participants were then asked to complete baseline questionnaires concerning their history of hypomania, current depression, trait anxiety and current mood. On completion, all participants, regardless of condition, were given a 3 minute practice of playing both Tetris and Pub Quiz. Participants were then asked to watch the positive film, imaging that the events being depicted were happening to them, right now. Immediately after film viewing, participants' mood was reassessed. According to group allocation, participants either played Tetris, Pub Quiz or sat quietly (No Task control) for 10 minutes. After the 10 minutes, participants' mood was reassessed and participants in the task conditions were asked to complete task compliance, enjoyment and difficulty ratings.

All participants were asked to record any IAMs of the film in an involuntary memory diary in the week following film viewing (Holmes, et al., 2004). Participants then returned to the laboratory and completed a measure of diary accuracy, a surprise visual recognition memory test of the film, a rating of predicted task effect (only participants in the task conditions) and ratings of emotional experience to individual film clips.

Results

Baseline measures

Of the 78 participants, 54 were female. Chi-Square found that the Tetris, Pub Quiz and No Task conditions (number female; 17, 20, 17 respectively) did not differ by gender [$\chi^2(2) = 1.08$, $p = .58$]

Exploratory data analysis suggested that Age and BDI-II scores were non normally distributed – non parametric tests were therefore employed. One-way ANOVA and Kruskal Wallis demonstrated no significant differences between conditions on the baseline measures [Age; $H(2) = 1.46$, $p = .48$; MDQ; $F(2,75) = .068$, $p = .94$, $\eta^2_p = .002$, BDI-II; $H(2) = .29$, $p = .87$, STAI-T; $F(2,75) = .53$, $p = .59$, $\eta^2_p = .014$]. Table 6.1 shows the means

and standard deviations of the baseline measures. Scores were within the non clinical range.

Emotional response

A repeated measures ANOVA was performed to investigate the effects of film viewing and task performance on mood, finding an effect of time on current positive mood [$F(2, 150) = 25.34$, $p < .001$, $\eta_p^2 = .25$]. No significant differences in mood change were found between the conditions [$F(2,75) = .36$, $p = .70$, $\eta_p^2 = .01$], nor was there a significant interaction between time and condition [$F(4, 150) = 1.13$, $p = .34$, $\eta_p^2 = .029$]. Positive emotional response increased across all participants from baseline (pre film) to post film viewing [$F(1, 75) = 20.10$, $p < .001$, η_p^2 .21], with no significant effect of condition [$F(2, 75) = .32$, $p = .72$, $\eta_p^2 = .009$], and decreased from post film viewing to post task [$F(1, 75) = 38.95$, $p < .001$, $\eta_p^2 = .33$], with no significant effect of condition [$F(2, 75) = .36$, $p = .70$, $\eta_p^2 = .01$]. Additionally, positive emotional response decreased from baseline to post task [$F(1, 75) = 10.10$, $p = .002$, $\eta_p^2 = .11$] with no significant effect of condition [$F(2, 75) = .55$, $p = .58$, $\eta_p^2 = .014$]. Mean positive emotional response by condition at each of the three time points, and the mean emotional response to the film can be seen in Table 6.1.

Table 6.1. Means and standard deviations of baseline measures and positive mood ratings assessed pre film, post film and post task.

Measure	Tetris		Pub Quiz		No Task	
	Mean	*SD*	Mean	*SD*	Mean	*SD*
Age	22.54	5.09	20.73	2.07	22.31	5.49
MDQ	5.62	3.16	5.65	4.41	5.27	4.71
BDI-II	6.12	6.51	5.73	7.09	7.08	8.03
STAI-T	37.50	9.94	38.27	9.89	40.31	10.71
PANAS-P pre film	25.23	6.87	24.38	5.53	25.92	6.29
PANAS-P post film	27.35	7.17	27.08	6.64	28.31	7.37
PANAS-P post task	24.85	7.04	22.31	5.20	23.27	7.73
PANAS-P change over film	2.12	4.40	2.69	4.95	2.39	4.80

Note. MDQ = Mood Disorders Questionnaire; STAI-T = State Trait Anxiety Inventory Trait version; BDI-II = Beck Depression Inventory Second Edition; PANAS-P = Positive subscale of Positive and Negative Affect Schedule 10.

Computer game task enjoyment and difficulty

Independent samples t-tests were performed on task compliance, enjoyment and difficulty ratings between the Tetris and Pub Quiz conditions. No significant difference was found between the two conditions on task compliance ($t(50) = 1.13$, $p = .26$, $d = .31$). A trend towards a significant difference was found for both enjoyment and difficulty [Enjoyment; $t(50) = 1.96$, $p = .056$, $d = .54$; Difficulty; $t(42.44) = 1.88$, $p = .067$, $d = .52$]. Participants in the Pub Quiz condition scored lower on enjoyment and higher on difficulty than those in the Tetris condition (Table 6.2).

Involuntary memory diary

In total 235 IAMs were reported in the diaries, with a range from 0 – 9 IAMs per person. Of the 235 reported IAMs, 109 (46.38%) were positive (range 0 – 8). An additional 29 IAMs were reported in the diaries that could not be matched to the film and were not included in the following analyses. Examples of IAMs written in the diaries include "Standing next to and watching the pianist" and "Going round a corner on a rollercoaster".

Emotional response and Positive IAM frequency

To investigate the first aim of the experiment, that positive emotional response to the film would be associated with positive IAM frequency, a negative binomial regression was performed on the participants in the No Task condition. Positive emotional response to the film was entered singularly into the model as it was the only predictor of positive IAMs in Chapter 5.

The regression model fit the data well [Pearson statistic for general linear models: $\chi^2 = 9.65$ (df = 24, $p = .91$)]. Against the hypothesis, positive emotional response to the film was not significantly associated with positive IAM frequency [$B = .0061$, $SE = .036$, $t(24) = .17$, $p = .87$, 95% CI = .94, 1.08].

Effect of task on positive IAM frequency

The critical outcome concerning IAMs was the mean frequency of positive IAMs in each group (Figure 6.3). As positive IAMs were non-normally distributed, Kruskal Wallis was employed. No significant difference was found between the groups [$H(2) = 2.13$, $p = .35$]

Effect of task on all IAM frequency

To test replication of the Davies et al. (2012) and to investigate whether these results could be extended to Pub Quiz, the difference in total number of all IAMs reported across the three groups was also investigated. As the total IAM frequency was also non-normally distributed Kruskal Wallis was employed. No significant difference was found between the groups [$H(2) = 1.76$, $p = .42$]

Diary accuracy

Mean diary accuracy (Table 6.2) differed between the conditions [$F(2,75) = 5.15$, $p = .008$, $\eta_p^2 = .121$]. Post hoc analysis using Turkey HSD found a significant difference in diary accuracy between the Tetris condition and the No Task condition ($p = .005$, $d = 0.85$), with participants in the Tetris condition reporting lower accuracy than the No Task condition. The Pub Quiz condition did not significantly differ on diary accuracy with either of the other conditions.

Predicted effect of task

Participants' mean predictions concerning the effect of the tasks in the Tetris and Pub Quiz conditions (Table 6.2) did not significantly differ [$t(50) = 1.26$, $p = .21$, $d = .35$].

Visual recognition memory

Performance on the visual recognition memory test (Table 6.2) did not significantly differ between conditions [$F(2,74) = .063$, $p = .94$, $\eta_p^2 = .002$]. Further analysis revealed no significant correlation between visual recognition memory score and positive IAM frequency [$r(76) = .16$, $p = .17$], however a significant correlation was found between

Figure 6.3. Positive IAM frequency in the 1-week involuntary memory diary for each of the experimental conditions**.** Error bars represent the standard error of the mean

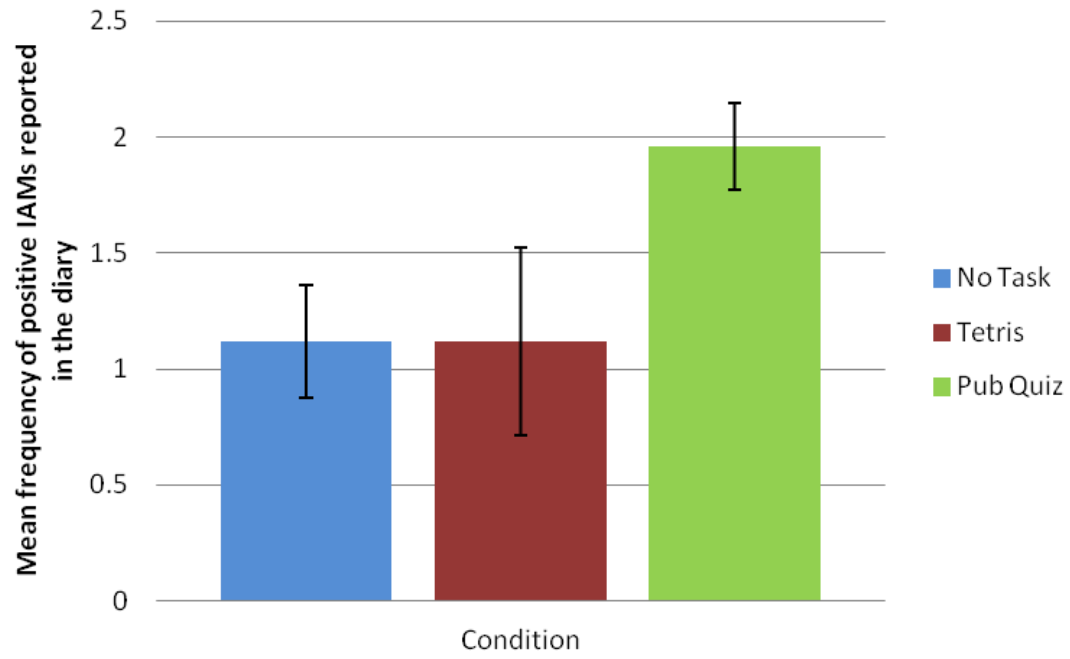
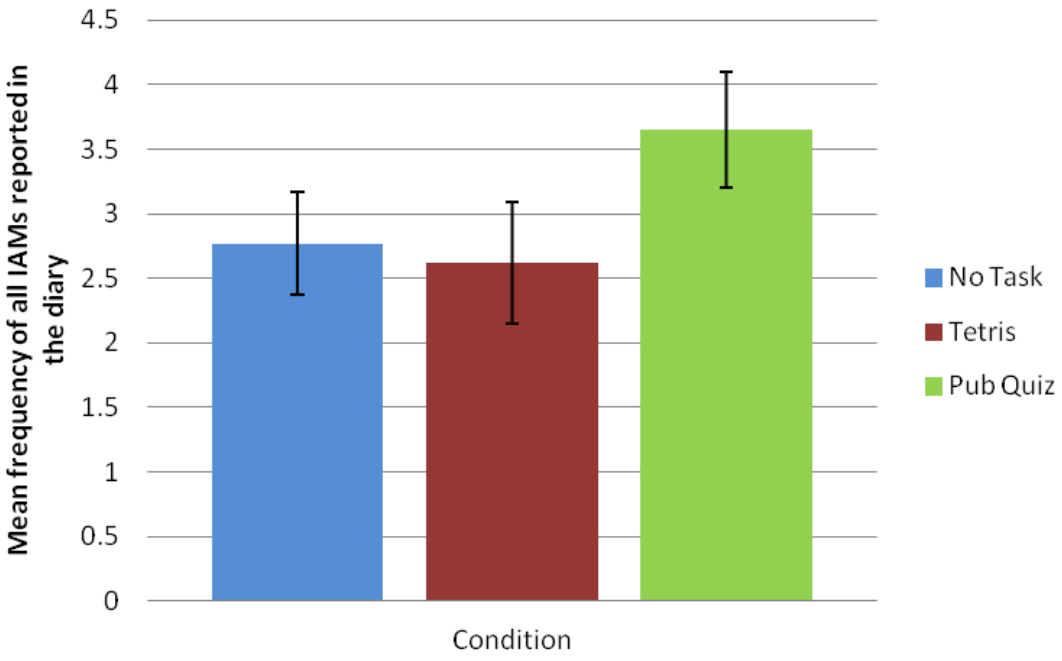


Figure 6.4. Frequency of all IAMs in the 1-week involuntary memory diary for each of the experimental conditions. Error bars represent the standard error of the mean



visual recognition memory score and all IAM frequency [r(76) = .31, p = .006].

Table 6.2. Means and standard deviations for measures of task compliance, enjoyment and difficulty, diary accuracy and the recognition memory test for each of the experimental conditions.

Measure	Tetris		Pub Quiz		No Task	
	Mean	*SD*	Mean	*SD*	Mean	*SD*
Task compliance	8.17	2.02	8.72	1.51	-	-
Task enjoyable	6.63	1.89	5.53	2.15	-	-
Task difficulty	3.61	2.21	4.58	1.41	-	-
Diary accuracy	7.54	1.90	8.19	1.30	8.85	1.08
Task effect	-1.62	3.41	-.46	3.20	-	-
Recognition memory test	75.12	6.93	75.00	5.30	74.52	7.05

Emotional experience ratings of film scenes

Emotional experience was analysed across all participants regardless of condition as participants viewed the positive film before randomisation to condition. Eleven participants reported no IAMs and were excluded from the analyses. The mean emotionality rating for IAM scenes was 6.58 (*SD* = 1.80), for Control scenes was 4.43 (*SD* = 1.24) and Potential scenes was 5.44 (*SD* = 1.40). Repeated measures ANOVA found a significant difference in emotionality between the scene types [$F(2,132) = 75.17$, $p < .001$, $\eta_p^2 = .53$]. Paired samples t-tests, corrected for multiple comparisons, found a significant difference in emotionality between IAM and Potential scenes [$t(66) = 5.47$, $p < .001$, $d = .71$], IAM and Control scenes [$t(66) = 10.61$, $p < .001$, $d = 1.39$], and Potential and Control scenes [$t(66) = 10.93$, $p < .001$, $d = .76$].

Comparison of participants in current experiment and participants in Chapter 5

Comparisons were made between the participant baseline characteristics, emotional response to the film and IAM frequency found in the current experiment and those reported in Chapter 5, the positive film study (means and standard deviations can be seen in Table 6.3).

Comparing across all of the participants in the two experiments regardless of condition, participants in the current experiment reported a non significant trend towards a lower emotional response to the film than in Chapter 5 [t(166.36) = 1.90, p = .059, d = .28]. However, both the frequency of all IAMs in the diaries, and positive IAMs were comparable across the experiments [U = 3323, p = .24, r = .09; U = 3443.5, p = .41, r = .06 respectively].

Additionally, scores on the MDQ, BDI-II and STAI-T were comparable [MDQ: t(171) = .89, p = .37, d = .11; BDI-II: U = 3668 p = .91, r = .009; STAI-T: t(171) = .31, p = .76, d = .05].,There were also no significant differences between the experiments on measures of diary accuracy and recognition memory [Diary accuracy: U = 3664.5, p = .90, r = .01; Recognition memory: t(168.14) = .067, p = .95, d = .01]. A trend towards a significant difference was found between the experiments on age and gender [Age*:*U = 3145, p = .085, r = .13; Gender: $\chi^2(1) = 3.28$, p = .070, ø = .14 (current experiment - 34.62% male, Chapter 5 - 44.21% male)].

