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Psychological and Neural Processing of Social Rejection and Inclusion in Major Depressive Disorder

Julia Alexandra Gillard

This dissertation is submitted for the degree of

Doctor of Philosophy

Murray Edwards College

University of Cambridge

15th May 2017

THESIS TITLE

Psychological and Neural Processing of Social Rejection and Inclusion in Major Depressive Disorder

CANDIDATE

Julia Alexandra Gillard

DISSERTATION SUMMARY

This thesis aimed to extend the existing psychological and neural basis of social processing in Major Depressive Disorder. This investigation was an attempt to resolve current conflicts and gaps in the social affective neuroscience literature regarding social functioning in depression. Chapter 1 consisted of a general introduction to the current evidence-base and theoretical frameworks surrounding social processing more generally, and in depression more specifically. Chapter 2 provided an exploration of the systemic behavioural biases in in those with depression compared to mentally healthy individuals using a range of social, affective and process measures implemented across the remaining chapters. Then followed a behavioural and neural investigation into self-relevant social processing in depression. Chapter 3 described the process of memory generation implemented across Chapter 4-6 using a script-driven paradigm. It further discussed the ecological validity of this paradigm using social autobiographical memories. Chapter 4 investigated the neural and behavioural responses to self-relevant autobiographical memories of social rejection and social inclusion in individuals with depression and in healthy controls. The next two chapters discussed the behavioural and neural basis of social processing in depression in response to others' memories of social rejection and inclusion, using traditional and novel fMRI analysis methodologies in Chapter 5 and Chapter 6, respectively. The latter applied a novel intersubject correlation analysis to the same population of depressed and healthy controls as in Chapter 5. Then, Chapter 7 presented a future application of the script-driven imagery paradigm by investigating the effectiveness of different emotion regulation strategies in response to socially salient autobiographical memories in a population of healthy controls. Finally, Chapter 8 provided a general discussion bringing together behavioural and neural findings to provide a clearer understanding of social processing in Major Depressive Disorder. Current theoretical frameworks were used to guide the interpretation of these findings.

DECLARATION

This dissertation is the result of my own work and includes nothing which is the outcome of work done in collaboration except as specified in the text. It is not substantially the same as any that I have submitted, or, is being concurrently submitted for a degree or diploma or other qualification at the University of Cambridge or any other University or similar institution except as specified in the text. I further state that no substantial part of my dissertation has already been submitted, or, is being concurrently submitted for any such degree, diploma or other qualification at the University of Cambridge or any other University or similar institution except as specified in the text. It does not exceed the prescribed word limit for the relevant Degree Committee.

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First and foremost, this thesis is dedicated to my parents, Karen and Frank. Your curiosity, and enthusiasm for all things great and small have contributed greatly to the person I am today, aided by the unwavering motivation to instil this pursuit of knowledge in your, at times, reluctant daughter. To dad, believe it or not, I *do* listen when you recite your historical facts and pearls of wisdom. To mum, your generosity, energy and strength know no limits. Having grown up amongst you, Rosie and Hans, in our Kraftshof enclave, I hope to have adopted at least some of these qualities. As such, this thesis presents the fruition of your parental mantra: *curiosity killed the cat, but satisfaction brought it back*. I will keep this in mind when seeking out the voyages of discoveries that lie ahead. For all of you have done, for all you continue to do, and for the exceptional parents you both are, I am grateful.

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TABLE OF CONTENTS

ABBREVIATIONS

AI	Anterior Insula
dACC	dorsal Anterior Cingulate Cortex
ANOVA	Analysis of Variance
AnG	Angular Gyrus
BAI	Beck's Anxiety Inventory
BDI	Beck's Depression Inventory
CBT/CT	Cognitive Behavioural Therapy / Cognitive Therapy
DERS	Difficulty in Emotion Regulation
fMRI	functional Magnetic Resonance Imaging
GLM	General Linear Model
ISC	Intersubject Correlation
IPSM	Interpersonal Rejection Sensitivity
IPT	Interpersonal Therapy
MCC	Middle Cingulate Cortex
MDD	Major Depressive Disorder
MDE	Major Depressive Episode
SAHP	Social Attention Holding Power
SIP	Social Investment Potential
SR	Social Risk (Hypothesis)

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CHAPTER 1. SOCIAL PROCESSING IN DEPRESSION – LITERATURE REVIEW AND CURRENT THEORETICAL MODELS

1.1 AIMS AND MOTIVATION

This thesis aims to extend our existing understanding of the psychological and neural bases of social processing in Major Depressive Disorder. This investigation is an attempt to resolve current conflicts and gaps in the social affective neuroscience literature regarding social functioning in depression.

First, it aims to challenge the long-held view that a dedicated neural network is selective for processing negative social emotions, such as social pain, in the human brain in response to being rejected or excluded. Recent suggestions indicate that this network may, in fact, reflect valence-independent and/or social evaluative processes. This debate thus requires further resolution.

Secondly, this thesis investigates the importance of these brain networks to the understanding of social functioning in depression, as deficits in this domain represent a hallmark symptom. The literature on depression and social functioning to date has focused its efforts on affective biases towards negative material. There is an evident gap as to the processing of positive affective information, and in particular, positive social signals. That will be a focus of the work reported here.

Finally, the thesis aims to marry these two lines of investigation within relevant theoretical frameworks of social processing in depression by extending current behavioural findings with neuroimaging data. The rich dynamic of complex social interactions will be explored by means of autobiographical memories of social rejection and inclusion.

1.2 Outline

This thesis consists of seven chapters spanning behavioural and neuroimaging experiments and discussions. See Figure 1.1 for an illustrated overview.

Chapter 1 (current chapter) consists of a general introduction to the current evidence-base and theoretical frameworks surrounding social processing more generally, and in depression more specifically, addressing the above questions. Chapter 2 will provide an exploration of the systemic behavioural biases in in those with depression compared to mentally healthy individuals on a range of social, affective and process measures implemented across the remaining chapters.

The next two chapters consist of a behavioural and neural investigation into self-relevant social processing in depression. Implementing a script-driven imagery paradigm, salient social emotions will be elicited in response to autobiographical memories of social rejection and inclusion experiences. Chapter 3 will first describe the methodology of generating memories as part of the script-driven imagery paradigm, before discussing its ecological validity in the context of socio-affective processing in depression. Then, the first neuroimaging study, described in Chapter 4, will investigate the neural and behavioural responses to self-relevant social cues derived from the generated autobiographical memories of social rejection and social inclusion in individuals with depression and in healthy controls,

The next two neuroimaging chapters will discuss the behavioural and neural basis of social processing in depression in response to *others'* memories of social rejection and inclusion, using traditional and novel fMRI analysis methodologies. Chapter 5 will explore neural responses to other's experiences of social rejection and inclusion, similarly using script-driven imagery. Chapter 6 applies a novel intersubject correlation analysis to the same population of depressed and healthy controls as in Chapter 5 (Hasson, Nir, Levy, Fuhrmann, & Malach, 2004a; Kauppi, Pajula, & Tohka, 2014). In this chapter, the degree of synchronisation across subjects is explored in response to listening to an *extended* negative and positive social narrative, as opposed to a series of brief autobiographical memories, as in Chapter 5.

Finally, the last two chapters describe future applications of the script-driven imagery paradigm and a general discussion of the work presented in this thesis. Chapter 7 will implement script-driven imagery in an emotion regulation task within healthy controls. This will investigate the effectiveness of different emotion regulation strategies in response to socially salient autobiographical memories. This provides a starting point for using script-driven imagery in a variety of social affective research areas. Then, Chapter 8 will provide a general discussion of the work presented, which aims to bring together both behavioural and neural findings to provide a clearer understanding of social processing in Major Depressive Disorder with respect to self- and other-relevant cues. Current theoretical frameworks will be used to guide our interpretation of these findings. The thesis will conclude with an outline of future directions for this fascinating area of research. To quote Paul Gilbert in "Depression, the evolution of powerlessness" (2nd edition): "That is the outline; let's begin the journey."

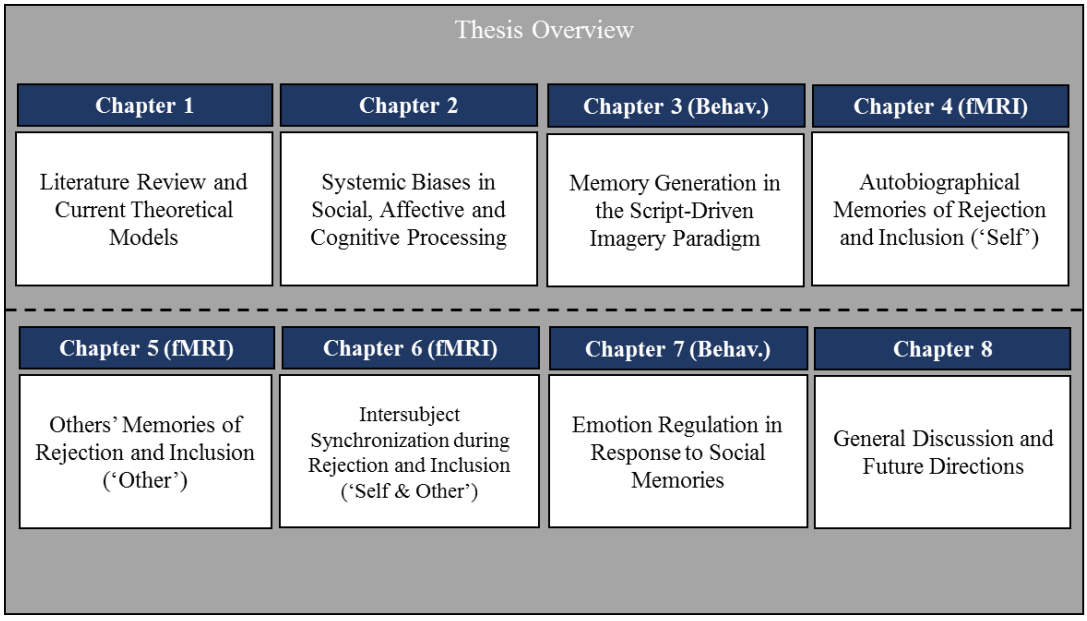


Figure 1.1. Thesis Overview

1.3 Major Depressive Disorder (MDD)

Major Depressive Disorder (MDD) is characterised by profound and persistent feelings of low mood or sadness and loss of interest or pleasure in daily activities, which severely alter an individual's mood, thoughts and behaviours. It is associated with an array of social, occupational and functional impairments (Diagnostic and Statistical Manual 5th Edition (DSM-5), American Psychiatric Association (APA), 2013). MDD is considered a common mental disorder with a global point prevalence estimated at 4.7%, elevated in females (5.9%) relative to men (3.8%), and a pooled annual incidence at 3.0%, (Ferrari et al., 2013). Further, lifetime prevalence rates for mood disorders, a group of diagnoses encompassing elevated mood (e.g. mania), depressed mood (e.g. MDD) and cyclical moods (e.g. bipolar depression) are estimated at 20.8%. Typically, the first onset occurs in childhood or early adolescence (Kessler et al., 2005). These findings emphasise the pervasiveness of depression as a severe psychological disorder which develops early with potentially detrimental impact.

Figure 1.2. Albrecht Durer's *Melancholia* still resonates today as the object's loneliness and sadness embodies our past and present conceptualisation of depression.

However, the heterogeneity of symptoms disrupting multiple domains of functioning highlights the difficulty in identifying MDD as a singular categorical entity. Since its first introduction, the diagnostic conceptualization of depression has undergone several revisions. This includes the introduction of the term *Major Depressive Disorder (MDD)* in DSM-III, formerly described as *Melancholia (*Figure 1.2), as depicted in Albrecht Durer's masterpiece above. It has also seen the emergence of multiple depressive subtypes, including reactive and endogenous depression, as well as atypical and melancholic depression (Dowrick & Frances,

2013). Reactive depression refers to depression that stems from situational factors, while endogenous depression arises in the absence of obvious environmental precipitants (Kessing, 2007). However, epidemiological studies suggest that these subtypes occur at much lower prevalence rates compared to the majority of depression, which is argued to develop in the continuous interplay between genes and stressful experiences (Flint & Kendler, 2014).

Since DSM-IV-TR (APA, 2000) diagnostic criteria for MDD include significant changes in weight, sleep quality or pattern, activity or energy levels, as well as feelings of guilt and worthlessness, difficulty in concentration and suicidality (See Appendix 1.1). A proportion of, but not all, symptoms need to be met to fulfil the diagnostic criteria for MDD and the list has not changed since the introduction of DSM-5. However, the introduction of DSM-5 allows for the characterization of additional symptoms without the assumption that these represent aetiologically true subtypes. These include severe depression with or without psychotic features, in partial or full remission, with anxious distress, catatonic features, perinatal, postpartum or atypical and mixed features (Uher, Payne, Pavlova, & Perlis, 2014). However, the ambiguous interpretations of these additional diagnoses in relation to MDD is still under discussion (Uher et al., 2014).

A hallmark symptom of MDD is a deficit in social functioning: an inability to fulfil a variety of roles across diverse, complex and dynamic social contexts (Hirschfeld et al., 2000). These difficulties are common across several other psychiatric and developmental disorders, for which social competency has long been conceptualised as a key diagnostic criterion, such as Autism Spectrum Disorder (ASD), several anxiety disorders, and Alzheimer's syndrome (D. P. Kennedy & Adolphs, 2012). Moreover, risk factors, such as major negative life events involving social rejection, loss or failure, and in particular early adverse life stress (Heim & Binder, 2012; Luterek, Harb, Heimberg, & Marx, 2004; van Harmelen et al., 2010, 2014) are known to precipitate the onset of depressive episodes (Slavich & Irwin, 2014a; Slavich, O'Donovan, Epel, & Kemeny, 2010).

In sum, depression is characterised by: (1) affective symptoms, such as persistent lowered mood, loss of pleasure in all or almost all activities, lack of emotional reactivity to pleasurable stimuli; (2) cognitive distortions, including negative thoughts about the world, self and future,

such as excessive or inappropriate feelings of worthlessness and guilt (Beck, 1987); (3) behavioural symptoms, including (social) withdrawal and inactivity, as well as psychomotor retardation or agitation; and (4) physical symptoms, which may include disruptions in diurnal variation in sleep patterns and significant weight loss or gain, and feelings of lethargy and tiredness. Given their high rate of occurrence, mood disorders and comorbid conditions are contributing to an increasing economic burden on health care systems worldwide (P. E. Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015; G. Miller, Chen, & Cole, 2009). This highlights the urgency for further research aimed at improving early detection, treatment interventions and relapse prevention.

In this chapter, we will discuss the behavioural and neural findings, and gaps in the literature, relating to the role of social pain processing within the social brain. We have chosen this as a starting point because many of the social difficulties associated with depression revolve around narratives of social rejection. Understanding normative models, both psychosocial and neural, of the impact of social rejection is thereby likely to be crucial. The discussion of social pain will therefore be followed by a discussion of the social functioning impairments observed in MDD. These findings will then be discussed in the context of current theoretical perspectives. Then, existing intervention approaches will be reviewed before concluding with a summary and overarching research questions that have emerged from this review.

1.4 A SELECTIVE NETWORK FOR SOCIAL PAIN?

SOCIAL COGNITION

Social cognition refers to both conscious and non-conscious psychological processes directed towards and derived from encounters or interactions with social agents and expressed in social behaviour. Impairments in social cognition are thought to result as a function of cognitive biases and deficits in emotion recognition at the perceptual-attentional level, and/or from an altered neural response to emotional stimuli (C. D. Frith & U. Frith, 2007; U. Frith & C.D. Frith, 2010; D. P. Kennedy & Adolphs, 2012a). On a neural level, several large-scale interacting networks have been implicated in social cognition (D. P. Kennedy & Adolphs, 2012). These networks are centred around the amygdala, which is thought to respond

selectively to socially salient emotional cues (Adolphs, Baron-Cohen, & Tranel, 2002); the so-called mentalising network, reflecting the brain while at rest or involved in inferring the mental states of others within social interactions (Baetens, Ma, Steen, & Van Overwalle, 2013; Centelles, Assaiante, Nazarian, Anton, & Schmitz, 2011); the so-called empathy network, involved in the ability to understand and share emotions experienced and/or expressed by another (Fan, Duncan, de Greck, & Northoff, 2011; Hein & Singer, 2008); and the so-called mirroring network, activated by action-observation and simulation (Barrett & Satpute, 2013; D. P. Kennedy & Adolphs, 2012). Taken together, these large-scale integrative neural networks encompass the notion of a social brain, optimised for social interactions within our social world (Barrett & Satpute, 2013; U. Frith & Frith, 2010). These key networks and regions underlying social functioning are illustrated in Figure 1.3, which will hopefully guide the reader across the anatomical landscape of the social brain in the following sections.

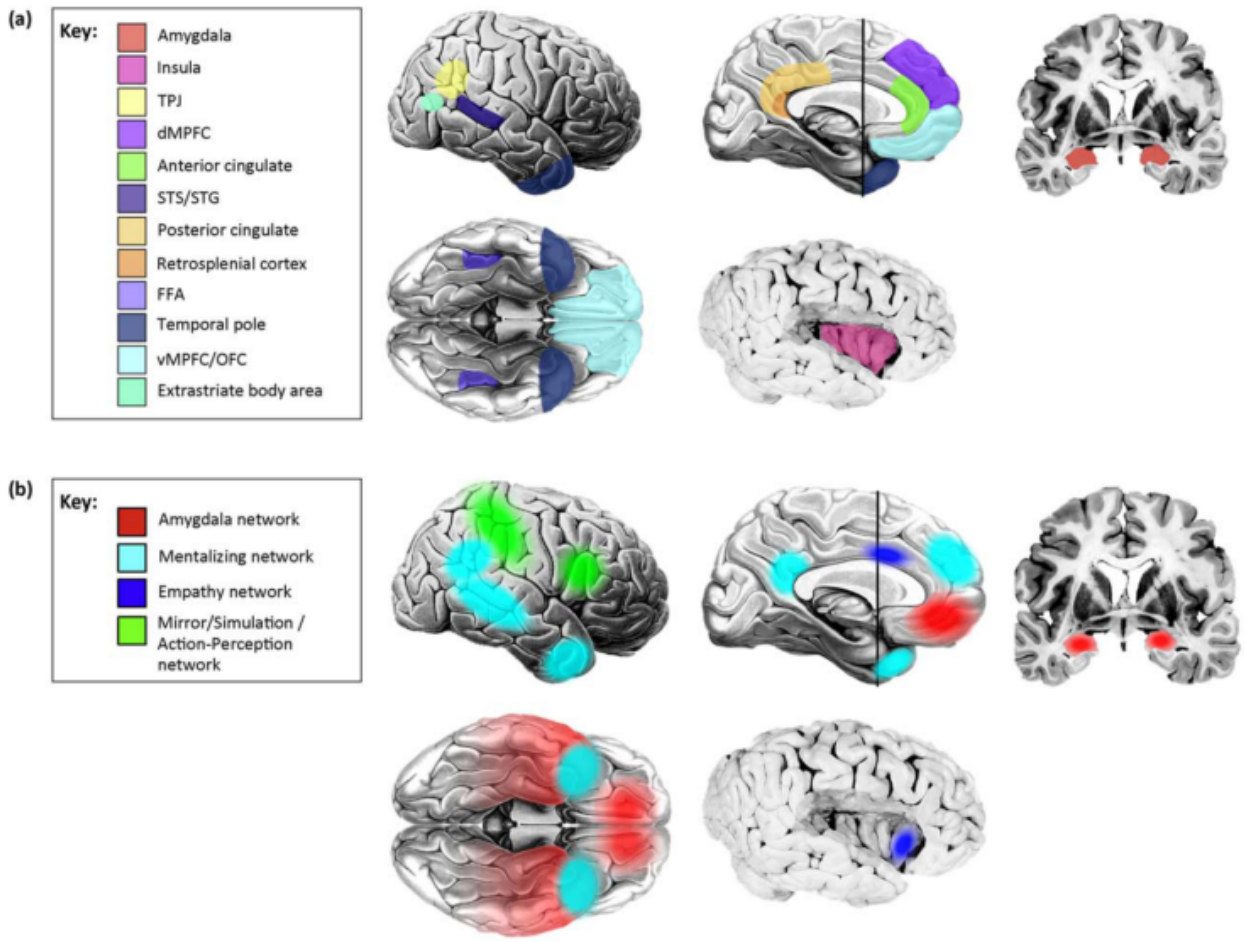


Figure 1.3 Adapted from Kennedy & Adolphs, 2012. The Social Brain from structures (a) to networks (b).

SOCIAL PAIN DEBATE

Central to the notion of a social brain is the continuing debate around the neural representation of 'social pain' - the experience of psychosocial pain following interpersonal exclusion, rejection or loss. 'Cyberball', a computerised ball-tossing game simulating social exclusion in participants by virtue of no longer receiving ball throws from two other virtual characters, has emerged as a paradigm of choice to study the relationship between social exclusion and self-reported distress, both on a behavioural and neural level (Eisenberger, 2012a; Eisenberger, Jarcho, Lieberman, & Naliboff, 2006; Eisenberger & Lieberman, 2003; Masten, Morelli, & Eisenberger, 2011a; K. D. Williams, Yeager, Cheung, & Choi, 2012).

In a seminal study in healthy individuals, the experience of social exclusion (relative to being included in the Cyberball game) was associated with increased neural activity in dorsal anterior cingulate cortex (dACC), anterior insula (AI), and the right ventral prefrontal cortex (vPFC) (see Figure 1.3), correlated with increased self-reported distress (Eisenberger, 2012a; Eisenberger & Lieberman, 2003). Interestingly, the effect was observable even when participants were explicitly informed that the other players were not real but instead computer-generated (Zadro, Williams, & Richardson, 2004), lending further weight to the findings. Crucially, the pattern of activation for social exclusion was proposed to share part of the underlying neural circuitry of somatosensory pain (Kross, Berman, Mischel, Smith, & Wager, 2011), thus leading to the term *social pain*. The notion of a 'social pain network', which co-opts the physical pain matrix, thus resonated with a populist scientific view on negative social interactions. In other words, the initial findings strongly supported the phenomenological experience that 'rejection really does hurt' (Eisenberger & Lieberman, 2003).

However, recent meta-analytical data have raised important questions about the existing social pain account (S. Cacioppo et al., 2013). Within the social domain, rather than having an exclusive role in social pain processing, the authors suggested that the dACC and bilateral AI co-activation may represent a more sophisticated index of the social dynamic at play (S. Cacioppo et al., 2013). A more in-depth multivariate fMRI pattern analysis further revealed distinct affective representations for physical pain and social pain within the social domain beyond the previous findings described at the gross anatomical level (Woo et al., 2014). Since

then, the central role of the dACC and its unique contribution to social pain remains the topic of much debate. Critical positions include meta-analytic evidence suggesting both dorsal and ventral ACC involvement in social pain elicitation and subjective distress (Rotge et al., 2015). In addition, authors have argued that activity in dACC in response to social exclusion within the Cyberball paradigm may be due to expectancy violation, given the sudden shift from a 'baseline' affiliative status of inclusion to the unexpected exclusion within the paradigm (Somerville, Heatherton, & Kelley, 2006).

Addressing these criticisms, a non-social alternative paradigm, "Cybershape", in which virtual players are replaced by neutral shapes, attempted to account for the notion of expectancy violation (Bolling et al., 2011). This revealed activation in ventral ACC and PCC but no selective activity in the social pain matrix when a shape was 'excluded' within the game. This suggests dissociable brain mechanisms for social pain and expectancy violation, with the latter activating a similar yet distinct region. Further, a study investigating saliency addressed the previous assumption that *inclusion* within Cyberball may represent a default state of mind. Based on this assumption, exclusion represents a departure from the norm and a highly salient event, as opposed to the less salient inclusion condition. Explicitly incorporating an *overinclusion* following the initial exclusion period revealed increased activity in dACC and right ventrolateral PFC during exclusion over-inclusion, suggesting a distinct role for social pain over inclusion (Kawamoto et al., 2012). Thus, these findings have gradually moved away from the notion of a selective network responding exclusively to negative social signals.

An important shift in the literature has suggested that within the domain of social processing the ACC may be more generally involved in tracking the motivation of other people (Apps, Balsters, & Ramnani, 2012; Apps, Rushworth, & Chang, 2016; Apps & Ramnani, 2014). Findings in this context are based on previous animal studies, revealing a role for ACC in social evaluation in macaque monkeys (Rudebeck, Buckley, Walton, & Rushworth, 2005). This would suggest that both social exclusion and inclusion would activate the ACC, to accurately monitor and evaluate social information. Interestingly, a recent study provides encouraging support for this suggestion with a novel social feedback paradigm revealing comparable neural activity in the dACC and AI in response to positive and negative social evaluation (Dalgleish

et al., 2017). This is aided by the finding that pleasure and physical pain may also share a common neural substrate in the same way as exclusion and physical pain were previously argued to overlap (Leknes & Tracey, 2008). With a particular role for ACC in the processing of pleasure (McLean et al., 2009), these results point towards a potential overlap between both pain and positive reward processing.

NO PAIN WITHOUT GAIN?

In general, the reward system has long been associated with key structures in the anterior cingulate cortex, OFC, ventral striatum and ventral pallidum, as well as affective areas in the amygdala, hippocampus, thalamus and dorsal PFC (Forbes, 2011; McClure, York, & Montague, 2004; Murray, 2007). These areas encompass regions previously described in negative emotional processing without specific mention of the *social* component of the affective material. However, when specifically contrasting *non-social* emotional-processing to *social* emotional processing in healthy controls, findings revealed *valence independent* heightened activity in overlapping areas (Frewen et al., 2011). These included the dorsomedial PFC, posterior cingulate cortex (PCC), precuneus, bilateral temporoparietal junction (TPJ) and right amygdala. These regions are crucially involved in social- and self-referential processing within the mentalising and empathy networks described within the social brain (see Figure 1.3).

This suggests that social emotional information evokes comparable activity independent of valence in key structures previously highlighted exclusively in negative emotional processing. Delving deeper into the neural representation of complex positive social information, a study investigating early-stage romantic love asked healthy control participants to recall specific positive memories with their romantic partner (Aron, 2005). In doing so, the aim was to induce a positive emotional state of social affiliation or inclusion. Interestingly, greater length of time in love correlated with increased activity in right mid-insular cortex and ACC. These regions echo previous findings of heightened activity in the insula and ACC while experiencing the arguably opposite experience of social pain (Eisenberger, 2003; Eisenberger et al., 2006). Thus, the recruitment of higher order cognitive processes during complex social-emotional

processing highlights areas previously attributed to negative emotional processing alone, in particular, social pain processing.

Interestingly, further drawing on the importance of the social context in processing negative emotions, reward processing in response to proximal social targets resulted in increased activity in dorsolateral PFC, bordering on the ACC (Fareri, Niznikiewicz, Lee, & Delgado, 2012). This is important as it highlights areas responding to inclusive signals, as well as negative social signals. Personal significance of social targets further modulated amygdalar responses to facial expressions (Vrtička, Andersson, Grandjean, Sander, & Vuilleumier, 2008). This was further illustrated in a game-show inspired paradigm, in which vicarious social reward revealed activity in ventral striatum and ventral ACC, modulated by the perceived interpersonal similarity with an unknown other (Mobbs et al., 2009). Thus, it is increasingly feasible to assume that altered neural responses to social reward in clinical and non-clinical populations are modulated by distinct social contexts and perceived interpersonal closeness, or by extension, interpersonal rejection sensitivity. Vrticka (2012) argues that this modulation by the social context in social affective processing is represented within an approach-aversion system. This system processes positive (social approach) and negative (social aversion) information. The former is argued to activate the ventral tegmental area, striatum and ventral medial OFC; the latter the amygdala, hippocampus, insula and ACC. See Figure 1.3 for illustration.