As the task conditions may have contributed to the difference in IAM frequency, the same comparisons with Chapter 5 were made using only the no task condition of the current experiment. As with the whole sample, the current experiment reported comparable total and positive IAM frequency [U = 1052, p = .25, r = .11; U = 1104, p = .39, r = .07 respectively]. The emotional response to the film was also comparable [t(119) = 1.18, p = .24, d = .26].

Further, there were no significant differences in age, gender, MDQ, BDI-II, STAI-T or recognition memory [Age: U = 1038.5, p = .21, r = .11; Gender: $\chi^2(1) = .77$, p = .38, ø = .08 (current experiment – 30.77% male); MDQ: t(119) = .82, p = .41, d = .18; BDI-II*:*U = 1153, p = .60, r = .05; STAI-T: t(119) = .88, p = .38, d = .20; Recognition memory: t(119) = .23, p = .82, d = .05]. Diary accuracy scores were found to be significantly

different between the two experiments, but they were higher in the current experiment [t(119) = 2.02, p = .045, d = .46]. Table 6.3 reports the means and standard deviations for each variable.

Table 6.3. Means and standard deviations for IAM frequency, emotional response to the film, baseline participant characteristics, diary accuracy and recognition memory for comparison between the current experiment and the previous experiment presented in Chapter 5.

Measure	Chapter 5 (n=95)		Current Experiment: Whole sample (n=78)		Current Experiment: Controls (n=26)	
	Mean	*SD*	Mean	*SD*	Mean	*SD*
IAM frequency	3.93	3.46	3.01	2.25	2.77	2.29
Positive IAM frequency	1.96	2.34	1.40	1.53	1.12	.95
PANAS-P change over film	4.05	6.76	2.40	4.67	2.38	4.80
Age	23.45	7.00	21.86	4.50	22.31	5.49
MDQ	6.11	4.55	5.51	6.12	5.27	4.71
BDI-II	5.62	5.81	6.31	7.16	7.08	8.03
STAI-T	38.19	10.86	38.69	10.12	40.31	10.71
Diary accuracy	8.27	1.32	8.19	1.55	8.85	1.08
Recognition memory test	74.96	8.92	74.88	6.40	74.52	7.05

Note. MDQ = Mood Disorders Questionnaire; STAI-T = State Trait Anxiety Inventory Trait version; BDI-II = Beck Depression Inventory Second Edition; PANAS-P = Positive subscale of Positive and Negative Affect Schedule 10.

Discussion

Experiment 2 aimed to replicate and extend the previous findings of the experiment presented in Chapter 5 and Davies et al., (2012), investigating the association of positive emotional response to positive footage on positive IAM frequency and the impact of playing Tetris or Pub Quiz compared to No Task after viewing positive footage on the frequency of IAMs. Participants watched positive film footage and then played Tetris or Pub Quiz, or were asked to sit quietly for 10 minutes. IAMs were recorded in a diary for the following week. Against hypotheses, the results of the current experiment did not replicate those of Chapter 5; there was no significant association of positive mood change and positive IAM frequency. Additionally, the results did not replicate Davies et al.,

(2012), finding no significant difference between the Tetris condition and No task on IAM frequency. There was also no significant increase in positive IAMs after participants played Pub Quiz compared to the No Task condition against the hypothesis that Pub Quiz would increase positive IAM frequency.

Although positive emotional response to watching the film footage was not associated with IAM frequency, emotional experience of viewing the film scenes (measured at one week as in Chapter 3) was reported as being higher for IAM scenes compared to both Potential and Control scenes. The results of the current study therefore partially support the findings of Chapter 5 suggesting that a larger emotional response at the time of viewing positive footage is associated with later positive IAM development (Clark, et al., 2013), if only by retrospective self report.

There are several limitations of Experiment 2 that may explain the non replication. The IAM frequency reported in the current experiment was low which may have lead to possible floor effects – if there is a low baseline of IAM frequency in the No Task condition it is difficult to reduce this in the Tetris condition. It should also be noted that the film used in the current experiment was different to that of both previous experiments. The film used in the current experiment was adapted for potential use with fMRI. The inclusion of additional control scenes (designed not to induce IAMs) may have had decreased both individual's emotional response at the time of viewing the film and IAM frequency over the following week.

Future work should seek to retest the impact of Tetris and Pub Quiz on positive IAM frequency using one of the previous films. This may help to clarify any impact of the film on emotional response and IAM frequency. The positive film paradigm has been developed over the course of this thesis. Further research to understand how to best induce

positive IAMs using this paradigm is required before firm conclusions across studies can be made.

Overall Discussion and Conclusion

Experiment 1 suggests that playing Tetris and Pub Quiz may not use differential levels of general working memory taxation. However, this was only a pilot study for a larger null hypothesis study and results should be interpreted with extreme caution. Future results could have implications for other research reducing flashback frequency (e.g. Holmes, et al., 2009; Holmes, et al., 2010), suggesting that modality may be more important than general working memory taxation for negative IAM reduction (Gunter & Bodner, 2008). Further research should continue to investigate why some cognitive tasks modulate IAM frequency, while others may not.

Experiment 2 did not replicate previous results of an association of positive IAMs and positive emotional response, nor that playing Tetris after film viewing would decrease IAMs. These preliminary results suggest that alteration of the emotion component of the clinical neuroscience framework may have larger effects than initially envisaged – the formation of positive IAMs and flashbacks may not be as similar as originally hypothesised.

However, further work is required to understand the similarities and differences between flashbacks and positive IAMs. Future work should focus on understanding the positive film paradigm and the subsequent development of IAMs. IAM frequency to positive footage is lower than flashbacks to the trauma film paradigm. Development of a stronger film inducing a greater frequency of IAMs may help clarify elements surrounding the formation of positive IAMs.

Chapter 7: General Discussion

Overview of the thesis

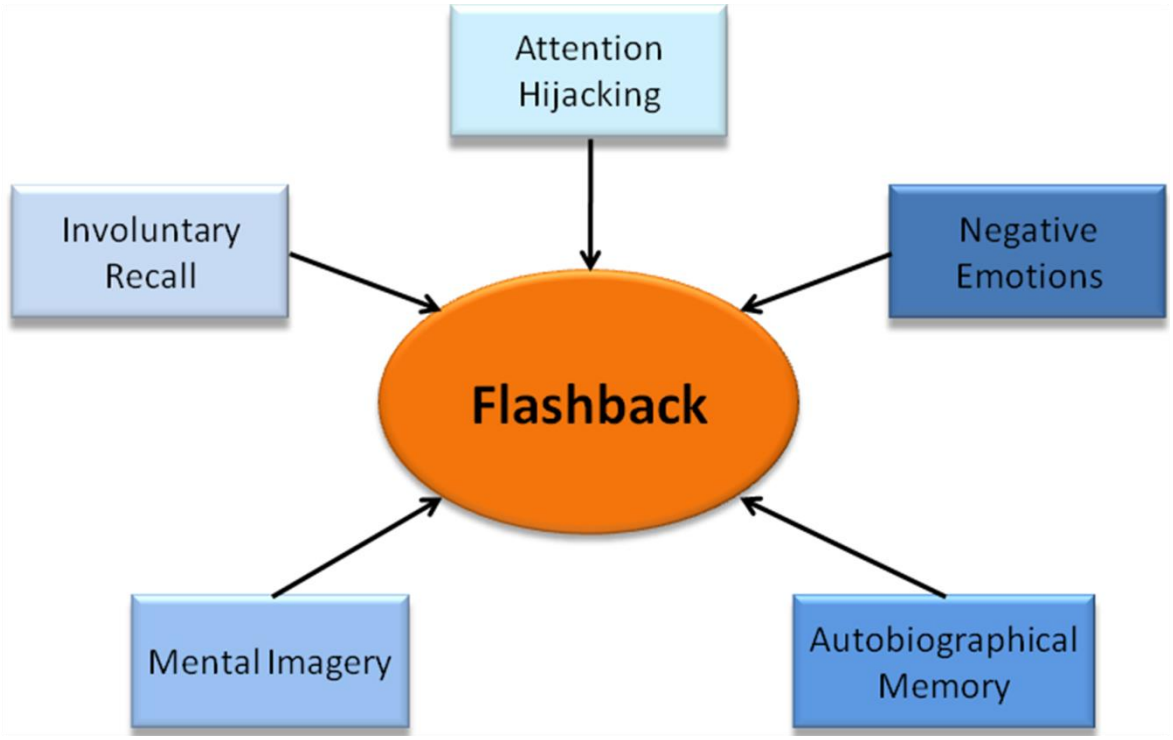
The term flashback has been used throughout this thesis to describe vivid, sensory-perceptual (predominantly visual images), emotional memories from a traumatic event that intrude involuntarily into consciousness. Flashbacks have been taken to be on a continuum of normal functioning, ranging from involuntary autobiographical memories in everyday life to intrusive memories in depression and bipolar disorder and recurrent flashbacks in PTSD.

A pragmatic clinical neuroscience framework of flashbacks was developed in Chapter 2, bringing together the clinical and neuroimaging understanding of flashbacks to guide work presented in this thesis. A flashback was described as comprising five component parts: autobiographical (trauma) memory, involuntary recall, negative emotions, mental imagery and attention hijacking (see figure 2.6, reproduced below). In all studies, participants recorded flashbacks in diaries and were given instructions in line with these components (see Table 2.1). The component of 'involuntary recall' was examined in the neuroimaging experiment presented in Chapter 3, the impact of 'negative emotions' in the behavioural study described in Chapter 4, and the emotional valence of the negative emotion component in Chapters 5 and 6.

Four studies were conducted in this thesis (1 fMRI and 3 behavioural). The neuroimaging study was conducted to investigate the neural basis of both the encoding and the recall of flashbacks. Details will be further discussed below. Next, as not all individuals develop flashbacks after trauma, an individual participant data analysis was conducted combining data from 16 previous behavioural trauma film paradigm experiments to investigate psychological factors that may be protective against flashback development. In the experiments presented in Chapters 5 and 6, I adapted the emotional

film paradigm to use a positive film to investigate flashback type memories arising from non-traumatic stimuli. The following section provides a brief overview of the main findings for each experiment.

Reproduction of Figure 2.6. A proposed pragmatic clinical neuroscience framework of flashbacks. All five components should be present for a flashback to be experienced



Main findings of the thesis

The neuroimaging experiment presented in Chapter 3 combined the trauma film paradigm with fMRI to investigate both the encoding and the recall of a flashback. Specifically, the study had four aims: 1) To replicate the previous findings (Bourne et al., 2013) of a distinct pattern of brain activity at the encoding of memories that later returned as flashbacks. 2) To extend the paradigm by dividing the trauma film according to whether or not moments of the film (stills) could be identified on a recognition memory test at one week – analysing only those stills which were successfully identified on a recognition memory test. It was hypothesised that there would be minimal encoding differences in

comparison to using both non-identified and identified stills. 3) To compare flashback events with potential events using identified and non-identified stills from the recognition memory test. As low numbers of events were expected, this analysis was exploratory and no hypotheses were made. 4) The paradigm was further extended to capture the brain activation involved at the moment of flashback involuntary recall in the scanner, hypothesising that flashback involuntary recall would involve brain regions associated with the components of the proposed clinical neuroscience framework.

Results supported 1) the existence of a distinct pattern of brain activity at flashback encoding for Flashback scenes compared to Potential scenes (scenes that returned as flashbacks in others) and Control scenes (scenes that never returned as a flashback). 2) Activation at the time of film encoding for flashback stills compared to non flashback stills that were identified on the recognition memory test was similar to the initial analysis. 3) Activation at the time of film viewing of Flashback identified stills versus non-identified and Potential identified versus non-identified were compared. This suggested an increase in activation at encoding in the insula, hippocampus and parahippocampus for flashback stills that were 'identified compared to flashbacks stills that were not identified on the recognition memory test. This difference was not seen for those unpleasant scenes in the film which did not return as flashbacks. 4) At the moment of flashback involuntary recall in the scanner, results suggest a predominant role for the middle and superior frontal cortices followed by activation in the frontal operculum and left IFG – reverse inference suggests that these are areas typically associated with emotion, autobiographical memory and attentional salience. The left IFG was associated with both the encoding of flashback memories and their involuntary recall. It is hypothesised that the left IFG may be processing the individual's hotspots or "worst thoughts" during the traumatic film (i.e. he's about to die), which 'flags' the event at encoding, leading to a high rating of importance

within selective attention, subsequently overriding normal functioning at recall. Future work could further examine this by qualitative analysis of flashback content and the nature of these worst moments.

Not everyone develops flashbacks after trauma. Understanding factors that protect against flashback development may help develop interventions aimed at reducing or preventing involuntary flashback recall. The individual participant data meta analysis presented in Chapter 4 investigated commonly studied psychological factors that may be associated with an absence of flashbacks using the same trauma film paradigm. Using binary regression, it was found that an absence of flashbacks was associated with low emotional response to the traumatic film footage, low trait anxiety and low current depression levels. These results underscore the importance of the role of emotional processing at the time of the trauma in the development of flashbacks.

The experiments presented in Chapters 5 and 6 examined the 'emotion' component of the clinical neuroscience framework, investigating whether the framework could also improve understanding of flashback type memories to a positive film. I adapted the emotional film paradigm to include scenes designed to be positive for a (predominantly) University of Oxford student audience. Scenes were therefore selected to be relevant to such participants – including, for example, Oxford students being enthusiastically greeted upon finishing final examinations, England coxless fours rowers winning the 2004 Olympic games and Oxford May day celebrations. Scenes were also included to capture the thrill seeking of some university students, for example, freestyle skiing and skydiving. Additionally, clips depicting high levels of accomplishment and the pride that accompanies this were included, including the end of the winning performance of the BBC young musician of the year in 2010 and Oxford University graduation. These clips were found to induce "positive flashbacks", referred to as positive involuntary autobiographical

memories (IAMs). After viewing the positive footage, participants kept a one week diary of any IAMs, rating their emotional experience of the IAM on a 5 point scale, from very negative to very positive (a rating of 4 or 5 was classed as a positive IAM, 3 as a neutral IAM) – allowing for identification of positive IAMs. The experiment described in Chapter 5 found that higher levels of positive mood change to the film were significantly associated with both the frequency of positive IAMs and the frequency of neutral IAMs. This suggests possible similarities between positive IAMs and flashbacks. The results also support the importance of the emotional response at the time of an event for the formation of memories that later return involuntarily.

In Chapter 6, two experiments were described. The visuospatial computer game Tetris has been previously found to reduce flashback frequency, while the verbal Pub Quiz computer game does not (Holmes, et al., 2010). However, whether these effects are due to the modality of the tasks or general working memory is unknown. Experiment 1 was a pilot experiment using a visual reaction time task to assess general working memory taxation required to play Tetris and Pub Quiz. Performance worsened on the task when played as a dual task with both Tetris and Pub Quiz, but did not significantly differ between the dual task conditions. This suggests that previous differences in flashback frequency after playing Tetris or Pub Quiz are unlikely to be due to general working memory taxation. However, a fully powered experiment with a larger sample size is required before firm conclusions can be made.

The second experiment aimed to replicate and extend the findings of the experiment presented in Chapter 5, and previous preliminary results suggesting that Tetris may reduce positive IAM frequency (Davies, et al., 2012). Results did not replicate previous work of an association between positive emotional response and positive IAMs, or find a significant effect of Tetris or Pub Quiz. Caution should be taken with

interpretation of the results as IAM frequency was low, suggesting possible methodological limitations, including the use of a different positive film, and a general need to develop and improve a "positive film" paradigm.