Empathic Processing of Social Signals

The social context and perceived interpersonal closeness are further closely associated with the notion of empathy. Empathy for positive and negative social emotions is crucial when engaging with and maintaining successful social interactions and can be described as an affective state caused by the shared experience of emotions or affective states of another person (Hein & Singer, 2008). On a neural level, empathy has been associated with activity in the AI, a key region implicated in social pain processing (Lamm & Singer, 2010). Additionally, focal lesions within AI cortex were associated with decreasing discrimination accuracy and increasing reaction times in response to processing other's physical pain; however, these deficits were not associated with lesions in the ACC (Gu et al., 2012). This is surprising given the earlier finding

that individuals high in trait empathy recruited affective areas including the AI and dACC in response to observing other's social pain (Masten et al., 2011a). In fact, this study highlights the complex neural pattern that emerges with additional activity in dorsomedial PFC, medial PFC and precuneus. These areas are predominately associated with mentalising and theory of mind, as described earlier. Empathy for social pain also has been found to activate sensory-discriminative areas, including posterior insula cortex and secondary somatosensory cortex (S2). However, only the subgenual cingulate cortex was recruited during empathic processing of both physical and social pain (Novembre, Zanon, & Silani, 2015).

To complicate matters further, higher levels of empathic concern were also related to increased subgenual cingulate activity in response to evoked guilt but not in response to evoked compassion (Zahn, de Oliveira-Souza, Bramati, Garrido, & Moll, 2009). This suggests that empathy for social pain may be differently mediated by complex social emotions such as guilt and compassion, which communicate important yet qualitatively distinct abstract social values relating to self and other respectively. Moreover, different components of empathetic pain processing may be modulated by distinct affective networks, including areas within the bilateral AI cortex, medial cingulate cortex (MCC) and ACC (Singer et al., 2004). For instance, concrete compared to abstract information used to elicit empathy revealed differential results. Concrete information activated action and perception networks, including somatosensory cortices. Abstract information activated mentalising networks, including STG, precuneus, vmPFC, and TPJ (Fan et al., 2011; Lamm, Decety, & Singer, 2011). These findings point towards discrepancies in the literature as a function of different experimental paradigms.

However, a shortcoming in the literature has been the limited evidence-base regarding the empathetic processing of positive emotions, such as social pleasure and social reward. While the anterior insula was previously implicated in the empathetic processing of negative social emotion, it also emerges in the empathic processing of compassion, compassion, perceived fairness and cooperation (Lamm & Singer, 2010). In addition, a novel study investigated gustatory empathic responses to negative and positive emotions by exposing individuals to both pleased, neutral and disgusted gustatory facial expressions. This revealed AI and adjacent frontal operculum (IFO) activity with self-reported empathy scores predictive of activity,

particularly within the gustatory IFO both during intense negative and positive information (Jabbi, Swart, & Keysers, 2007). This study is unique in exploring empathy in response to both negative and positive emotions and suggests valence-independent social affective processing. Finally, a study investigating emotional contagion, or the transfer of emotion within a group, also revealed that the observation of happy facial expressions resulted in increased activity in left anterior cingulate gyrus; further, both happy and sad expressions evoking activity in the right inferior frontal gyrus (Harada, Hayashi, Sadato, & Iidaka, 2016). These results point towards social affective processing that encompasses positive and negative information and questions previous assumptions of a selective network for processing social pain.

SUMMARY

In sum, the notion of a selective network for social pain has emerged as a topic of much debate and research within the last decade. It falls within the long-held view that "bad trumps good" in relation to events spanning everyday and major life events (e.g., trauma), as well as *close other* relationship outcomes, social group hierarchies and interpersonal social interactions (Baumeister, Bratslavsky, Finkenauer, & Vohs, 2001). However, a further review suggests that autobiographical memories are an exception to this "bad trumps good" rule, with stronger affect fading biases for negative compared to positive memories (Walker, Skowronski, & Thompson, 2003). While the literature on social pain has thus proposed the exclusive co-opting of the dACC-AI matrix, recent results have questioned both the unique contribution of dACC, as well as the importance of saliency and rule violation in processing social exclusion, within the social domain. In addition, results have highlighted the importance of distinguishing between non-social and social-emotional processing, independent of valence and the overlapping contribution of positive social signals within the social pain network. The social context and personal self-relevant significance of social signals are further seen to modulate neural activity in key regions. This emerging evidence thus suggests a more distributed social network that may respond both to negative and positive social signals and demands a serious reconsideration of the literature on social pain processing, as well as providing insights into potential disruptions in depression.

This section has considered social signals as distinct emotional phenomena which contribute to social functioning of individuals. These findings may provide a viable target for investigating social functioning with an emphasis on the altered socio-affective profile in depression. However, psychological and neural mechanisms underlying the depressed socio-cognitive profile have yet to be comprehensively examined. The next section, therefore, aims at exploring how social signals are processed in depression.

1.5 How are social signals processed in depression?

Individual differences in detecting and responding to *social* signals in depression have previously been operationalised along a dimension of interpersonal rejection sensitivity, encompassing either enhanced or diminished sensitivity to the behaviour and emotions of others (Boyce & Parker, 1989). Altered sensitivity further extends to receiving social feedback, concern about behaviour and verbal statements of others, and fears of perceived or actual criticism. This may result in feelings of inadequacy, inferiority and the misinterpretation of social cues signalling rejection and/or inclusion, correlated with low mood (Gilbert & Allan, 1998). Behaviourally, individuals with high rejection sensitivity tend to socially withdraw in an attempt to avoid actual social exclusion (Slavich & Irwin, 2014b). This gradual withdrawal may be especially heightened in those already experiencing social anhedonia, the loss or decreased interest in engaging in social activities – with depressed individuals reportedly experiencing more positive affect and less negative affect in the absence of other people (Kwapil et al., 2009). The withdrawal, loss or disconnection from social networks, as well as the mere threat of social exclusion, is argued to activate an immune response to adversity in the same way as experiencing actual physical threat or injury, thereby protecting the physical and emotional integrity of an individual (Slavich & Irwin, 2014b). Thus, social rejection, loss or failure represent key risk factors in the development and maintenance of depression (Slavich & Irwin, 2014a; Slavich et al., 2010).

However, cognitive biases towards negative information as well as a reduced reactivity and orientation towards positive affective material (Roiser & Sahakian, 2013), difficulties in

emotion recognition and differential empathic processing may account for altered interpersonal rejection sensitivity in depression.

Cognitive Deficits and Biases

Considering cognitive processes first, a distinction is drawn in the literature between 'hot' (affect-laden) and 'cold' (affect-independent or neutral) cognitive processes. Hot cognition refers to the cognitive processing of affective material, while cold cognition relates to the processing of information *independent* of any emotional context or motivational demands (Roiser & Sahakian, 2013). In depression, emotion-independent 'cold' deficits are evident throughout the acute phase of the disorder across multiple domains spanning executive dysfunction, attention and memory (Hammar & Ardal, 2009; Snyder, Miyake, & Hankin, 2015). This is illustrated in marked impairments in timed visuospatial attention tasks, (Hammar & Ardal, 2009), difficulties in attentional disengagement away from negative stimuli (Christopher & MacDonald, 2005) and impairments on pattern and spatial recognition memory (i.e. matching to sample, spatial span, spatial working memory and planning (Elliott, 1998; Elliott et al., 1996). Interestingly, the latter study also noted a motivational deficit in recovering from poor performance on the above measures. In other words, in depressed individuals, failure or poor performance on a task detrimentally affected subsequent performance. The authors argued that this may reflect heightened sensitivity to negative feedback and/or the activation of negative self-schema. This mirrors the notion of heightened interpersonal rejection sensitivity in response to negative social feedback. An alternate interpretation is that 'cold' cognition may 'turn hot' in the presence of depression (Roiser & Sahakian, 2013), thus leading to deficits traditionally associated with 'cold' cognitive tasks.

Biases in hot cognition are also found across a variety of domains, including attention, decision-making, and various aspects of memory functioning, e.g. experience of overgeneral memory and intrusive memories (Baddeley, 2013; Whalley, Rugg, & Brewin, 2012). A long-held view posits that cognitive biases favour the processing of negative affective material while promulgating avoidance or neglect of positive affective material, referred to frequently as a negative response bias (Roiser & Sahakian, 2013). A body of evidence illustrates this

dichotomy in the context of affective facial processing. Depressed individuals exhibit slower reaction times for affective face identification overall (Surguladze et al., 2004), require greater intensity for happy facial expressions, and lower intensity in response to sad expressions (Joormann & Gotlib, 2006). This persists into remission (Lemoult & Sherdell, 2010). Aside from facial processing, cognitive impairments extend to the processing of affective body movements. Depressed individuals rate social interactions, depicted through point-light displays, as more negative and more intense for negative compared to positive interactions, compared to healthy controls (Kaletsch et al., 2014). However, facial expressions and body movements are inherently social in nature beyond their basic affective properties. It is therefore perhaps unsurprising that lower-order cognitive deficits observed in affective processing extend to higher-order deficits across multiple domains of social cognition. This includes theory of mind, social perception and metacognition and is present even in individuals experiencing their first depressive episode (Ladegaard, Roj, Videbech, & Lysaker, 2014; Lee, Hermens, Porter, & Redoblado-Hodge, 2012).

ALTERED REWARD SENSITIVITY

In addition to cognitive biases and deficits, depressed individuals exhibit blunted anticipatory reactivity to rewarding (positive) stimuli, but not to non-rewarding (neutral) stimuli or (negative) stimuli indicative of punishment (McFarland & Klein, 2009). An altered sense of reward derived typically from engaging in pleasurable (social and non-social) activities is thought to be driven by a variety of factors. These include reduced reward sensitivity, and impairments in reward encoding and positive reinforcement learning (Dillon et al., 2015; Huys, Pizzagalli, Bogdan, & Dayan, 2013; Pizzagalli, 2014), persisting beyond recovery (Pechtel, Dutra, Goetz, & Pizzagalli, 2013). These findings assume blunted emotional reactivity to positive stimuli, such as reward, in contrast to a heightened negative response bias. However, an alternative account suggests that depression is characterised by deficits in emotional reactivity independent of valence (Bylsma, Morris, & Rottenberg, 2008). Specifically, the emotion context-insensitivity hypothesis posits that depressed individuals exhibit overall lowered reactivity in response to both negative and positive information (Bylsma et al., 2008; Rottenberg, Gross, & Gotlib, 2005).

A further interpretation draws on differences in recognition accuracy as a function of emotional intensity, correlated with depression severity and difficulty in emotion regulation (Gollan, McCloskey, Hoxha, & Coccaro, 2010). Impaired recognition of affective social signals may detrimentally impact on an individual's ability to engage with *regulatory* goal-directed actions. The occurrence, magnitude, duration, and expression of this response may encompass both voluntary and automatic processes (Gross, 1998; Sheppes, Suri, & Gross, 2015), including the effortful cognitive reappraisal of meaning associated with an emotional context, the active attentional disengagement from negative stimuli, as well as labelling emotions, thereby reducing subjective distress (Gross, 1998; Moyal, Henik, & Anholt, 2014). In depression, individuals tend to engage in maladaptive emotion regulation strategies, such as rumination or distraction, intrinsically linked to greater symptom severity and deficits in cognitive processing. However, the use of emotion regulation strategies in response to social emotions has revealed inconsistent and limited results thus far (see Aldao, Nolen-Hoeksema, & Schweizer, 2010).

A MATTER OF PERSPECTIVE?

In addition to emotion recognition and regulation, the ability to infer and empathise with other people's mental and affective states, i.e. empathic processing, underpins our ability to engage in successful social interactions. In depression, there are varying accounts of empathic processing deficits. For instance, there are suggestions that depression is associated with heightened levels of empathetic stress, but reduced empathic concern and perspective-taking ability (Schreiter, Pijnenborg, & Aan Het Rot, 2013). These findings are frequently correlated with greater depressive symptom severity (Cusi, MacQueen, Spreng, & McKinnon, 2011). Perspective taking as a mechanism underpinning the ability to infer other's mental representations is crucial to the empathic response with reduced empathic concern thus appearing at odds with the observation of heightened empathic stress in depression. One possible interpretation of these findings assumes heightened proneness to self-blaming emotions in depression (Green, Moll, Deakin, Hulleman, & Zahn, 2012). As such, the presence of self-relevant negative emotions, such as guilt, shame or self-contempt within a social interaction may increase empathic stress. In contrast, other-relevant social emotions, such as

contempt or anger may be more greatly associated with heightened empathic concern, although it is worth noting that these emotions can also be directed at the self (Zahn et al., 2015). As a result, reduced other-referential processing in depression may account for increased empathic stress alongside reduced other-oriented empathic concern.

This interpretation is aided by evidence suggesting heightened self-focused attention in depression, with ruminative self-focused attention (SFA) previously posited as an explanatory factor in depressed individuals' negative response bias (Ingram, 1990). Specifically, SFA is the heightened awareness for internally generated or self-relevant information as opposed to externally derived information. Interestingly, maladaptive SFA is associated with greater negative affect and negative appraisal across multiple psychopathologies, including depression (Beck & Clark, 1997; David M. Clark, 2001; Mor & Winquist, 2002; Spurr & Stopa, 2002). However, the observation of heightened empathic stress may also merely reflect prior personal negative experiences. In an interesting study, the heightened prior exposure to social exclusion in depressed individuals was associated with greater levels of empathy during subsequent vicarious exposure to other's social pain of exclusion (Nordgren, Banas, & MacDonald, 2011). Discrepancies in the empathy literature in depression may thus reflect altered processing of self- (empathic stress) versus other- (empathic concern) relevant affective information. They also highlight the importance of the social context in which the interaction is taking place.

Neural Basis of Socio-Affective Processing in Depression

On a neural level, affect-independent processes, such as decision-making and reasoning, are argued to activate large areas of the PFC, including OFC, and ACC (Phillips, Ladouceur, & Drevets, 2008). However, when processing negative affective information, a voxel-based morphometry study revealed a volumetric reduction in the OFC in depression, with increased functional activity in the middle frontal gyrus, caudate, precuneus and lingual gyrus (Scheuerecker et al., 2010). In addition, regional lesions are associated with emotional disturbances (see Levy & Dubois, 2006, for review). This suggests that hyperactivity in (extended) limbic areas, such as the ACC and OFC, may underpin abnormalities in processing negative affective material in depression (Miskowiak & Carvalho, 2015). In contrast, reward

or positive affective processing in depression revealed decreased activity in medial PFC, with greater activity in inferior frontal gyrus (IFG), ACC, thalamus, putamen and insula. As already noted, this region had previously been associated with (negative) social aversion (Forbes, 2011; Forbes et al., 2009; Mitterschiffthaler et al., 2003). In addition, reduced medial PFC activation in response to positive social interaction images extended to remitted depressed individuals, lending support to the notion of persistent deficits in social processing post recovery (Elliott et al., 2012). Thus, areas previously implicated in negative affective processing, including reduced prefrontal activation and increased limbic activation extend also to the processing of rewarding positive affect in depression.

This imbalanced neural response in the fronto-limbic network extends to other key regions involved in social affective processing. The amygdala has been described as central to the recognition of socially salient signals within the social brain (Adolphs et al., 2002). There are several lines of evidence supporting this notion. Lesion studies revealed that unilateral and bilateral amygdala damage was associated with impairments in recognising basic and complex social emotions, such as shame, jealousy, or pride (Adolphs et al., 2002). Further, functional evidence revealed that depressed individuals' perceived negative evaluation by others, expressed in feelings of shame, was associated with preferential activation in the amygdala (Pulcu et al., 2014). This was juxtaposed to the decreased activity observed in response to self-referential feelings of guilt, persisting into remission. This suggests that the frame of reference, the comparison of self-versus other, and social context impacts on the neural processing of emotion in depression, and may maintain depressive vulnerability, as behavioural findings have previously suggested (Green, Lambon Ralph, Moll, Deakin, & Zahn, 2012; Green, Moll, et al., 2012). Results also suggest a negative response bias, with meta-analytic findings revealing heightened functional activation in response to negative facial expressions in the amygdala. In contrast, processing positive facial expressions evoked decreased activity in the amygdala, as well as the insula, parahippocampal gyrus, fusiform face area, and putamen (Stuhrmann, Suslow, & Dannlowski, 2011). However, the research to date may be erroneous in its assumption, and in particular, studies contributing to this meta-analysis, as research on emotional processing in depression is based almost exclusively on behavioural and neural

responses to negative stimuli and not comparably salient positive stimuli. This presents a clear gap in the literature and begs further investigation.

SUMMARY

In sum, individuals with depressed mood exhibit marked cognitive impairments and biases in neutral and affective contexts. These findings reinforce the notion of a negative response bias in depression, with greater cognitive attention directed towards negative information, and altered sensitivity towards positive signals. These deficits and biases in depression further extend to the recognition of socio-emotional stimuli, such as faces, gestures or even motivational demands within a social context. This detrimentally affects depressed individuals' ability to effectively maintain or engage with adaptive goal-directed emotion regulation strategies. With differential empathic responses to self- and other-referential processing, an impaired ability to mentalise other's emotional states might entail a greater likelihood of negative social experiences, and thus correlate with heightened sensitivity to social rejection. This raises some interesting questions, as higher-order deficits in socio-cognitive processing at the neural level remain to be fully explored.

Thus, negative cognitive biases in depression are thought to be facilitated by increased influence from subcortical emotion processing regions in combination with reduced top-down regulation in prefrontal cognitive control regions. This fronto-limbic imbalance is further evident in social reward and positive emotion processing, indicating widespread cognitive impairments in depression that extend to social and emotional processes. However, importantly, emerging findings do not explicitly rule out a comparable pattern of activation in response to both positive and negative social signals. Furthermore, no research to date has carried the debate around a selective network for social pain into the depression literature, despite the obvious functional impairments in social functioning. This requires resolution, as underlying psychological and neural insights into social functioning can aid our understanding in the context of theoretical accounts of depression, the topic of the next section.

1.6 How do these findings relate to theoretical accounts of depression?

The theoretical study of depression underwent a cognitive revolution in the 1960s (G. A. Miller, 2003). Rather than focusing on analytical psychodynamic approaches, the literature experienced a shift toward the adoption of models stressing cognitive mediation. This was based on the emerging assumption that cognitive distortions in depression affected behaviour and mood, but were nonetheless open to change. This cognitive restructuring involved a rigorous focus on negative cognitions about the self, others and the world, frequently incorporating impairments from within the social domain. Notable models include the cognitive model of depression (Beck, 1967, 1987a; Beck, Rush, Shaw, & Emery, 1979; Ellis, 1962), Seligman's model of learned helplessness (Seligman, 1972) and its reformulation based on the revised attribution theory (Abramson, Seligman, & Teasdale, 1978) and finally, the model of self-control (Rehm, 1977). These theories have made significant contributions to the understanding and treatment of depression. The social domain is thus the playing field of distorted cognitions central to the models noted above. From this, interpersonal theories of depression emerged, more closely investigating the contribution of social deficits to the development and maintenance of depression.

Early interpersonal theories

Contrary to the recent (2016) referendum results voting in favour of Great Britain exiting the European Union, humans have commonly been ascribed with a fundamental need to belong, motivated by an evolutionary drive for self-preservation and survival within a hierarchy of needs (Maslow, 1943). This is accomplished by securing access to limited resources and ultimately reproductive privileges within the safety of a social group (Baumeister & Leary, 1995). However, there exist competing theoretical accounts of how depression has evolved and is maintained within the context of this social dynamic. Central to all theories is the notion that individuals are highly sensitive to how the social world perceives and values them and that there is a dedicated mechanism in place to monitor and regulate human behaviour to satisfy the fundamental need to belong.

Early interpersonal theories of depression, such as Coyne's interactional model, argued that feelings of low mood in depression result as a function of maladaptive social behaviour which in turn entails a greater likelihood of experiencing social rejection and other negative life events (Coyne, 1998; Segrin & Dillard, 1992). Similarly, Lewinsohn posited that depressed individuals lack social skills, thereby preventing the experience of positive reinforcement or social reward (Lewinsohn & Libet, 1972; Libet & Lewinsohn, 1973; Youngren & Lewinsohn, 1980). This social skills deficit model argues that poor social competency and/or the lack of a supportive social environment are essential maintaining factors for depressive symptoms. Poor social skills may be attributed to a range of interpersonal characteristics associated with greater symptom severity in depression, for instance the automatic expression of negative facial expressions (e.g. contempt), less positive expressions (e.g. smiling) (Girard, Cohn, Mahoor, Mavadati, & Rosenwald, 2013), and impaired adaptation to other's emotional expressions, gaze direction or social motivational demands (Radke, Güths, André, Müller, & de Bruijn, 2014). Impaired perception and understanding of interpersonal social signals and the inability to respond appropriately might further account for other's appraisal of poor social skills in depressed individuals (Tse & Bond, 2004), in addition to the dominant negative narrative.

Sociometer Theory

In line with early interpersonal theories, the sociometer theory of depression relies on other's appraisals. Based on our fundamental need to belong, the sociometer theory posits that self-esteem functions as an internal monitor for interpersonal relationships, guided by perceptions of social rejection or acceptance that alert the individual to changes in relational status (Baumeister & Leary, 1995). The ability to attend and respond to signals of social rejection and inclusion therefore provides a mechanism for the modification and adaptation of various social strategies and behaviours in response to negative and positive social feedback. On an intra-individual level, the quality of relationships has been found to account for short-term fluctuations in self-esteem, while higher (and more stable) trait self-esteem was associated with higher quality relationships (Denissen, Penke, Schmitt, & van Aken, 2008). Moreover, low self-esteem, conceptualised as negative beliefs about the self, has long been posited as a causal risk factor for depression, with robust evidence for the predictive power of low self-esteem in

depression (Orth & Robins, 2013; Sowislo & Orth, 2012). Tajfel's social identity theory provided early evidence for this inherent human drive to attain social affiliation and positive self-identity via in- versus out-group social categorization, followed by in-group favouritism on a par with out-group derogation, to maintain said affiliation (Tajfel, 1978). Moreover, the threat of social exclusion was associated with greater motivation and attention to cues signalling affiliation with novel social targets (DeWall, Maner, & Rouby, 2009; Maner, DeWall, Baumeister, & Schaller, 2007). It thus reflects the motivation of individuals to maintain a minimum level of group affiliation and modify behaviour in response to the mere threat of social exclusion (Leary, 2010; Maner et al., 2007).

However, other evidence suggests that social exclusion does not consistently motivate affiliative behaviour, as originally suggested by the sociometer theory. Such behaviours could range from reduced prosocial behaviour (Twenge, Baumeister, DeWall, Ciarocco, & Bartels, 2007) to increased aggressive behaviour towards perpetrators of negative feedback and exclusion (Twenge, Baumeister, Tice, & Stucke, 2001). Despite being one of the early leading theoretical accounts of the function of self-esteem and positive self-regard in interpersonal interactions, the sociometer theory has not been consistently supported in the literature. Higher levels of self-esteem are not consistently associated with greater subjective interpersonal success, positive affect and even health outcomes, while objective measures of self-esteem, as opposed to self-reported levels, fail to predict duration or quality of interpersonal relationships and social success in other domains. (Baumeister, Campbell, Krueger, & Vohs, 2003). Moreover, the sociometer theory requires a medium degree of self-esteem contingency for an optimal response, in which greater variability in self-esteem fluctuations is suggestive of a miscalibrated system (Leary, 2004; Oosterwegel, Field, Hart, & Anderson, 2001). However, there was no evidence for a curvilinear relationship between the contingency of depressive symptoms on self-esteem (J. Sowislo, Orth, & Meier, 2014), suggesting that depression may be a relatively distal outcome of a potentially miscalibrated sociometer.

HIEROMETER AND SOCIAL RANK THEORY

Thus, a recent challenge to the sociometer theory has come in the form of the hierometer theory (Mahadevan, Gregg, Sedikides, & De Waal-Andrews, 2016), which argues that it is not merely the fundamental need to belong that drives human behaviour, but rather the fundamental need for status (Anderson, Hildreth, & Howland, 2015). This builds on earlier work conceptualised within social rank theory, which provides an initial framework for understanding the relationship between defensive submissive strategies in depression, anxiety and social rank (Gilbert, 2000). The central notion of the hierometer and social rank theories derives from intra-species competition for physical and social resources which requires the ability to negotiate, challenge and ascertain social status within a social hierarchy, operationalised as resource-holding power (RHP). Furthermore, in line with the hierometer, humans are ascribed a need for other's positive appraisals. This provides an extension of RHP, incorporating social attention holding power (SAHP) as a useful tool in maintaining affiliative status and high self-esteem within a social hierarchy. The absence of SAHP and RHP may contribute to the development of depressive symptoms. In fact, low social rank has been associated with a range of psychopathologies, including depression, anxiety and psychosis (L. Wood & Irons, 2015). Submissive behaviours expressed as a result of low rank in a social hierarchy include many of the features described in the social skills deficit model of depression (Lewinsohn & Libet, 1972; Libet & Lewinsohn, 1973; Youngren & Lewinsohn, 1980), including averting gaze and social withdrawal. The latter is perhaps better conceptualised as subordinate or avoidance behaviour, with depressed individuals more likely to identify themselves as more inferior than others when engaging in social comparisons (Allan & Gilbert, 1995).

While sociometer theory posits a minimal threshold for inclusion as an evolutionary advantage for survival, hierometer and social rank theory argue that higher social rank bestows greater evolutionary advantage, including greater reproductive success, increased access to potential partners, community-wide allies and deference from competitors (Anderson & Kilduff, 2009; von Rueden, Gurven, & Kaplan, 2011). This is achieved not merely by displays of dominance, but also by enhancing and exhibiting an individual's subjective value to a group within a social infrastructure, echoing Gilbert's assertion of the importance of social attention holding power

(Anderson & Kilduff, 2009; Cheng, Tracy, Foulsham, Kingstone, & Henrich, 2013). Low self-esteem in depression is found to inhibit this assertive-affiliative behaviour; while, greater submissive behaviour in depression may be preferable to maintain a more stable social rank. This approach is the result of an evolutionary driven risk-benefit calculation, considering other's rank and power relative to the self, as well as the likelihood of competitive success.

A Social Risk Hypothesis of Depressed Mood

Finally, the social risk (SR) hypothesis of depressed mood (Allen & Badcock, 2003) encompasses many of the features described both in the sociometer, hierometer and social rank theory, and brings together evolutionary, psychosocial, and neurobiological perspectives. For a schematic overview, see Figure 1.4. In the SR hypothesis, the adaptive mechanism is conceptualised as the social investment potential (SIP), which represents the ability of an individual to successfully invest in socially relevant endeavours. Or in other words, the extent to which an individual can maintain beneficial social relationships. An individual's SIP is derived from the ratio between their perceived social value (S_V), or benefit to others, and the perceived social burden (S_B), or the cost or loss of current or potential resources to others because of participation in social interactions. These two components are informed by positive and negative interpersonal experiences, the perceived control of the social environment, achievement or failure of socially relevant or important goals, as well as the perceived SIP of others' or competitors', and investments gained from others. These, in turn, can be broadly categorised into two dimensions of interpersonal relatedness - an individual's level of agency and affiliation. Thus, SIP will fluctuate according to feedback from the social world or the context that individuals find themselves in. For instance, if social value exceeds social burden in a current relationship, resulting in high estimated SIP, an individual may be motivated to extract more resources from social investments using opportunistic social strategies; whereas if social value and social burden approach equivalent states, estimated SIP decreases, thereby leading to less risky social endeavours and increased sense of failure and lack of agency and importantly, threat of exclusion. Phenomenologically, these changes in SIP may be expressed as fluctuations in self-esteem and status, as conceptualised within the sociometer and hierometer theories.

From an evolutionary perspective, depression is argued to evolve because of critically low SIP. Similar to the sociometer (Baumeister & Leary, 1995) and hierometer theories (Mahadevan et al., 2016), the Allen and Badcock (2003) argue that to maintain affiliation within a group, individuals have developed a sophisticated capacity to judge their (social) value to others against their burden on others. Thus, the SR hypothesis places a greater emphasis on the ratio between an individual's social value and social burden, reflected in fluctuations of SIP, which in turn affect behaviour and cognition. In depression, precipitants for low or unsatisfactory SIP may include negative interpersonal experiences (such as losses or rejections), as described by the sociometer theory (Baumeister & Leary, 1995; Leary, 2004; Slavich & Irwin, 2014b); the failure to achieve socially relevant goals resulting in perceived or actual loss of social status, as described within the hierometer theory (Mahadevan et al., 2016); or perceptions of a lack of control, defeat or entrapment in social situations, exemplified in the social rank theory (Abramson et al., 1978; Gilbert & Allan, 1998; Gilbert & Gilbert, 2003). Establishing SIP further relies on other-relevant processing of competitors perceived SIP, as well as social investments gained from others. As a result, critically low SIP motivates the individual to adopt a risk-averse approach to social interactions in the context of perceived threat of exclusion (see Figure 1.5). Once this risk-averse state of depressed mood has been activated, the individual tailors behaviour and cognitive process to the social context, resulting in further low mood and anhedonia. Socio-cognitive deficits and impairments in social functioning consistently observed in behavioural and neuroimaging findings in depression can be understood in the context of this theory.