Implications of the findings

The results of the experiments presented are discussed in line with the proposed clinical neuroscience flashback framework of Chapter 2. Specifically, reverse inference from the results of the neuroimaging study potentially implicates brain regions associated with the components of the flashback framework developed in Chapter 2 (mental imagery, autobiographical memory, attention hijacking, negative emotions and involuntary recall) in the encoding or recall of a flashback memory. The importance of emotional response at the time of flashback formation was also shown by the association of low emotional response with an absence of flashbacks, and by the association of a high positive emotional response with positive IAM frequency. Future research could further test the mechanisms involved in each individual component and how these components can be disrupted to prevent or decrease flashback recall and formation. There are currently no established preventative treatments for PTSD (see Rothbaum et al., 2012) or flashback formation – understanding the individual components of a flashback may help to suggest potential targets to prevent or reduce flashback development.

The results of the neuroimaging study also demonstrate the potential of applying neuroimaging to symptoms of psychological disorders and cognitions. A recent special edition of *Perspectives on Psychological Science* (Mather, Cacioppo, & Kanwisher, 2013) highlights the argument of some researchers that neuroimaging has not significantly added to current psychological theories about cognitive processing. However, although a number of the brain regions identified in flashback encoding and recall would be predicted by cognitive theories of PTSD (e.g. emotional regions – amygdala, thalamus, putamen,

insula), psychological theories would not necessarily predict either the lack of any hippocampal or parahippocampal change, or the predominant involvement of the left IFG. The left IFG, although suggested to be involved in autobiographical memory (e.g. Spaniol, et al., 2009) and selective attention, predominantly for verbal stimuli (Jonides & Nee, 2006; Nelson, et al., 2009), is often thought of as a language area of the brain (Binder, et al., 1997; Vigneau, et al., 2006). Flashbacks, on the other hand, have been defined here as image based. The results of the neuroimaging study implicate the left IFG as playing an important role in both flashback encoding and recall, possibly acting as a "flag" for the worst moment. One possible implication is that language processing as well as mental imagery processing should be taken into account for the treatment, and possible prevention, of flashbacks.

Finally, although involuntary memories have traditionally been studied in the form of flashbacks in clinical psychology, there is emerging evidence that involuntary autobiographical memory recall is a "basic mode of remembering" (Berntsen, 2010) in the same vein as voluntary recall and implicit memories. The results presented in this thesis may also be relevant for more general autobiographical memory theories, suggesting, at least tentatively, that autobiographical memories that are later recalled involuntarily may be encoded differently to normal "healthy" autobiographical memories".

Limitations of the research presented in this thesis

Limitations specific to each study have been outlined in the corresponding chapter. However, there are some limitations that are more general of the work presented in this thesis as a whole.

The use of emotional films as both an analogue of trauma to induce flashbacks, and an analogue of positive events to induce positive IAMs should be acknowledged as a potential limitation. Analogue laboratory experiments offer a prospective controlled setting

to study the formation of flashbacks and IAMs, but viewing film footage is not the same as experiencing events in real life. However, the traumatic film depicts images of real death and injury, in line with the criteria for a traumatic event (American Psychiatric Association, 2000). Further, the newly released DSM-5 includes "the individual experiences first-hand repeated or extreme exposure to aversive details of the traumatic event (not through media, pictures, television or movies unless work related)" within the trauma exposure criterion (American Psychiatric Association, 2013). This suggests that individuals can develop posttraumatic symptoms, including flashbacks, from viewing traumatic footage as in the trauma film paradigm.

Additionally, all studies in this thesis used the pen and paper diary methodology to measure flashbacks and IAMs. The pen and paper diary offers an opportunity to measure flashbacks and IAMs in the context of everyday life and is a widely used methodology in the literature (e.g. Berntsen, 2001; Laposa & Alden, 2008). However, the use of a diary may have distorting effects – some participants may have been more conscientious in noticing and reporting flashbacks and IAMs, and the diary itself may act as a reminder and trigger for flashbacks and IAMs (see Bolger, Davis, & Rafaeli, 2003). On the other hand, Schlagman and Kvavilashvili (2008) found no differences between IAMs reported in a written diary and IAMs reported during an undemanding vigilance task conducted in the laboratory, suggesting a limited distorting effect of the pen and paper diaries. Future studies could consider using alternative methodology to record flashbacks over the following week, for example via Short Messaging Service (SMS; Malik, Goodwin, & Holmes, 2012) or smart phone apps.

Throughout the thesis, only a small subset of psychological measures were investigated for possible associations with flashbacks and IAMs. Other psychological factors not included may therefore also be involved in protection against flashbacks or

predicting the frequency of positive IAMs. The trauma film paradigm has been used in 50 published experiments since 2008, investigating, for example the effects of Cognitive Bias Modification (e.g. Woud, et al., 2012), a prior ability to remove information no longer relevant from mind (Verwoerd, et al., 2011), the influence of contextual information (Pearson, Ross, & Webster, 2012) and the effects of peritraumatic self referent processing and dissociation (Laposa & Rector, 2012) on flashback frequency. While these factors may also be important for the development of flashbacks, it is beyond the scope of this thesis to investigate them at this time.

Additionally, the positive film paradigm was developed during this thesis. Although this paradigm represents an opportunity to study positive IAMs, the low number of IAMs induced represents a weakness that could be addressed for future research with this paradigm. Further validation of the clips used in terms of the positive emotional response induced and the subsequent frequency of IAMs over the following week may help develop a more efficient and reliable positive film paradigm.

Future directions

The results described in this thesis provide multiple directions for future work, some of which are discussed in the individual chapters.

Further research should attempt to elucidate the unexpected predominant involvement of the left IFG and the proposed protective activation it may have against flashback encoding. This may be particularly important in the immediate aftermath of trauma. Activation in the left IFG is traditionally associated with language processing (Vigneau, et al., 2006)**.** Although psychological debriefing as a technique for the reduction of PTSD and associate symptoms is widely discouraged (Rose, Bisson, Churchill, & Wessely, 2002), single session "instant psychological interventions", as outlined in a recent newspaper article, remain a common response after trauma (Bell, 2013). If

suppressing activation in the left IFG is protective against flashback formation, as hypothesised from the results of the neuroimaging study, then talking based therapies in the immediate aftermath of trauma may contribute to the development of flashbacks and possible later PTSD. Further understanding at a neuroscientifc level about how flashback memories are formed may help to suggest ways to prevent flashback formation, as well as the potential dangers of performing certain treatments.

General memory theories suggest that regardless of whether a memory is later recalled involuntarily or voluntarily, the neural basis of the encoding of the memory remains the same – the difference between the memories lies at recall (e.g. Berntsen, 2010; Henson & Gagnepain, 2012; Ramponi, et al., 2011). However, the neuroimaging findings presented here suggest that there are surprisingly large differences in brain activation at encoding for memories that are later remembered involuntarily. Future work should explore differences into the encoding of involuntary and voluntary memories using neuroimaging techniques.

Additionally, the neuroimaging study is the first to capture brain activation at the moment of flashback involuntary recall in the scanner. Replication of this finding is therefore warranted. A recent laboratory paradigm was designed to behaviourally compare involuntary and voluntary autobiographical memory recall of non emotional stimuli using a non demanding vigilance task (Schlagman & Kvavilashvili, 2008). Combining this paradigm with neuroimaging may offer a further experimental technique to induce flashback memories while participants undergo neuroimaging and directly monitor the brain activation at the moment of involuntary and voluntary recall.

Recent advances in neuroimaging analysis and techniques present further opportunities for better understanding of the encoding and recall of flashback memories. Multivariate pattern analysis has recently been used to predict whether an aversive

experience will develop into a fear memory from the brain activation at the time of the aversive experience (Kriegeskorte, Goebel, & Bandettini, 2006; Visser, Scholte, Beemsterboer, & Kindt, 2013). The same techniques could also be applied to the flashback encoding data collected for this thesis, predicting the occurrence of a flashback solely from the neural patterns at the time of encoding.

In terms of flashback recall, the development of multiband fMRI allows for more precise timing information than traditional fMRI techniques. This would allow for more precise observation of the brain activation involved at the moment of flashback involuntary recall. In addition, machine learning and decoding models have recently been used to reconstruct visual imagery from brain activity during sleep (Horikawa, Tamaki, Miyawaki, & Kamitani, 2013) and from brain activity when participants viewed a neutral film (Nishimoto et al., 2011). It may therefore be possible to decode the visual experience of an individual flashback from brain activation at flashback recall, and to predict what image an individual may experience as a flashback from the brain activation at encoding. This would allow for reconstruction of emotional perceptual experiences, informing general understanding of how the brain processes negative and traumatic information, and may help to further validate and objectively identify brain regions and cognitive processes that may be targetable to reduce, and possibly prevent, flashback occurrence.

Combining data collected across studies using similar protocols (as in Chapter 4) allows for larger scale studies investigating the effects of commonly collected measures or tasks on flashback frequency. Psychological studies often have small sample sizes and are at risk of being inadequately powered (Bertamini & Munafò, 2012). Performing individual participant data meta analyses on data sets using similar protocols may help to overcome this, creating larger sample sizes that are better powered to examine associations between collected measures and flashbacks.

The results concerning positive IAMs are unclear due to the non replication within the final chapter. The positive film paradigm used in this thesis successfully induced positive IAMs, however, the frequency of positive IAMs is low compared to the frequency of flashbacks after viewing traumatic footage. Future work should seek to refine this paradigm, using the most effective clips to encourage a larger positive emotional response to the film. Current research has behaviourally investigated the recall of positive IAMs, suggesting potential similarities between positive IAMs and flashbacks (Berntsen, 2001). However, the encoding of positive IAMs has received limited attention. Further research in this area will help illuminate similarities and differences between flashbacks and positive IAMs.

In summary, the work presented in this thesis provides evidence that processing at the time of an event is important for the encoding of memories which later flashback. Further, it highlights that a specific area of the brain – the left inferior frontal gyrus – may be involved in both the encoding and involuntary recall of a flashback memory, and suppression of activation in the left IFG may be protective against flashback encoding. Future research could build upon these findings to better understand the neural processes of flashback formation and potentially seek to inform treatment developments, directly targeting the left inferior frontal gyrus to reduce the encoding and later involuntary recall of debilitating flashback memories.

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Appendix I

Ethical Approval for the neuroimaging experiment presented in Chapter 3 from Central University Research Ethics Committee (CUREC), Medical Sciences Division, Oxford University

MEDICAL SCIENCES DIVISIONAL OFFICE
LEVEL 3, JOHN RADCLIFFE HOSPITAL
HEADINGTON, OXFORD, OX3 9DU

Tel: +44(0)1865 228974 Fax: +44(0)1865 750750
www.medsci.ox.ac.uk

Mrs Rosie Mortimer
Senior Assistant Registrar (Planning and Resource Allocation)

CONFIDENTIAL

Ref: MSD/IDREC/C1/2012/31

2 April 2012

Ian Clark
Department of Psychiatry
Warneford Hospital

Dear Ian

CUREC checklist

I am writing to acknowledge receipt of your CUREC/1 form for your project: **The Neural Correlates of Involuntary Memories**

On the basis of the information you have provided this has now been approved by the Medical Sciences IDREC **subject to:**

a) it is your responsibility to comply with the requirements for administering any tests or questionnaires and if in doubt to contact the publisher of those tests or questionnaires.

b) On the evidence you have submitted and the understanding you will strictly follow protocol MSD/IDREC/2010/P17.1 (for non-invasive magnetic resonance investigations in healthy volunteers) the committee considers your research is ethically sound. However this approval does not provide assurance that fMRIB/OCMR will be able to provide the facilities for this research. You should, if you have not already done so, undertake discussion with the relevant unit about this.

The reference number for this project is **MSD/IDREC/C1/2012/31** 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

Rosie Mortimer
Senior Assistant Registrar

Appendix II

Ethical Approval for the behavioural experiment presented in Chapter 5 from Central University Research Ethics Committee (CUREC), Medical Sciences Division, Oxford University

University of Oxford

Medical Sciences Office
John Radcliffe Hospital, Headington, Oxford OX3 9DU

From Carol Green

CONFIDENTIAL
Mr Ian Clark
c/o Dr Emily Holmes
Department of Psychiatry
Warneford Hospital

Ref.
MSD/IDREC/C1/2011/2

31st January 2011

Dear Mr Clark,

CUREC checklist

I am writing to acknowledge receipt of your CUREC/1 form for your project: Involuntary memories following a positive film; what factors make it more likely that a positive memory is recalled involuntarily?

On the basis of the information you have provided this has now been approved by the Medical Sciences IDREC **subject to receipt of the hard copy of your application signed by your head of department (Please note that should this not appear or the head of department is unwilling to sign then this approval would not be valid).**

The reference number for this project is MSD/IDREC/C1/2011/ 2 and may I remind you that your project may be reviewed at some stage during an annual audit of projects.

Amendments
Should you at some stage alter some of the techniques or procedures then you should first undertake a checklist (CUREC/1) to see whether these changes alter the ethics of the research. If these remain the same then the committee will require notification of the changes to lodge with the project. If they do not remain the same then you may need to complete a CUREC/2 form and undergo further scrutiny by the committee.

Please do not hesitate to contact me if you have any queries about this.

Yours sincerely,

Carol Green (Miss)
Secretary to the
MSD IDREC

Appendix III

Ethical Approval for the behavioural experiments presented in Chapter 6 from Central University Research Ethics Committee (CUREC), Medical Sciences Division, Oxford University

University of Oxford

Medical Sciences Office
John Radcliffe Hospital, Headington, Oxford OX3 9DU

From Carol Green

CONFIDENTIAL
Mr I Clark
c/o Dr Emily Holmes
Department of Psychiatry
Warneford Hospital

Ref.
MSD/IDREC/C1/2011/85

28th July 2011

Dear Mr Clark,

CUREC checklist

I am writing to acknowledge receipt of your CUREC/1 form for your project: An investigation into the modulation of positive involuntary memories.

On the basis of the information you have provided this has now been approved by the Medical Sciences IDREC **subject to:**

(a) receipt of the hard copy of your application signed by your head of department (Please note that should this not appear or the head of department is unwilling to sign then this approval would not be valid);

(b) it is your responsibility to comply with the requirements for administering any tests or questionnaires and if in doubt to contact the publisher of those tests or questionnaires.

The reference number for this project is MSD/IDREC/C1/2011/85 and may I remind you that your project may be reviewed at some stage during an annual audit of projects.

Amendments
Should you at some stage alter some of the techniques or procedures then you should first undertake a checklist (CUREC/1) to see whether these changes alter the ethics of the research. If these remain the same then the committee will require notification of the changes to lodge with the project. If they do not remain the same then you may need to complete a CUREC/2 form and undergo further scrutiny by the committee.

Please do not hesitate to contact me if you have any queries about this.

Yours sincerely,

Carol Green (Miss)
Secretary to the
MSD IDREC

Appendix IV

Trauma film used in the neuroimaging experiment presented in Chapter 3

Experiment 1: Trauma film used in fMRI

Running time: 21 minutes 19 seconds

Description: A compilation of 15 individual clips depicting the aftermath of real road traffic accidents, real surgical procedures, edited versions of road safety adverts, an edited short film by Martin Scorsese depicting a man shaving until bleeding and an elephant rampage. The film contained 20 potential scenes and 16 control scenes. The film was identical to that of Bourne et al. (2013) apart from the eye makeup clip was shortened to allow for more time on the scene explanations later in the film without overly lengthening the film. The three control scenes in the eye makeup scene were kept the same length as in Bourne et al. meaning that the average length of control scene was kept identical.

Film Clips

Clip 1 – The aftermath of a road traffic accident involving multiple vehicles. Notable incidents include a dismembered head on the road, a leg sticking out of an upturned car and a firefighter carrying a baby away from the accidents.

Clip 2 – Excerpt of close up shots of a woman applying eye make up

Clip 3 – Excerpt of an operation on an eye, viewed close up with just the eye showing and the lens being cut by surgical instruments.

Clip 4 – The aftermath of a collision involving a grey saloon car and a minivan. A man is stuck in the car and a woman in the van. The man is removed from the car and receives medical attention for his wounded leg at the roadside. The fire fighters attempt to remove the woman from the van by cutting off the roof and pulling the front of the van away from her legs. The woman faints during the attempts.

Clip 5 – An excerpt from a "don't drink and drive advert". A man goes to the pub after winning a football match. On his drive home, he rolls the car through a fence, killing a young boy who was playing football in his back garden.

Clip 6 – The aftermath of a second multiple vehicle road traffic accident. The clip depicts a car under the back of a lorry with a body under a blanket lying half out of the car and emergency personal lifting and moving bodies.

Clip 7 – Nurses preparing an operating theatre, interviewing each other as the go about their routine tasks. As the video is played without sound the conversation of the nurses is not know

Clip 8 – Excerpt of a operation of a compound fracture of the leg. The operation involves scraping the flesh off the bone fracture

Clip 9 – The aftermath of a third multiple vehicle road traffic accident. An individual is shown trapped in their car, bodies on the road and bodies being placed in metal coffins.

Clip 10 – Excerpt from the Martin Scorsese short depicting a man shaving in front of a mirror. As he progresses, he starts to cut himself and blood appears. The final cut is a large transverse cut across his neck.

Clip 11 – A female student after surviving a road traffic accident is intuabated – a pipe is being placed down her throat to allow her to breathe.

Clip 12 – Excerpt of a road safety advert about the dangers of not wearing a seatbelt. A couple meet some friends and go for a drive. At a junction, they are involved in a head on collision. The boy in the back seat is shown in slow motion ricocheting around the inside of the car, injuring the other passengers.

Clip 13 – A group of elephants perform tricks in a circus ring

Clip 14 – A single elephants is shown mauling his keeper during a circus act. A second man tries to distract the elephants but is also attacked and trampled.

Clip 15 – Excerpt of a road safety advert about the dangers of speeding. A girl is sitting on a wall with her boyfriend standing facing her. A car going too fast spins around a corner pinning the couple to the wall.

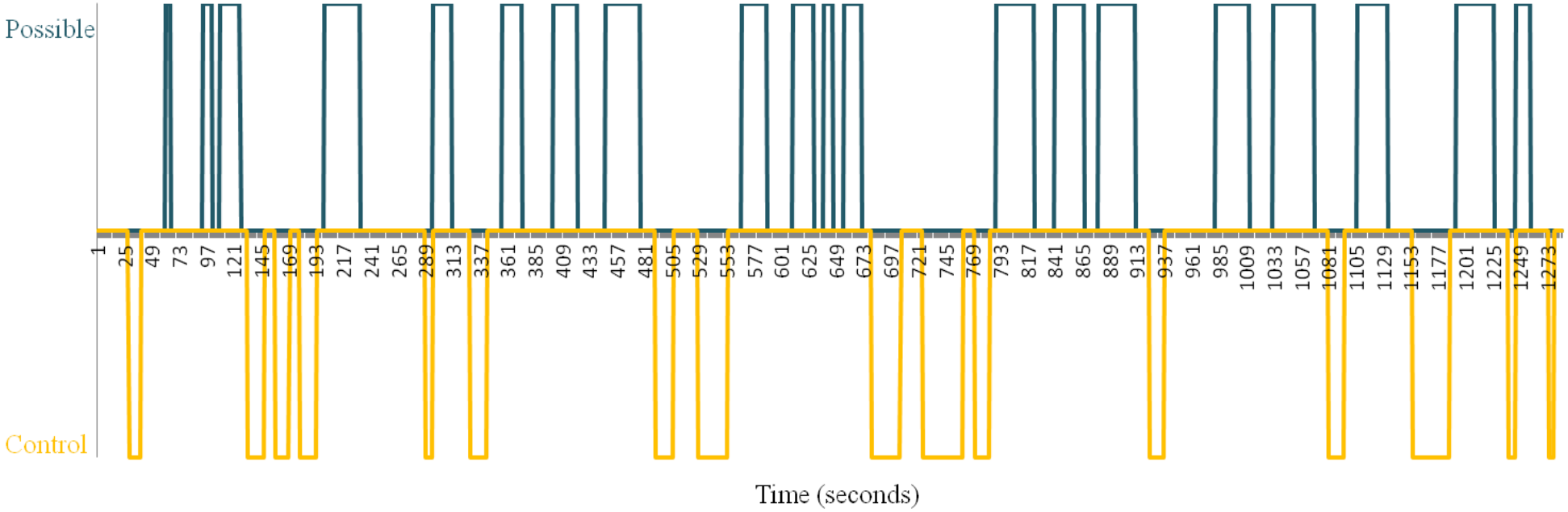
Table IV.I. "Potential" Scenes in fMRI study

Clip	Scene Description	Start Time (secs)	End Time (secs)	Duration (secs)
1	Dismembered head	60	64	5
1	Leg sticking up out of car	93	100	7
1	Fire fighter carrying baby	108	125	18
3	Eye Operation	199	230	32
4	Man trapped in grey car	295	310	16
4	Woman trapped in van	355	372	18
4	Woman faints in van	400	421	22
4	Leg wound	446	476	31
5	Car hitting the boy	565	587	23
6	Body sticking out of car	610	628	19
6	Bodies moved and covered	637	645	9
6	Firemen lifting bodies	655	670	16
8	Leg operation	789	821	33
9	Bodies on the street	840	865	26
9	Bodies being placed into coffins	878	910	33
10	Shaving cut across throat	981	1010	30
11	Student being intubated	1031	1067	37
12	Slow motion ricocheting of boy inside the car injuring the others	1105	1131	27
14	Elephant mauling keepers	1192	1225	34
15	Couple pinned to wall	1244	1256	13

Table VI.II. "Control" Scenes in fMRI study

Clip	Scene Description	Start Time (secs)	End Time (secs)	Duration (secs)
1	Arrival of Fire truck	28	38	11
2	Eye make up 1	132	146	15
2	Eye make up 2	156	168	13
2	Eye make up 3	178	192	15
4	St John's ambulance men	288	294	7
4	Fire men with equipment to try and rescue woman from van	327	341	15
4	Paramedics checking the man's non damaged leg	490	505	16
5	Boy playing in the garden	527	552	26
7	Nurses in operating theatre 1	679	704	26
7	Nurses in operating theatre 2	724	759	36
7	Nurses in operating theatre 3	770	782	13
10	Man shaving as normal	923	935	13
12	Couple in town square before meeting friends	1080	1093	14
13	Elephants performing in circus tent	1154	1185	32
15	Couple on wall	1238	1243	6
15	Girl in hospital bed	1273	1277	5

Figure IV.I. Film time course by scene type. The timing and duration of the 20 possible scenes (which became either Flashback or Potential scenes) and the 16 Control scenes in the fMRI study.



Appendix V

Positive film used in the behavioural experiment presented in Chapter 5

Positive Film used in Chapter 5

Running time: 24 minutes 55 seconds

Description: A compilation of 19 individual clips depicting positive emotions, including excitement, jubilation and high levels of enthusiasm. The clips were selected with a predominantly student audience in mind. The positive films were developed by the author for the experiments presented in this thesis.

Film Clips

Clip 1 – Colossus Rollercoaster. The scene depicts 30 seconds of a rollercoaster ride "Colossus" in Thorpe Park, a theme park located in the South of England. The scene involves a number of loops and turns that the watcher experiences.

Clip 2 – Oxford May Day Celebrations. The May Day Celebrations are an Oxford tradition that occurs in the early hours of the morning on May 1st. Due to the locations of the celebrations Magdalen Bridge is closed off by the police until later in the morning. There are two scenes in the clip that may cause involuntary memories; protestors getting through police barriers and students jumping off the bridge. The clip starts with students attempting to get past the police onto the bridge, leading into the first possible involuntary memory scene as one of them makes it over the barrier. The clip then moves onto the bridge. The clip ends with the second possible involuntary memory scene as students jump off the bridge into the river below.

Clip 3 - Tom Cruise on the Oprah Winfrey Show. The clip is taken from the Oprah Winfrey show aired in May 2005. The involuntary memory scene focuses on Tom Cruise declaring his love for Katie Holmes and jumping up and down on the sofa in his elevated mood.

Clip 4 - Pendulum at Glastonbury, 2009. Pendulum is a British-Australian Drum and Bass/electronic rock band. The clip is the beginning of Pendulums remix of Calvin Harris, I'm not alone. After the build up, the involuntary memory scene is characterised by shots of the crowd and stage with multiple lasers coming from the stage.

Clip 5 - Freestyle Skiing. The clip follows a series of skiers travelling up a mountain. The involuntary memory scene is that of the skiers performing a jump, in the first person.

Clip 6 – Young musician of the year 2010. Lara Omeroglu was the winner of the BBCs Young musician of the year in 2010. The clip shows her performance from different angles, including angles where the viewer can directly observe her playing. The scene then

ends with the rapturous applause, seen from both close up shots of the audience and short from the stage.

Clip 7 - Sky Diving. The clip is part of the footage from a sky dive that took place over Lake Taupo in New Zealand. The clip follows the sky diver as they make their way to the plane, and in the plane itself. The involuntary memory scene is that of the sky diver jumping out of the plane and the subsequent footage of their fall.

Clip 8 - Finishing Oxford Final University Examinations. A more recent tradition at Oxford University is to meet finalists after they finish their last exam with champagne/sparklers/party poppers etc. The clip depicts people coming out of exams, with the involuntary memory scene focusing on the moment when a friend of the people filming emerges, greeting her with champagne and throwing confetti

Clip 9 – Oxford University Graduation. This clip focuses on an individual whose graduation it is. The scene has two main points of interest. This first is the interview with the individual graduating, talking about how he feels about graduating. The second is the graduation itself, with the gowned students being congratulated by the chancellor of Oxford University.

Clip 10 - Night Clubbing. This scene is taken from a promotional video for a night club. The clip shows a series of shots of people dancing, taking photos and of lasers across the club.

Clip 11 - England rowing win; 2004 Olympic games. The scene depicts the end of the coxless fours rowing race in which England marginally beat Canada to win their 4th Gold in 4 Olympic Games. The end of the scene shows the England rowers celebrating and congratulating each other on their win.

Clip 12- Base Jumping. Base jumping involves jumping from an elevated object (either a cliff, bridge, building or antenna tower) with only a late release parachute, or, more recently, a 'wing suit' which allows the jumper to glide before releasing a parachute to land. The clip shows two jumps. The first jump scene is a man on his own, who counts down and then jumps off a cliff, the clip ending just after the parachute release. The second scene is a group jump with wing suits, where the gliding ability of the suits can be seen before the scene ends.

Clip 13 – The Oscars. This clip is the announcement of the winner of best actor in a leading role, the award going to Tom Hanks for his performance in Forest Gump. The involuntary memory scene is that of the audience applause and the standing ovation given

to Tom Hanks, seen both as close ups of individual members of the audience, and more general larger shots of the audience.

Clip 14 - Seattle Flash mob. A flash mob is the sudden assembling of a large group of people in a public space who perform an act, and then subsequently rapidly disperse. They have no particular reason; they are designed purely for entertainment. The clip is taken from a flash mob that occurred in Seattle, Westlake district in April 2010. The clip begins with general shots of people in the area. The involuntary memory scene occurs when music suddenly begins and people start dancing, gradually including more and more people, with spectators gathering to watch.

Clip 15 - Philip DeFranco Show. The Philip DeFranco show is a YouTube channel in which Philip DeFranco presents a roundup of the news in a chatty and spontaneous manner. The involuntary memory scene focuses around the spontaneous deaths of thousands of fish and birds at the start of January 2011. DeFranco talks about possible reasons for why this might be, ranging from global warming to vampire robots, and then changing the subject to a map of how most people view Europe.

Clip 16 – Psychedelic. This scene is based around bipolar patients' descriptions of mental images that they have during mania. The scene contains various shapes moving around the screen, changing form and colour, before merging into a stripped colour tunnel which the viewer then passes through.

Clip 17 – Gambling win. In 2004 Ashley Revell gambled his life savings (after selling all his possessions) on a roulette spin in a casino in Las Vegas. The clip shows the build up to the moment where Ashley chooses red. The involuntary memory scene depicts the celebration of Ashley and his friends and family when the roulette wheel stops on red.

Clip 18 - "You in love?" You in love is an artistic piece created by Sarah Cane in 2002. This clip is a slightly shorter version of the full piece. The scene shows people walking past a camera, subtly looking into the camera and smiling.

Clip 19 - Michael McIntyre's Comedy Roadshow. Michael McIntyre's comedy roadshow features stand-up comedy from Michael McIntyre and up and coming new comedians. The clip starts with Michael McIntyre, with the involuntary memory scene focusing on him pretending to go nightclubs called "Man United" and "Man City". Comedian Daniel Sloss is then introduced, with the second involuntary memory scene involving his story of him and his girlfriend's father.

Table V.I. Possible involuntary memory scenes for the positive film used in Chapter 5

Clip	Scene Description	Start Time (secs)	End Time (secs)	Duration (secs)
1	Colossus Rollercoaster	8	38	30
2	May Day; Police Barrier	52	75	23
2	May Day; Jumping from the bridge	132	158	26
3	Tom Cruise; Jump on sofa	202	230	28
4	Glastonbury; Start of Pendulum	244	263	19
4	Glastonbury; Pendulum lasers	294	327	33
5	Skiing; Jump	356	370	14
6	Young Musician; Applause	454	478	24
7	Sky Diving; Jump & fall	532	558	26
8	Finishing Oxford Exams	595	619	24
9	Graduation; Ceremony	649	683	34
10	Night clubbing	723	751	28
11	Rowing; England win gold	764	799	35
12	Base Jumping; Single jump	822	837	15
12	Base Jumping; Group jump	869	880	11
13	Oscar win; Tom Hanks announced	952	989	37
14	Flashmob; Dancing	1017	1043	26
15	Philip DeFranco Show	1081	1108	27
16	Psychedelic shapes	1121	1150	29
17	Gambling; Win & celebrating	1281	1303	23
18	“You in love?”	1319	1349	30
19	Michael McIntyre; Dancing	1392	1418	26
19	Daniel Sloss; Story	1460	1494	34

Appendix VI

Positive film used in Experiment 2 of Chapter 6

Positive Film used in Experiment 2 of Chapter 6

Running time: 18 minutes 21 seconds

Description: A compilation of 16 individual clips depicting positive emotions, including excitement, jubilation and high levels of enthusiasm. The clips were selected with a predominantly student audience in mind. The film was refined from study 1 to be suitable for future work involving fMRI. Edits were made to each scene to encompass the exact moment of each involuntary memory. Scene times and the number of potential involuntary memory scenes were also matched to the trauma film developed for fMRI (used in study 3). Additional "control" scenes (expected not to induce involuntary memories) were included that were not present in the film used in study 1 to provide suitable matched controls for each of the potential scenes. The film contained 19 "potential scenes" (possibly inducing involuntary memories) and 16 control scenes.