To illustrate, deficits in executive function (Hammar & Ardal, 2009; Snyder et al., 2015), attention or emotion recognition and regulation (Gollan et al., 2010; Hammar & Ardal, 2009; Joormann & Gotlib, 2006; Snyder et al., 2015) may serve to maintain vigilance to indicators of further social threat with attentional and inferential biases to negative (social) information. Feelings of low mood and anhedonia serve to reduce risk-taking behaviour, which would require motivation to engage in (social) activities (Kwapil et al., 2009; Mitterschiffthaler et al., 2003; Pizzagalli, 2014). Moreover, to further reduce social risk, individuals exhibit social withdrawal and/or signal submissiveness and subordination to conspecifics to avoid defeat or elicit help (Allan & Gilbert, 1997; Kupferberg, Bicks, & Hasler, 2016; Slavich & Irwin, 2014a;

Sturman, 2011). This maintains low mood and negative views on self, others and the future. In addition, the model emphasises that individual SIP may fluctuate as a result of responding to others' perceived heightened SIP, and others' received investments. This is a compelling component, as depressed individuals may respond with complex social emotions such as guilt, shame or disgust relative to the social transaction (Gilbert, 2000; Green, Moll, et al., 2012; Pulcu et al., 2014; L. Wood & Irons, 2015). The extent of the reciprocal social transaction might also reflect fluctuations in levels of empathic concern and empathic stress, given the importance of monitoring and responding to others' SIP relative to one's own SIP (Cusi et al., 2011; Feng et al., 2016; Schreiter et al., 2013; Zahn et al., 2009).

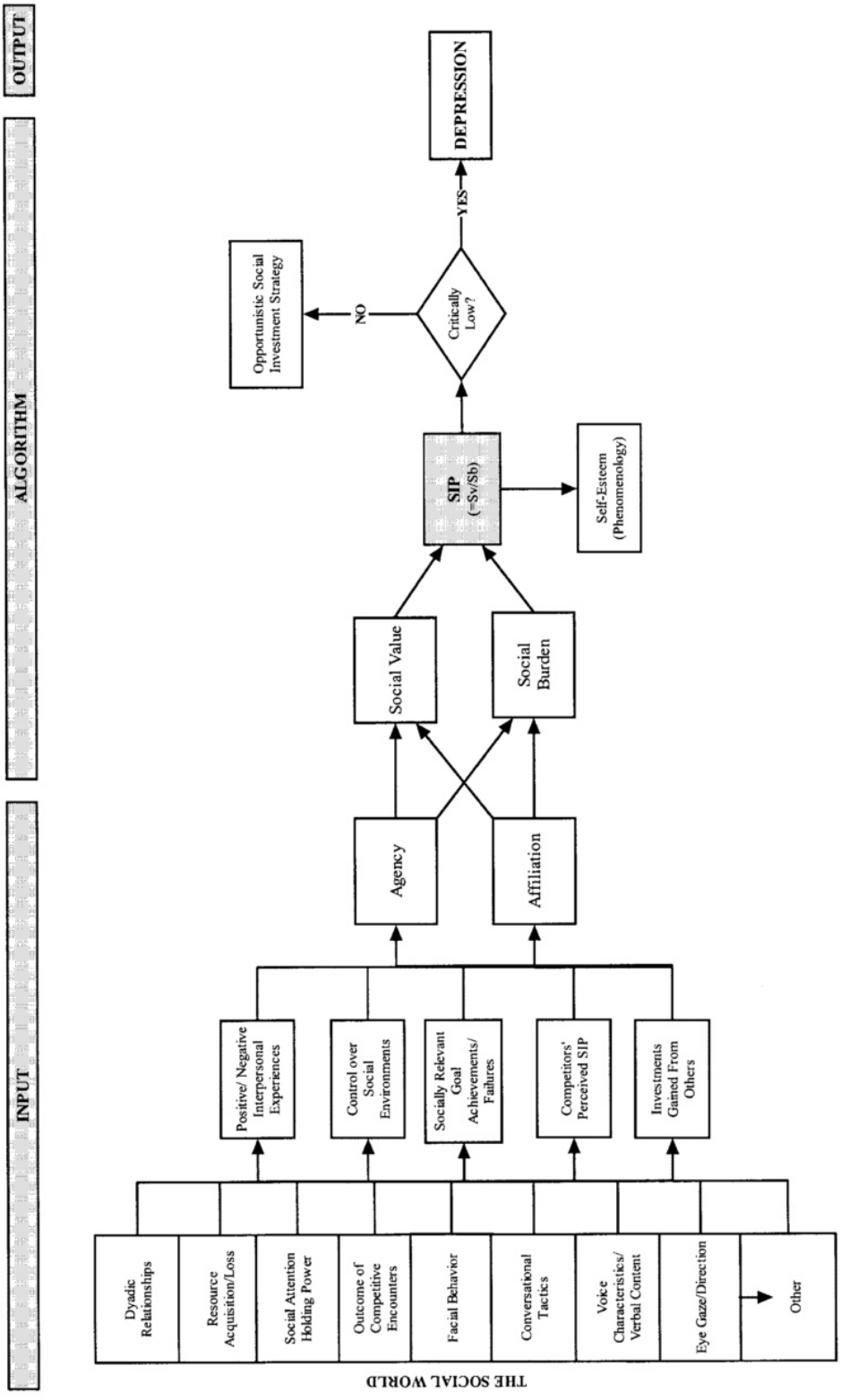


Figure 1.4 Adapted from Allen and Badcock, 2003, p987. Hypothesised inputs and the algorithm of the depression mechanism. SIP = social investment potential; Sv = social value; Sb = social burden.

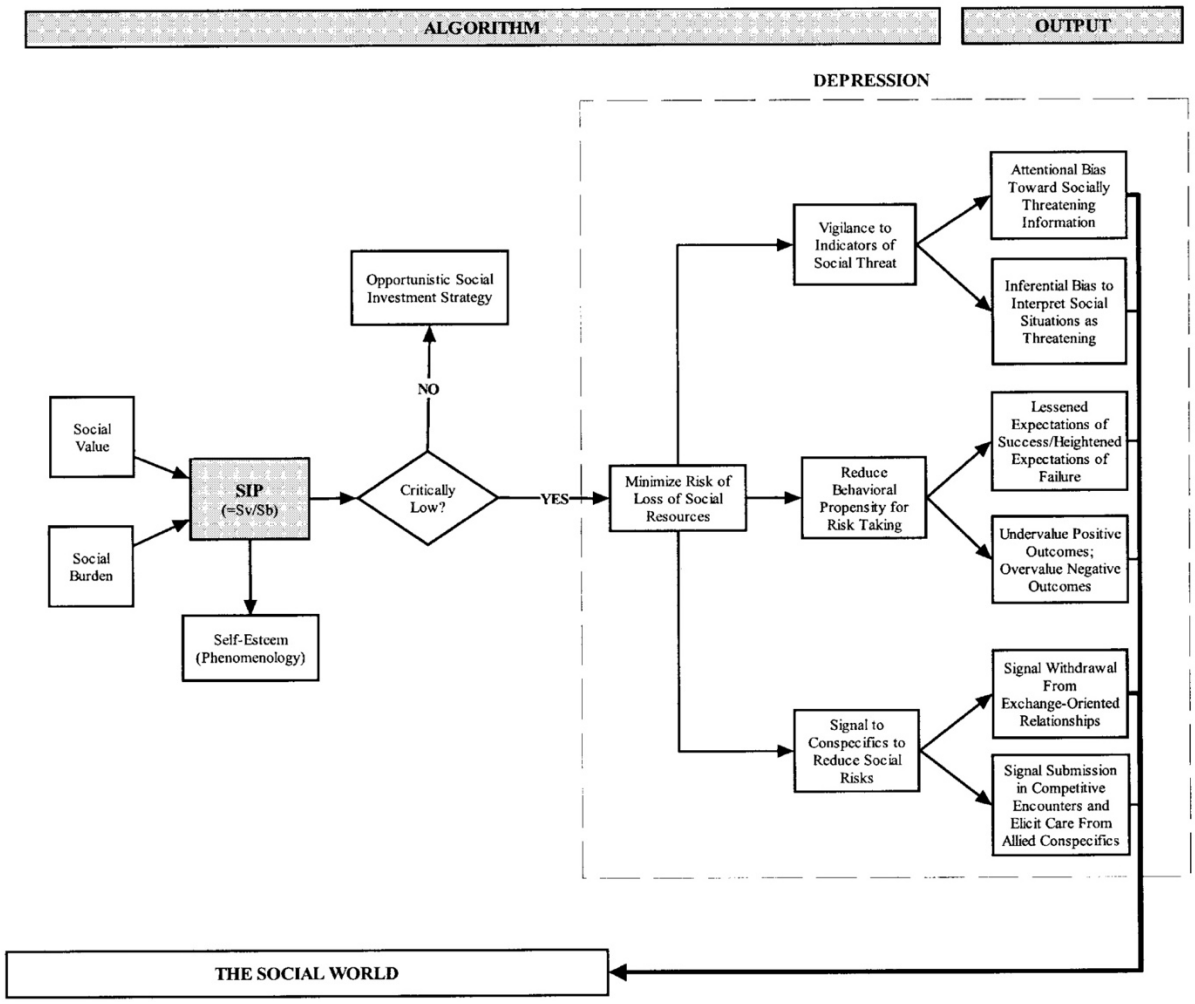


Figure 1.5. Adapted from Allen and Badcock, 2003, p987. Hypothesised *outputs* and *actions* of the depression mechanism. SIP = social investment potential; Sv = social value; Sb = social burden.

SUMMARY

In sum, all of the above theories build on the fundamental human need to belong and have posited different mechanisms by which individuals with and without depression navigate the social straits of group membership and hierarchy. The consensus is that successful social interaction requires dedicated and adaptive psychological and neural systems able to detect and respond to social signals of inclusion and rejection. The sociometer theory argues that self-esteem tracks levels of inclusion and regulates affiliative behaviour with the aim of avoiding exclusion. The hierometer theory posits that self-esteem tracks social status or rank, and regulates assertive behaviour with the aim of matching or exceeding the current social status and social attention holding power (SAHP). Finally, the social rank hypothesis conceptualises depressed mood as an evolutionary rooted risk-averse motivational state, which is informed by the social world, social status or rank and interpersonal experiences. The risk-averse individual with depressed mood thus tailors behaviour and cognition to the social context to maintain his or her social investment potential (SIP); i.e. the ratio of perceived social value over social burden and clinical depression represents a case of being chronically 'stuck' in a state of perceived low SIP. Thus, the social risk hypothesis provides a compelling framework, encompassing concepts and assumptions held within the sociometer, hierometer and social rank theories. In addition, behavioural findings appear to provide strong evidence in support of the SR hypothesis. The neural territory, however, remains relatively uncharted. This presents an important gap in the literature, which the work reported in this thesis will aim to begin to address.

1.7 Intervention approaches

In this section, we will briefly review current intervention approaches to the treatment of depression. While pharmacological interventions with antidepressant (AD) medication are effective in treating acute symptoms of depression, residual symptoms persist in the majority of patients, alongside well-documented side-effects (Adams, Miller, & Zylstra, 2008). Together, these make non-pharmacological approaches appealing alternatives in preventing further depressive episodes, especially when the risk of recurrence and chronicity in depression is considered. In addition, incorporating theoretical findings from above sections will aid in the development of existing treatment approaches, with the aim of preventing relapse.

One of the main non-pharmacological or psychological therapies is Cognitive Behavioural Therapy (CBT) (Beck, 1967; Beck et al., 1979; A. Butler, Chapman, Forman, & Beck, 2006). It is based on the assumption that emotional distress and behavioural problems are maintained by cognitive factors: for example, distortions in core beliefs or assumptions about the world and the self would trigger negative automatic thoughts and lead to low mood (Hofmann, Asnaani, Vonk, Sawyer, & Fang, 2012). More, recently, mindfulness-based cognitive therapy (MBCT) has emerged as a third-wave approach (Kuyken et al., 2016) to preventing relapse in depression. MBCT is a structured group treatment that incorporates mindfulness training, such as body scan meditation, alongside cognitive therapy. The emphasis of MBCT on relapse prevention and the psychological benefits of mindfulness have garnered attention both in the scientific and general population (Bockting, Hollon, Jarrett, Kuyken, & Dobson, 2015; Teper, Segal, & Inzlicht, 2013). Increasingly, transdiagnostic (TD) perspectives have been successfully integrated into primary care, evidenced in recent meta-analyses comparing face-to-face CBT to clinician-guided internet/computerised or face-to-face TD-CBT and mindfulness-based treatments. Results revealed that both traditional and TD approaches provide comparable efficacy in reducing depression and anxiety (Newby, McKinnon, Kuyken, Gilbody, & Dalgleish, 2015; Vollenbroek-Hutten et al., 2015).

Despite advances in the development of cognitive-based interventions, there is still a lack of understanding regarding the underlying *cognitive* mechanisms contributing to the development and maintenance of depressive symptoms, as described in the previous sections (Flint &

Kendler, 2014). Moreover, treatment outcomes do not tend to include improvements in cognitive processing, such as decision making and concentration, but predominantly target the nature of cognitions themselves: negative thoughts about the self, others and the world (McIntyre et al., 2013). This is despite residual deficits being commonly observed in cognitive domains following recovery, including attention, executive function or verbal memory (Godard, Baruch, Grondin, & Lafleur, 2012).

The importance of treating cognitive deficits in MDD is particularly pertinent to social functioning, as psychosocial impairments in depression are largely mediated by underlying cognitive deficits, and not merely by poor social skills as assumed in early interpersonal theories of depression (McIntyre et al., 2013). However, unsurprisingly, existing pharmacological and non-pharmacological interventions offer only limited or short-lived improvements to social functioning. Moreover, measures of social functioning are seldom included as functional treatment outcomes (Hirschfeld et al., 2000; N. Kennedy, Foy, Sherazi, McDonough, & McKeon, 2007; Park, Cuijpers, van Straten, & Reynolds, 2014; Renner, Cuijpers, & Huibers, 2014). This was exemplified in a three-year follow-up highlighting the long-term debilitating impairments in social and physical functioning even after recovery from depressive disorders, including unipolar MDD, dysthymic disorder and bipolar depression (Rhebergen et al., 2010). Thus, existing interventions will improve if we can gain a better understanding of the social and cognitive mechanisms involved in depression.

Noteworthy social interventions, which place a greater emphasis on social functioning include interpersonal therapy (IPT) and compassion focused CBT. IPT addresses current or recent life events, interpersonal difficulties, and symptoms (Feijo De Mello, De Jesus Mari, Bacaltchuk, Verdeli, & Neugebauer, 2005). It is based on the interactional principle put forward by Coyne (1998) and discussed above. The interactional perspective on depression emphasises the relationship between past personal events, the role of significant others, and depressed individuals' cognitions about themselves in relation to their interpersonal context. While IPT shares some phenomenological characteristics with psychodynamic therapy in that it advocates an exploratory approach, the two are nonetheless distinct. Instead, IPT shares both the time-limited, active approach of CBT as well as the diagnostic focus on the "here and now" with

some suggestions of greater efficacy in treating depression compared to CBT (Feijo De Mello et al., 2005). However, the therapy focuses on active changes and solutions for interpersonal problems, primarily acting on reactive as opposed to endogenous processes. While CBT takes a wider perspective on both the presenting problem and underlying aetiology, IPT arguably provides a more effective approach within the social domain.

In comparing intervention approaches, there is evidence to suggest that CBT and psychodynamic approaches are as effective as pharmacological therapies for treating mild depression (Furukawa, McGuire, & Barbui, 2002). One study, in particular, suggested that CBT delivered in response to acute MDD can provide prolonged recovery, augmented by continued psychological interventions (Bockting et al., 2015). Moreover, a recent meta-analysis of randomised controlled trials (RCTs) compared the efficacy of psychological interventions CBT, MBCT and IPT to treatment as usual and anti-depressant use in preventing recurrence. Results indicated that psychological interventions may prolong the recovery or reduce the risk of relapse following non-pharmacological intervention over a 12-month period. Nonetheless, this meta-analysis still implied greater efficacy following pharmacological treatment in the first instance (Biesheuvel-Leliefeld et al., 2015; Clarke, Mayo-Wilson, Kenny, & Pilling, 2015). However, a large RCT investigating the effectiveness of MBCT relative to maintenance antidepressant medication revealed no evidence that antidepressant medication was superior to MBCT in preventing relapse in at-risk individuals (Kuyken et al., 2015). In fact, both treatments showed promising positive effects on residual symptoms and quality of life, see also Kuyken et al. (2016). This finding contradicts previous results and is of great importance, given the well-documented side-effects of pharmacological medication.

However, the relative benefits and harms of the different approaches outlined above are yet to be definitively established (Furukawa et al., 2002). Moreover, in cases where common psychotherapeutic and psychopharmacological interventions fail to remedy chronic, severe or treatment-resistant depression, alternative interventions have been sought. These include deep brain stimulation (Mayberg et al., 2005), repetitive transcranial magnetic stimulation (rTMS) and electroconvulsive therapy (ECT) (Pagnin, de Queiroz, Pini, & Cassano, 2004; Schulze-Rauschenbach, 2005). However, evidence for their respective efficacy remains mixed, with the

trade-off between therapeutic doses, treatment response and side-effects confounding the benefits and risks of these latter treatment approaches.

In sum, depression is one of the most common psychiatric disorders marked by a heightened risk of relapse and recurrence, amplified in the presence of social risk factors. Despite efficacious interventions in response to acute phase depression, the residual deficits observed in cognitive and social functioning following recovery warrant further investigation into underlying mechanisms. Moreover, incorporating measures of cognitive *and* social functioning would aid in the development of more targeted treatment approaches, allowing for earlier identification and treatment of at-risk individuals. This would thereby alleviate the increasing global economic health burden that depression and other mood disorders represent today.

1.8 Summary and questions

In summary, depression is a debilitating heterogeneous disorder, characterised by an early onset, heightened risk of recurrence and vulnerability to a range of risk factors, such as negative interpersonal experiences. Impairments in social and cognitive functioning are evident, with residual symptoms persisting beyond recovery. However, targeted interventions have yet to be developed which incorporate outcome measures specifically addressing the altered socio-cognitive profile observed in MDD. Furthermore, difficulties in emotion recognition and regulation contribute to the systemic biases underlying affective information processing, observed both on a behavioural and neural level. However, the literature has largely focused on affective processing *per se*, with less regard given to the complexities of interpersonal or *socio*-affective processing that may account for deficits in social functioning in depression. This is despite extensive findings detailing the heightened interpersonal rejection sensitivity and contribution of social risk factors to the development and maintenance of depressive symptomology.

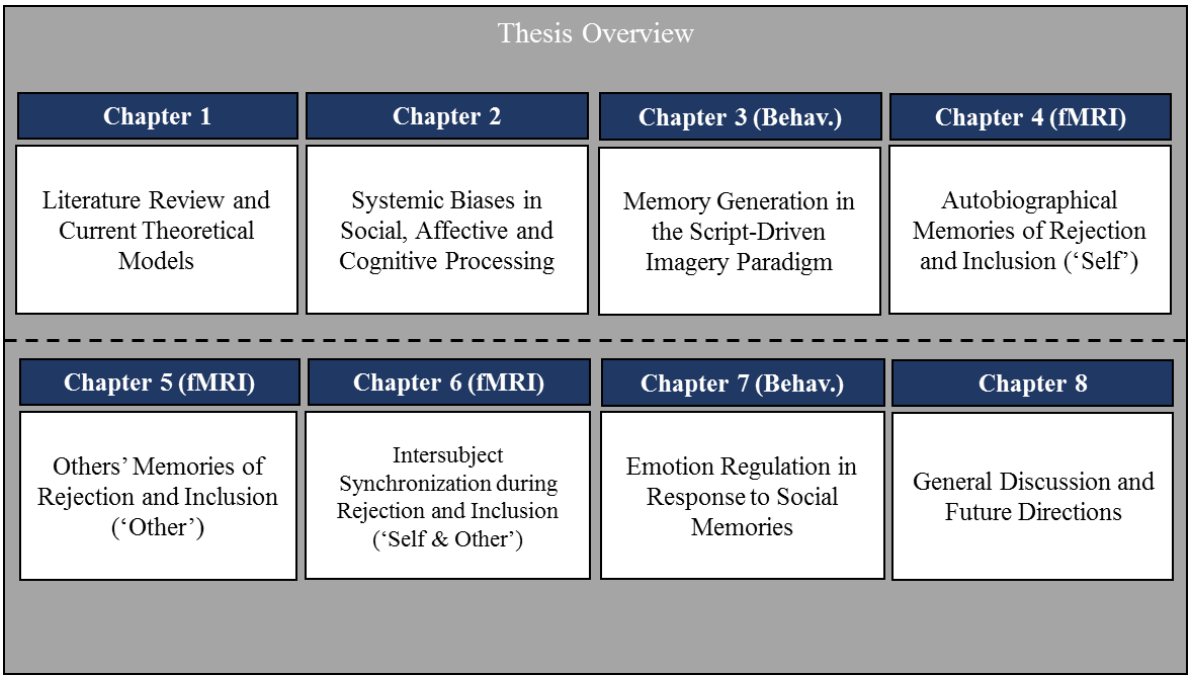
Investigating social pain as a key interpersonal phenomenon represents a step in the right direction within the context of social functioning in depression. However, this literature has also revealed conflicting accounts and the debate surrounding a selective network for social pain continues. In addition, theoretical accounts of social processing in depression have to date

mostly been implemented on a behavioural level with limited evidence validating these theories on a neural level. In particular, within clinical populations, for whom impaired social processing is arguably a key deficit. Furthermore, interpersonal theories of social processing suggest that social impairments may be as a result of either a mis-calibrated system for tracking signals of inclusion and rejection, including emotion recognition, impaired understanding or appraisal of these social signals or dysfunctional emotion regulation, and subsequently maladaptive social behaviour (Segrin, 2000; Segrin, Mcnelis, & Swiatkowski, 2016; Tse & Bond, 2004).

Finally, there is a lack of ecologically valid paradigms that sufficiently capture and elicit the dynamic real-world experiences of social rejection and inclusion or social interaction more generally. Despite promising findings in social affective neuroscience, experimental results generalise to real life only when they reflect automatic perceptual processes, and not response strategies adopted to satisfy the particular demands of laboratory tasks, such as Cyberball (De Gelder & Bertelson, 2003). One approach to this problem is the use of autobiographical memories. Personal memories serve as a rich repository of social interactions and have in the past been used to elicit salient emotions using a script-driven imagery approach. Previously used primarily in research on posttraumatic stress disorder, as well as in healthy control populations, studies have found this paradigm to be successful at eliciting highly arousing, intense emotions in response to recollected real-world social scenarios (Beckham et al., 2007; Frewen et al., 2008, 2010, 2011; Kleim, Wilhelm, Glucksman, & Ehlers, 2010; Lanius et al., 2002, 2003; Lindauer et al., 2004). Within the social pain literature, script-driven imagery has been used to investigate whether re-lived experiences of social and physical pain revealing heightened self-reported emotional distress and heightened activity in affective pain regions (dACC, AI) and mentalising networks (dorsomedial PFC) during the recall of socially painful experiences, while recall of physical pain activates the somatosensory system (S1, S2) in the absence of self-reported distress (Meyer, Williams, & Eisenberger, 2015). This suggests that the use of autobiographical memories may serve as a useful proxy for eliciting real-world social emotions both in healthy and clinical populations.

Thus, an overall aim of this thesis is to investigate individual differences in detecting and responding to interpersonal emotional signals on a behavioural and neural level, as well as differences in cognitive mechanisms involved in emotion recognition and emotion regulation. This will be achieved by implementing script-driven imagery of autobiographical memories as an ecologically valid approach, as opposed to the existing paradigms. This method will be used to elicit salient social emotions providing the basis for two neuroimaging studies of social rejection and inclusion; these studies will be aimed at elucidating the neural mechanisms underlying social processing. Results will be interpreted within explanatory theoretical frameworks, with an emphasis on the social risk hypothesis of depression. In the future, gaining a richer understanding of the individual differences in processing cues of social rejection and social inclusion at the behavioural and neural level in depressed and non-depressed individuals will allow for more focused interventions. This is of relevance for therapeutic success given the high frequency of residual symptoms in the socio-cognitive domain, with poor social functioning indicative of future relapse into depressive episodes. In the next chapter, we will address general issues and procedures pertaining to all experimental investigations presented in this thesis, as well as describing the first research study on systemic biases in social, affective, and cognitive processing in depression.

CHAPTER 2. SYSTEMIC BIASES IN SOCIAL, AFFECTIVE AND COGNITIVE PROCESSING IN MDD



2.1 Introduction

This chapter aims to outline general issues and procedures pertaining to the work presented in this thesis as a whole, including recruitment procedures, ethical considerations, and the general statistical approach to the data. These considerations can be applied to the data presented across the remaining chapters, and where different, modifications will be presented. In addition, this chapter aims at investigating systemic biases in social affective and cognitive processing in MDD and remitted depressed participants based on a battery of social, affective and process measures administered across all samples presented in this thesis. This will serve to validate the diagnostic screening and recruitment process using established measures of affective and cognitive processing, as well as validating existing social measures in a sample of depressed, remitted depressed and healthy controls.

Two of the most well-known measures of low mood and anxiety, the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI), are well suited for assessing symptom severity, and allow for the identification of residual affective symptoms in remitted depressed individuals (Beck, Guth, Steer, & Ball, 1997; Lasa, Ayuso-Mateos, Vázquez-Barquero, Díez-Manrique, & Dowrick, 2000; Osman et al., 2002; Storch, Roberti, & Roth, 2004). However, as outlined in the general introduction in Chapter 1, depression is further characterised by impairments in social functioning attributed to underlying socio-affective and cognitive deficits (Hirschfeld et al., 2000; N. Kennedy et al., 2007; Ladegaard et al., 2014), including reduced emotional awareness as one of five facets of mindfulness (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006) and difficulty in emotion regulation (Aldao et al., 2010; Bardeen, Fergus, & Orcutt, 2012; Gratz & Roemer, 2004; Gratz, Rosenthal, Tull, Lejuez, & Gunderson, 2006).

Furthermore, central to the work presented in this thesis, social rejection is posited as one of the strongest risk factors for developing depression, with early interpersonal difficulties viewed as potential psychosocial antecedents (Heim & Binder, 2012; Luterek et al., 2004; Slavich & Irwin, 2014b; Slavich et al., 2010; van Harmelen et al., 2010, 2014). In addition, sensitivity to social rejection is associated with symptom severity in social anxiety (Harb, Heimberg, Fresco, Schneier, & Liebowitz, 2002) and depression (Luty, Joyce, Mulder, F. Sullivan, & McKenzie,

2002) and is associated with greater neuroticism (Wilhelm, Boyce, & Brownhill, 2004) and higher rates of internal life stressors (Liu et al., 2014).

The importance of identifying biases in social processing in relation to symptoms of anxiety and depression is conceptualised within the social rank theory (Allan & Gilbert, 1997; Gilbert et al., 2007) and social risk (SR) hypothesis of depressed mood (Allen & Badcock, 2003), outlined in more detail in the general introduction. According to these theories, depressed mood is argued to develop as an evolutionary adaptive coping mechanism to reduce agonistic social interactions. In striving to gain access to shared resources, differential behavioural strategies might be advantageous when in competition with others. In other words, maintaining low social rank could be argued to be evolutionarily advantageous as opposed to challenging the status quo. This includes appeasing aggression or threats by a more dominant other, and inhibiting socially risky behaviour in response to the perceptions of defeat, inferiority or low social rank. The social rank theory thus proposes an internal gauge, which determines the likelihood of social defeat or success based on incoming social cues, with the hierometer further advocating a need for positive self-regard. Similarly, the SR hypothesis (Allen & Badcock, 2003) specifically argues that depressed mood is the result of critically low social investment potential, which represents the ratio of perceived social value and social burden. Moreover, impairments in social processing in remitted depressed may point towards a 'learned "lower rank" mind-set', in which the internal gauge of social rank or critically low SIP, once initiated, motivates (mal)adaptive behaviour even in the absence of current low mood. Thus, entrenched engagement in (mal)adaptive behaviours, such as greater submissiveness and subordinate behaviours aimed at restoring optimal social investment potential (SIP) or rank, now heighten the risk of chronic depression or depressive relapse.