Film Clips

Clip 1 – Thorpe park. The clip starts with a children's "merry-go-round" ride as a control scene. The clip then continues into the 32 second scene of the rollercoaster ride "Colossus" involving a number of loops and turns that the watcher experiences.

Clip 2 – Oxford May Day Celebrations. The May Day Celebrations are an Oxford tradition that occurs in the early hours of the morning on May 1st. The clip starts on May morning, seeing the early risers enjoying the morning on Magdalen Bridge. The clip then moves towards a group of people watching students jump off the bridge into the river below.

Clip 3 - Tom Cruise on the Oprah Winfrey Show. The clip is taken from the Oprah Winfrey show aired in May 2005. The involuntary memory scene focuses on Tom Cruise declaring his love for Katie Holmes and jumping up and down on the sofa in his elevated mood.

Clip 4 - Freestyle Skiing. The clip follows a series of skiers travelling up a mountain. The involuntary memory scene is that of the skiers performing a jump, in the first person.

Clip 5 – Young musician of the year 2010. Lara Omeroglu was the winner of the BBCs Young musician of the year in 2010. The clip shows her performance from different angles, including angles where the viewer can directly observe her playing. The scene then ends with the rapturous applause, seen from both close up shots of the audience and short from the stage.

Clip 6 - Sky Diving. The clip is part of the footage from a sky dive that took place over Lake Taupo in New Zealand. The clip follows the sky diver as they make their way to the plane, and in the plane itself. The involuntary memory scene is that of the sky diver jumping out of the plane and the subsequent footage of their fall.

Clip 7 - Finishing Oxford Final University Examinations. A more recent tradition at Oxford University is to meet finalists after they finish their last exam with champagne/sparklers/party poppers etc. The clip depicts people coming out of exams, with the involuntary memory scene focusing on the moment when a friend of the people filming emerges, greeting her with champagne and throwing confetti

Clip 8 – Oxford University Graduation. This clip focuses on an individual whose graduation it is. The scene has two main points of interest. This first is the interview with the individual graduating, talking about how he feels about graduating. The second is the graduation itself, with the gowned students being congratulated by the chancellor of Oxford University. In addition to the same clip used in study 1, a longer introduction to the ceremony is shown, providing a control scene for the graduation

Clip 9 - Night Clubbing. This scene is taken from a promotional video for a night club. The clip shows a series of shots of people dancing, taking photos and of lasers across the club.

Clip 10 - Base Jumping. Base jumping involves jumping from an elevated object (either a cliff, bridge, building or antenna tower) with only a late release parachute, or, more recently, a 'wing suit' which allows the jumper to glide before releasing a parachute to land. The clip shows two jumps. The first jump scene is a man on his own, who counts down and then jumps off a cliff, the clip ending just after the parachute release. The second scene is a group jump with wing suits, where the gliding ability of the suits can be seen before the scene ends. An additional control scene was included in between the two jumps.

Clip 11 - England rowing win; 2004 Olympic games. The scene depicts the end of the coxless fours rowing race in which England marginally beat Canada to win their 4th Gold in 4 Olympic Games. The end of the scene shows the England rowers celebrating and congratulating each other on their win.

Clip 12 – The Oscars. This clip is the announcement of the winner of best actor in a leading role, the award going to Tom Hanks for his performance in Forest Gump. The involuntary memory scene is that of the audience applause and the standing ovation given

to Tom Hanks, seen both as close ups of individual members of the audience, and more general larger shots of the audience.

Clip 13 - Seattle Flash mob. A flash mob is the sudden assembling of a large group of people in a public space who perform an act, and then subsequently rapidly disperse. They have no particular reason; they are designed purely for entertainment. The clip is taken from a flash mob that occurred in Seattle, Westlake district in April 2010. The clip begins with general shots of people in the area. The involuntary memory scene occurs when music suddenly begins and people start dancing, gradually including more and more people, with spectators gathering to watch.

Clip 14 – Psychedelic. This scene is based around bipolar patients' descriptions of mental images that they have during mania. The scene contains various shapes moving around the screen, changing form and colour, before merging into a stripped colour tunnel which the viewer then passes through.

Clip 15 – Gambling win. In 2004 Ashley Revell gambled his life savings (after selling all his possessions) on a roulette spin in a casino in Las Vegas. The clip shows the build up to the moment where Ashley chooses red. The involuntary memory scene depicts the celebration of Ashley and his friends and family when the roulette wheel stops on red.

Clip 16 - Michael McIntyre's Comedy Roadshow. Michael McIntyre's comedy roadshow features stand-up comedy from Michael McIntyre and up and coming new comedians. The clip starts with Michael McIntyre on stage, with the involuntary memory scene focusing on him pretending to go nightclubs called "Man United" and "Man City".

Table VI.I. "Potential" Scenes for positive film used in Chapter 6

Clip	Scene Description	Start Time (secs)	End Time (secs)	Duration (secs)
1	Colossus Rollercoaster	38	69	32
2	May Day; Jumping from the bridge	127	133	7
3	Tom Cruise; Jump on sofa	187	202	16
4	Skiing; Jump	227	242	16
5	Young Musician Playing	274	299	26
6	Sky Diving; Jump & fall	377	390	14
7	Finishing Oxford Exams	426	438	13
8	Graduation; Interview	451	467	17
8	Graduation Ceremony in Sheldonian theatre	506	541	36
9	Night clubbing	554	569	16
10	Base Jumping; Single jump	592	608	17
10	Base Jumping; Group jump	636	655	20
11	Rowing; England win gold	668	692	25
12	Oscar win; Tom Hanks announced	779	811	33
13	Flashmob; Dancing	839	866	28
14	Psychedelic shapes	877	898	22
15	Gambling; Placing bet and spin	998	1028	31
15	Gambling Win & celebration	1029	1051	23
16	Michael McIntyre; Dancing	1076	1100	25

Table V.II. "Control" Scenes for positive film used in Chapter 6

Clip	Scene Description	Start Time (secs)	End Time (secs)	Duration (secs)
1	Merry-go-round	10	31	22
2	Spectators on the bridge	83	99	17
2	Spectators looking at the river	106	120	15
3	Crowd on the Oprah Winfrey show	155	173	19
4	Skiers after the ski jumps	250	262	13
5	Applause for the young musician	305	324	20
6	Skydivers going to the plane and view from the plane	337	369	33
7	Friends waiting for students to finish examinations	399	419	21
8	View in Sheldonian theatre waiting for graduation ceremony to begin	476	498	23
10	Basejumpers preparing before group jump	616	629	14
12	Oscar nominations	717	738	22
12	Oscar nominations	747	770	24
13	Normal street before flashmob	824	830	7
15	Gambling Explanation by croupier	910	926	17
15	End of gambling explanation, talking to the croupier	933	951	19
15	Gambling build up before placing bet	958	983	26

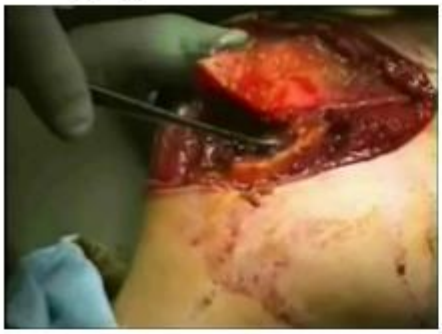
Appendix VII

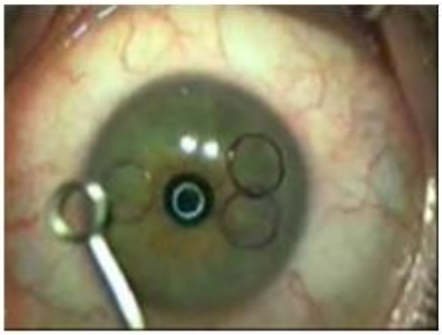
Sample of visual recognition memory test used in the neuroimaging experiment presented in Chapter 3

Example possible stills from film

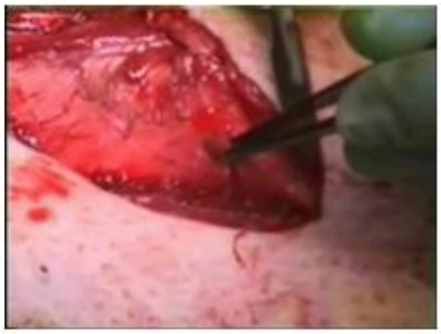
Example emotional stills used as foils

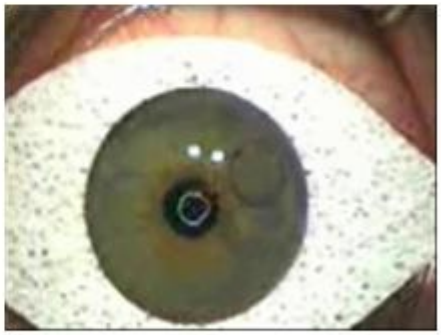
Example possible stills from film





Example emotional stills used as foils





Example control stills from film

Example control stills used as foils

Example control stills from film

Example control stills used as foils

Appendix VIII

Visual recognition memory test used in the behavioural experiment presented in Chapter 5

Instruction Slide:

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celebrity01.blogspot.com


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Appendix IX

Visual recognition memory test used in Experiment 2 of Chapter 6

Instruction Slide:

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Appendix X

Involuntary memory diary used across studies

Thank you for completing the diary. Your participation is very much appreciated. Don't forget to give back the completed diary, then you will then be given payment and information about the purpose of the study.

Thank you!!!

Follow up Session Appointment Card

Date:

Time:

Duration:

If you have any questions or problems, please do not hesitate to contact me at ian.clark@psych.ox.ac.uk

If you would like to discuss anything related to the experiment or your reactions to it, please do not hesitate to contact the responsible Investigator, Dr Emily Holmes at any point in the week after the film or beyond. Dr Holmes can be contacted at the University Department of Psychiatry Warneford Hospital, Warneford Lane, Oxford, OX3 7JX tel: 01865223912 or emailed at emily.holmes@psych.ox.ac.uk

PARTICIPANT DIARY

Participant No.:

Date started:

Date completed:

Introduction

❖If over the next week you experience any **involuntary memories about the film you have just watched,** I would be very grateful if you could note them down in the diary.

❖What goes through our minds can either take the form of words and phrases ("verbal thoughts"), or it can be like mental pictures ("images") in your minds eye. Although mental 'images' often take the form of pictures they may also involve sounds and bodily sensations too. Please note down all involuntary memories from the film in this diary.

❖For each intrusion, mark 'I' (mental image), 'T' (thought) or 'IT' (image and thought) on pages 3 and 4 for the corresponding time of day, or **write down that you have had Zero** in that time frame. Then <u>for every single involuntary memory</u> you have had fill in the details of the content on pages 5, 6 and 7. **Please write an entry for each involuntary memory even if you have several the same or involuntary memories that occur one after the other.**

❖If you are on occasion unable to record details, please make sure you record that an involuntary memory has occurred and the date.

❖Remember, **involuntary memories of the film can be very short/fleeting and fragmented**. We still would like to know about them in the diary!

PLEASE KEEP THIS DIARY – IT IS VITAL FOR THE EXPERIMENT.

THANK YOU!!!!

Date / Day of involuntary memory	What was the content of the involuntary memory of the film? (e.g. subject matter)	What, if anything, triggered the involuntary memory?	Your emotional rating and vividness rating of the involuntary memory on a scale of 1-5 Emotion: 1-Very Negative to 5-VeryPositive Vividness: 1-Cloudy and imageless to 5-Vivid as experiencing again	
			Emotion	Vividness

Mark each involuntary memory as either an 'i' for a mental image, a 't' for a verbal thought or an 'it' if both happen together. Otherwise write '0' for that time frame.

Example Day	
Morning	0
Afternoon	0
Evening & Night	i i

Day 1 Date:	
Morning	
Afternoon	
Evening & Night	

Day 2 Date:	
Morning	
Afternoon	
Evening & Night	

Day 3 Date:	
Morning	
Afternoon	
Evening & Night	

Please remember to fill in the content page for each involuntary memory indicated. Thank you

p3

Date / Day of involuntary memory	What was the content of the involuntary memory of the film? (e.g. subject matter)	What, if anything, triggered the involuntary memory?	Your emotional rating and vividness rating of the involuntary memory on a scale of 1-5 Emotion: 1-Very Negative to 5-Very Positive Vividness: 1-Cloudy and imageless to 5-Vivid as experiencing again	
			Emotion	Vividness

p6

Day 4 Date:	
Morning	
Afternoon	
Evening & Night	

Day 5 Date:	
Morning	
Afternoon	
Evening & Night	

Day 6 Date:	
Morning	
Afternoon	
Evening & Night	

Day 7 Date:	
Morning	
Afternoon	
Evening & Night	

Please remember to fill in the content page for every involuntary memory indicated. Thank you

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Content Page

Involuntary memories of the film can take the form of **mental images** (that is 'you see' or 'hear' it in your minds eye) or **verbal thoughts** (words or phrases; an internal dialogue)

Date / Day of involuntary memory	What was the content of the involuntary memory of the film? (e.g. subject matter)	What, if anything, triggered the involuntary memory?	Your emotional rating and vividness rating of the involuntary memory on a scale of 1-5 Emotion: 1-Very Negative to 5-Very Positive Vividness: 1-Cloudy and imageless to 5-Vivid as experiencing again	
			Emotion	Vividness
Day 1 EVE	I saw a crowd cheering me on	Playing rugby for college	5	4
Day 1 EVE	I saw the broken wreckage of a car	Hearing the sound of brakes in the rain	2	2

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Appendix XI

Protocol used in the neuroimaging experiment presented in Chapter 3

When Booking in Participant

1. Ensure that the participant is scanner safe before confirming fMRI slot. Email them the fMRI screening form
2. Book interview room in OCMR for (preferably) before the scanning session (30 mins) and after the scanning session (15 mins)
3. Create participant pack with Info Sheet, Consent from, fMRI Screening Questionnaire, MDQ, SUIS, BDI, Altman, EPQ, IFES, STAI-T, PICS, pre film PANAS 10, VAS. Post film, PANAS10, VAS. Attention to film, processing style of film. Diary. Diary checklist. Recognition test (verbal and visual), diary compliance, IES-R, behaviour change, emotionality ratings. Debrief, debrief sig, payment form

Before starting to test

1) Arranged to meet participant at OCMR 30 mins before start of scanner slot.
2) Fill-in participant number on all forms before participant arrives.

After participant arrives

1) Greet Participant:

*"Good morning/afternoon…, Thank you for coming. First we have to get some preliminary paper work done. Then I will get you to do a few questionnaires for about **30 mins**, following which we will be going into the scanner room and starting the main part of the experiment. We will need to spend about **60 mins** in the scanning room although the film is only 20 mins long. After the scanning session we will need **15 mins** to finish some more measures before we are finished for today.*

Now, I previously e-mailed you a copy of the Information Sheet but could you read it again, ask any questions you may have, and if you are happy with it sign the Consent Form. I also need you to complete this form regarding the scanner and your safety. Feel free to ask any questions."

2) Give **Information Sheet** to read. *Do you have any further questions?*
3) Give **Informed Consent form** to them to fill in, make sure participants signs and adds contact details (phone and email). *Would you like a copy?*

4) Give **OCMR Participant Form** – Yellow Sheet

5) Give **Participant Details** form to them to fill in.

Can I check you have placed all metal objects, credit cards, mobile phone etc. in this bag. I will lock this away for you and return everything to you once you are out of the scanner room. Thanks

6) Give **MDQ, SUIS, BDI, Altman, EPQ, IFES, STAI-T, PICS**

7) Give **Pre-film PANAS and VAS mood ratings**:

Please fill in this short questionnaire about how you are feeling right now. Do not think about your answers too much, but give the first response that comes to mind. Please use the full scale, not just the extremes.

8) Explanation of film & scanner:

OK in a few minutes I will take you into the Scanner Room. I will introduce you to the radiographer who will be conducting the scans and who will be speaking to you once you are in the scanner via an intercom. The radiographer will also help you to lie in the scanner and get you settled. There will be a headpiece that will sit over your head and allow you to see the screen where we will be projecting the film.

Once you are lying down, I would like you to check that you can see all the text that will be displayed on the screen. We will then slide you into the scanner and you will be asked to check that you can still see all the text on the screen. If not we can adjust the headpiece so that you can. Once you are settled we will start the first scan. Once the machine is scanning it can get quite noisy but you will have headphones to reduce the noise and so that you can hear the radiographer speaking to you.

After the first short scan the radiographer will speak to you and when you are ready the film will then start and will run for 20 mins and the scanner will be running continuously during this time.
After the film has finished we will take you out of the scanner for a short break and to let you walk around. I'll then get you to fill out a few more questionnaires. We'll then put you back in the scanner to do the final set of scans, which takes about 15 minutes.

Please remember that the film consists of 15 or so scenes of potentially distressing footage, including: real police footage of road traffic accidents, real footage of surgical operations, and road safety film.

The film will start with the same blue screen you saw when you first got in the scanner and it will have text reminding you to lie still and be absorbed in the film. Then you will get a new screen with text introducing the first scene. Each scene will start with the same blue screen and some text explaining the events that are about to occur.

Please lie still otherwise the scans will be blurred (it is just like taking a photograph) and pay close attention to the video. Imagine you are really there, at the scene. Watch the film and do not look away, shut your eyes, or flinch. You may be asked questions about the content of the film later on. It is really important that you are absorbed or immersed in the events you are witnessing as if you were really there taking part. Please don't distance yourself from the events.

Both the radiographer and I will be in the control room next door watching you at all times. You will also have a button to press if you want to stop the session at any time.

OK, so what are the three things you need to remember about watching the film:
(i) make sure you can see all the text on the screen even once you have been slid into the scanner;
(ii) watch the film at all times, remaining still, not flinching or closing your eyes;

(iii) watch the film as if you are really involved in the scenes, as if you are really there watching the events unfold.

Taking participant into Scanner room:

1) **Scanning Sequence is in N12_05**

2) Set Up **N12_05, Trauma film experiment.** Make sure this starts loading after the participant has confirmed they can see the screen

3) Check the projector is on and that the participant can see everything.
4) Remind participant about keeping still and being absorbed in the film as if really there.
5) **Remind radiographer to tell participate to lie still and be absorbed in the film after localiser and before EPI series.**

After the Video/ Scans

Take participant out of the scanner.

Ask participant to fill out **post-film PANAS and VAS mood ratings, Attention to film, processing style of film**

Please fill in these short questionnaires about how you are feeling right now, after the film. Do not think about your answers too much, but give the first response that comes to mind.

On completion say:

We now need to do a few final scans. This will take about 10-15 mins. During this time images about the film you've just seen may spontaneously pop into your mind without you thinking about it. These images can be fuzzy or fragmented as well as clear; they can also be brief and very fleeting. This is called an involuntary memory. If you do happen to experience an image based involuntary memory then please press one of the buttons on the box as soon as it occurs. Please keep doing this for as many image intrusions as you have (You may well have none and that is fine to simply don't press the buttons!) If you deliberately bring an image to mind during this time please don't record it by pressing the buttons, only images that just seem to appear to you should be counted.

Put participant back in the scanner.
Load sequence **N12_05; Free think**
On completion, perform structural scan.

Remove participant from scanner

Finishing experiment:

1) Explanation of weekly **diary**.
    a. Move to sit next to participant at desk
    b. Open diary and go through introduction/explanation text on page 1

*It may that over the next few days bits of the film will **pop to your mind** when you **weren't expecting** them to. This is what we call an **involuntary memory or a flashbacks***

*What goes through our minds can either take the form of words and phrases, "verbal thoughts" or mental images. Although mental images often take the form of pictures they could also include sounds and bodily sensations too. These flashbacks can be fuzzy or fragmented as well as clear; they can also be brief and very fleeting – like a quick flashback of the film. We are interested in knowing about **all** these types of images that you have of the film.*

[Check participant understands by asking one or several of the following & giving feedback.] *Do you understand what I mean by a mental image? Can you give me an example?*

If you have any intrusions/ involuntary memories of the film you have just watched over the next week, please record each one as soon as possible in this diary. Please keep the diary in your bag or next to your bed and start filling it in from now. It's really important that you keep it as accurately as possible.

On page 3 and page 4, fill in one of the little boxes every single time you have an involuntary memory of the film **[demonstrate what to do on the diary]***; **I** for image, **T** for thought or **IT** if it was both. So if you have 3 intrusions in the afternoon, then 3 of the little boxes should be filled. If you have had none during that time period then write zero or cross that section of the day out. Make sure that you have completed each of the three time periods (Morning, Afternoon and Evening/Night) as they occur. If you are unable to complete the diary at the time when you experience an involuntary memory please make sure you complete each time period at least once a day. Next, fill in the details of each involuntary memory you have had on page 5, putting down the day and time. We then need to know the content of the intrusion. This can be brief but we need to be able to match any intrusions you have to the film so please be as clear as possible* **[refer to examples]** *for example you may spontaneously remember a car crash, which you would describe like this* **[point to example].** *We would also like to know your emotional and vividness rating of each flashback, could you please write a number, 1 to 5, in this box, from 1 being very negative/cloudy & imageless to 5 being very positive/as clear and vivid as if it was experienced again.*

For <u>every little box you fill in after having an intrusion there should be a matching line in the back of the diary</u>. If you are unsure of the detail, please just note it down in the diary anyway and we will go over it with you later when you return.

2) Check understanding of the diary. If unsure that the participant understands then ask them to explain back to me.
3) If they had any flashbacks in the scanner, get them to write what they were in now
4) Reemphasise the importance of keeping the diary

5) Explanation of **follow up session**

You will finish this diary on ……, in 7 days time. At that point, you will be invited to return for a follow-up session (at OCMR) Please bring this diary with you to the follow up session. You will be asked to fill in a couple of questionnaires, and you will then be given the payment and information about the purpose of the study. Any questions?

6) Fill in dates on diary. & show participant out

Follow-Up Session:

DIARY INTRUCTIONS [Information for the experimenter]:
When a participant returns with their diary you must go though it straight away. Do not leave it until the participant has gone, this way you can check the details in person while the information is still fresh in their minds:

Check diary is completed correctly. Complete any missing information, with the participants help if necessary, e.g. check there is a description for every single box checked with an intrusion on page 3 and 4 of the diary. If not then ask the participant if they can remember and describe the intrusion that went with the checked box, or mark if not.

Read all the intrusion descriptions in the diary. If they are unclear or you don't recognise them as being from the film ask for more details until you can identify it. If the intrusion is not from the film it cannot be included.

It might be helpful to create a list of film clips with a brief description if you are not familiar with the film.

Note

Sometimes participants do not realise that very fleeting or fragmented pictures are the kind of mental images that should have been recorded in the diary. Participants often think experiencing an intrusion will be like having an almost complete memory for the film, like a photograph or complete movie in their minds eye, but this is not the case. This is why it is important to give a good definition at the start.

Instructions for follow up session

1) Welcome back!
2) Check diary is completed correctly.
3) Check each intrusion in the content sheet for its spontaneity. (Discount intrusion that is not spontaneous.)

Was this intrusion spontaneous, rather than being part of a conscious attempt to remember parts of the film or experiment.

4) Do **Visual Memory Test**
5) Do **Verbal Memory Test**
6) Give **Diary Compliance**
7) Give **Impact of Events Scale.**
8) Give **Behaviour Change**

9) **Ask participants to rate the Emotionality of each Scene and Clip based on how the felt when the originally saw the film.**

10) Ask participants if they have any concerns having taken part in the experiment or if they feel disturbed. (Contact responsible investigator if feel concerned.)
11) Debrief participants
12) Fill out payment sheet
13) Future Participant Form.
14) Thank participants for taking part.
15) Show participants out.

Appendix XII

Protocol used in the behavioural experiment presented in Chapter 5

Before participant arrives:

1) Create a Participant Pack. This should have a complete set of forms (Participant Info, Consent Form, Demographics, MDQ, BDI, HPS, STAI-T, Altman, O-LIFE, EPQ, SUIS, Attetnional Control Scale, IFES, PICS, VAS, (pre film, post film), emotional response to film questionnaire, film compliance, involuntary memory checklist, Diary, post diary VAS, involuntary memory questionnaire, diary compliance, recognition memory test, behavioural change questionnaire, IES positive version, post task VAS.
2) Determine subject number from random number sequence and write participant number on all questionnaires.
3) Equipment Check: Always check the computers and projetor are working before running a participant.
4) Open the Film on Desktop of PC and reduce, ready to play when needed
5) Check all items are ready: Timer, participants pack, pens

After participant arrives

6) Greet Participant:

> *"Good morning/afternoon…, Thank you for coming. First we have to get some preliminary paper work done but then we will be starting the experiment. The experiment will take roughly 1 hour. Could you read this, and if you are happy with it sign the consent form. Feel free to ask any questions."*

7) Give **Information Sheet** to read. *Do you have any further questions?*
8) Give **informed consent form** to them to fill in, make sure participants signs and adds contact details (phone and email). *Would you like a copy?*

9) Give **Participant Detail** form to them to fill in.
10) Can I check you turned off your mobile phone please? Thanks
11) Give **MDQ**
12) Give **BDI**

> *Please fill this in, about how you've been feeling for the past two weeks, including today.*

13) **HPS**
14) Give **Trait questionnaire** (STAI-Y2)

> *Please fill this in, about how you generally feel; whether it's Almost Never or Almost Always. Notice that Questions are phrased so your answers will probably swap sides.*

15) Give Altman; *Most of us have normal fluctuations in attention and mood. These questions are looking for something a bit more marked, think as to whether other people, friends/family would notice these changes, are they out of character for you? Are they lasting for a sustained period of time? It is these changes that we are interested in.*
16) Give **O-LIFE, EPQ, SUIS, ACS, IFES, PICS**

17) Give **Pre-film VAS** mood ratings (Anxious, motivated, irritable, sad, impulsive, hyper, depressed, elated, good) and **PANAS**: Emphasise to respond with how they are feeling **right at this very moment**. Don't let participant know film is about to be played

Please fill in this short questionnaire about how you are feeling right now, while you've been filling out the questionnaires here in the lab. Do not think about your answers too much, but give the first response that comes to mind. Please use the full scale, not just the extremes.

18) Explanation of film:

In a few minutes you will see a short film of about 25 minutes. Please sit still and pay close attention; you will be asked questions on it later. I don't want you to watch the film like you normally would, I want you to immerse yourself in the events depicted, imagine you are ***really there****, at the scene, taking part in the events, as though it's happening to you. For example, the first scene is of a rollercoaster, so I want you to imagine that you're actually on it, experiencing the twists and turns as they are happening. So if you're really immersed you might feel the emotions and physical sensations as if you were at the event. Some of the events might be ones that you haven't been involved in before, even so try and focus on feeling involved in the event as well as you can*
Do you know what I mean? How I want you to watch the film [get them to explain it back to you].
Watch the film and try not to look away or shut your eyes. I will be just outside should there be any problems, and will come in when the film ends. Any questions?

19) Turn off the lights / close blinds.
20) Start the video, the timer and the heart rate monitor
Experimenter exits room and waits outside.

<u>After the video</u>

1) Experimenter enters room.
2) Turn on the lights and turn off the film
3) Participant to fill out **VAS mood ratings, PANAS Post film [how you feel after watching the film], emotional response to film and attention to film rating**

Please fill in this short questionnaire about how you are feeling right now. Do not think about your answers too much, but give the first response that comes to mind.

Finishing experiment:

<u>Explanation of weekly diary</u>
It may that over the next few days bits of the film will ***pop to your mind*** *when you* ***weren't expecting*** *them to. This is what we call an* ***involuntary memory or a flashbacks***

What goes through our minds can either take the form of words and phrases, "verbal thoughts" or mental images. Although mental images often take the form of pictures they could also include sounds and bodily sensations too.

Mental images can be fuzzy or fragmented as well as clear; they can also be brief and very fleeting – like a quick flashback of the film. We are interested in knowing about ***all*** *these types of images that you have of the film.*
[Check participant understands by asking one or several of the following & giving feedback.] *Do you understand what I mean by a mental image? Can you give me an example?*

If you have any intrusions/ involuntary memories of the film you have just watched over the next week, please record each one as soon as possible in this diary. Please keep the diary in your bag or next to your bed and start filling it in from now. It's really important that you keep it as accurately as possible.

[Explanation on how to fill out the diary]

On page 3 and page 4, fill in one of the little boxes every single time you have an involuntary memory of the film **[demonstrate what to do on the diary]***; **I** for image, **T** for thought or **IT** if it was both. So if you have 3 intrusions in the afternoon, then 3 of the little boxes should be filled. If you have had none during that time period then write zero or cross that section of the day out. Make sure that you have completed each of the three time periods (Morning, Afternoon and Evening/Night) as they occur. If you are unable to complete the diary at the time when you experience an involuntary memory please make sure you complete each time period at least once a day. Next, fill in the details of each involuntary memory you have had on page 5, putting down the day and time. We then need to know the content of the intrusion. This can be brief but we need to be able to match any intrusions you have to the film so please be as clear as possible* **[refer to examples]** *for example if there were images of crowds cheering in the film, you may have an involuntary memory of this moment which you would describe like this* **[point to example],** *or if this was a negative film, you may have witnessed a car crash, which you would describe like this* **[point to example].** *We would also like to know your emotional rating of each involuntary memory, could you please circle a number, 1 to 5, in this box, where one is very unpleasant, three is neutral and 5 is very pleasant.*
For <u>every little box you fill in after having an intrusion there should be a matching line in the back of the diary</u>. If you are unsure of the detail, please just note it down in the diary anyway and we will go over it with you later when you return.

Fill in dates on the diary with them to get them to engage. Make them do a brief example to check they understand.

Give involuntary memory checklist. Make sure participant is paying attention to the checklist. Get them to read it aloud.

So remember:

Mental images can be pictures in your mind, but also sounds and sensations

Mental images may be fuzzy, very brief or almost like a flash in your mind's eye.

Even if you have several intrusions that are the same please record each individual one in the diary every single time it occurs.

Reemphasise the importance of keeping the diary

Explanation of follow-up session.

> *You will finish this diary on ……, in 7 days time. At that point, you will be asked to return for a follow-up session of this experiment.* (Arrange date and time). *Please bring this diary with you to the follow up session. You will be asked to fill in a couple of questionnaires, and you will then be given the payment and information about the purpose of the study. Any questions?*

Fill in Appointment Card on Diary for follow up session.