Social comparison encapsulates this tendency for monitoring our social position within a hierarchy (Giacolini et al., 2013; Gibbons & Buunk, 1999; Terol, Lledo, Quiles, & Martin-Aragon, 2015). It is argued that such comparison motivates affiliative behaviour, including greater submissiveness and involuntary subordination, to maintain a stable social position within the hierarchy rather than risk expulsion (Allan & Gilbert, 1997; Baumeister & Leary, 1995; Gilbert et al., 2007; Leary, 2004). Evidence in support of this notion derives from studies observing changes in behaviour when threatened with social exclusion, such as increased

attention to positive social targets and motivation to seek novel sources of affiliation (DeWall et al., 2009; Maner et al., 2007). It does not, however, fully explain findings observing decreases in prosocial behaviour and increased aggression towards both former in and current out-group members (Twenge et al., 2007, 2001).

Previous work aimed at identifying social biases in affective and social processing outlined in these theories has led to the development of an array of measures targeting known areas of social impairment in depression. These include assessing for social comparisons, such as feelings of low rank (Allan & Gilbert, 1995), but extend to submissive behaviour (Allan & Gilbert, 1997), striving to avoid inferiority (Gilbert et al., 2007), and involuntary subordination (Sturman, 2011). These measures are central to understanding social impairments in clinical disorders, with previous studies focusing on perceptions of low social rank associated with depression, anxiety (L. Wood & Irons, 2015), paranoid thoughts (Freeman et al., 2005), low self-esteem and perceived stigma in adults with intellectual disability (Paterson, Mckenzie, & Lindsay, 2012). Insecure striving to avoid inferiority is further associated with fear of rejection, submissiveness and depressive symptoms, mediated by external shame and anxious attachment in both healthy and depressed populations (Gilbert et al., 2007; Gilbert, McEwan, Bellew, Mills, & Gale, 2009). In young adults, self-harm and depression are further found to causally relate to insecure striving (K. D. Williams, Gilbert, & McEwan, 2009), which in turn moderate low self-perception of rank and importance of thinness in an eating disordered population (Ferreira, Gouveia, & Duarte, 2013). Secure non-striving and acceptance are further negatively associated with appearance anxiety, fear of rejection and depressive symptoms, again, in an eating disordered sample (Bellew, Gilbert, Mills, McEwan, & Gale, 2006). Finally, a measure of involuntary subordination was developed with the aim of encompassing previous measures of negative social comparison, feelings of inferiority, and submissiveness, revealing high correlations with self-criticism, neuroticism, and low self-esteem (Sturman, 2011). The involuntary subordination scale predicts short-term changes in social anxiety symptoms, and mediates the relationship between defeat and depressive symptoms in healthy undergraduate students (Sturman, Rose, McKeighan, Burch, & Evanico, 2015), but has not been further validated in samples of depressed or remitted depressed individuals per se, despite defeat and entrapment in particular being associated with symptoms of depression, anxiety, suicidality

and post-traumatic stress disorder (PTSD) (Siddaway, 2013), and increased suicidal ideation amongst men who have sex with men (Li et al., 2016).

In addition, these deficits in social functioning persist beyond recovery (Elliott et al., 2012; N. Kennedy et al., 2007; Pechtel et al., 2013), with biases in social affective processing in remitted depressed individuals previously described in reward sensitivity (Pechtel et al., 2013), and emotion recognition and regulation (Lemoult & Sherdell, 2010). In fact, greater self-reported difficulties in emotion regulation in recovered populations have been highlighted as a risk factor for future depressive episodes (Ehring, Fischer, Schnülle, Bösterling, & Tuschen-Caffier, 2008; Muntingh et al., 2011). However, the literature has yet to fully examine the extent of residual social impairments in remitted depressed individuals. Identifying residual deficits in social processing on specific measures of submissive behaviour, involuntary subordination or interpersonal rejection sensitivity in remitted depressed would therefore point towards potential risk factors from within the social domain specifically. This presents an important gap that needs addressing, as partial remission or the presence of residual symptoms in individuals with a past history of depression presents an important problem given the high rate of relapse and chronicity, with recurring depressive episodes further contributing to the economic and mental health burden (P. E. Greenberg et al., 2015; Paykel, 2008).

Implementing the measures of social processing outlined above in samples of depressed and remitted depressed individuals may therefore shed important light on how impairments in perceived social status and subsequent defensive behaviours negatively impact the ability to form or maintain positive social relationships within social hierarchies, even in the absence of marked current depressive symptoms. Few studies have directly administered the existing measures in clinically depressed samples, and much less often in remitted depressed participants, despite significant overlap in social deficits across psychopathologies (D. P. Kennedy & Adolphs, 2012). However, a recent review highlighted the difficulty in accounting for potential biases when implementing subjective measures of social functioning per se, due to the heterogeneity of comparable measures across different studies (Santini, Koyanagi, Tyrovolas, Mason, & Haro, 2015). Reducing the variability of subjective social measures by identifying meaningful underlying constructs may help to address this heterogeneity and

identify functional treatment outcomes, alongside targeting well-established symptoms of depression, anxiety and difficulties in emotion dysregulation.

In sum, this chapter aims to directly test the hypothesis that depression is characterised by systemic biases in social and affective processing compared to the presentation of healthy controls, as well as seeking to further investigate the pattern of residual social impairments in remitted depressed individuals, using the battery of measures outlined above. This serves to further validate and replicate findings from existing measures assessing submissive behaviour, subordination, striving to avoid insecurity, interpersonal sensitivity, mindfulness and emotion dysregulation. Following the outline of general issues and procedures pertaining to the work presented in this thesis, the array of social, affective and process measures, administered across all studies, will be outlined and results presented towards the end of this chapter.

The hypotheses for the present study were as follows;

HYPOTHESES

- Depressed individuals will show significant impairments on affective, social and process measures, compared to remitted depressed and healthy controls
- Remitted depressed individuals will be impaired on social and process measures relative to controls and to depressed individuals, and on affective measures compared to depressed individuals but not to controls.

2.2 General methods and materials used across all studies

Participants

Forty-one participants experiencing a current Major Depressive Episode (MDE) and meeting criteria for a diagnosis of MDD (31 female; 37.12±13.63 years), 82 healthy controls who had never met criteria for MDD (47 female; 33.54±15.35 years) and 27 remitted depressed participants who had previously experienced at least one previous MDE but currently did not meet diagnostic criteria for MDD (19 female; 38.73±14.92 years) were recruited into the studies described within this thesis. These participants also comprise the samples for the current study described in this chapter.

Recruitment

Healthy control participants were recruited from the department mainstream participant panel at the MRC Cognition and Brain Sciences Unit (CBU) and the University of Cambridge. The mainstream participant panel volunteers had previously been recruited via local advertisement, through the MRC CBU website, open days, science fairs and word-of-mouth. Healthy control participants had no history of significant mental health problems, such as depression or anxiety. Depressed participants were recruited from the research group depression panel and met diagnostic criteria for current MDD. The depression panel contains the details of individuals who had previously agreed to take part in research conducted by the research group on cognition, emotion and mental health at the MRC CBU and who had previously met criteria for a diagnosis of MDD in a structured clinical interview. Remitted depressed participants were recruited from the same depression panel, had experienced at least one previous Major Depressive Episode (MDE), but did not currently meet diagnostic criteria for MDD.

Participants were not eligible for the depression research panel if they had a diagnosis of psychosis, bipolar disorder, current or past drug or alcohol problems, or a personality disorder. Moreover, the co-occurrence of multiple psychological disorders (comorbidity) is a common problem when recruiting participants in social affective neuroscience, with 7.7% and 17.3% lifetime prevalence for 2 or more and 3 or more disorders, respectively (Kessler et al., 2005, 2012). In line with the existing literature, it would be unfeasible to exclude all participants with

additional diagnoses if these are not thought to impact largely on, for instance, the phenomenon of interest. Thus, participants with common co-morbidities (past or present) were not excluded. See Table 2.1.

All participants were aged between 18-65, were right-handed, were native or near-native English speakers, had normal or corrected-to-normal vision and no self-reported hearing impairments, as the tasks required auditory presentation of stimuli. Additional exclusion criteria included the presence of head injury or neurological impairments, as this may have confounded the interpretation of the neuroimaging findings. All recruited participants completed either neuroimaging experiments (Chapter 4, Chapter 5, and Chapter 6), or the behavioural experiment (Chapter 7). Full demographics for all participants can be found in Table 2.5, with demographics for each specific study presented in each respective chapter. For all behavioural studies, participants were paid an honorarium to reimburse them for their time at a rate of £6/hour (minimum £12 guaranteed) and £2.50-£3 to cover travel expenses (rate depending on living proximity from the research unit). This was anticipated to amount to a maximum of 2 hours for each subject (£12 per subject) plus travel expenses. For all studies involving neuroimaging, participants were paid £10/hour (minimum £20 guaranteed) and £2.50-£3 to cover travel expenses. This was anticipated to amount to £20 per subject plus travel expenses. This was the standard method of recruitment applied across all studies contained within this thesis which had previously been approved by the Cambridge Psychology Research Ethics Committee (CPREC) (Appendix 2.1).

Medication Use Across All Studies

Identifying significant abnormalities in functioning on a behavioural and neural level within clinical samples that are generalizable, relies on recruiting a representative sample. However, the heterogeneity of symptoms in depression and sample selection issues more generally at times impede the generalisability of the findings (Hughes-Morley, Young, Waheed, Small, & Bower, 2015). While this thesis aimed to recruit a representative sample, it is important to note the potentially limited representativeness given the effects of medication use when interpreting neuroimaging findings. Having said this, 44% of the MDD group reported currently using medication, compared to 26% of the remitted depressed sample. The use of medication and

range of dosages within the remitted depressed and currently depressed sample are presented below. Healthy control participants indicated no current or past use of antidepressant medication (Table 2.2).

Table 2.1

Co-morbidities in MDD participants across studies

Co-morbidity	Presence	Chapter 4	Chapter 5 & 6	*Total*
Generalized Anxiety Disorder	Current	1	6	*7*
	Past	0	1	*1*
Post-traumatic Stress Disorder	Current	1	1	*2*
	Past	0	2	*2*
Obsessive-Compulsive Disorder	Current	1	1	*2*
	Past	0	1	*1*
Social Anxiety Disorder	Current	1	1	*2*
	Past	0	1	*1*
Panic Disorder	Current	1	1	*2*
	Past	0	2	*2*
Eating Disorder	Current	0	0	*0*
	Past	1	1	2
Total	*Current*	*5*	*10*	*15*
	Past	*1*	*8*	*9*

Table 2.2

Medication use in MDD and remitted depressed across all studies

	Remitted (N=27)	MDD (N = 41)	Total	Min Dosage (mg)	Max Dosage (mg)
Citalopram	3	3	6	10	40
Venlafaxine	2	2	4	150	375
Fluoxetine	2	2	4	20	60
Mirtazapine	0	4	4	15	30
Sertraline	0	3	3	100	100
Zopiclone	0	1	1	3.75	3.75
Propranolol	0	1	1	30	30
Other	0	2	2	-	-
Total	7	18	25		

Ethical Considerations Across All Studies

Much of the research contained within this thesis involved the recall or presentation of negative memories, a procedure which may elicit negative emotions. To reduce the likelihood that participants may recall overly upsetting personal memories as part of the script-driven imagery procedure outlined in the following chapters, participants were asked to identify memories which feel personally relevant but which they would feel comfortable thinking or talking about in the study context. The recall of negative memories was preceded and followed in fixed order by neutral and positive memories respectively to counteract any negative emotion and ensure mood repair prior to the end of the experiments. The use of questionnaires and measures enquiring about emotions including mood and stress symptoms may also be difficult for some participants, particularly those who are experiencing low mood. Nonetheless, script-driven imagery is a widely-used procedure for symptom provocation in PTSD research with no long-term negative outcomes reported in clinical and control populations (Lanius et al., 2006). In the present thesis, no trauma-related memories were probed, with social memories being much lower in valence and arousal.

These studies were conducted under the supervision of on-site clinical psychologists (Dr. Tim Dalgleish, Dr Caitlin Hitchcock), in case any participant became distressed or other clinical issues arose. In the unlikely case that a participant did become distressed, we had a protocol in place to ensure their wellbeing. A full description of this protocol is included in Appendix 2.6. In brief, in case of distress the participants were provided with a safe space, were offered a confidential consultation with a clinical psychologist, were ensured safe transport home and were followed up if necessary. In the event of clinical issues arising from the structural MRI data, the following summarised procedure was put in place with a full description of this protocol found in Appendix 2.7. In the event that a significant abnormality was noticed by the qualified MRI operator, this was brought to the attention of the CBSU medical monitor, who was responsible for acting on this information. If a volunteer later contacted a researcher to ask about possible abnormal findings, the researcher only took their contact details, and then told the medical monitor and radiographers, one of whom contacted the volunteer if requested. The behavioural data were stored in a locked filing cabinet and imaging data continue to be stored on the secure server located at the CBU which only the investigators have access to. The

information on the computers is linked to personal information only via ID number and is fully encrypted. The data will be retained for a minimum of 5 years. Data collected during the study were stored and used in compliance with the UK Data Protection Act.

For all studies, participants were told they were participating in projects investigating the processing of social emotions in response to autobiographical memories of rejection and inclusion memories. In Chapter 4, Chapter 5 and Chapter 6 participants were explicitly informed that the studies involve fMRI. No information was withheld that was not made available to participants in the respective information sheets detailed in Appendix 2.4 (Chapter 4 and Chapter 7), and Appendix 2.5 (Chapter 5 & Chapter 6). Participants were fully debriefed at the conclusion of the respective study with ample opportunity to ask questions (see Appendix 2.8). To ensure the confidentiality and anonymity of participants, participant numbers were allocated to each person, and data were recorded in a database according to this number (i.e., not participants' personal information). The analysis between groups depends on average differences between numerical scores and statistical parametric maps on the imaging data, as do publication of results, thereby protecting the anonymity of participants.

Clinical Interview and Social, Affective and Process Self-Report measures used across all Studies

Across all studies, a comprehensive diagnostic interview and a battery of social, affective and process self-report measures were undertaken with respect to all participants, preceding and following participation in the studies outlined in this thesis. These are detailed below. The behavioural data obtained from these measures form the basis for the research study described in this chapter.

Affective and Diagnostic Measures

Structured Clinical Interview for DSM Axis-IV Disorders (SCID-I; First, Spitzer, Gibbon., & Williams, 1996).

The SCID-I is a standardised diagnostic interview schedule designed to assist clinicians and researchers in making reliable DSM-IV Axis I psychiatric diagnoses. The SCID-I involves a series of questions concerning current and past symptoms of a range of psychological disorders

and usually takes between ½ and 1 hour. The SCID is only administered by experienced research staff who have undergone comprehensive SCID training. The mood module is used to verify whether participants are currently experiencing low mood of clinical severity or not. See Appendix 2.9.

Beck Depression Inventory (BDI-II: Beck, Steer & Brown, 1996).

The BDI-II is a 21-item multiple-choice self-report measure assessing depressive symptomatology including low mood. It is one of the most widely used instruments for measuring the severity of depression with good internal consistency, test-retest reliability and convergent validity with standardised clinician assessments (Beck et al., 1997; Richter, Werner, Heerlein, Kraus, & Sauer, 1998; Storch et al., 2004), enabling comparison across studies. The internal consistency has been estimated at around 0.9, with retest reliability ranging from 0.73 to 0.96, as well as high correlations between BDI-II and the BDI-I (Wang & Gorenstein, 2013). The BDI-II is widely used as an assessment tool by health care professionals and researchers in a variety of settings and is well-suited as a screening instrument for depression in the general population sample, with high predictive diagnostic value (Lasa et al., 2000). As this thesis included the recruitment of remitted and currently depressed individuals, the BDI was used to assess current and residual symptoms of depression. See Appendix 2.10.

Beck Anxiety Inventory (BAI: Beck, Epstein, Brown & Steer, 1988).

The BAI is a 21-item self-report measure assessing current or state anxiety symptomatology. Like the BDI-II, the BAI it is widely used in research and has well-established psychometric properties, reliability and validity (Osman et al., 2002), including the ability to assess the severity of anxiety in adult and adolescent populations (Muntingh et al., 2011) and a relatively good ability to discriminate anxious from depressive presentations (Beck et al., 1988). Participants indicate the extent to which they have experienced anxiety symptoms over the previous week. Scores on the BAI indicate change in mood symptoms over time. As this thesis recruited MDD and remitted depressed individuals, the BAI was used to assess the presence of anxiety symptoms in addition to current depressive symptoms assessed by the BDI-II. See Appendix 2.11.

Positive and Negative Affect Scale (PANAS: Watson, Clark & Tellegen, 1988).

The PANAS is a 20-item mood scale with good internal consistency and convergent validity (Watson et al., 1988) which can be used to measure state positive and negative affect, respectively. The items are derived from a principal components analysis of Zevon and Tellegen's (1982) mood checklist; Respondents are asked to rate the extent to which they have experienced each particular emotion within a specified time period, with reference to a 5-point scale. The scale points are: 1 'very slightly or not at all', 2 'a little', 3 'moderately', 4 'quite a bit' and 5 'very much'. The PANAS is shown to have high internal consistency, and good test-retest reliability. Factorial analysis confirmed independent loading of the adjectives on the two scales. A longer, extended version also assesses specific, embedded emotional states such as fear, joviality, shyness, attentiveness and serenity (Watson & Clark, 1994). The PANAS was used in this thesis to check that participants' baseline emotional state did not vary significantly across individuals within each group, as well as to compare participants' baseline emotional states between groups over the last week. See Appendix 2.12.

PROCESS MEASURES

Difficulties in Emotion Regulation (DERS: Gratz, K. L., & Roemer, L., 2004).

The DERS is a brief, 36-item, self-report questionnaire designed to assess multiple aspects of emotion regulation and dysregulation. The DERS items reflect difficulties within the following dimensions of emotion regulation: (a) awareness and understanding of emotions (e.g., "I pay attention to how I feel" [reversed]); (b) non-acceptance of emotions (e.g., "When I'm upset, I feel guilty for feeling that way"); (c) the ability to engage in goal-directed behaviour (e.g., "When I'm upset, I have difficulty concentrating") and refrain from impulsive behaviour (e.g., "When I'm upset, I become out of control"), when experiencing negative emotions; and (d) access to emotion regulation strategies perceived as effective (e.g., "When I'm upset, it takes me a long time to feel better"). Participants rate how often statements such as "I feel at ease with my emotions" apply to them on a 5-point scale (1='almost never', to 5='almost always'). The scale demonstrates good psychometric properties, with good internal consistencies (α's > .80) and stabilities (ϱtt's > .69) across its subscales and significant correlations with other emotion regulation measures (Ehring et al., 2008; Gratz & Roemer, 2004). As greater difficulties in emotion regulation contribute to generalized anxiety disorder (GAD) (Roemer et

al., 2013), borderline personality disorder (Gratz et al., 2006), and PTSD symptoms (Tull, Barrett, McMillan, & Roemer, 2007), this well-established measure was used to further assess the presence of emotion regulation deficits in depression. See Appendix 2.13.

Five Facet Mindfulness Questionnaire (FFMQ: Baer, R. A., Smith, G. T., Hopkins, J., Krietemeyer, J., & Toney, L., 2006).

The FFMQ is a 39-item measure based on a factor analytic study of five independently developed mindfulness questionnaires, encompassing the five facets of observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. Participants are asked to indicate what 'best describes your own opinion of what is generally true for you' on a 5-point scale (5 = Always or Very Often True to 1 = Never or Very Rarely True). This measure was used to assess aspects of mindfulness in healthy controls in Chapter 7 only, as the study involved comparing emotion regulation strategies based on mindfulness principles. See Appendix 2.14.

Spontaneous Use of Imagery Scale (SUIS; Reisberg, et al., 2003).

The SUIS is a 12-item questionnaire aimed at measuring the spontaneous use of imagery during daily life. Participants use a 5-point scale to rate the degree to which each item is appropriate for them (from "never appropriate" to "always completely appropriate"). A sample item is: "When I think about visiting a relative, I almost always have a clear mental picture of him or her". A total score can be calculated by summing the 12 item scores, resulting in a total score ranging from 12 to 60 with higher scores indicating more use of mental imagery in everyday life. As this thesis implements a script-driven imagery paradigm, which relies on using vivid imagery of autobiographical memories, this measure allows for between-group comparisons of baseline differences in everyday use of imagery. See Appendix 2.15.

National Adult Reading Test (NART; Nelson, 1982).

The NART consists of participants reading aloud 50 difficult-to-pronounce words and is scored based on pronunciation errors made. The NART is widely used in clinical and research settings to estimate a person's premorbid level of intellectual ability as a function of verbal intelligence, in neuropsychological research (Bright, Jaldow, & Kopelman, 2002). In addition, Nelson and O'Connell (1978) showed the NART to be a robust predictor of premorbid levels on the

Wechsler Adult Intelligence Scale (WAIS, Wechsler, 1955), suggesting that it has high construct validity as a measure of general intelligence, even when used in populations with neurological or psychiatric disorders (Crawford, Stewart, Cochrane, Parker, & Besson, 1989; McGurn et al., 2004). A study comparing participants' NART scores at age 80 with intelligence scores collected at age 11 demonstrated the robustness of the NART at estimating verbal IQ across the lifespan (McGurn, et al., 2004). In the present thesis, the NART was used to measure verbal IQ and to enable matching across groups. See Appendix 2.16.

Social Measures

Interpersonal Sensitivity Measure (IPSM: Boyce, P., & Parker, G., 1989).

The IPSM is a 36-item measure assessing excessive sensitivity to the interpersonal behaviour of others, to social feedback and to (perceived or actual) negative evaluation by others. The IPSM generates a total score as well as five sub-scale scores: interpersonal awareness, need for approval, separation anxiety, timidity and fragile inner-self. Its reliability is demonstrated by high internal consistency in two separate groups, and by stability in scores over time in a non-clinical group: in a clinical sample of depressed patients and a non-clinical student sample, internal consistency estimates for the total score were 0.86 and 0.85, respectively, and a six-week retest reliability of 0.70 in the student sample. Moreover, this measure has separately been implemented in social anxiety (Harb et al., 2002) and depression (Luty et al., 2002). Moderate to high correlations with neuroticism (r=0.66), self-esteem (r=0.39), and a low correlation with emotional arousability (r=0.11) highlight the convergent and divergent validity of the IPSM (Harb et al., 2002). The 36 items are completed on a 4-point Likert-type scale (1= 'very unlike me', 2='moderately unlike me', 3='moderately like me', 4='very like me'). As this thesis is investigating individual differences in responding to experiences of social rejection and inclusion on a neural level, this measure provides a baseline measure of sensitivity to social signals and allows for group comparisons. See Appendix 2.17.

Involuntary Subordination Questionnaire (ISQ: Sturman, E. D., 2011).

The ISQ is a 32-item questionnaire designed to interrogate involuntary subordination, indexing tendencies of feeling stuck (entrapment), defeated, inferior, and seeing the self as submissive. Involuntary subordination may be adaptive in species that compete for resources as a

mechanism to switch off fighting behaviours when loss is imminent (thus saving an organism from injury). In humans, major depression is thought to occur when involuntary subordination becomes prolonged. In healthy individuals, scores on the involuntary subordination scale are found to predict short-term changes in social anxiety symptoms, and mediates the relationship between defeat and depressive symptoms (Sturman et al., 2015). This measure has predominantly been implemented in healthy undergraduates (Sturman et al., 2015), PTSD populations (Siddaway, 2013), and amongst men who have sex with men (Li et al., 2016), but not with depressed samples per se. As this thesis involves the recruitment of currently and remitted depressed samples, this measure was included to further validate its use within clinical groups. See Appendix 2.18.

Striving to Avoid Inferiority Scale Part I and Part II (SAIS-I/II: Gilbert, et al., 2007). Part I of the SAIS is a 31-item scale to measure beliefs about striving to compete to avoid inferiority (e.g., 'If I don't strive to achieve I'll be seen as inferior to other people') and feelings of acceptance by others whether one succeeds or fails (e.g., 'Others will accept me even if I fail'). Part II of the SAIS focuses on the reasons for people feeling under pressure to compete and avoid inferiority. Participants respond to statements on a 10-point scale ranging from 'don't agree' to 'completely agree'. Parts I and II of the SAIS have shown good reliability with Cronbach's alphas of .84 - insecure striving; .69 - secure non-striving; .84 - losing out; .80 - overlooked and .79 - rejection (Gilbert et al., 2007). This measure has been implemented in healthy and depressed populations (Gilbert et al., 2007, 2009), young adults with depressive symptoms g (K. D. Williams et al., 2009), and eating disordered populations (Bellew et al., 2006; Ferreira et al., 2013). This thesis aimed to further validate this measure in depressed and remitted depressed samples. See Appendix 2.19.

Submissive Behaviour Scale (SBS: Allan, S. & Gilbert, P., 1997).
Derived from the work of Buss and Craik (1986), the Submissive Behaviour Scale was developed by Gilbert and Allan (1994) and refined by Allan and Gilbert (1997). It consists of 16 examples of submissive behaviour (e.g. "I agree that I am wrong even though I know I'm not") which people rate as a behavioural frequency (from 0 = Never to 4 = Always). The scale has good reliability, with a Cronbach's alpha of .89, and four-month test-retest reliability of $r = .84$, $p < .001$ with a student population (Gilbert et al., 1996). This scale has predominantly

been used in studies examining social comparison (social ranking) and evolutionary theory (Gilbert and Allan, 1994), and has been previously validated in a limited number of depressed samples (O'Connor, Berry, Weiss, & Gilbert, 2002). This thesis aimed to further validate this measure in depressed and remitted depressed samples. See Appendix 2.20.

Social Comparison Scale (SCS: Allan, S. & Gilbert, P., 1995).

The SCS was developed by Allan and Gilbert (1995) to measure self-perceptions of social rank and relative social standing. This scale uses a semantic differential methodology and consists of 11 bipolar constructs. Participants are required to make a global comparison of themselves in relation to other people and to rate themselves on a ten-point scale. The 11-items cover judgements concerned with rank, attractiveness and how well the person thinks they 'fit in' with others in society. Low scores point to feelings of inferiority and general low-rank self-perceptions. The scale has been found to have good reliability, with Cronbach alphas of .88 and .96 with clinical populations and .91 and .90 with student populations (Allan and Gilbert, 1995, 1997) and in cross-cultural comparisons (Terol et al., 2015). This thesis aimed to further validate this measure in depressed and remitted depressed samples, as previous work found that self-perceptions of low rank resulting from social comparisons may result in depression, anxiety and psychosis (L. Wood & Irons, 2015). See Appendix 2.21.

Procedure Across All Studies

This section describes the procedure as it pertains only to the administration of the social, affective and cognitive measures across all studies. Specific procedures for the remaining studies and main experimental tasks are outlined within their respective chapters.

Immediately prior to the main experimental task, outlined in detail within each respective chapter, all participants provided informed consent and were then administered the BDI and BAI, as well as the National Adult Reading Test (NART). At the end of each session, participants were provided with the battery of social, affective and process self-report measures to be completed and returned in their own time, by post or email. Finally, participants were thanked for their time and debriefed. Informed consent was obtained from the participants, and the studies and consent procedures were approved by the Cambridge Psychology Research Ethics Committee (Appendix 2.1).

Statistical Analysis Across All Studies

Exploratory data analysis was carried out across all studies to assess whether the data met requirements for parametric data analysis, and where this was not the case, non-parametric statistics were implemented. For all behavioural data, an alpha level of $p = 0.05$ was set as the statistical threshold of significance. For neuroimaging data, the majority of results are reported at $p = 0.001$, uncorrected with an extent cluster threshold of $k=20$, unless otherwise indicated in the neuroimaging chapters.

Demographic data were analysed using Pearson's chi-squared significance test to assess for differences between populations using frequency of cases and Fisher's exact test when the cell size count was below 5. Self-report affective, process and social measures were analysed using Pearson and Spearman correlation analyses and independent samples t-tests, as well as one-way analyses of variance (ANOVA) with group (controls/MDD/remitted) as the between-subjects factor. Mixed between- and within-subject ANOVAs were used to investigate between group differences and within-group variability in response to different memory types or emotion regulation strategies as outlined in the relevant chapters.