Note date of the experiment and follow up date on Participant record sheet.

Say goodbye.

> *Please do not speak to anyone who may take part about the details of the experiment, so as not to affect the behaviour of future participants. Please feel free to contact me at any point in the future if you feel that you need to. Remember your bank details for our next meeting so we can reimburse you as soon as possible, Thank you!*

Show participant out.
File all questionnaires away securely and ensure follow up appointment is in the calendar.

Follow-up Session

DIARY INTRUCTIONS [Information for the experimenter]:
When a participant returns with their diary you must go though it straight away. Do not leave it until the participant has gone, this way you can check the details in person while the information is still fresh in their minds:

Check diary is completed correctly. Complete any missing information, with the participants help if necessary, e.g. check there is a description for every single box checked with an intrusion on page 3 and 4 of the diary. If not then ask the participant if they can remember and describe the intrusion that went with the checked box, or mark if not.

Read all the intrusion descriptions in the diary. If they are unclear or you don't recognise them as being from the film ask for more details until you can identify it. If the intrusion is not from the film it cannot be included.

It might be helpful to create a list of film clips with a brief description if you are not familiar with the film.

Note

Sometimes participants do not realise that very fleeting or fragmented pictures are the kind of mental images that should have been recorded in the diary. Participants often think experiencing an intrusion will be like having an almost complete memory for the film, like a photograph or complete movie in their minds eye, but this is not the case. This is why it is important to give a good definition at the start.

Make sure PowerPoint is open on the computer and the intrusion triggering task is loaded, keep screen off, but PowerPoint show ready.
When participant arrives:

1) Welcome back!
2) VAS post diary.

> *Please fill in this short questionnaire about how you feel right now. Do not think about your answers too much, but give the first response that comes to mind.*

3) Check diary is completed correctly, complete any missing information.
4) Get the participants to recall as much detail about their involuntary memories.
5) Give **recognition memory test**

6) Give **demand / follow up** diary compliance questions.
7) Give **Behaviour Change Questionnaire** and **Impact of Event Scale (for positive film)**
8) Intrusion triggering task:
   Turn on computer screen to show instructions screen:
   I am about to show you a selection of pictures from the film you watched earlier, please sit still and pay close attention to the pictures. There will then be a short break. Please stay seated and do not talk to the experimenter during this period. You can think about anything, with no restrictions. If parts of the film happen to spontaneously pop into your mind during this period I'd like you to make a mark on this piece of paper. Any questions?

9) Show PowerPoint presentation
10) *Remember to mark down any time you have an involuntary thought of the film.* [Start timer: 2 minutes]
11) **VAS post task**
12) Ask participants if they have any concerns about taking part of the experiment or if they feel disturbed. (Contact responsible investigator if feel concerned.)
13) Debrief participants fully and give debrief information sheet.
14) Ask the participant to sign **end of the experiment form**.
15) Fill out payment sheet **if being reimbursed**
    a. **Full name**
    b. **Address**
    c. **Bank account number & sort code**
16) Thank participants for taking part.

Appendix XIII

Protocol used in Experiment 1 of Chapter 6

Before participant arrives:

1) Equipment Check: Always check the computers are working before running a participant.
2) Open the reaction time task on one PC and have the computer games ready on the other PC
3) **Determine subject number and order of conditions [counterbalanced across participants] from random number sequence**

After participant arrives

1) Greet Participant:

> *"Good morning/afternoon…, Thank you for coming. First we have to get some preliminary paper work done but then we will be starting the experiment. The experiment will take roughly 20 minutes. Could you read this, and if you are happy with it sign the consent form. Feel free to ask any questions."*

2) Give **Information Sheet** to read. *Do you have any further questions?*
3) Give **informed consent form** to them to fill in, make sure participants signs and adds contact details (phone and email). *Would you like a copy?*
4) Give **Participant Detail** form to them to fill in.
5) *Can I check you turned off your mobile phone please? Thanks*

6) Say:

"We are now going to start the experiment. The main task you will be performing is a visual reaction time task – you will perform this task with your non dominant hand"

7) Check that the computers are correctly set up so that the reaction time task is on the computer corresponding to the participant's non dominant hand (i.e. if participant is right handed, visual reaction time task should be on left computer). Load visual reaction time task

8) Visual Reaction Time task explanation:

"The visual reaction time task requires you to respond as quickly and accurately as possible to coloured circles that will be presented on the screen. Using your non dominant hand please press the "H" key on the keyboard whenever a green circle appears in the middle of the screen and the "F" key whenever a yellow circle appears. Please try and respond as quickly and accurately as you can to all of the circles. Do you have any questions?

I will now ask you to perform a practice run of the visual reaction time task"

9) Run Visual Reaction Time practice (10 trials). Watch the participant to ensure they have understood the task and are responding correctly and within good time

10) Check with participant that they understand the task

11) Depending on participant number and condition order, ask participant to perform the Visual Reaction Time task as a single task, as a dual task with Tetris or a dual task with Pub Quiz:

Visual Reaction Time task as a single task
1) *"I am now going to ask you to perform the visual reaction time task as a single task. Please respond as quickly and accurately as you can to the coloured circles as they are presented on the screen. Remember; H for a green circle and F for a yellow circle. Any questions?"*

2) Tell participants to start the task when they are ready using the space bar [Lasts approximately 3 minutes depending on participant reaction time]

3) *"Great, thank you very much"*

Visual Reaction Time task as a dual task with Tetris
1) Load Tetris onto computer corresponding to participant's dominant hand

2) *"I am now going to ask you to perform the visual reaction time task as a dual task with the computer game Tetris. You will be playing Tetris with your dominant hand"*

Tetris Explanation:

"*Tetris consists of 7 different shaped blocks which fall from the top of the screen one at a time. Each time you fill a whole horizontal line with the blocks, with no gaps, that line will disappear and give you points. The aim is to make as many of these lines disappear as possible before the screen is filled completely.*

In this particular game I want you to focus on the three blocks that will be falling immediately after the one being played on the right of the screen. Try and work out in your minds eye where best to place these blocks in order to make the most complete lines and get the best score.

Blocks are moved using the 4 arrow keys. Left and right using the left and right cursor keys and rotated using the up cursor key. Each press of the up key rotates the block 90° clockwise. If you are confident that you have the block at the desired rotation and position, you can speed up its descent by pressing the down key.

Do you have any questions concerning Tetris?

While playing Tetris, I'd also like you to perform the visual reaction time task as before using your non dominant hand. Please respond as quickly and accurately as you can to the coloured circles as they are presented on the screen. Remember; H for a green circle and F for a yellow circle. Please try your best to perform both tasks as well as possible. Any questions?

3) Start Tetris. Tetris will count down from 3 seconds. When Tetris game starts press space on the visual reaction time task to start. [Task lasts approximately 3 minutes depending on participant reaction time]

4) *"Great, thank you very much"*

Visual Reaction Time task as a dual task with Pub Quiz
1) Load Pub Quiz onto computer corresponding to participant's dominant hand

2) *"I am now going to ask you to perform the visual reaction time task as a dual task with the computer game Pub Quiz. You will be playing Pub Quiz with your dominant hand"*

Pub Quiz Explanation:

"The Pub Quiz game consists of a single question presented on the screen with 4 possible answers. The aim is to correctly answer as many questions as possible to get as many points as you can.

You do this by using the mouse to select the answer you think is correct. You will then be told whether you are right or wrong. Each time you get an answer right you get awarded points. Get an answer wrong and you lose a life. You have three lives, but if you lose them all we just start again – the main advantage is that you get more points for correct answers the more questions you answer correctly. You have 15 seconds to answer each question, otherwise the question times out and you lose a life.

Some of the questions are harder than others, so just try your best to get as many right as you can. The game is designed to be fun but please do your best to get a good score.

Do you have any questions concerning Pub Quiz?

While playing Pub Quiz, I'd also like you to perform the visual reaction time task as before using your non dominant hand. Please respond as quickly and accurately as you can to the coloured circles as they are presented on the screen. Remember; H for a green circle and F for a yellow circle. Please try your best to perform both tasks as well as possible. Any questions?

3) Start Pub Quiz and the visual reaction time task. [Task lasts approximately 3 minutes depending on participant reaction time]

4) *"Great, thank you very much"*

Finishing Experiment
When participant has performed the visual reaction time task in all of the three conditions:

1) Ask participants if they have any concerns about taking part of the experiment
2) Debrief participants fully
3) Fill out payment sheet **if being reimbursed**
    a. **Full name**
    b. **Address**
    c. **Bank account number & sort code**
4) Thank participants for taking part.

Appendix XIV

Protocol used in Experiment 2 of Chapter 6

Before participant arrives:

1) Create a Participant Pack. This should have a complete set of forms (Session 1: Participant Info, Consent Form, Demographics, MDQ, BDI, STAI-T, Altman, O-LIFE, EPQ, SUIS, IFES, PICS, PANAS, VAS, (pre film, post film), emotional response to film questionnaire, film compliance, attention to task, task enjoyment and difficultly, Diary, involuntary memory checklist. Session 2: Post diary PANAS and mood VAS, involuntary memory questionnaire, diary compliance, recognition memory test (verbal and visual), behavioural change questionnaire, IES-R positive version, post task PANAS and mood VAS.
2) **Determine subject number and condition from random number sequence** and write participant number on all questionnaires.
3) Equipment Check: Always check the computers and projector are working before running a participant.
4) Open the Film on Desktop of PC and reduce, ready to play when needed
5) Check all items are ready: Timer, participants pack, pens

After participant arrives

Greet Participant:

"Good morning/afternoon…, Thank you for coming. First we have to get some preliminary paper work done but then we will be starting the experiment. The experiment will take roughly 1 hour. Could you read this, and if you are happy with it sign the consent form. Feel free to ask any questions."

1) Give **Information Sheet** to read. *Do you have any further questions?*
2) Give **informed consent form** to them to fill in, make sure participants signs and adds contact details (phone and email). *Would you like a copy?*
3) Give **Participant Detail** form to them to fill in.
4) *Can I check you turned off your mobile phone please? Thanks*
5) Give **MDQ**
6) Give **SUIS**
7) Give **BDI**

   Please fill this in, about how you've been feeling for the past two weeks, including today.
8) Give **Altman**; *Most of us have normal fluctuations in attention and mood. These questions are looking for something a bit more marked, think as to whether other people, friends/family would notice these changes, are they out of character for you? Are they lasting for a sustained period of time? It is these changes that we are interested in.*
9) Give **EPQ-N, OLIFE, IFES**
10) Give **Trait questionnaire** (STAI-Y2)

    Please fill this in, about how you generally feel; whether it's Almost Never or Almost Always. Notice that Questions are phrased so your answers will probably swap sides.
11) Give **PICS**

12) Ensure Tetris or PubQuiz programmes are loaded. Double click on desktop icons.

(Tetris: Username = HolmesEA. password = windmill if not already logged on in Lab 26. For lab 24: username: EPACT1, password: pubquiz)

13) Say:

Now, you are going to play the computer game Tetris. Have you heard of this game before or played it?
(If yes say "I'll just give you a brief explanation" but still give same explanation. If no, then give an explanation and ask if they require a demonstration of the game)*:*
The game consists of 7 different shaped blocks which fall from the top of the screen one at a time. Each time you fill a whole horizontal line with the blocks, with no gaps, that line will disappear and give you points. The aim is to make as many of these lines disappear as possible before the screen is filled completely.
In this particular game I want you to focus on the three blocks that will be falling immediately after the one being played on the right of the screen. Try and work out in your minds eye where best to place these blocks in order to make the most complete lines and get the best score.
Blocks are moved using the 4 arrow keys. Left and right using the left and right cursor keys and rotated using the up cursor key. Each press of the up key rotates the block 90° clockwise. If you are confident that you have the block at the desired rotation and position, you can speed up its descent by pressing the down key.

Now before you play, do you have any questions? [Emphasise that it is not important what score they get, but to enjoy themselves and keep trying all the way through]

14) Start timer (duration of Tetris: 3 minutes).

15) Say:

"Now, you are going to play a computer quiz game. The Pub Quiz game consists of a single question presented on the screen with 4 possible answers. The aim is to correctly answer as many questions as possible to get as many points as you can.

You do this by using the mouse to select the answer you think is correct. You will then be told whether you are right or wrong. Each time you get an answer right you get awarded points. Get an answer wrong and you lose a life. You have three lives, but if you lose them all we just start again – the main advantage is that you get more points for correct answers the more questions you answer correctly. You have 15 seconds to answer each question, otherwise the question times out and you lose a life.

Some of the questions are harder than others, so just try your best to get as many right as you can. The game is designed to be fun but please do your best to get a good score."

16) Start timer (duration of PubQuiz: 3 minutes).

17) Give **Pre-film VAS** mood ratings (Anxious, motivated, irritable, sad, impulsive, hyper, depressed, elated, good) and **PANAS**: Emphasise to respond with how they are feeling **right at this very moment**. Don't let participant know film is about to be played

> *Please fill in this short questionnaire about how you are feeling right now, while you've been filling out the questionnaires here in the lab. Do not think about your answers too much, but give the first response that comes to mind. Please use the full scale, not just the extremes.*

18) Explanation of film:

> *In a few minutes you will see a short film of about 20 minutes. Please sit still and pay close attention; you will be asked questions on it later. I don't want you to watch the film like you normally would, I want you to immerse yourself in the events depicted, imagine you are **really there**, at the scene, taking part in the events, as though it's happening to you. For example, the first scene is of a rollercoaster, so I want you to imagine that you're actually on it, experiencing the twists and turns as they are happening. So if you're really immersed you might feel the emotions and physical sensations as if you were at the event. Some of the events might be ones that you haven't been involved in before, even so try and focus on feeling involved in the event as well as you can*
> *Do you know what I mean? How I want you to watch the film* [get them to explain it back to you].
> *Watch the film and try not to look away or shut your eyes. I will be just outside should there be any problems, and will come in when the film ends. Any questions?*

19) Turn off the lights / close blinds.
20) Start the video and leave the room. Video is 18mins.
Experimenter exits room and waits outside.

<u>After the video</u>

21) Experimenter enters room.
22) Turn on the lights and turn off the film
23) Participant to fill out **VAS mood ratings, PANAS Post film [how you feel after watching the film], emotional response to film and attention to film rating**

> *Please fill in this short questionnaire about how you are feeling right now, i.e. after watching the film. Do not think about your answers too much, but give the first response that comes to mind.*

Experimental Condition

According to initial allocation;

Tetris

1) Say:

> *Now, you are going to play the computer game Tetris that you practiced earlier. Don't forget to try and manipulate the blocks to form the most complete lines, and pay attention to the blocks coming up next on the right of the screen, and how they might be rotated to fit best.*
>
> *Now before you play, do you have any questions?* [Emphasise that it is not important what score they get, but to enjoy themselves and keep trying all the way through]

Start timer (duration of Tetris: 10 minutes). Record scores of each game completed – include: time, points, number of lines, level.