Cases with missing values pose a significant challenge during data collection (Scheffer, 2002). However, when present, missing cases for individual items on a measure were considered to be missing at random, therefore the univariate analyses of variances implemented list wise deletion, followed by a missing value analysis using EM (expectation-maximisation) (Dong & Peng, 2013). This method assumes a distribution for the partially missing data and bases inferences on the likelihood under that distribution, considering the conditions under which missing data occurred. Each iteration consists of an E step and an M step. The E step finds the conditional expectation of the "missing" data, given the observed values and current estimates of the parameters. These expectations are then substituted for the "missing" data. In the M step, maximum likelihood estimates of the parameters are computed as though the missing data have been filled in. "Missing" is enclosed in quotation marks because the missing values are not being directly filled in. Instead, functions of them are used in the log-likelihood.

POWER AND EFFECT SIZE ACROSS ALL STUDIES

In setting up behavioural and neuroimaging experiments, a priori power analyses are the preferable approach to determining the sample sizes required to detect an existing effect within the data. However, in neuroimaging experiments, this approach is hampered by lengthy simulations and statistical constraints (Desmond & Glover, 2002). Further difficulties in controlling the sample size are due to limited time and/or logistical resources, heightened given the unique demands of recruiting vulnerable groups (Phillips, 2012). Nonetheless, sample sizes reported in this thesis fall well within the range of reported sample sizes within the clinical and social affective neuroscience literature (Linden, 2012). Specifically, the sample sizes meet the demands when implementing specific analyses, such as the Intersubject Correlation Analysis (ISC) described in Chapter 6 (Pajula & Tohka, 2016). As a result, post-hoc power analyses were conducted and calculated using the given sample size, probability level and a medium effect size, as described by (Cohen, 1992). This analysis was implemented using the software package GPower (Faul, Erdfelder, Buchner, & Lang, 2009).

The achieved power for detecting a medium sized effect (0.25) employed the traditional 0.05 statistical significance criterion and uses the respective sample sizes for each study (Table 2.2). For example, the post hoc analysis for the battery of measures to investigate systemic biases presented in this chapter achieved a statistical power of 79% using an alpha level of $p < .05$ and an overall sample size of 150. However, given cases of missing data, less respective power was seen with respect to specific measures: BAI (0.73), BDI-II (0.75), DERS (0.73), FFMQ (0.55), IPSM (0.73), ISQ (0.75), PA (0.75), NA (0.75), SAIS-I/II (0.75), SBS (0.75), SCS (0.75), and SUIS (0.75). The behavioural study in Chapter 7 achieved a power of 81% in the post-hoc analysis for the repeated measures ANOVA. The behavioural results of the neuroimaging study in Chapter 4 achieved a power of 86%, while the neuroimaging studies Chapter 5 and Chapter 6 achieved a respective power of 97% when including and 88% when excluding the remitted sample from the post-hoc analysis (Table 2.2).

Table 2.3

Sample sizes and post-hoc power analyses for key analyses across all studies

Study	Chapter	*N*	Controls	MDD	Remitted	Power
Systemic Biases (Behavioural)	Chapter 2	*150*	82	41	27	79%
'Self' Memory (fMRI)	Chapter 4	*39*	21	18	-	86%
'Others' Memory and ISC of Social Interactions (fMRI)	Chapter 5 & 6	*77*	27	23	27	97%
Emotion Regulation (Behavioural)	Chapter 7	*34*	34	-	-	81%

2.3 Cross-study results pertaining to self-report measures

Participants Characteristics

Table 2.4 and Table 2.5 show the sample characteristics of healthy controls, remitted depressed and currently in episode MDD participants recruited as part of this thesis. Chi-squared analyses revealed significant associations between group and ethnicity ($\chi(2) = 30.55$, $p = .000$), with a greater frequency of individuals of Caucasian ethnicity within the healthy control population, compared to MDD and remitted depressed group. There was no significant association between group and employment type ($\chi(4) = 6.98$, $p = .137$), employment status ($\chi(6) = 4.51$, $p = .609$), education ($\chi(10) = 17.92$, $p = .056$), marital status ($\chi(6) = 8.58$, $p = .199$), or gender ($\chi(2) = 5.23$, $p = .073$) (see Table 2.5). Participant groups did not differ in terms of age ($F[2,130]=1.58$, $p=0.210$) or reading ability assessed using the NART ($F[2,130]=1.119$, $p=0.330$), commonly used to estimate premorbid intelligence levels (Table 2.4).

Table 2.4

Demographic characteristics across all studies. Numbers are ns unless otherwise stated.

	Group	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval	
						Lower Bound	Upper Bound
NART	Control	73	9.62	6.11	0.72	8.19	11.04
	MDD	37	9.43	6.40	1.05	7.30	11.57
	Remitted	21	11.95	9.17	2.00	7.78	16.13
	Total	131	9.94	6.76	0.59	8.77	11.11
Age	Control	82	33.54	15.36	1.70	30.16	36.91
	MDD	41	37.12	13.63	2.13	32.82	41.42
	Remitted	26	38.73	14.92	2.93	32.71	44.76
	Total	149	35.43	14.89	1.22	33.02	37.84

Table 2.5

Demographic characteristics across all studies cont'd. Numbers are ns unless otherwise stated.

	Controls n=82	MDD n=41	Remitted n=27	*Total N=150*	X^2	p
Sex					5.23	.073
Male	35	10	8	*53*		
Female	47	31	19	*97*		
Age, years						
Mean	33.54	37.12	38.73	*35.43*		
SD	15.36	13.63	14.92	*14.89*		
National Adult Reading Test						
Mean	9.62	9.43	11.95	*9.94*		
SD	6.11	6.40	9.17	*6.76*		
Ethnicity					30.55	<0.001
Other	22	23	23	*68*		
Caucasian	60	18	4	*82*		
Marital Status					8.58	.199
Single / Unmarried	56	21	11	*88*		
Married	12	9	8	*29*		
Separated / Divorced	6	4	2	*12*		
Other	8	7	6	*21*		
Education					17.92	.056
Completed Year 10	2	4	2	*8*		
Completed Year 12	27	16	7	*50*		
Completed Bachelors	33	7	6	*46*		
Completed Masters	9	4	2	*15*		
Completed PhD	0	2	2	*4*		
Other	11	8	8	*27*		
Employment Status					4.51	.609
Employed	50	23	11	*84*		
Unemployed	19	12	9	*40*		
Student	7	2	3	*12*		
Other	6	4	4	*14*		
Employment Type					6.98	.137
Full Time	27	20	8	*55*		
Part Time	23	6	4	*33*		
Other	32	15	15	*62*		

Social, Affective and Process Measures

Table 2.6 presents the univariate results across groups for the battery of social, affective and process measures. Results reveal significant group differences between remitted depressed, MDD and healthy control participants on all measures except for the Spontaneous Use of Imagery Scale ($p=0.274$). In terms of affective measures, MDD participants were significantly more anxious (BAI), depressed (BDI) and exhibited significantly dampened positive affect and heightened negative mood (PANAS) compared to remitted depressed and followed by healthy control individuals. In terms of process measures, MDD revealed higher scores on the DERS suggesting greater problems with emotion regulation, greater interpersonal rejection sensitivity (IPSM), again followed by remitted and then control participants. MDD also exhibited lower levels of mindfulness (FFMQ) compared to healthy controls, while this measure was not administered in the final study and therefore no data are available for remitted depressed participants. Finally, social measures revealed higher levels of involuntary subordination (ISQ), greater scores on striving to avoid inferiority (SAIS-I/II), higher scores on the submissive behaviour scale (SBS) indicating more submissive behaviour, and lower scores on the social comparison scales (SCS), suggesting greater feelings of inferiority and low rank self-perceptions in MDD compared to both remitted and healthy controls.

Planned Comparisons

Planned comparisons revealed that MDD participants were significantly different from control participants on all measures (all $p<0.001$). In comparison to the remitted sample, MDD participants were only significantly different on affective measures ($p<0.001$), with greater scores on the BAI (8.49±2.11), BDI-II (13.52±2.03), NA (8.59±1.89) and IPSM (12.34±3.85), indicating higher levels of anxiety, depression, negative affect and interpersonal rejection sensitivity. MDD participants were not significantly different from the remitted sample on the DERS (8.10±6.36, $p=0.62$), ISQ (10.36±4.49, $p=0.07$), SAIS-I (0.53±5.15, $p=1.00$), SAIS-II (1.75±5.16, $p=1.00$), SBS (7.43±2.33, $p=0.15$), SCS (-9.13±4.80, $p=0.18$), SUIS (3.60±2.35, $p=0.38$), and PA (1.57±2.20, $p=1.00$). This suggests residual deficits in social processing following recovery not evident from purely affective measures. Conversely, remitted depressed participants were not significantly different from control participants on BAI (-3.16±1.92,

p=0.31), BDI-II (-3.18±1.85, p=0.26), SAIS-I (-8.96±4.72, p=0.18), SCS (10.52±4.40, p=0.05), SUIS (3.17±2.16, p=0.38), and NA (-2.50±1.72, p=0.44). In contrast, healthy controls were significantly different to the remitted sample on the DERS (-32.32±5.83, p=0.001), IPSM (-10.33±3.50, p=0.01), ISQ (-22.08±4.13, p=0.001), SAIS-II (-14.75±4.73, p=0.01), SBS (-7.43±2.33, p=0.01), and PA (10.82±2.01, p=0.001).

As the remitted and control groups differed on levels of depression, the other differences between these groups could be a function of this elevated symptomatology in the remitted sample. A further sensitivity analysis was carried out after seeking to match the groups more closely. Outliers were removed from the analysis, whereby individuals who scored zero on the BDI-II were set aside from the control group. This sensitivity analysis revealed an identical pattern of results, as described above, with one exception reported here. See Appendix 2.22 for full descriptive and ANOVA results of the sensitivity analysis. Results now revealed no significant difference between groups on the SAIS-I (F[2,133]=2.56, p=0.08). This suggests that remitted depressed, matched in levels of depression with the control group, retained their pattern of results with regards to the consistent residual deficits observed across measures of social processing when compared to control participants. See Appendix 2.23 for full table of planned comparisons of the sensitivity analysis results.

Table 2.6

Descriptive and ANOVA results for all measures across all studies.

	Group	Mean	Std. Error	95% Confidence Interval		df	F	Sig.
				Lower Bound	Upper Bound			
BAI	Controls	5.09	0.55	4.00	6.18	[2,132]	29.38	.000
	MDD	16.74	1.91	12.88	20.60			
	Remitted	8.25	1.47	5.17	11.33			
	Total	8.89	0.79	7.33	10.46			
BDI-II	Controls	6.72	0.61	5.52	7.93	[2,139]	65.97	.000
	MDD	23.43	1.63	20.13	26.72			
	Remitted	9.90	1.83	6.09	13.72			
	Total	11.97	0.89	10.22	13.73			
DERS	Controls	71.78	2.42	66.96	76.60	[2,134]	46.18	.000
	MDD	112.10	3.60	104.81	119.39			
	Remitted	104.00	6.58	90.18	117.82			
	Total	87.96	2.53	82.95	92.97			
IPSM	Controls	98.77	1.70	95.38	102.15	[2,134]	34.33	.000
	MDD	121.55	2.05	117.40	125.70			
	Remitted	109.10	2.74	103.37	114.83			
	Total	106.71	1.47	103.81	109.62			
ISQ	Controls	71.13	1.88	67.38	74.88	[2,135]	57.17	.000
	MDD	103.58	2.45	98.62	108.53			
	Remitted	93.21	3.59	85.67	100.76			
	Total	83.76	1.87	80.06	87.46			
SAIS-I	Controls	55.79	1.94	51.93	59.66	[2,136]	4.13	.018
	MDD	65.28	3.51	58.17	72.38			
	Remitted	64.75	4.03	56.32	73.18			
	Total	59.87	1.64	56.62	63.12			
SAIS-II	Controls	43.95	2.04	39.88	48.02	[2,136]	12.08	.000
	MDD	60.45	2.92	54.55	66.35			
	Remitted	58.70	5.10	48.03	69.37			
	Total	50.92	1.74	47.49	54.35			
SBS	Controls	22.17	1.00	20.17	24.17	[2,136]	24.81	.000
	MDD	34.65	1.71	31.19	38.11			
	Remitted	29.60	1.67	26.11	33.09			
	Total	26.90	0.92	25.08	28.72			
SCS	Controls	59.32	2.18	54.98	63.67	[2,136]	16.92	.000
	MDD	39.68	2.20	35.23	44.12			
	Remitted	48.80	3.93	40.57	57.03			
	Total	52.05	1.66	48.76	55.34			
SUIS	Controls	38.52	0.95	36.63	40.41	[2,136]	1.31	.274
	MDD	38.95	1.38	36.17	41.73			
	Remitted	35.35	2.08	30.99	39.71			
	Total	38.18	0.74	36.73	39.64			
FFMQ	Controls	127.89	2.81	122.25	133.52	[1,69]	5.32	.024

	MDD	114.94	4.64	105.11	124.77			
	Total	124.74	2.48	119.79	129.69			
PA	Controls	34.27	0.86	32.56	35.98	[2,138]	24.24	.000
	MDD	25.03	1.29	22.41	27.64			
	Remitted	23.45	2.30	18.68	28.23			
	Total	29.90	0.81	28.29	31.51			
NA	Controls	14.64	0.62	13.39	15.88	[2,138]	32.29	.000
	MDD	25.73	1.45	22.79	28.66			
	Remitted	17.14	1.70	13.61	20.67			
	Total	18.22	0.73	16.78	19.66			

Note: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PA, NA, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups assumed equal.

Correlation Matrices

Next, to address the heterogeneity of comparable social measures used across different studies (Santini et al., 2015), correlations between the different social measures were explored.

Results revealed that in depressed participants, the IPSM, ISQ, SAIS-I, SAIS-II, SCS and SBS were strongly inter-correlated, although the SCS was not correlated with the SAIS-I (Appendix 2.26). In remitted depressed participants, the IPSM was significantly correlated with the SAIS-I and the SCS; the ISQ was significantly correlated with the SAIS-I, SAIS-II, SBS and SCS and the SAIS-I was additionally correlated with the SBS, and SCS. Finally, the SBS was correlated with the ISQ, SAIS-I, SAIS-II and SCS, while the SCS was correlated with IPSM, ISQ, SAIS-II, and SBS (Appendix 2.27). In healthy controls, the IPSM, ISQ, SAIS-I, and SAIS-II were significantly correlated, while the SBS was only significantly correlated with the IPSM, ISQ and SAIS-II. The SCS was significantly correlated with IPSM and SBS only (Appendix 2.28). Finally, for all participants' data combined, all social measures were significantly intercorrelated (Appendix 2.29). For an overview of correlational matrices and results for all social, affective and process measures, see Appendix 2.25-Appendix 2.29.

Given these high correlations, we sought to further explore the heterogeneity between the social measures by using a principal component factor analysis to reduce the data into a meaningful "social" construct, alongside the affective and process measures. The scores on the social measures IPSM, ISQ, SAIS-I, SAIS-II, SBS and SCS were entered into a Principal Components Factor Analysis using an oblique rotation in all participants combined. The aim was to extract meaningful latent structures consolidating the range of social measures encompassing submissiveness, social rank and inferiority behaviours that could be implemented in subsequent analyses to minimise multiple testing of overlapping measures. Principal components analysis is based on the correlation matrix of the variables involved, and correlations usually need a large sample size before they stabilize. A sample size between 100-200 is considered fair (Osborne & Costello, 2004). The social measures loaded significantly onto one component explaining 59.14 % of the variance, best described by involuntary subordination and submissiveness (see Appendix 2.24).

Finally, we correlated the resulting 'social factor' with the main affective and process measures, specifically, the BAI, BDI-II, and DERS. This aimed to explore the relationship between symptoms of anxiety, depression, and emotional dysregulation and social functioning within and across groups (see Table 2.7), as outlined in the literature (see introduction).

In healthy controls, results revealed a significant correlation between the social factor, and the BAI, BDI-II, and DERS. In remitted depressed, the social factor was significantly correlated with the BDI-II and DERS only, while in depressed participants the social factor was significantly correlated with the BAI, BDI-II and the DERS. Finally, across all participants combined, results revealed significant positive correlations between the social factor and all remaining measures. See Figure 2.1 for a correlation plot of the social factor and affective and process measures, across all groups and studies combined. These results suggest that the social component, encompassing greater involuntary subordination and submissiveness, is associated with an increase in symptoms of anxiety, depression and emotional dysregulation. This provides strong evidence for the relationship between depressive symptoms and involuntary subordination and submissiveness, as the main measures contributing to the social factor derived from the PCA.

Table 2.7

Correlation matrix of social factor with affective and process measures across all groups and studies

Measure		MDD	Remitted	Controls	All Participants
BAI	Pearson's r	0.34	0.29	0.40	0.53
	p-value	*0.03*	*0.17*	*< .001*	*< .001*
BDI-II	Pearson's r	0.40	0.54	0.45	0.63
	p-value	*0.01*	*0.01*	*< .001*	*< .001*
DERS	Pearson's r	0.71	0.67	0.58	0.77
	p-value	*< .001*	*< .001*	*< .001*	*< .001*

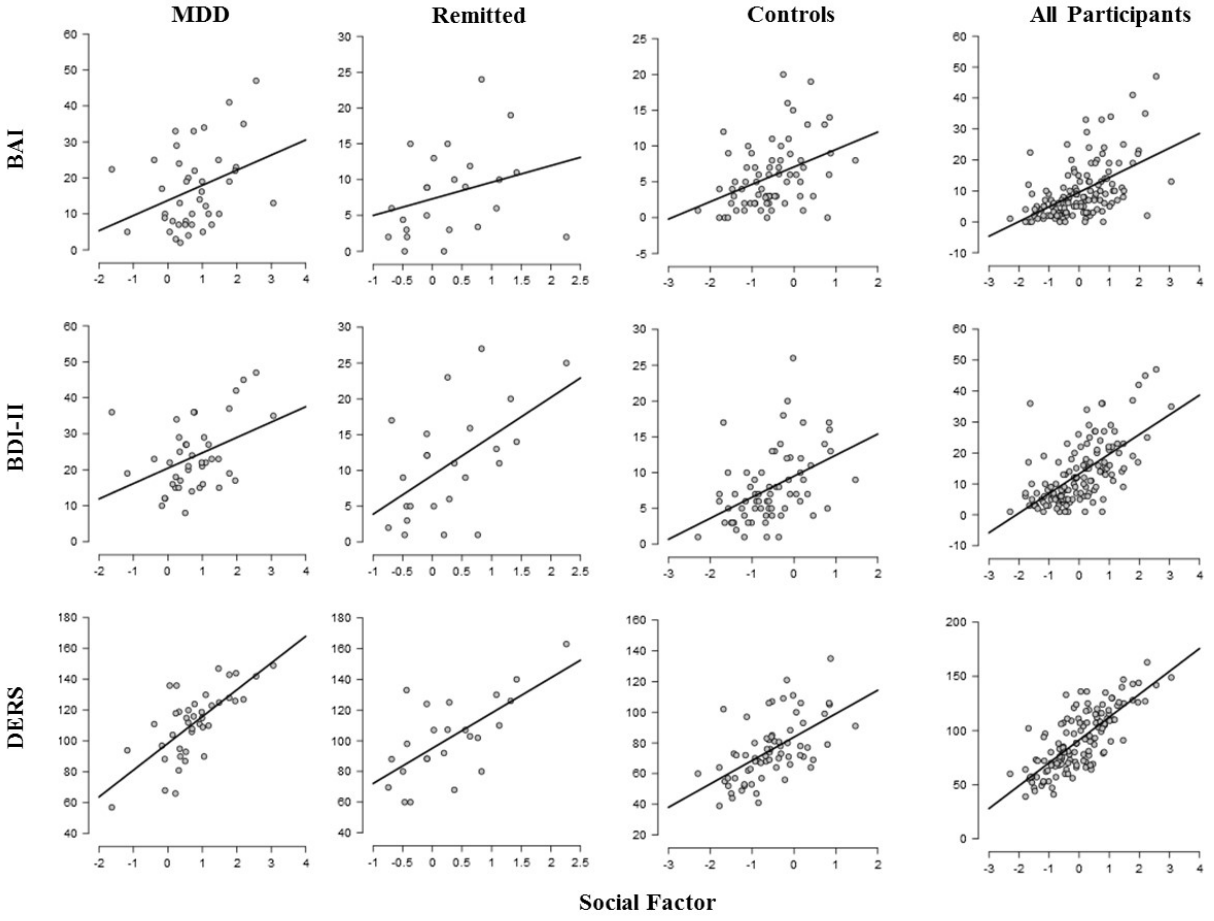


Figure 2.1. Correlation plot of the 'social factor', and the main affective and process measures (BAI, BDI-II and DERS) across all studies and groups combined. Results reveal significant correlations between the latent social component indicating involuntary subordination and submissiveness, and measures of anxiety, depression and difficulty in emotion regulation.

2.4 Discussion

This chapter presented the general methods including recruitment and assessment procedures, measures used, ethical considerations and issues pertaining to the statistical analyses and power for all studies presented in this thesis. In addition, we explored the hypothesis that depression is characterised by significant systemic biases in social and affective processing compared to healthy controls, and investigated the pattern of residual social impairments in remitted depressed individuals, using a series of self-report measures. In line with our hypotheses, results highlight significant impairments in social, affective and cognitive processing between MDD and control participants, with persistent residual deficits in social and cognitive processing exhibited in remitted participant relative to controls. In addition, correlational results revealed significant relationships between symptoms of anxiety, depression and social measures, including involuntary subordination and submissiveness within- and across-groups. Finally, this chapter reduced the heterogeneity of existing social measures to better account for potential biases in social functioning (Santini et al., 2015). This revealed submissiveness and involuntary subordination as the main candidate maladaptive behaviours, significantly correlated with symptoms of depression, anxiety and difficulties in emotion regulation.

Furthermore, findings from this study replicate previous results highlighting the usefulness and validity of the BDI and BAI as reliable indicators of symptom severity and as screening tools within the general population (Beck et al., 1997; Muntingh et al., 2011; Osman et al., 2002; Storch et al., 2004). In the current thesis population, depressed individuals fell well within the moderate range of depression and anxiety, with remitted depressed individuals scoring within the normal range of mood fluctuations, bordering on a mild mood disturbance and anxiety, alongside healthy controls. Additional sensitivity analyses confirmed the suitability of our screening and recruitment process to ensure matching across groups. Moreover, our results reveal a significant relationship between depressive symptom severity and difficulties in emotion regulation, in line with previous studies (Aldao et al., 2010; Bardeen et al., 2012; Gratz & Roemer, 2004; Gratz et al., 2006). Broad impairments on affective and process measures thus validate the distinct groups outlined within this thesis as a function of symptom severity and allow for mood-dependent interpretations based on subsequent between-group comparisons on a behavioural and neural level.

In addition, our findings extend the relationship between well-established deficits in affective and cognitive processing to incorporate systemic biases in social processing on a range of social measures in remitted depressed and currently depressed samples. Our findings suggest that for instance, across all groups, but most strongly for those with MDD, difficulty in emotion regulation is significantly associated with a range of social measures, including submissive behavior, interpersonal sensitivity, involuntary subordination, striving to avoid inferiority and perceptions of low social rank. This suggests that emotion regulation is strongly linked to inherently social affective contexts, with social behaviours fulfilling regulatory goals, including submissiveness and subordination. Interestingly, greater difficulties in emotion regulation in depressed and remitted depressed individuals compared to healthy controls further highlights the importance of residual impairments in a remitted population (Ehring et al., 2008; Muntingh et al., 2011).

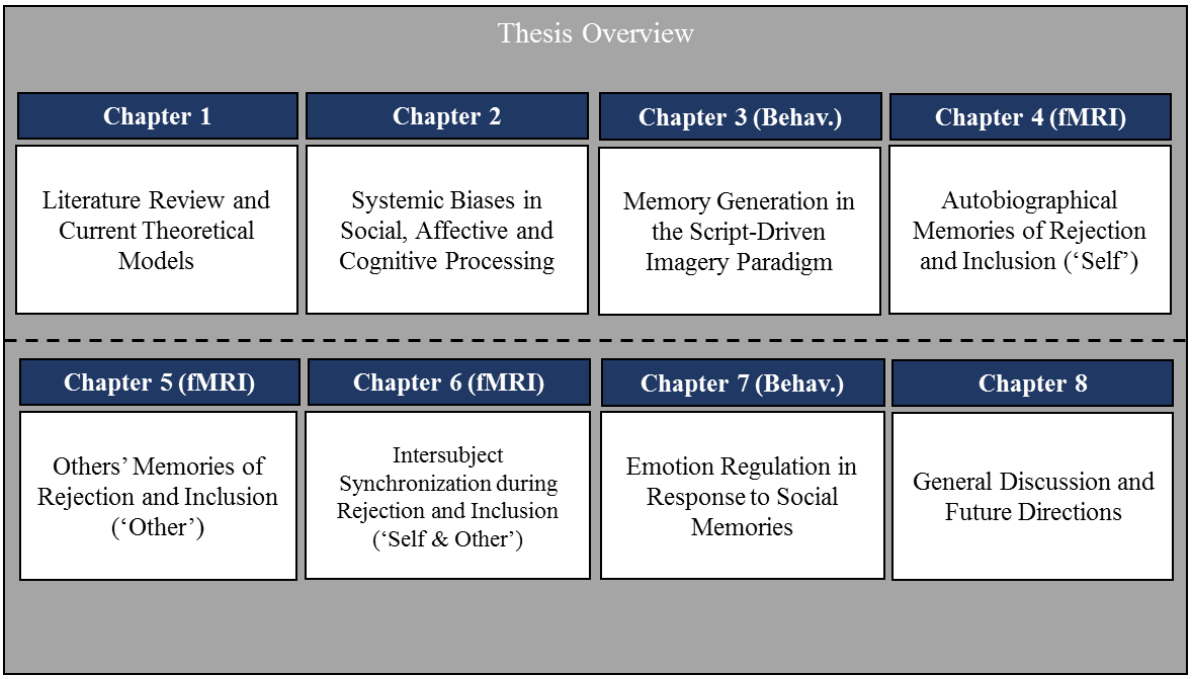
As described within the social rank theory (Allan & Gilbert, 1997; Gilbert et al., 2007) and in line with the social risk hypothesis of depression (Allen & Badcock, 2003), depressed individuals with low perceptions of social rank are argued to employ a range of defensive behavioural strategies in response to internalised feelings of inferiority and low self-esteem (Gilbert, 2000). Findings from this chapter emphasise this notion, as depressed individuals experience significant low rank self-perceptions, and feelings of inferiority, they engage in greater levels of involuntary subordination and submissiveness. Further, perceptions of insecure relationships, encapsulated in measures assessing defensive and regulatory behaviours, such as involuntary subordination, and submissive behaviour, were highly correlated with interpersonal rejection sensitivity, and depressive symptoms. These findings fit will within the existing literature, which identifies an association between negative social comparisons and increased rumination and depressive symptoms (Feinstein & Hershenberg, 2013), eating disorder (Troop, Andrews, Hiskey, & Treasure, 2014), chronic illness (Terol et al., 2015), increased stigma in intellectual disability (Paterson et al., 2012) and increases in paranoid thoughts (Freeman et al., 2014).

Similarly, remitted depressed individuals within this study exhibited impairments on measures of submissive behaviour, involuntary subordination and interpersonal rejection sensitivity. This emphasises the notion of a ‘learned “lower rank” mind-set’, in which maladaptive

behaviour even in the absence of current low mood is initiated by systemic biases in social processing. Similarly, in line with the social risk hypothesis (Allen & Badcock, 2003) persistent submissive and subordinate behaviours aimed at restoring optimal SIP contribute to the maintenance and risk of depressive relapse. This underscores the importance of these findings in the current study, given the deficits in social functioning in depressed and remitted depressed samples previously described across a variety of socio-affective domains (Elliott et al., 2012; N. Kennedy et al., 2007; Pechtel et al., 2013), including emotion recognition and regulation (Lemoult & Sherdell, 2010), reward sensitivity (Pechtel et al., 2013), and altered neural responses to social interactions (Elliott et al., 2012).

In sum, depressed individuals are found to be more sensitive to social rejection, and engage in negative social comparisons, submissive behaviour and involuntary subordination, while striving to avoid inferiority, discussed within the framework of the main social theories of depression. Moreover, the results within the remitted sample point towards a need for a more complex index of social functioning to account for socio-cognitive deficits even in the absence of a current clinical diagnosis. These findings may indicate vulnerability to future episodes as well as providing a scientific rationale for incorporating functional treatment outcomes from within the social domains into existing intervention approaches to alleviate and maintain recovered symptoms of low mood and anxiety. Thus, this chapter has served to validate and replicate well-established findings using common affective and process measures, and extend these findings to other measures of social relevance within currently depressed and remitted depressed individuals. Finally, this chapter outlined the general issues and procedures pertaining to the work presented in this thesis, starting with the next chapter.

CHAPTER 3. MEMORY GENERATION IN THE SCRIPT-DRIVEN IMAGERY PARADIGM



3.1 Introduction

This chapter aims at investigating the phenomenological qualities of autobiographical memories of social rejection, inclusion and emotionally-neutral social experiences generated and recalled for use in the script-driven imagery paradigm in Chapter 4 and Chapter 7. The validation of the script-driven imagery paradigm may present a viable experimental approach to understanding the relationship between specific psychological processes underlying complex social interactions. However, a long-cited challenge in social affective neuroscience is the low ecological validity of existing paradigms (Bem & Lord, 1979; Bronfenbrenner, 1977), where the research to date has relied on the presentation of experimentally constrained emotional stimuli (Amodio, 2010; Burgess et al., 2006; Poldrack, 2008). The benefits and costs of real-life or naturalistic approaches, compared to traditional or laboratory-based approaches, are outlined in more detail in Chapter 8; however, the gist of the debate concerns the trade-off between the need for experimental control and the drive to preserve the psychological phenomenon of interest (Burgess et al., 2006).

Topical reviews suggest the implementation of a variety of tasks and stimuli to capture the social dynamic (Amodio, 2010; Poldrack, 2008). Efforts to address these suggestions have embraced novel methodological approaches to increase ecological validity, ranging from individual experience sampling (Trull & Ebner-Priemer, 2009), virtual reality environments (Parsons, 2015), and brain-as-predictors approaches, in which brain activity complements self-report and other physiological measures to predict real-world outcomes and inform interventions (Berkman & Falk, 2013). One further approach to the problem of limited ecological validity is to reflect real-world social encounters as closely as possible through the use of highly self-relevant autobiographical memories (Whalley et al., 2012).

Autobiographical recollections are temporary mental representations derived from an underlying knowledge-based system with varying levels of specificity, which are guided by goals and beliefs currently held within a working model of self (M. A. Conway & Pleydell-Pearce, 2000). Retrieval within the autobiographical memory model is initiated by executive control processes, which in turn activate sensory perceptual episodic concepts (M. A. Conway & Pleydell-Pearce, 2000). Moreover, memory representations feed into person and event

schemas, which provide templates for interpersonal relationships and patterns of response within role-relationship models (Horowitz, 1989). With interpersonal schemas being inherently affective in nature (Horowitz, 1989), there is a preferential recall of affective experiences over more descriptive memories (M. A. Conway & Pleydell-Pearce, 2000). Autobiographical memories thus encompass multifaceted affective environments and socially salient negative and positive emotions (Kuyken & Moulds, 2009).

The use of autobiographical memories also allows for the investigation of complex neural processes, including the distinct phenomenological qualities of emotion, emotion recognition and regulation (Gross, 2015). For instance, a study investigating emotion regulation strategies in response to (negative) emotional memories revealed novel patterns of activity in regions relevant to affective disorders, including depression (Kross, Davidson, Weber, & Ochsner, 2009). These regions had not previously been identified in traditional 'laboratory' paradigms using isolated normative stimuli. Autobiographical memories may therefore further provide an ecologically valid alternative route to elucidating patterns of brain activity relevant for both emotional and social processing (Kross et al., 2009). However, understanding the functional neuroanatomy of our personal past and present requires innovative methods for eliciting personal memories in the scanner and may be subject to idiosyncratic limitations.

A paradigm which has thus specifically adapted the recall of autobiographical memory for use in fMRI research is script-driven imagery. This paradigm consists of the prompted recall of one or multiple specific autobiographical memories with an emphasis on sensory, visceral and affective characteristics aimed at eliciting salient emotions (Lanius et al., 2002). These memories generated in an initial interview session are then presented to participants in a second memory presentation session. Initial studies investigated dissociative responses in PTSD through the explicit recall and script-driven imagery of traumatic memories in individuals with sexual-abuse related PTSD (Lanius et al., 2002). However, the elicitation of less severe more 'everyday' negative and positive memories has also successfully evoked socially salient emotions (Frewen et al., 2010, 2011a). To date, script-driven imagery has been successfully implemented in both clinical and non-clinical groups, to examine social and emotional processes at the behavioural and neural level (Lanius et al., 2003; Lindauer et al., 2004; Beckham et al., 2007; Frewen et al., 2008, 2010, 2011b; Kleim et al., 2010).

It is important to consider potential limitations to the feasibility of implementing script-driven imagery within the context of depression. Depression is associated with distinct alterations in memory functioning, such as mood-congruent recall, intrusive memories and negative biases in autobiographical memory recall (Dalgleish et al., 2007; Dalgleish & Brewin, 2007; Kuyken & Howell, 2006; Whalley et al., 2012; J. M. G. Williams et al., 2007), such as the tendency to recall over-general memories (Dalgleish et al., 2007; Raes, Hermans, de Decker, Eelen, & Williams, 2003; J. M. G. Williams et al., 2007). Overgeneral memory, the reduced ability to retrieve specific autobiographical memories, presents perhaps the biggest challenge in implementing script-driven imagery in depressed samples (J. M. G. Williams & Broadbent, 1986). This is thought to be due in part to a faulty retrieval process in response to cue words which involuntarily invokes dysfunctional schemas in depression, thereby preventing the specific recall of memories (Dalgleish et al., 2007; Dalgleish & Brewin, 2007; Kuyken & Howell, 2006; J. M. G. Williams et al., 2007).

Alongside the tendency to recall over-general memories (Dalgleish & Brewin, 2007; J. M. G. Williams et al., 2007), depressed individuals are also found to recall memories at a slower pace, thereby lengthening the time required per individual per memory within a memory generation session (Liu, Kraines, Massing-Schaffer, & Alloy, 2014). In contrast to the recall of single traumatic memories as part of the original script-driven imagery study in PTSD populations (Lanius et al., 2002), the recall of multiple memories may therefore interfere with successful memory generation, especially in clinical populations. Other common autobiographical memory deficits in depression describe biases towards preferentially recalling events of negative emotional valence; difficulty in retrieving positive memories and the role of rumination and avoidance when recalling autobiographical memories (Koehler et al., 2015). These considerations should be taken into account when designing studies implementing script-driven imagery, as they might interfere with successful memory generation.

However, research also suggests that the ability to retrieve specific memories when explicitly prompted eliminates the overgeneralising effect and negative response bias (Watkins et al., 2000). Specifically, over-general memory in depression has been found to be modifiable through cognitive interventions and manipulations reflecting a dynamic cognitive style, thus highlighting the importance of executive control for autobiographical memory recall (Watkins

et al., 2000; Dalgleish et al., 2007). It is important to emphasize the latter point as over-general memory relates to the cued recall of voluntary memories, as opposed to the prompted recall of specific autobiographical memories within the script-driven imagery paradigm. These findings suggest that the script-driven imagery paradigm may be implemented even in clinical contexts, where memory functioning presents a contributing factor to the aetiology and maintenance of depressive symptoms.

In addition, while the notion of ecological validity and memory deficits in depression may be addressed more satisfactorily, a further consideration concerns the stability and intensity of emotions over time. Considerations regarding the temporal latency between memory recall and original experience are conceptualised within the affective fading bias literature. The fading affect bias refers to the observation that the affective intensity for unpleasant events fades faster or to a greater degree than the affect associated with pleasant events (Walker et al., 1997, 2003, 2014; Lindeman et al., 2016). The term was first coined by Cason (1932) who asked participants to rate the affective intensity at the time of experiencing a positive or negative event, followed by ratings of affect when recalling the event at a later point in time. Taking the affect fading bias into account, an observed attenuation in affect, intensity, and vividness between experience and recall as a function of memory type would further speak to the validity of the script-driven paradigm overall. Moreover, recent findings suggest that positive events are recalled more vividly compared to negative events (Lindeman et al., 2016), suggesting that that vividness may be a plausible mediator between the valence of an event and its degree of affective fading. The fading bias is further modulated by the type of audience to which the memory is disclosed, in this case, the experimenter. Social disclosure to an interactive listener decreased the affective intensity of unpleasant events, while non-responsive listeners prompt an increase in affective intensity (Muir et al., 2017). This is important in the context of script-driven imagery, given the interactive nature of the memory generation session.

Overall, the fading affect bias is thought to lessen the impact of negative experiences, simultaneously emphasising the impact of positive experiences (Walker et al., 2003; Ritchie et al., 2009; Lindeman et al., 2016). The bias thus reflects a healthy coping mechanism pertaining to autobiographical memory, which may be disrupted in clinical disorders, including depression, dysphoria and anxiety (Walker et al., 2003, 2014). In particular, low mood was

found to diminish the effect with unpleasant and pleasant emotions fading comparably over time, correlated with dysphoric symptom severity (Walker et al., 2003). Similarly, increased levels of trait anxiety diminished the fading affect bias across both positive and negative events, although not eliminating it altogether (Walker et al., 2014). In the context of script-driven imagery, it is therefore unclear to what extent this bias may interfere with the memory generation process, especially considering the importance of matching memories in emotional saliency across groups.

In sum, social neuroscience has strived towards bridging the gap between experimentally constrained presentations of stimuli to investigate tightly controlled psychological phenomena, while preserving the ecological qualities of the phenomenon in question. The use of autobiographical memories within the script-driven imagery paradigm, appears as a potential approach in this context, with the recall of rich multi-faceted affective environments allowing for the investigation of complex psychological constructs. However, memory disturbances in depression, the affect fading bias and sensitivity regarding personal disclosure may provide stumbling blocks for the successful implementation of this paradigm.

The aims of the present chapter were, therefore, two-fold: (i) to validate the experimental use of autobiographical memory recall and script-driven imagery to manipulate mood in depressed and non-depressed individuals across the experimental studies in this thesis; (ii) to deepen our understanding of the carry-over over effects between initial memory recall and script-driven imagery with respect to valence, vividness and intensity, as markers of saliency. This chapter will address these aims by comparing affective, vividness and intensity ratings of the rejection, inclusion and neutral memories obtained in the initial memory generation sessions between groups and between the time of experience and time of recall within session.

HYPOTHESIS

- Memories generated involving social rejection, inclusion, and emotionally-neutral social experiences in an initial memory generation session will reliably modify mood across participants, with the recall of rejection memories resulting in more negative mood, the recall of inclusion memories resulting in more positive mood, and neutral memories resulting in relatively unchanged mood. This will validate the script-driven imagery paradigm, in line with previous implementations (Lanius et al., 2002).

3.2 METHODS AND MATERIALS

PARTICIPANTS

This chapter will report analyses on pooled data obtained from two separate samples described in Chapter 4 and Chapter 7, respectively. This serves to ensure that the memories obtained from the initial memory generation sessions within these studies meet the demands of the script-driven imagery paradigm with respect to eliciting salient memories, which modify mood as a function of valence. Thus, participants for "sample 1" were recruited as part of the neuroimaging study investigating psychological and neural processes in response to autobiographical memories of rejection and inclusion in depressed and healthy controls (Chapter 4). Participants for "sample 2" were recruited for the behavioural study investigating emotion regulation strategies in response to autobiographical memories of rejection and inclusion in healthy controls only (Chapter 7). Both samples were recruited from volunteer and research panels at the MRC Cognition and Brain Sciences Unit and the University of Cambridge. For details on recruitment and inclusion and exclusion criteria see Chapter 2. All participants completed two research sessions, an initial behavioural memory generation session described here, followed by either i) a neuroimaging memory presentation session described in Chapter 4 or ii) a behavioural memory presentation session described in Chapter 7. This chapter will describe the memory-generation procedure in the initial session only.

fMRI study – Sample 1 (Chapter 4)

The neuroimaging study involved eighteen participants experiencing a current Major Depressive Episode and meeting criteria for a diagnosis of Major Depressive Disorder (MDD;

13 female; 34.11±10.9 years) and 21 healthy controls who had never met criteria for MDD (10 female; 35.30±16.1 years). Full demographics are presented in Table 4.2 and a full description of the study procedure can be found in Chapter 4.

Behavioural study – Sample 2 (Chapter 7)

The behavioural study involved the recruitment of thirty-four healthy participants (22 female; 39.32±16.73 years) with no history of Major Depressive Disorder or other mental health problems. Full demographics are presented in Table 7.2 and a full description of the study procedure can be found in Chapter 7.

Clinical Interview and Social, Affective and Process Self-Report measures

A comprehensive diagnostic interview and battery of social, affective and process self-report measures was undertaken with respect to all participants in each sample. See Chapter 2 for a full description.

Experimental Task

Memory Generation Session

In the memory-generation session, participants provided autobiographical memories consisting of social rejection memories, social inclusion, memories and neutral social memories, and affective ratings with respect to current mood state at the time of memory recall and mood state at the time of the original experience. In the neuroimaging study (sample 1 - Chapter 4), the number of memories to be recalled consisted of 18 autobiographical memories and extended to both healthy controls and currently depressed individuals. In the behavioural study (sample 2 - Chapter 7), healthy control participants provided 9 autobiographical memories consisting of three memories in each category of social rejection (e.g. being romantically rejected by a partner), social inclusion (e.g. being elected team captain), and neutral social memories (e.g. shopping in the presence of other people). See Table 3.1 for overview of memories obtained.

For all memories, participants were asked to verbally provide a social personal memory from their life that they very clearly remember and that still feels important to them, which was audio-recorded by the experimenter and later transcribe. Participants were asked to recall a memory that involves other people, with at least one other person, and a memory that still

evokes strong feelings even when remembering it in the present. Participants were encouraged using a series of prompts (see Figure 3.1) to emphasise sensory details and visceral reactions to maximise the emotiveness when recalling the narratives. For a full protocol of the memory generation session, see Appendix 3.1. A description of what constitutes a social compared to a non-social memory, as well as examples of each memory category were provided to participants on cue cards (see Table 3.2). See Appendix 3.2 for example memories obtained within the memory generation session. The generated memories were then later used in the script-driven imagery paradigm designed to elicit the salient emotional experiences and adapted for fMRI (Frewen et al., 2008, 2011; Lanius et al., 2002). The procedure for the memory presentation session is described in Chapter 7 and Chapter 4, respectively.

Participants rated each memory on vividness and intensity, and with respect to four elicited subjective mood states (distress, rejection, inclusion, positivity) with respect to current mood state at the time of memory recall and mood state at the time of the original experience to ensure that memories were elicited with comparable emotional salience across time and groups. All affective ratings were obtained on Likert scales ranging from 0 ("Not at all") to 10 ("Extremely"). The four subjective mood states were compiled into a negative mood index (the reverse scored average of the distress and rejection ratings), and a positive mood index (the average of the inclusion and positivity ratings). The negative mood index was then subtracted from the positive mood index, resulting in an overall composite measure of affect ranging from -10 (very negative/rejected) to +10 (very included/positive). Following the memory generation session, each memory narrative was transcribed and edited down into a 30-second transcript narrated in the first person, present tense. These transcripts were used to generate audio-recordings with memories narrated by a research assistant gender-matched to the participant and where possible matched geographically to account for regional varieties in language. These recordings were then used as individualised stimuli in the memory presentation session described in Chapter 4 and Chapter 7.

Table 3.1

Numbers of social memories obtained in the memory generation sessions for each sample

Sample	Chapter	Group	Rejection	Inclusion	Neutral	*Total (Session)*	*Total (Study)*
1	Chapter 4	MDD & Controls	6	6	6	*18*	*702*
2	Chapter 7	Controls	3	3	3	*9*	*304*

Note: MDD = Major Depressive Disorder; samples pooled for analysis

A (social) personal memory …

- Is a memory from your life that you very clearly remember and that still feels important to you
- Is a memory that involves other people, with at least one other person
- Evokes strong feelings

Describe the situation in your own words – what happened?

- How long ago was it?
- Where did it happen?
- What kind of day was it?
- What did your surroundings look like?
- What did you say? How did you act?
- Were other people there? What where they saying? How were they acting?
- Any sensations: Sights, Sounds, Smells, Touch?
- How long did it last?

Figure 3.1 Memory generation cue card and prompts used in the memory generation session

Table 3.2

Examples of social compared to non-social memories used in memory generation sessions

	Social Memories	**Non-Social Memories**
Inclusion	- Being elected class representative - Receiving a (surprise) birthday party by your friends - Travelling together in a group - Being asked to be the best man/maid of honour - Starting a relationship with someone you feel very strongly about OR Getting married - Scoring the winning goal in a football match	- Academic achievement, such as passing your exam - Being promoted at work - Getting a job you really wanted
Rejection	- Being rejected by your romantic partner - Having a group of friends turn on you / not invite you - Being humiliated by your boss in front of everyone - Bereavement - Getting your divorce papers through	- Failing an exam - Being fired from your job - Losing at an important tennis match
Neutral	- Standing in a queue in the supermarket - Waiting in a group for the bus - Standing on the platform waiting for a train/underground - Commuting on a packed train - Sitting in assembly at school - Being part of the school class - Being part of a sports team	- Having a new kitchen installed - Landscaping the garden - Reading a book in a café - Buying groceries

Procedure

In the 1.5-hour memory generation session, participants provided informed consent and were then asked to recall a series of autobiographical memories. For all memories, participants were asked to emphasise sensory details and visceral reactions. Participants rated their memories on vividness and intensity, and with respect to four subjective mood states (distress, rejection, inclusion, positivity). At the end of the session participants were thanked for their time and reminded of the scheduled second research session.

Statistical Analysis

The composite affective ratings and vividness and intensity scores acquired in the memory-generation sessions for both samples were pooled and averaged for each memory type. Composite affective ratings, vividness and intensity scores between time of experience and time of recall were entered into a series of univariate analyses of variance (ANOVAs) with memory type (rejection/inclusion/neutral) and time (experience/recall) as within-group factors and group (MDD/controls) as a between-group factor. This served to validate that the emotional saliency of the memories had been maintained over time as had been outlined in the instructions to the participant ('…should be a memory that still evokes strong emotions even when remembering it in the present…') with respect to vividness and intensity, and could thus be reliably re-elicited in the memory presentation task in session two. It also served to validate that mood is modified non-significantly differently across depressed and non-depressed participants recruited as part of this thesis, with changes in mood differing significantly as a function of the valence of the memories recalled, in line with our hypothesis, but not as a function of group.

3.3 RESULTS

For participant characteristics and social, affective and process measures for the individual samples please refer to Chapter 4 and Chapter 7. In the pooled sample, we investigated whether the memories recalled in the memory-generation sessions had maintained their emotional saliency over time since the original event had been experienced considering both memory type and group. For this purpose, differences between affective ratings of mood, vividness and intensity were investigated both at time of experience and recall.

Firstly, exploratory data analysis ensured that the data met the criteria for parametric analysis for subsequent between-groups and within-group analyses. Kolmogorov-Smirnov's test of normality and Levene's test of homogeneity of variance, as well as assumptions of sphericity were assessed and any deviations reported accordingly. Where data violated the assumption of sphericity, Greenhouse-Geisser or Huynh-Feldt corrections are reported, depending on the value of the Greenhouse-Geisser estimate. If the estimate was less than 0.75, Greenhouse-Geisser correction was used, otherwise Huynh-Feldt, if the estimate exceeded 0.75 (Field, 2005). Kolmogorov-Smirnov's test of normality and Levene's test of homogeneity of variance revealed that affective ratings were normally distributed and homogenous across groups.

For the affective ratings, the within-subject factor memory type (x^2=38.31, p=0.001) and the interaction between time and memory type (x^2=24.36, p=0.001) violated Mauchly's test of sphericity and will be reported using a Greenhouse-Geisser correction. Similarly, for vividness and intensity ratings, memory type (vividness: x^2=12.55, p=0.002; intensity: x^2=17.41, p<0.001) and the interaction between time and memory type (vividness: x^2=13.59, p=0.001; intensity: x^2=10.29, p=0.006) violated Mauchly's test of sphericity and will be reported using a Greenhouse-Geisser correction.

BEHAVIOURAL RATINGS

Affective Ratings

Mean composite mood ratings by memory type are presented in Table 3.3, suggesting that mood was most positive following inclusion memories, followed by neutral and lastly rejection memories, across groups and time. Moreover, mean mood ratings by time (Table 3.4) suggests

that overall mood was slightly elevated at recall compared to experience irrespective of memory type and group. Finally, the interaction of group, memory type and time is presented in Table 3.5. Mean descriptives for the raw non-composite affective ratings are presented in Appendix 3.3.

ANOVA results revealed a significant main effect for memory type ($F[1.39,134]=392.40$, $p<0.001$, $\eta_p^2=0.85$). Planned comparisons indicated that mood ratings in response to rejection, neutral and inclusion memories all differed significantly from each other (all $p<0.001$). Mood following inclusion memories was significantly elevated relative to neutral (3.80±0.41) and rejection memories (11.19±0.41), followed by neutral memories relative to rejection memories (7.39±0.41), the latter resulting in lowest (most negative) mood. There was also a main effect of time ($F[1,67]=68.48$, $p<0.001$, $\eta_p^2=0.51$), with significantly more positive mood ratings at time of recall compared to time of experience (1.05±0.13), across groups. There was no main effect for group ($F[1,67]=3.38$, $p=0.07$, $\eta_p^2=0.05$).

There was a significant interaction between memory type and time ($F[1.53,134]=69.20$, $p<0.001$, $\eta_p^2=0.47$). On closer inspection, this revealed that across both groups inclusion memories were rated as marginally less positive at time of recall compared to time of experience, while rejection memories were rated as significantly more positive at time of recall compared to time of experience (see Figure 3.2). This is line with the fading affect bias discussed in the introduction ((Ritchie, Skowronski, Hartnett, Wells, & Walker, 2009; Walker et al., 2003)). There was a significant interaction between memory type and group ($F[1.39,93.03]=20.56$, $p<0.001$, $\eta_p^2=0.26$), suggesting that MDD participants relative to controls reported greater negative mood in response to rejection memories, as well as greater positive mood in response to inclusion memories, with marginal differences for neutral memories (see Figure 3.3). There was no significant interaction between time and group ($F[1,67]=0.14$, $p=0.71$, $\eta_p^2=0.002$) or a three-way interaction between time, memory and group ($F[1,67]=0.43$, $p=0.60$, $\eta_p^2=0.006$).

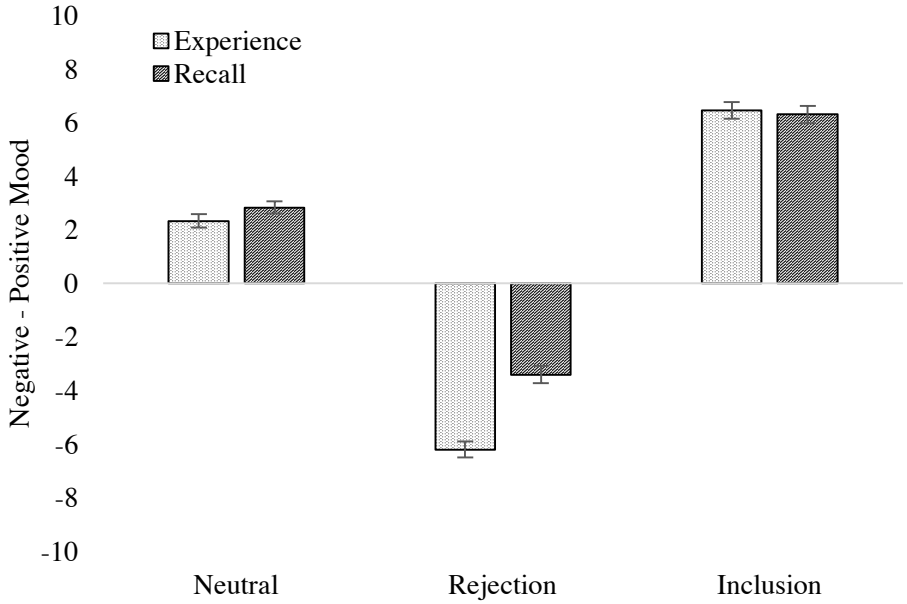


Figure 3.2 Mean ± 1SE of the mean interaction of time and memory type for composite affective ratings reveals a positive shift in mood for rejection memories over time, as compared to marginal changes in mood for neutral and inclusion memories, respectively.

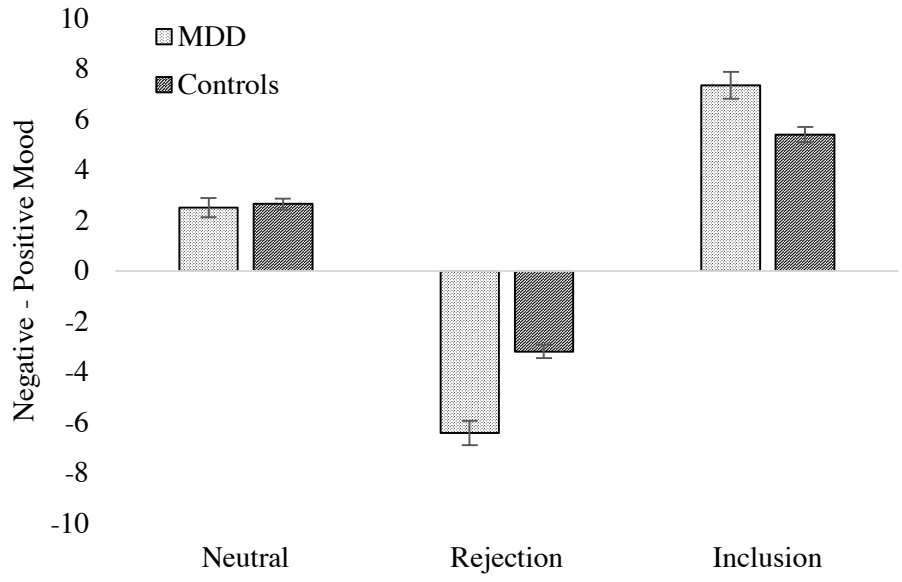


Figure 3.3 Mean ± 1SE of the mean interaction of group and memory type for composite affective ratings reveals greater negative mood for rejection and greater positive mood for inclusion memories in MDD relative to controls across time, with marginal differences in mood for neutral memories.

Table 3.3

Mean composite affective ratings by social memory type across memory generation sessions

Memory Type	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Neutral	2.58	0.22	2.14	3.03
Rejection	-4.80	0.27	-5.35	-4.26
Inclusion	6.38	0.30	5.78	6.99

NB: Lower scores represent more negative mood with a range of -10 to +10 (most positive)

Table 3.4

Mean composite affective ratings by time across memory generation sessions

Time	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Experience	.87	.13	.61	1.12
Recall	1.91	.16	1.59	2.23

NB: Lower scores represent more negative mood with a range of -10 to +10 (most positive)

Table 3.5

Mean composite affective ratings by group, memory type and time across memory generation sessions

Group	Memory Type	Time	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
Controls	Neutral	Experience	2.50	0.24	2.01	2.98
		Recall	2.82	0.22	2.37	3.27
	Rejection	Experience	-4.56	0.29	-5.13	-3.99
		Recall	-1.82	0.33	-2.47	-1.17
	Inclusion	Experience	5.44	0.30	4.84	6.04
		Recall	5.38	0.31	4.75	6.01
MDD	Neutral	Experience	2.18	0.43	1.32	3.03
		Recall	2.84	0.39	2.06	3.62
	Rejection	Experience	-7.84	0.50	-8.85	-6.84
		Recall	-4.99	0.57	-6.13	-3.85
	Inclusion	Experience	7.48	0.52	6.43	8.53
		Recall	7.24	0.55	6.14	8.34

NB: Lower scores represent more negative mood with a range of -10 to +10 (most positive)

Vividness and Intensity Ratings

Mean ratings of vividness and intensity obtained for each memory are summarised by memory type (Table 3.6), suggesting comparably high vividness and intensity scores across rejection and inclusion memories and dampened scores for neutral memories. Ratings at time of recall compared to time of experience (Table 3.7) similarly reveal comparable high scores of vividness and intensity, while group comparisons reveal a similar pattern as that across time, with marginally higher scores for vividness compared to intensity across both MDD and controls (Table 3.8). The interaction of group, memory type and time is presented in Table 3.9.