2) Give **post-task VAS and PANAS mood ratings**, say:

> *OK, please stop now. Please fill in these short questionnaire about how you are feeling **right now, i.e. after playing Tetris**. Do not think about your answers too much, but give the first response that comes to mind.*

3) **Give attention to task, task enjoyment and difficultly VAS**

Pub Quiz

1) Say:

> *Now, you are going to play the computer quiz game that you practiced earlier. Remember to use your dominant hand to select the answer you think is correct out of a choice of the four possible answers using the mouse. There is a 15 second time limit for each question. Remember that some of the questions will be harder than others and to try your best to get the highest score possible. Now before you play, do you have any questions?*
> *The game is designed to be fun but please do your best to get a good score. If the game ends we will start a new game straight away*

Start timer (duration of PubQuiz: 10 minutes). Record scores of each game completed.

2) Give **post-task VAS and PANAS mood ratings**, say:

> *OK, please stop now. Please fill in these short questionnaire about how you are feeling **right now, i.e. after playing PubQuiz**. Do not think about your answers too much, but give the first response that comes to mind.*

3) Give **attention to task, task enjoyment and difficultly VAS**

Control

1) Say:

> *I would now like you to have a short break. During this time please stay seated and do not talk. You can think about anything, with no restrictions during this time.*

Start timer (10 minutes).

2) Give **post-task VAS and PANAS mood ratings**, say:

> *OK, please stop now. Please fill in these short questionnaire about how you are feeling **right now, i.e. after the break**. Do not think about your answers too much, but give the first response that comes to mind.*

Finishing experiment:

Explanation of weekly diary

*It may that over the next few days bits of the film will **pop to your mind** when you **weren't expecting** them to. This is what we call an **involuntary memory or a flashbacks***

What goes through our minds can either take the form of words and phrases, "verbal thoughts" or mental images. Although mental images often take the form of pictures they could also include sounds and bodily sensations too.

*Mental images can be fuzzy or fragmented as well as clear; they can also be brief and very fleeting – like a quick flashback of the film. We are interested in knowing about **all** these types of images that you have of the film.*
[Check participant understands by asking one or several of the following & giving feedback.] *Do you understand what I mean by a mental image? Can you give me an example?*

If you have any intrusions/ involuntary memories of the film you have just watched over the next week, please record each one as soon as possible in this diary. Please keep the diary in your bag or next to your bed and start filling it in from now. It's really important that you keep it as accurately as possible.

[Explanation on how to fill out the diary]

On page 3 and page 4, fill in one of the little boxes every single time you have an involuntary memory of the film **[demonstrate what to do on the diary]***; **I** for image, **T** for thought or **IT** if it was both. So if you have 3 intrusions in the afternoon, then 3 of the little boxes should be filled. If you have had none during that time period then write zero or cross that section of the day out. Make sure that you have completed each of the three time periods (Morning, Afternoon and Evening/Night) as they occur. If you are unable to complete the diary at the time when you experience an involuntary memory please make sure you complete each time period at least once a day. Next, fill in the details of each involuntary memory you have had on page 5, putting down the day and time. We then need to know the content of the intrusion. This can be brief but we need to be able to match any*

intrusions you have to the film so please be as clear as possible **[refer to examples]** *for example if there were images of crowds cheering in the film, you may have an involuntary memory of this moment which you would describe like this* **[point to example],** *or if this was a negative film, you may have witnessed a car crash, which you would describe like this* **[point to example].** *We would also like to know your emotional and vividness rating of each involuntary memory, could you please circle a number, 1 to 5, in this box, from 1 being very negative/cloudy & imageless to 5 being very positive/as clear and vivid as if it was experienced again.*

For every little box you fill in after having an intrusion there should be a matching line in the back of the diary. If you are unsure of the detail, please just note it down in the diary anyway and we will go over it with you later when you return.

Fill in dates on the diary with them to get them to engage. Make them do a brief example to check they understand.

Give involuntary memory checklist. Make sure participant is paying attention to the checklist. Get them to read it out loud.

So remember:

Mental images can be pictures in your mind, but also sounds and sensations

Mental images may be fuzzy, very brief or almost like a flash in your mind's eye.

Even if you have several intrusions that are the same please record each individual one in the diary every single time it occurs.

Reemphasise the importance of keeping the diary

1) Explanation of follow-up session.

> *You will finish this diary on ……, in 7 days time. At that point, you will be asked to return for a follow-up session of this experiment.* (Arrange date and time). *Please bring this diary with you to the follow up session. You will be asked to fill in a couple of questionnaires, and you will then be given the payment and information about the purpose of the study. Any questions?*

2) Fill in Appointment Card on Diary for follow up session.
3) Note date of the experiment and follow up date on Participant record sheet.
4) Say goodbye.

> *Please do not speak to anyone who may take part about the details of the experiment, so as not to affect the behaviour of future participants. Please feel free to contact me at any point in the future if you feel that you need to. Remember your bank details for our next meeting so we can reimburse you as soon as possible, Thank you!*

5) Show participant out.
6) File all questionnaires away securely and ensure follow up appointment is in the calendar.

Follow-up Session

DIARY INTRUCTIONS [Information for the experimenter]:
When a participant returns with their diary you must go though it straight away. Do not leave it until the participant has gone, this way you can check the details in person while the information is still fresh in their minds:

Check diary is completed correctly. Complete any missing information, with the participants help if necessary, e.g. check there is a description for every single box checked with an intrusion on page 3 and 4 of the diary. If not then ask the participant if they can remember and describe the intrusion that went with the checked box, or mark if not.

Read all the intrusion descriptions in the diary. If they are unclear or you don't recognise them as being from the film ask for more details until you can identify it. If the intrusion is not from the film it cannot be included.

It might be helpful to create a list of film clips with a brief description if you are not familiar with the film.

Note

Sometimes participants do not realise that very fleeting or fragmented pictures are the kind of mental images that should have been recorded in the diary. Participants often think experiencing an intrusion will be like having an almost complete memory for the film, like a photograph or complete movie in their minds eye, but this is not the case. This is why it is important to give a good definition at the start.

Make sure PowerPoint is open on the computer and the intrusion triggering task is loaded, keep screen off, but PowerPoint show ready.

When participant arrives:

5) Welcome back!

6) PANAS and VAS post diary.

> *Please fill in this short questionnaire about how you feel right now. Do not think about your answers too much, but give the first response that comes to mind.*

7) Check diary is completed correctly, complete any missing information.
8) Get the participants to recall as much detail about their involuntary memories to fit them to the film
9) Give **verbal recognition memory test**
10) Do **visual recognition memory test**
11) Give **demand / follow up** diary compliance questions [For Tetris and Pub Quiz give predited effects of task VAS as well]
12) Give **Behaviour Change Questionnaire** and **Impact of Event Scale (for positive film)**

13) Intrusion triggering task:
    Turn on computer screen to show instructions screen:
    I am about to show you a selection of pictures from the film you watched earlier, please sit still and pay close attention to the pictures. There will then be a short break. Please stay seated and do not talk to the experimenter during this period. You can

think about anything, with no restrictions. If parts of the film happen to spontaneously pop into your mind during this period I'd like you to make a mark on this piece of paper. Any questions?

14) Show PowerPoint presentation
15) *Remember to mark down any time you have an involuntary thought of the film.* [Start timer: 2 minutes]
16) **Emotional rating** task.

    Please rate how much positive emotion (i.e. excitement, enjoyment, happiness etc) comes back to you right now in relation to each picture and explanation. I am not asking you to rate how pleasant or unpleasant each one is, I'm asking you to rate the positive emotion that you felt at the time of viewing the film.
17) **VAS and PANAS** to finish
18) Ask participants if they have any concerns about taking part of the experiment or if they feel disturbed. (Contact responsible investigator if feel concerned.)
19) Debrief participants fully and give debrief information sheet.
20) Ask the participant to sign **end of the experiment form**.
21) Fill out payment sheet **if being reimbursed**
    a. **Full name**
    b. **Address**
    c. **Bank account number & sort code**
22) Thank participants for taking part.

Appendix XV

Publications and presentations during the time of this thesis

Publications arising from this thesis

Clark, I. A., Mackay, C. E., & Holmes, E. A. (2013). Positive involuntary autobiographical memories: You first have to live them. *Consciousness and Cognition, 22*(2), 402-406. doi: 10.1016/j.concog.2013.01.008

Clark, I. A., Holmes, E. A., & Mackay, C. E. (in press). Intrusive imagery and Post Traumatic Stress Disorder; an experimental psychopathology approach to flashbacks. In Mishara, A., Corlett, P., Fletcher, P., Schwartz, M. (Eds.), *Phenomenological Neuropsychiatry: How Patient Experience Bridges Clinic with Clinical Neuroscience.* Springer

Pending publications arising from this thesis

Clark, I.A., Mackay, C.E., & Holmes, E.A. (2013). Why doesn't everyone get flashbacks after trauma? Low emotional response to traumatic footage predicts an absence of flashbacks. *Manuscript in preparation*

Clark, I. A., Holmes, E. A., & Mackay, C. E. (in prep). The neural basis of flashback encoding and recall. *Manuscript in preparation*

Conference presentations arising from this thesis

Clark, I.A., Holmes, E.A., Mackay, C.E (September 2013).Using neuroimaging to understand flashbacks: Can the brain inform treatments? in Arntz, A. (Chair), *Recent developments in treatment and understanding of posttraumatic stress disorder and symptoms related to aversive autobiographical memories in other disorders.* Symposium at the *43rd annual European Association for Behavioural and Cognitive Therapies (EABCT) conference.* Marrakesh

Clark, I.A., Mackay, C.E., Holmes, E.A. (July 2013).Using cognitive neuroscience to understand the aetiology of flashbacks. in Moulds, M. (Chair), *Rumination and Intrusive Memories: Understanding the Basic Processes Underlying these Transdiagnostic Phenomena in Clinical Disorders.* Symposium at the *7th World Congress of Behavioural and Cognitive Therapies (WCBCT).* Lima.

Clark, I.A., Holmes, E.A., Mackay, C.E (June 2013). Neuroimaging Flashbacks: The Formation and Occurrence of Involuntary Autobiographical Memories. Poster session presented at Human Brain Mapping, Seattle.

Clark, I.A., Mackay, C.E., Holmes, E.A. (August 2012). Protection against flashbacks: What factors predict the absence of flashbacks? *Poster session presented at the 42nd annual European Association for Behavioural and Cognitive Therapies (EABCT) conference*. Geneva, Switzerland, 29th August – 1st September 2012 (Vol. book abstracts, P.272)

Clark, I.A., Mackay, C.E., Holmes, E.A. (June 2012).Susceptibility to involuntary autobiographical memories of a positive film. *Poster session presented at the Clinical perspectives on autobiographical memory conference*. Aarhus University, Denmark, 11th - 12th June 2012 (Vol. book abstracts P. 21)

Clark, I.A., Holmes, E.A., Mackay, C.E. (March, 2012). A Clinical Neuroscience Model of Flashbacks. *Poster session presented at the Oxford Neuroscience Symposium*. 21st March 2012, Oxford University, UK

Other publications during the time of this thesis

Murray, A. M., Nobre, A. C., **Clark, I. A.,** Cravo, A. M., & Stokes, M. G. (2013). Attention Restores Discrete Items to Visual Short-Term Memory. *Psychological Science, 24*(4), 550-556. doi: 10.1177/0956797612457782

Clark, I. A., James, E. L., Iyadurai, L., & Holmes, E. A. (in press). Mental imagery in psychopathology: From the lab to the clinic. In D. Berntsen & L. Watson (Eds.), *Clinical Perspectives on Autobiographical Memory*: Cambridge University Press

Pending publications

Clark, I.A., Mackay, C.E., & Goodwin, G. (in prep). No difference in pituitary gland volume between bipolar patients and matched controls. *Manuscript in preparation.*

Appendix XVI

Changes to the Posttraumatic Stress Disorder diagnosis for DSM-5

Posttraumatic Stress Disorder

American Psychiatric Publishing

Posttraumatic Stress Disorder (PTSD) will be included in a new chapter in DSM-5 on Trauma- and Stress-or-Related Disorders. This move from DSM-IV, which addressed PTSD as an anxiety disorder, is among several changes approved for this condition that is increasingly at the center of public as well as professional discussion.

The diagnostic criteria for the manual's next edition identify the trigger to PTSD as exposure to actual or threatened death, serious injury or sexual violation. The exposure must result from one or more of the following scenarios, in which the individual:

- directly experiences the traumatic event;
- witnesses the traumatic event in person;
- learns that the traumatic event occurred to a close family member or close friend (with the actual or threatened death being either violent or accidental); or
- experiences first-hand repeated or extreme exposure to aversive details of the traumatic event (not through media, pictures, television or movies unless work-related).

The disturbance, regardless of its trigger, causes clinically significant distress or impairment in the individual's social interactions, capacity to work or other important areas of functioning. It is not the physiological result of another medical condition, medication, drugs or alcohol.

Changes in PTSD Criteria

Compared to DSM-IV, the diagnostic criteria for DSM-5 draw a clearer line when detailing what constitutes a traumatic event. Sexual assault is specifically included, for example, as is a recurring exposure that could apply to police officers or first responders. Language stipulating an individual's response to the event—intense fear, helplessness or horror, according to DSM-IV—has been deleted because that criterion proved to have no utility in predicting the onset of PTSD.

DSM-5 pays more attention to the behavioral symptoms that accompany PTSD and proposes four distinct diagnostic clusters instead of three. They are described as re-experiencing, avoidance, negative cognitions and mood, and arousal.

Re-experiencing covers spontaneous memories of the traumatic event, recurrent dreams related to it, flashbacks or other intense or prolonged psychological distress. Avoidance refers to distressing memories, thoughts, feelings or external reminders of the event.

Negative cognitions and mood represents myriad feelings, from a persistent and distorted sense of blame of self or others, to estrangement from others or markedly diminished interest in activities, to an inability to remember key aspects of the event.

Finally, arousal is marked by aggressive, reckless or self-destructive behavior, sleep disturbances, hypervigilance or related problems. The current manual emphasizes the "flight" aspect associated with PTSD; the criteria of DSM-5 also account for the "fight" reaction often seen.

The number of symptoms that must be identified depends on the cluster. DSM-5 would only require that a disturbance continue for more than a month and would eliminate the distinction between acute and chronic phases of PTSD.

PTSD Preschool Subtype and PTSD Dissociative Subtype

DSM-5 will include the addition of two subtypes: PTSD in children younger than 6 years and PTSD with prominent dissociative symptoms (either experiences of feeling detached from one's own mind or body, or experiences in which the world seems unreal, dreamlike or distorted).

PTSD Debate within the Military

Certain military leaders, both active and retired, believe the word "disorder" makes many soldiers who are experiencing PTSD symptoms reluctant to ask for help. They have urged a change to rename the disorder posttraumatic stress injury, a description that they say is more in line with the language of troops and would reduce stigma.

But others believe it is the military environment that needs to change, not the name of the disorder, so that mental health care is more accessible and soldiers are encouraged to seek it in a timely fashion. Some attendees at the 2012 APA Annual Meeting, where this was discussed in a session, also questioned whether injury is too imprecise a word for a medical diagnosis.

In DSM-5, PTSD will continue to be identified as a disorder.

DSM is the manual used by clinicians and researchers to diagnose and classify mental disorders. The American Psychiatric Association (APA) will publish DSM-5 in 2013, culminating a 14-year revision process. For more information, go to www.DSM5.org.

APA is a national medical specialty society whose more than 36,000 physician members specialize in the diagnosis, treatment, prevention and research of mental illnesses, including substance use disorders. Visit the APA at www.psychiatry.org and www.healthyminds.org. For more information, please contact Eve Herold at 703-907-8640 or press@psych.org.