Vividness ratings revealed a significant main effect for memory type ($F[1.71,114.22]=57.45$, $p<0.001$, $\eta_p^2=0.46$). Planned comparisons deconstructing the main effect of memory type, indicated that vividness ratings for neutral memories were significantly ($p<0.001$) lower compared to both rejection (-1.22±0.19) and inclusion memories (-1.68±0.16), with rejection memories also significantly different in vividness from inclusion memories (-0.46±0.13, $p=0.002$). There was a main effect for time ($F[1,67]=5.12$, $p=0.03$, $\eta_p^2=0.07$), with memories rated marginally more vivid at the time of experience than at time of recall (0.35±0.16). There was no main effect for group ($F[1,67]=1.18$, $p=0.28$, $\eta_p^2=0.02$), suggesting that independent of memory type, there was no support for vividness ratings differing over time and between groups. There no significant interaction between time and group ($F[1,67]=0.11$, $p=.74$, $\eta_p^2=0.00$). However, there was a significant interaction between memory type and time ($F[1.69,112.98]=20.50$, $p<0.001$, $\eta_p^2=0.23$). Ratings at time of recall revealed memories being rated as most vivid for inclusion, followed by rejection memories relative to neutral memories, while vividness ratings at time of experience exhibited greater distinctions between memory types, with sharp increases in vividness for rejection and inclusion memories relative to neutral memories. Neutral memories were rated as more vivid at time of recall compared to time at experience (see Figure 3.4). There was no significant interaction between memory type and group ($F[1.71,114.22]=1.29$, $p=0.28$, $\eta_p^2=0.02$), nor a three-way interaction between group, memory type and time ($F[2,134]=1.71$, $p=0.19$, $\eta_p^2=0.03$).

Intensity ratings also revealed a significant main effect for memory type ($F[1.63,110.67]=190.62$, $p<0.001$, $\eta_p^2=0.74$) with planned comparisons revealing that neutral memories were rated as significantly less intense compared to rejection (-3.94±0.24, $p<0.001$) and inclusion memories (-3.73±0.26, $p<0.001$), which in turn were comparably intense to rejection memories (0.21±0.17, $p=0.63$). There was also a significant main effect for time ($F[1,68]=45.47$, $p<0.001$, $\eta_p^2=0.40$), with pairwise comparisons across groups revealing that memories were rated as significantly more intense at time of experience compared to time of recall (1.03±0.15). There was no main effect for group ($F[1,68]=2.21$, $p=0.14$, $\eta_p^2=0.03$) or interaction between time and group ($F[1,68]=0.01$, $p=.94$, $\eta_p^2=0.00$). A significant interaction between memory type and time ($F[1.75,119.06]=15.20$, $p<0.001$, $\eta_p^2=0.18$), suggested a similar trend to vividness, in that memories are comparable low in intensity for neutral memories, and marginally lower at time of experience (Figure 3.5). Memories are rated as most intense at time of experience for both rejection and inclusion, with slightly lower intensity ratings at time of recall. However, the overall trend nonetheless suggests increased intensity and vividness for valenced compared to neutral memories. There was no significant interaction between memory type and group ($F[2,68]=0.68$, $p=0.51$, $\eta_p^2=0.01$), or three-way interaction ($F[2,136]= 0.29$, $p=0.75$, $\eta_p^2=0.04$).

Table 3.6

Mean vividness and intensity ratings by social memory type across memory generation sessions

Measure	Memory Type	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Vividness	Neutral	6.49	0.19	6.12	6.86
	Rejection	7.71	0.16	7.39	8.02
	Inclusion	8.17	0.13	7.90	8.43
Intensity	Neutral	3.93	0.23	3.47	4.40
	Rejection	7.87	0.15	7.58	8.16
	Inclusion	7.66	0.19	7.28	8.04

Table 3.7

Mean vividness and intensity ratings by time across memory generation sessions

Measure	Time	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Vividness	Experience	7.63	0.16	7.32	7.95
	Recall	7.28	0.15	6.99	7.57
Intensity	Experience	7.00	0.14	6.72	7.29
	Recall	5.97	0.18	5.61	6.33

Table 3.8

Mean vividness and intensity ratings by group across memory generation sessions

Measure	Groups	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Vividness	MDD	7.31	0.14	7.04	7.59
	Controls	7.60	0.22	7.15	8.04
Intensity	MDD	6.28	0.15	5.98	6.57
	Controls	6.70	0.24	6.21	7.19

Table 3.9

Mean vividness and intensity ratings by memory type and time across memory generation sessions

Measure	Memory Type	Time	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
Vividness	Neutral	Experience	6.18	0.27	5.65	6.71
		Recall	6.80	0.17	6.47	7.14
	Rejection	Experience	8.23	0.21	7.82	8.64
		Recall	7.19	0.20	6.79	7.58
	Inclusion	Experience	8.48	0.15	8.19	8.77
		Recall	7.85	0.16	7.53	8.17
Intensity	Neutral	Experience	4.13	0.28	3.57	4.69
		Recall	3.74	0.23	3.28	4.19
	Rejection	Experience	8.73	0.15	8.44	9.03
		Recall	7.01	0.21	6.58	7.44
	Inclusion	Experience	8.15	0.20	7.76	8.55
		Recall	7.17	0.23	6.72	7.62

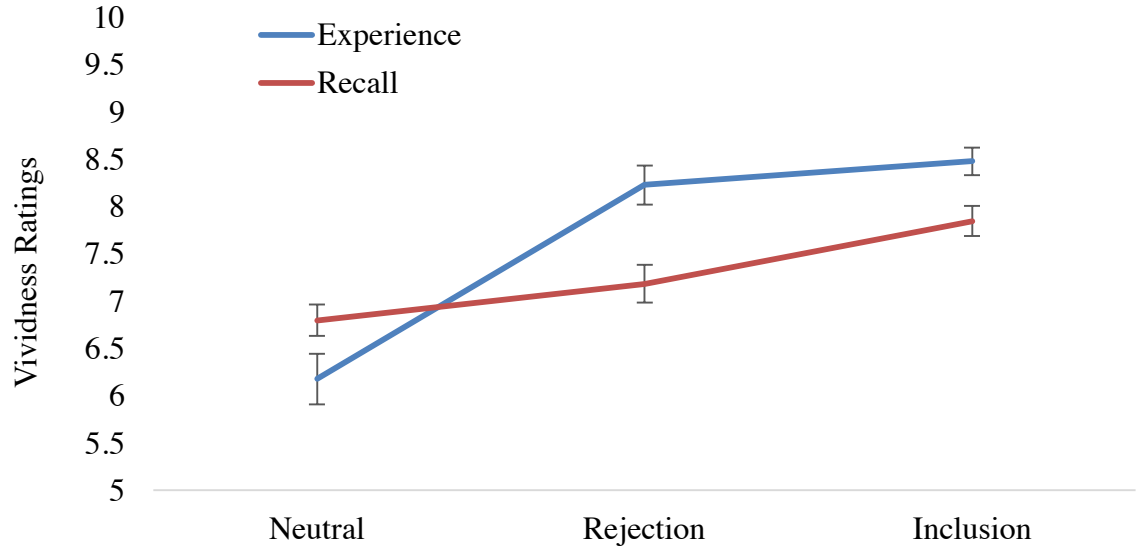


Figure 3.4 Mean interaction ± 1SE of the mean of time and memory type for vividness ratings. Rejection and inclusion memories are rated as more vivid overall than neutral memories.

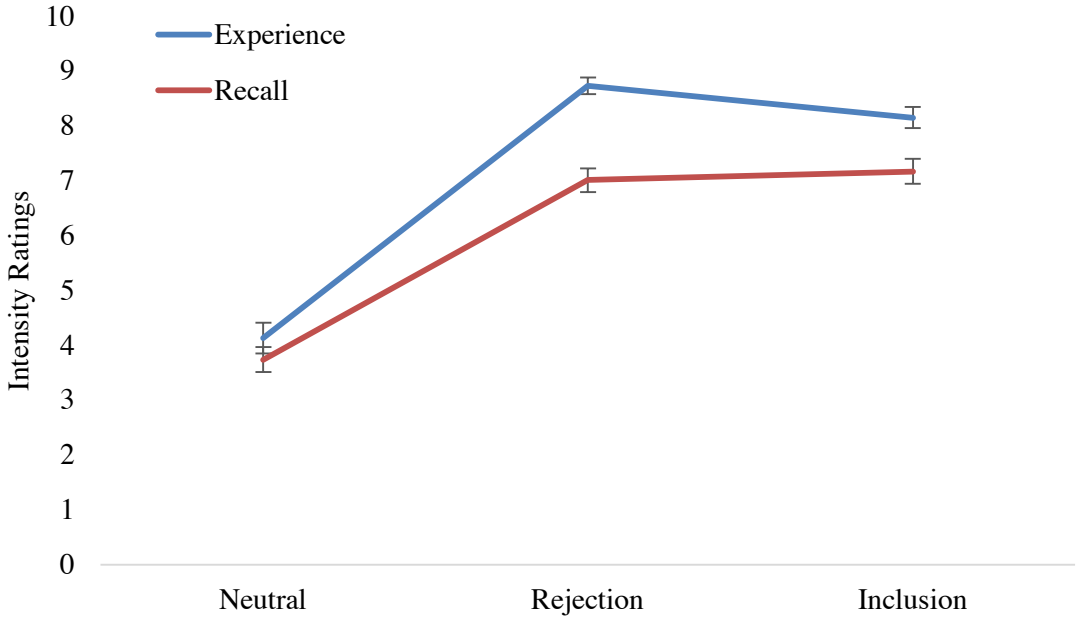


Figure 3.5 Mean interaction ± 1SE of the mean of time and memory type for intensity ratings. Rejection and inclusion memories are rated as more intense relative to neutral memories, with intensity at recall lower than at experience overall.

Summary of Findings Across Samples

Findings for the pooled data for depressed and healthy control participants obtained from the neuroimaging study (sample 1) and the behavioural study (sample 1), reveal that mood, intensity and vividness differed as a function of memory type, and but not, importantly, as a function of group. Thus, both groups appeared to experience comparable changes in mood, vividness and intensity as a function of memory type, despite mood, intensity and vividness ratings declining from the time the individual experienced the event to the time of recall as reported retrospectively within the memory generation session. The successful memory manipulation and sufficient saliency in emotion across groups thus indicates that the memory generation sessions met the conditions necessary in the script-driven imagery paradigm, as outlined in the introduction. The memories generated were therefore assumed to be suitable stimuli for the memory presentation sessions reported in Chapter 4 and Chapter 7.

3.4 Discussion

This chapter reported the procedure for validating the recall of autobiographical memories of social rejection, inclusion and neutral social experiences for use in the script-driven imagery paradigm described in the two studies reported in Chapters 4 and 5. In line with our predictions, the recall of social rejection memories resulted in greater negative mood, while recall of inclusion memories improved mood, and neutral memories revealed no change in mood. We further established that mood manipulations were comparable across depressed and non-depressed participants recruited as part of this thesis, and maintained sufficient saliency in terms of mood, intensity, and vividness over time.

The present study aimed at validating the script-driven imagery paradigm using socially salient autobiographical memories of rejection and inclusion within the context of depression. As such, our findings are twofold; firstly, this chapter illustrates that salient social autobiographical memories can be generated across depressed and non-depressed samples with comparable phenomenological qualities regarding intensity, vividness and valence. Secondly, generated memories can be successfully employed to manipulate mood within an ecologically valid framework, again both in depressed and non-depressed individuals.

This latter finding is of particular importance, given the memory deficits previously described in depression. The tendency to recall over-general memories (Dalgleish & Brewin, 2007; J. M. G. Williams et al., 2007), preferential recall of negative relative to positive memories (Koehler et al., 2015) and attentional limitations were previously noted as potential barriers to the process of memory generation in a depressed sample. However, despite an increase in numbers of memories retrieved in each sample and sessions lasting up to two hours, these potential limitations were not found to interfere with successful memory generation. However, it is worth noting that these disturbances are more likely to be encountered when spontaneously recalling memories, as opposed to the recall of explicitly generated, and where necessary, cued, memories.

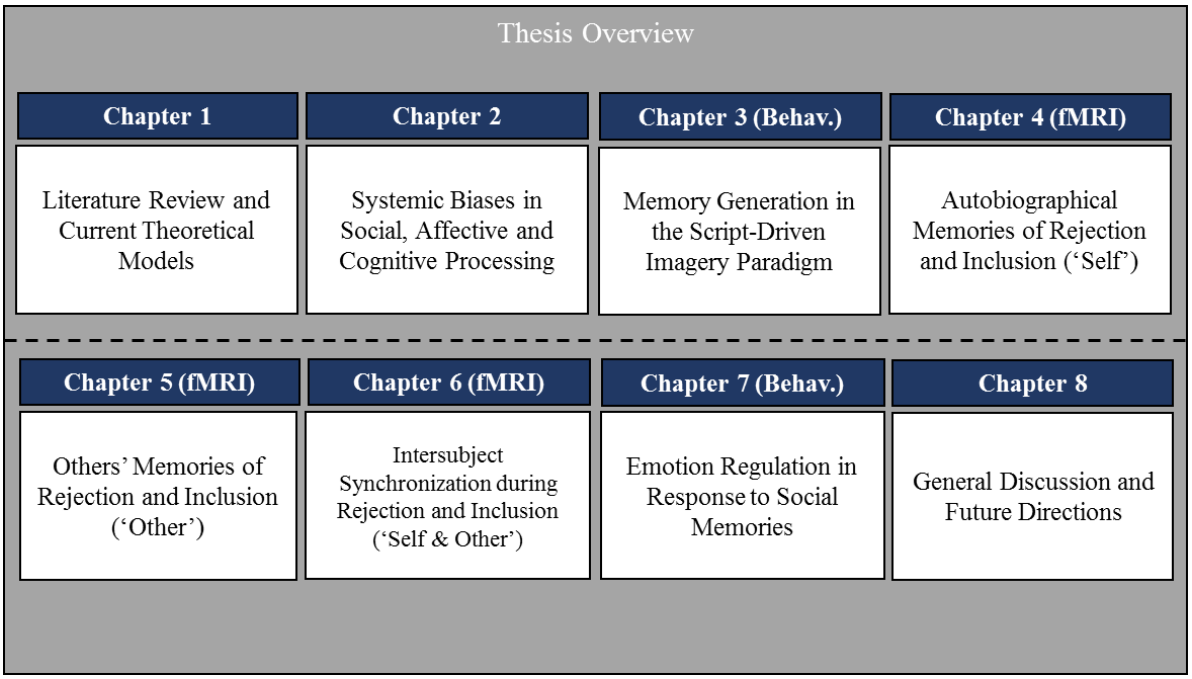
In line with the affect fading bias described in the introduction, our results reveal an attenuation in affect, intensity, and vividness between experience and recall, in particular for healthy controls. This is consistent with previous findings that affective intensity decreases more for rejection compared to inclusion memories (Lindeman, Zengel, & Skowronski, 2016; Ritchie et al., 2009; Walker et al., 2003), despite participants being explicitly asked to report memories with current affective impact. In addition, reductions in vividness over time exhibited a valence-independent effect, although inclusion memories were rated as more vivid overall. This mirrors recent findings that positive events are recalled more vividly compared to negative events (Lindeman et al., 2016). Finally, as outlined in the introduction, this paradigm instrumentally relies on personal (social) disclosure. In the context of the work presented in this thesis, the interviews were all carried out by the main experimenter; however, future implementations may want to be mindful of the interactive effect, when using multiple experimenters. However, in our findings, both groups maintained comparable emotional saliency of the recalled memories over time, despite marginally elevated mood in controls relative to depressed participants across memories. Thus, importantly, our findings overall suggest that the fading affect bias was present with respect to memory type but not as a function of group, due to the explicit instructions about recalling memories with current emotional salience. In future, while this study ensured saliency across sessions, the latency between experience and recall should be incorporated more explicitly into the memory generation session, as there might be phenomenological differences between more or less recently

experienced events. As part of the script-driven imagery paradigm this omission was apparent when reviewing previous studies implementing this approach, with limited reference either to the time since the original event or saliency across sessions (Lanius et al., 2003, 2006; Beckham et al., 2007; Frewen et al., 2008, 2011a; Kleim et al., 2010).

However, the question at the forefront of these studies is whether the recalled memories can reliably elicit salient emotions in the present and that the saliency can be comparable across groups and valence. Considering our findings from this very specific perspective, our results strongly suggest that in line with other script-driven imagery paradigms, autobiographical memories of both positive and negative valence serve to powerfully elicit salient emotions for use in behavioural and neuroscience social affective research. Previously, recalling trauma memories triggered high levels of negative affective intensity and vividness (Lanius et al., 2002, 2006; Frewen et al., 2008). However, this was the first time this paradigm was implemented using multiple social autobiographical memories. Contrary to the notion of 'bad is stronger than good' (Baumeister et al., 2001), as outlined in the introduction in Chapter 1, autobiographical memories of both rejection and inclusion experiences revealed comparable intensity and vividness ratings compared to memories describing neutral or low-level social interactions. This suggests that the generation of socially salient memories in depression for use in a script-driven imagery paradigm is thus both feasible and ecologically valid.

In sum, when comparing mood, affective intensity, and vividness ratings in response to recalling autobiographical memories of rejection and inclusion, both depressed and healthy controls were able to successfully retrieve and elicit memories that provoked salient emotions in the present. Further, affective fading effects were present for both groups between the retrospective ratings for the time of the event being experienced to the contemporary ratings at the time of recall within the memory generation session, but there was no support for differential affective fading across groups. Critically, therefore, the memories elicited sufficiently heightened mood, affective intensity, and vividness required for script-driven imagery. Given the comparable saliency across groups, the generated memories were thus deemed suitable as stimuli for use in the subsequent memory presentation sessions described in more detail in the subsequent chapters.

CHAPTER 4. PSYCHOLOGICAL AND NEURAL PROCESSING OF AUTOBIOGRAPHICAL MEMORIES OF SOCIAL REJECTION AND INCLUSION



4.1 Introduction

The previous chapter determined the suitability of social autobiographical memories for use in the script-driven imagery paradigm. This chapter will present the first neuroimaging experiment to implement this paradigm to examine individual differences in detecting and responding to social signals at the behavioural and neural level in response to autobiographical memories of social rejection, inclusion and neutral social experiences, with depressed and healthy samples.

Interpersonal rejection sensitivity encompasses both enhanced or diminished sensitivity to the behaviour and emotions of others as they pertain to the perceived level of inclusivity within a social group or relationship (Boyce & Parker, 1989). At the behavioural level, this involves heightened sensitivity to the receipt of social feedback, concern about behaviour and verbal statements of others, and fears of perceived or actual criticism. Enhanced rejection sensitivity may result in feelings of inadequacy, inferiority and the misinterpretation of social cues signalling rejection and/or inclusion, correlated with low mood (Gilbert & Allan, 1998). Behaviourally, individuals with high rejection sensitivity tend to modify their interpersonal behaviour and socially withdraw in an attempt to avoid actual social exclusion (Slavich & Irwin, 2014b), with the mere threat of social exclusion increasing selective attention to social signs of acceptance (DeWall et al., 2009), and the motivation to forge novel social affiliations (Maner et al., 2007). See Chapter 1 for more detailed discussion.

As discussed in Chapter 1, at a neural level, processing of interpersonal rejection signals in healthy individuals has been investigated using the virtual ball-tossing game 'Cyberball' (Eisenberger & Lieberman, 2003), designed to generate feelings of social exclusion. Results revealed increased activity in the dorsal anterior cingulate cortex (dACC), anterior insula (AI), and the right ventral prefrontal cortex (vPFC) regions alongside qualitatively distinct self-reported feelings of 'social pain', as opposed to physical pain (Eisenberger, 2012a; Eisenberger & Lieberman, 2003). It was further argued that inducing a state of social distress may result in a diminished sensitivity to pain (Eisenberger, 2012b; Eisenberger et al., 2006). Finally, patients with somatoform pain disorders and fibromyalgia who experience pain with no medical explanation also reported greater levels of early social trauma, including emotional abuse or

family conflict (Imbierowicz & Egle, 2003).This suggests a similar underlying neural circuitry as somatosensory pain regions (Kross et al., 2011).

On a theoretical level, these findings provided empirical support for the sociometer theory (Baumeister & Leary, 1995, see also Chapter 1, page 38), which posits that perceptions of social rejection and acceptance are translated into state self-esteem, which serves as a gauge of interpersonal relationship status, alerting individuals to the threat of exclusion. This proposed neural 'alarm system' or 'sociometer' may provide the mechanism for the modification and adaptation of social strategies and behaviours (Eisenberger, Inagaki, Muscatell, Byrne Haltom, & Leary, 2011). However, more in-depth multivariate fMRI pattern analysis has revealed distinct affective representations for physical pain and social pain beyond the previous findings described at a gross anatomical level (Woo et al., 2014). Moreover, a meta-analysis that specifically focused on the contribution of the dACC in processing social pain suggested a more distributed pattern of activation including both dorsal and ventral ACC (Rotge et al., 2015). Additionally, reconciling findings from the pain and reward processing literatures, there have been suggestions that physical pleasure and physical pain may similarly share a common neural substrate (Leknes & Tracey, 2008). Further, recent meta-analytical data investigating social rejection paradigms revealed distinct activations in the left ACC, bilateral AI and inferior orbito-frontal cortex (OFC) suggesting a more sophisticated index of the social dynamic than the dACC-AI co-activation initially proposed (S. Cacioppo et al., 2013). Finally, Somerville et al. (2006) argued that the 'Cyberball' paradigm (Eisenberger & Lieberman, 2003) is limited by its brief social inclusion condition, which precedes the salient exclusion event. Activity in dACC may therefore reflect expectancy violation rather than affective responses to social rejection per se (Somerville et al., 2006). This limitation may be addressed with a paradigm, which more adequately addressed the saliency across social conditions, such as the recall of highly emotionally salient autobiographical memories.

Therefore, while the underlying neural mechanism of the social pain account had previously been discussed only with respect to processing of social rejection in healthy individuals (Eisenberger, Inagaki, Muscatell, Byrne Haltom, & Leary, 2011), emerging evidence warrants further investigation as to whether this social pain network may be similarly implicated in the

processing of inclusive social signals, considering the comparable saliency of social signals. Recently, a study investigating social processing in a population of healthy adolescents provided encouraging support for this notion of a common neural circuitry underlying positive and negative social evaluation with a novel social feedback paradigm (Dalgleish et al., 2017). Results revealed comparable activation in the dACC and AI to inclusive social feedback provided by virtual 'peers', suggesting that the social pain network may respond to socially salient information regardless of valence.

This social pain debate is of importance in depression, as it begs the question of how social pain regions may respond to signals of inclusion in depression on a neural and psychological level. As described in Chapter 2, our behavioural findings suggest that depressed participants are significantly elevated in their sensitivity to interpersonal rejection compared to healthy controls. This builds on previous suggestions that individual differences in interpersonal rejection sensitivity mediate the relationship between early adverse life events, and depressive symptoms in later adult life (Luterek et al., 2004). Further, higher self-reported need for social acceptance and high investment in interpersonal relationships is associated with greater vulnerability to depression (Ayduk, Downey, & Kim, 2001). While early interpersonal theories of depression argued that feelings of low mood resulted as a function of maladaptive social behavior or poor 'social skills', greater rejection sensitivity may increase the likelihood of experiencing social rejection in the first place (Coyne, 1998; Segrin & Dillard, 1992), alongside impairments in recognition and response to interpersonal social signals (Tse & Bond, 2004). However, Beck's cognitive model (Beck, 1987) posits that emotional distress and behavioural problems are maintained by distortions in core beliefs or assumptions about the world, others and the self, which in turn trigger negative automatic thoughts, once activated. The experience of rejection thus sustains people's view of themselves as unworthy of love and acceptance, thereby maintaining self-directed hostile cognitions and negative core beliefs in depression (Breines & Ayduk, 2015).

As discussed in Chapter 1, heightened interpersonal sensitivity in depression is conceptualised within the social risk hypothesis of depressed mood (Allen & Badcock, 2003), which posits that both positive and negative interpersonal experiences are computed within a zero-sum

game, in which the trade-off between social value and social burden determines an individual's social investment potential (SIP). This in turn impacts the extent to which an individual maintains beneficial social relationships, with critically low SIP triggering a range of behavioural coping strategies. The SR hypothesis suggests that depressed individuals may exhibit a heightened sensitivity to social cues of rejection, or inclusion aimed at restoring the optimal ratio of social value relative to social burden, as this would cease or maintain the adaptive social behaviours. Empirical support comes from recent findings suggesting a social processing network dedicated to evaluating social signals independent of valence. For instance, a study in a depressed community sample investigated expectations and affective responses to positive and negative social interactions using a social evaluation "Chatroom" task (Caouette & Guyer, 2015). Initial results suggested a dampened affective response to social acceptance; however these findings were modulated by the source of the evaluation (Steger & Kashdan, 2009). Thus, tasks with an emphasis on social evaluation by a familiar source as opposed to unknown others revealed a heightened sensitivity to positive and negative social cues, in line with the SR hypothesis. This suggests that a threat to the social investment potential may be amplified in the presence of close other's, as opposed unfamiliar others.

At the neural level, recent evidence suggests heightened vulnerability to social signals in previously depressed women, with hyperactivity in dACC in response to repeated negative social evaluation (Dedovic, Slavich, Muscatell, Irwin, & Eisenberger, 2016), in line with the social pain account. However, emotional processing in depression is also associated with heightened amygdala response and attenuated dorsolateral prefrontal cortex (DLPFC) activation (Hamilton et al., 2012), alongside hyperconnectivity within the brain's default network associated with internally oriented and self-referential processing (R. H. Kaiser, Andrews-Hanna, Wager, & Pizzagalli, 2015). Further, findings have revealed large-scale network dysfunction in fronto-parietal and midline cortical structures involved in attentional control, emotion and salience processing (R. H. Kaiser et al., 2015). This is seemingly at odds with the notion of heightened sensitivity to external signals of social salience. These network dysfunctions may reflect the maladaptive tendency for ruminative self-focus in the context of social evaluation, centred around negative self-schema communicating feelings of worthlessness in relation to others (B. Bradley & Mathews, 1983; Swallow & Kuiper, 1988).

This negative self-schema within a depressed individual's cognitive framework acts to interpret events and may lead to distorted interpretations (Beck et al., 1979), such as negative appraisals of social signals. It might further account for previous findings of a negative response bias and reduced reward sensitivity described in more detail in the introduction (Chapter 1).

In sum, it can thus be argued that the experience of social rejection can be both the cause and the consequence of depression, with implications both at the behavioural and neural levels. However, the psychological and neural processing of social signals pertaining to inclusivity have received less attention within the literature in healthy controls. In the context of depression, this question deserves particular attention, given the dysfunctions in emotional and social processing at the behavioural and neural levels and suggestions of heightened rejection sensitivity in depression. This chapter draws on self-generated autobiographical memories as a repository for salient social experiences and emotions that can inform, establish or maintain our current social narrative and interpersonal relationships and consequently, our emotional state. Autobiographical memories are explicit personal experiences, which can powerfully re-elicit salient emotions experienced in the past in both healthy and depressed individuals using a script-driven imagery approach (Lanius et al., 2002). This would also address the notion of self-relevance and familiarity in the context of social evaluation, as autobiographical memories provide a platform for the elicitation of salient social emotions from highly self-relevant personal social narratives within distinct cultural and social contexts (Wilbers, Deuker, Fell, & Axmacher, 2012).

The aim of the present study is thus to investigate the differential processing of social rejection and social inclusion information at behavioural and neural levels, in individuals with a diagnosis of clinical depression and those who have never been depressed. This will be achieved by using the script-driven imagery paradigm to elicit salient social emotions in the present and to investigate the neural and behavioural response while listening to and imagining a series of previously self-generated autobiographical memories of social rejection, social inclusion and socially neutral experiences, as described in the previous chapter.

Our hypotheses were as follows;

HYPOTHESES

Behavioural Hypotheses

- Behavioural ratings of mood, vividness and intensity obtained in the memory presentation session will differ as a function of memory type, but not with respect to group, consistent with the findings in the memory generation session described in the previous chapter.

Neural Hypotheses

- We hypothesise that a common neural architecture exists for processing memories of social rejection and social inclusion (relative to neutral memories) within the previously described 'social pain' network, replicating previous findings in healthy controls (Dalgleish et al., 2017) and building on an emerging consensus (S. Cacioppo et al., 2013). This consists of affective areas including the dACC and AI, as well as the OFC, consistent with the meta-analytic evidence (S. Cacioppo et al., 2013; Rotge et al., 2015). We aimed to replicate findings experimentally inducing feelings of social rejection and to extend this to the experience of social inclusion.
- Individuals with depression will show heightened activation to cues of social rejection and social inclusion, relative to healthy controls within the same 'social pain' network (dACC, AI, OFC) described above, in line with the SR hypothesis and sociometer theory.

4.2 Methods and Materials

Participants

Eighteen participants experiencing a current Major Depressive Episode and meeting criteria for a diagnosis of Major Depressive Disorder (MDD; 13 female; 34.11±10.9 years) and 21 healthy controls who had never met criteria for MDD (10 female; 35.30±16.1 years) were recruited from volunteer panels at the MRC Cognition and Brain Sciences Unit and the University of Cambridge. All participants completed two research sessions, a behavioural memory generation session (described in Chapter 3) and a neuroimaging memory presentation session. All participants were right-handed, with no history of brain injury, normal or corrected-to-normal vision and no hearing impairments. MDD participants previously underwent a structural clinical interview to confirm their diagnosis and current episode. Full demographics can be found in the results section in Table 4.2. For further information on general methods and recruitment see also Chapter 2.

Clinical Interview and Social, Affective and Process Self-Report measures

A comprehensive diagnostic interview and battery of social, affective and process self-report measures was undertaken with respect to all participants. See Chapter 2 for a full description.

Experimental Task

Stimuli

In the initial behavioural memory-generation session, participants provided 18 autobiographical memories consisting of 6 social rejection memories, 6 social inclusion, memories and 6 emotionally neutral social memories (e.g. shopping in the presence of other people) and affective ratings with respect to current mood state at the time of memory recall and mood state at the time of the original experience. See Chapter 3 for memory generation methodology and data. The generated autobiographical memory scripts represented the stimuli for the following memory presentation session. Audio scripts of the autobiographical memories were recorded and edited using Adobe® Audition® (2009 Adobe Systems, version 3.0).

'Self' Memory Presentation (SEMP) Task

In the neuroimaging session, participants were presented with the memory audio-scripts generated within the initial memory-generation session. In the present 'self' memory presentation task, the autobiographical memory scripts were presented within fMRI utilising a block-design comprising two functional runs with three blocks of three memories per block, in each run. The blocks were presented in a fixed order – social neutral, social rejection, and finally, social inclusion to facilitate overall mood repair (Figure 4.1). This gives six memories of each type. During the three 30-second memory audio scripts within each of the three blocks, participants were instructed to close their eyes and listen carefully to the memory. After each audio script, there was a 20-second period of silence during which participants were asked to mentally elaborate on the emotionally salient aspects of the previous memory (Lanius et al., 2002). This 'silent imagery period' was the event of interest for our main analyses, in line with the previous script-driven imagery studies (Lanius et al., 2002).

A tone cue followed each silent imagery period to indicate to participants to open their eyes and provide baseline and post-script mood ratings. Participants rated their current mood prior to each block following a brief 30-second closed-eye baseline period and following each audio script. Participants rated levels of current subjective distress, rejection, inclusion and positivity on the same 11-point Likert scale as in the initial behavioural session. The positive and negative scores were combined for the analyses into composite mood scores (See Chapter 3). An additional 30-second washout clip depicting an ocean sunset was presented between the rejection and inclusion blocks to facilitate mood repair. The order of individual scripts within each block was randomised. The total approximate duration was 25 minutes per run.

Auditory presentation of the stimuli inside the scanner was delivered via Sensimetric's S14 headphones following the application of a custom equalization filter (© 2010 Sensimetric Corporation – www.sens.com, version 2.1) in combination with ear defenders to attenuate scanner noise. The headphones were connected via a desktop PC running Matlab (Mathworks) and presented using the psychophysics toolbox (Brainard, 1997; Pelli, 1997). Simultaneously, participants were asked to provide mood ratings on a Likert scale using a button box. Visual presentation was provided via a custom-built mirror stereoscope, with the participant's head

stabilised by a chin-and-head rest. The effective viewing distance was 50 cm with a resolution of 1024 x 768 and a visual angle of 16.7 degrees.

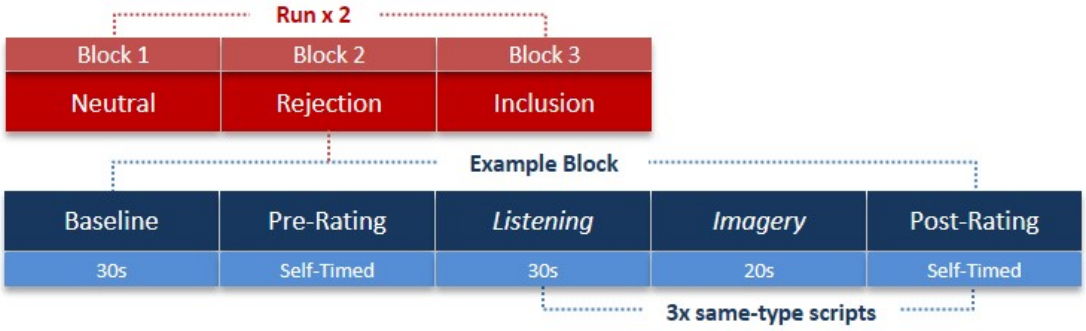


Figure 4.1. Script-driven imagery paradigm for 'Self' Memory Presentation (SEMP) task adapted for fMRI (Lanius et al., 2002).

PROCEDURE

The procedure for the memory generation session is described in Chapter 3. One week later, in this 1.5-hour memory presentation session, participants provided informed consent once more and then performed the fMRI memory presentation task within the scanner. A practice run outside of the scanner preceded the experimental block to familiarise participants with the procedure. In the scanner, participants were instructed to keep their eyes closed throughout the baseline, listening and silent imagery periods. Following the tone cue, participants were instructed to open their eyes to provide the affective ratings. Immediately after the fMRI session, participants provided post-scanning ratings of overall intensity and vividness for each memory category, followed by a battery of social, affective and process self-report measures (described in Chapter 2). At the end of the session participants were thanked for their time and debriefed.

fMRI Data Acquisition

A 3T Siemens Tim Trio MRI scanner with a 32-channel head coil was used to acquire a structural T1-weighted MPRAGE image (1-mm isotropic voxels) and functional data of ~600 whole-brain T2*-weighted EPI volumes with 32 oblique axial slices that were 3.5 mm thick, and an in-plane 64×64 matrix with resolution of 3×3 mm, TR 2 s, and TE 30 ms (two runs). FMRI data were pre-processed and analysed using MATLAB R2013a (Mathworks, Sherbon, Massachusetts) and SPM12 (Statistical Parametric Mapping Software, Wellcome Trust Centre for Imaging Neuroscience, London, United Kingdom; http://www.fil.ion.ucl.ac.uk/spm/software/spm12/). For details on fMRI preprocessing and analysis see below.

Statistical Analysis

Behavioural Ratings

Affective ratings acquired in the memory-generation session ('session I') at time of recall were compared to the ratings obtained during the memory presentation session ('session II') acquired within the scanner. See Appendix 4.2. In session II, the affective ratings acquired in the fMRI session were averaged for each memory type and change in affective ratings calculated. These affective ratings of current mood, as well as ratings of vividness and intensity were analysed in a series of univariate analyses of variance (ANOVAs) with group (MDD/controls) as a between-group factor and memory type (rejection/inclusion/neutral) as a within-group factor. Self-report measures of affective, process and social processing were analysed using Pearson and Spearman correlational analyses and independent samples t-tests.

fMRI Pre-processing and analysis

Raw Digital Imaging and Communication in Medicine (DICOM) images were converted to Neuroimaging Informatics Technology Initiative (NIFTI) format, realigned within and across both runs to correct for motion, and then each of the images was matched/resliced to the first image of the time series and a mean of these aligned images was generated. The mean BOLD image was co-registered with the T1 image, segmented and spatially normalised to Montreal Neurological Institute (MNI) template space. The resulting warps were applied to all volumes,

with a 3mm isotropic voxel interpolation, followed by a 3D 8mm isotropic Gaussian kernel smoothing. For fMRI statistical analysis we ran a two-level RFX analysis using SPM12. At the first level, a linear convolution general linear model (GLM) was applied to the time series within each voxel across both runs. For each run, the blood oxygen-level dependent (BOLD) response was modelled by convolving a canonical haemodynamic response function (HRF) to each memory type (neutral, rejection, inclusion) during listening, silent imagery, closed-eye baseline, baseline ratings, post-script ratings, washout movie clip, and text instructions. At the second level, these contrasts were then entered into independent-samples t-tests and a full factorial ANOVA with group (2 levels: controls, MDD) and memory type (3 levels: neutral, rejection, inclusion) as the conditions of interest with separate sets of regressors generated per run for the separately modelled listening and silent imagery periods respectively, as well as six additional regressors generated per run to account for rigid-body movement (realignment parameters). Contrasts of these parameters were generated for negative rejection and positive inclusion memories relative to neutral social memories, as well as contrasts of negative rejection relative to positive inclusion memories for each participant during the listening and silent imagery periods. These silent imagery contrasts were taken to the second level for group level analysis. All whole-brain results were thresholded at $p<0.001$ uncorrected ($k=20$). It is important to note that this level of thresholding reduces the power to detect subtle differences of interest when correcting for multiple comparisons (Han et al., 2017). However, at this exploratory stage of the field, the statistical approach is in line with the previous literature (c.f. Eisenberger & Lieberman, 2003) and is further strengthened by the region of interest analysis described below. Nonetheless, it is important to consider the increased likelihood for Type I error when interpreting neuroimaging findings.

Region of Interest Analyses

For region of interest (ROI) analyses, peak voxel coordinates were obtained from a meta-analysis examining the virtual ball-tossing game Cyberball and Romantic Rejection paradigms (S. Cacioppo et al., 2013), as described in the introduction and Chapter 1. In addition, further independent ROIs were obtained from a meta-analysis more closely examining the contribution of the ACC to social pain (Rotge et al., 2015), also described in the introduction. These functionally independent ROIs were defined by 10mm spheres centred on the respective peak

voxels. Anatomically overlapping ROIs were combined into conglomerate ROIs. ROI extraction was carried out using the MARsBaR toolbox within SPM (MARSeille Boîte À Région d'Intérêt; Brett et al., 2002). MARsBaR treats all voxel values within the region as repeat samples of the identical signal and calculates a single summary value to represent all the voxels in the ROI, resulting in a single ROI summary value per image on which the statistical model is run, extracting the signal using a finite impulse response (FIR) deconvolution. The contrast value represents the effect size. The uncorrected p is the one-tailed p value for the t statistic given the degrees of freedom for the analysis. The corrected p is the uncorrected p value with a Bonferroni correction for the number of ROIs analysed. MARsBaR does not correct the p value for the number of contrasts as the contrasts may not be orthogonal and this will make a Bonferroni correction too conservative. However, as the activity in the given ROI is assumed to be relatively homogenous, MARsBaR is the preferred analysis compared to small volume correction, which assumes potentially different responses in different part of the defined ROIs. See Table 4.1 for an overview of the ROIs examined here.

Table 4.1

Peak coordinates for region of interest (ROI) analyses derived from meta-analyses on social pain

Meta-Analysis	Description	x	y	z	Labels
Cacioppo et al. 2013	Rejection by a stranger during Cyberball paradigms	38	18	-6	Right Anterior Insula*[1]
		38	18	-6	Right Anterior Insula *[1]
		34	14	-6	Right Anterior Insula *[1]
		-36	20	-10	Left Anterior Insula *[4]
		-2	52	10	Left ACC
		-32	16	-20	Left Inferior Orbito-Frontal Cortex
		0	48	38	Superior Medial Frontal region
Cacioppo et al. 2013	Feelings of rejection by a significant other	10	40	16	Right ACC*[2]
		10	38	12	Right ACC*[2]
		10	40	18	Right ACC*[2]
		12	12	-2	Right Caudate Nucleus*[3]
		18	20	6	Right Caudate Nucleus*[3]
		-42	30	10	Left Inferior Frontal Lobe
		-34	32	-12	Left Inferior Orbito-Frontal Cortex*[4]
		32	26	8	Right Anterior Insula
Rotge et al. 2015	dACC social pain	4	36	-4	Dorsal ACC 25/32
		8	24	24	Dorsal ACC 24/32

Note: * and superscript numbers indicate combined (anatomically overlapping) ROIs in final MARsBaR analysis.

4.3 RESULTS

DEMOGRAPHIC CHARACTERISTICS

Table 4.2 shows the demographic characteristics of healthy controls and MDD participants. Appendix 4.1 presents the descriptives and group comparison of social, affective and process measures for the current sample. All measures revealed significant group differences between MDD and healthy controls, except for the Spontaneous Use of Imagery Scale (p=0.12). Our groups were well matched in age (t(37)=0.51, p=0.61), reading ability (NART (t(37)=.21, p=0.83), and in other characteristics (see Table 4.2).

Table 4.2

Demographic Characteristics for Chapter 4. Numbers are ns unless otherwise stated.

	Controls n=21	MDD n=18	Total N=39	X^2	p
Sex					
Male	11	5	16	2.43	0.12
Female	10	13	23		
Age, years					
Mean	35.05	34.11	34.62		
SD	15.68	10.92	13.53		
National Adult Reading Test					
Mean	8.71	7.78	8.28		
SD	5.90	5.48	5.66		
Ethnicity					
Caucasian	20	16	36	1.4*	0.72
Other	1	2	3		
Marital Status					
Single/Unmarried	17	8	25	6.29*	0.05
Married	2	7	9		
Separated/Divorced	1	2	3		
Other	1	1	2		
Education					
Completed HSC/Yr 12	9	8	17	4.37*	0.57
Other	2	0	2		
Employment Status					
Employed	17	13	30	1.75*	0.43
Unemployed	4	5	9		
Employment					
Full-Time	12	12	24	2.45*	0.89
Part-Time	5	3	8		
Other	4	3	7		

Note: * indicates Fisher's Exact Test

BEHAVIOURAL RATINGS

Memory Generation (Session I)

In the first step, we investigated whether the memories recalled in the memory-generation session had maintained their saliency over time since the original event considering both group and memory type. These results are presented in Chapter 3. Results suggested both groups maintained comparable emotional saliency of the recalled memories over time. Then, session I and session II were compared in a further manipulation check to ensure comparable saliency across sessions. See Appendix 4.2 for results. The generated memories were deemed appropriate for use in the neuroimaging memory presentation session.

'Self' Memory Presentation Task (Session II)

To investigate the response to the emotional memories within the neuroimaging session, we compared the change in affect during the memory presentation session immediately before and after each memory was presented (see Table 4.3), as well as vividness and intensity ratings (see Appendix 4.9). Affective change ratings were analysed using a series of univariate ANOVAs with group (MDD/controls) as a between-group factor and memory type (rejection/inclusion/neutral) as the within-group factor. Normality and homogeneity assumptions were met. Within-subject factor memory type violated Mauchly's test of sphericity (x^2=13.26, p=0.001) and will be reported using a Greenhouse-Geisser correction.

Affective ratings are presented as a function of memory type and group in Table 4.4. Results revealed a significant main effect for memory type (F[1.51,52.91]=188.91, p<0.001, η_p^2=0.84). Planned comparisons of the main effect of memory type corrected using a Bonferroni adjustment, indicated significant differences in mood ratings between memory types (all p<0.001). Mood was significantly more negative for rejection memories relative neutral (-8.11±0.59) and inclusion memories (-12.63±0.82), while inclusion memories were rated as highest in positive mood relative to neutral (4.52±0.52). Overall, mood across groups was significantly decreased following rejection memories compared to relatively unchanged mood following neutral and significantly increased mood following inclusion memories (see Table 4.3). This is further illustrated in Figure 4.2. There was no main effect for group (F[1,35]=0.155, p=0.70, η_p^2= 0.004). The same pattern of results emerged when run was

included as a variable in the analysis, suggesting an absence of practice effects across runs. This was therefore not reported in the final analysis. There was no significant interaction between memory type and group ($F[2,70]= 0.46$, $p=0.63$, $\eta_p^2 = 0.01$), suggesting change in mood solely differed as a function of memory type and not group, in line with our expectations based on the comparability of memories across groups in the initial memory generation session (see Table 4.4).

Vividness ratings obtained in the neuroimaging session between groups and across memories revealed a main effect for memory type ($F[2,58]= 52.52$, $p<0.001$, $\eta_p^2=0.64$). Planned comparisons revealed a significant difference ($p<0.001$) between neutral memories and both rejection (-1.54±0.20) and inclusion memories (-1.86±0.21), while rejection and inclusion memories were not significantly different from each other (0.32±0.17, $p=0.214$). There was no significant main effect for group ($F[1,29]= 0.42$, $p=0.52$, $\eta_p^2=0.01$) nor an interaction between memory type and group ($F[2,58]=0.25$, $p=0.78$, $\eta_p^2=0.01$). See Appendix 4.9.

Intensity ratings revealed that Mauchly's assumption of sphericity had been violated, $x^2(9.49)$, $p<0.009$), therefore results will be reported using a Greenhouse-Geisser correction. The results show that there was a main effect for memory type ($F[1.55,45.05]=72.89$, $p<0.001$, $\eta_p^2=0.72$), but no main effect for group ($F[1,29]=1.84$, $p=0.19$, $\eta_p^2=0.06$) and no significant interaction ($F[1.55,45.05]=0.45$, $p=0.59$, $\eta_p^2=0.02$). Planned comparisons revealed a significant difference ($p<0.001$) between neutral memories and both rejection (-.437±0.38) and inclusion memories (-4.06±0.50), while rejection and inclusion memories were not significantly different from each other (-0.31±0.31, $p=1.000$). This suggests comparable vividness for valenced memories compared to neutral memories across groups. See Appendix 4.9.

Table 4.3

Mean mood ratings by memory type (Chapter 4)

			95% Confidence Interval	
Memory Type	Mean	Std. Error	Lower Bound	Upper Bound
Neutral	-7.55	0.63	-8.82	-6.28
Rejection	0.56	0.24	0.06	1.05
Inclusion	5.08	0.47	4.13	6.03

NB: Lower scores represent more negative mood with a range of -10 to +10 (most positive)

Table 4.4

Interaction between group and memory type (Chapter 4)

	Memory		Std.	95% Confidence Interval	
Group	Type	Mean	Error	Lower Bound	Upper Bound
MDD	Neutral	.78	.35	.07	1.50
	Rejection	-7.20	.90	-9.02	-5.38
	Inclusion	4.83	.67	3.47	6.19
Controls	Neutral	.33	.34	-.37	1.02
	Rejection	-7.90	.87	-9.68	-6.13
	Inclusion	5.32	.65	4.00	6.65

NB: Lower scores represent more negative mood with a range of -10 to +10 (most positive)

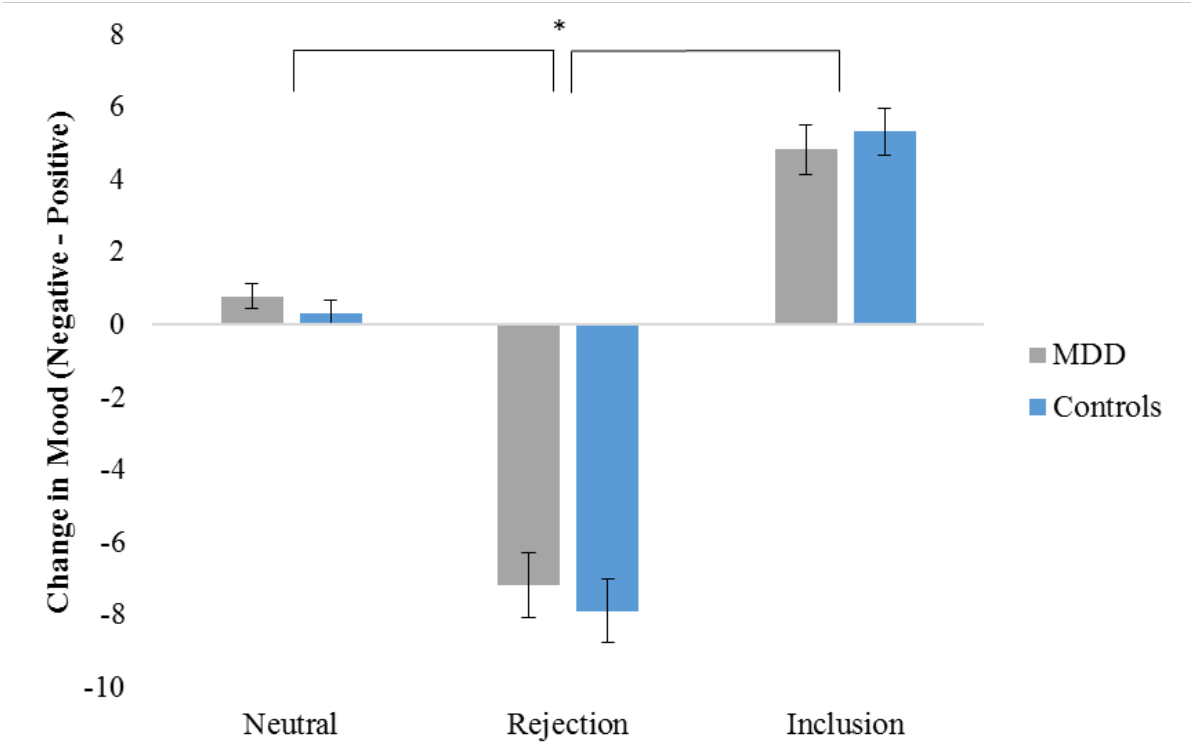


Figure 4.2. Mean change ± 1SE in mean positive and negative mood in response to autobiographical memories from the fMRI session. Results showed significant mood deterioration and mood enhancement following social rejection and social inclusion memories, respectively with mood remaining unchanged following neutral memories. There were no significant group differences in mean change in mood.

fMRI Results

Region of Interest Analyses

The first analysis was designed to look at differential patterns of activation across all participants and within groups in response to silent imagery of rejection relative to neutral and inclusion relative to neutral memories across a group of selected ROIs. The two main contrasts of interest of rejection relative to neutral and inclusion relative to neutral were derived from previous studies investigating 'social pain' (S. Cacioppo et al., 2013; Eisenberger, 2012b; Eisenberger & Lieberman, 2003; Rotge et al., 2015). The ROIs were derived from meta-analyses investigating the neural basis of social pain and are presented in Table 4.3.

One-sample t-test results are presented in Table 4.5. It is important to note that one MDD and three healthy participants were excluded from the final ROI and whole-brain fMRI data analyses due to acquisition difficulties. Analysis of all remaining participants revealed activation in dACC during inclusion versus neutral and inclusion and rejection versus neutral, but not for rejection versus neutral or rejection versus inclusion and vice versa. Next, we investigated the pattern of activation within each group separately. One-sample t-tests in MDD participants suggest the results from all participants might be driven by MDD participants, who revealed greater activation in dACC and right caudate nucleus during rejection relative to neutral memories and significant activity in dACC, inferior orbito-frontal and left AI during inclusion relative to neutral memories. as well as in the bilateral AI and left inferior orbital frontal cortex during rejection *and* inclusion relative to neutral for MDD. For control participants, one-sample t-tests did not reveal significant activity within the selected ROIs.

We then sought to explore between-group differences at the second level with independent sample t-tests between MDD and controls (see Table 4.5). Results revealed greater bilateral AI and dACC activation in MDD compared to controls for inclusion relative to neutral and inclusion and rejection relative to neutral, as well as dACC activation only in rejection relative to neutral again heightened in MDD relative to controls. A full factorial with group (MDD/controls) and memory type (neutral, rejection, inclusion) is presented in Appendix 4.13. Across all levels of analysis there were no significant activations across ROIs for inclusion compared to rejection and rejection compared to inclusion and no significant interactions.

Table 4.5

Region of interest analysis for one sample T-tests of silent imagery of autobiographical memories of rejection and inclusion

	MNI Coordinates			Rejection > Neutral			Inclusion > Neutral			Rejection & Inclusion > Neutral		
Region of Interest	x	y	z	Controls	MDD	All	Controls	MDD	All	Controls	MDD	All
Right Anterior Insula	38	18	-6	1.00	0.11	0.72	1.00	0.08	0.88	1.00	0.08	0.75
Left ACC	-2	52	10	1.00	0.05	0.20	0.30	0.05*	0.01*	0.81	0.03*	0.02*
Left Inferior Orbito-Frontal Cortex	-32	16	-20	1.00	0.41	0.90	1.00	0.03*	0.23	1.00	0.04*	0.43
Left Anterior Insula	-36	20	-10	1.00	0.24	0.90	1.00	0.22	0.99	1.00	0.19	0.95
Superior Medial Frontal Gyrus	0	48	38	1.00	0.43	0.81	0.99	0.30	0.41	1.00	0.23	0.53
Right ACC	10	40	16	1.00	0.05	0.47	1.00	0.32	0.53	1.00	0.08	0.37
Right Caudate Nucleus	12	12	-2	1.00	0.05*	0.33	1.00	0.16	0.85	1.00	0.05	0.51
Left Inferior Frontal Lobe (Trigerminalis)	-42	30	10	0.86	0.15	0.13	0.99	0.72	0.71	0.94	0.31	0.26
Right Anterior Insula	32	26	8	1.00	0.09	0.84	1.00	0.06	0.99	1.00	0.04*	0.90
Left Anterior Insula	-34	32	-12	1.00	0.31	0.90	1.00	0.04*	0.67	1.00	0.08	0.75
dACC 25/32	4	36	-4	0.86	0.00*	0.08	0.34	0.02*	0.01*	0.67	0.00*	0.02*
dACC 24/32	8	24	24	0.80	0.02*	0.08	0.86	0.00*	0.03*	0.84	0.01*	0.03*

*denotes p-values significant at $p<0.05$

Table 4.5 cont'd.

	Coordinates			Rejection > Inclusion			Inclusion > Rejection		
Region of Interest	x	y	z	Controls	MDD	All	Controls	MDD	All
Right Anterior Insula	38	18	-6	0.98	1.00	0.97	1.00	1.00	1.00
Left ACC	-2	52	10	1.00	1.00	1.00	0.48	1.00	0.82
Left Inferior Orbito-Frontal Cortex	-32	16	-20	1.00	1.00	1.00	0.99	0.95	0.91
Left Anterior Insula	-36	20	-10	0.91	1.00	0.97	1.00	1.00	1.00
Superior Medial Frontal Gyrus	0	48	38	1.00	1.00	1.00	0.99	0.99	0.98
Right ACC	10	40	16	1.00	0.97	1.00	0.99	1.00	1.00
Right Caudate Nucleus	12	12	-2	0.98	0.97	0.90	1.00	1.00	1.00
Left Inferior Frontal Lobe (Trigerminalis)	-42	30	10	0.90	0.98	0.84	1.00	1.00	1.00
Right Anterior Insula	32	26	8	0.86	1.00	0.97	1.00	1.00	1.00
Left Anterior Insula	-34	32	-12	1.00	1.00	1.00	1.00	0.97	1.00
dACC 25/32	4	36	-4	1.00	0.96	1.00	0.86	1.00	1.00
dACC 24/32	8	24	24	1.00	1.00	1.00	1.00	0.50	0.92

*denotes p-values significant at $p<0.05$

Table 4.6

Regions of interest for two-sample T-tests during silent imagery of autobiographical memories of rejection and inclusion

	MNI Coordinates			Rejection > Neutral		Inclusion > Neutral		Rejection & Inclusion > Neutral		Rejection > Inclusion		Inclusion > Rejection	
Region of Interest	x	y	z	Controls > MDD	MDD > Controls	Controls > MDD	MDD > Controls	Controls > MDD	MDD > Controls	Controls > MDD	MDD > Controls	Controls > MDD	MDD > Controls
Right AI	38	18	-6	1.00	0.19	1.00	0.02*	1.00	0.04*	0.99	1.00	1.00	1.00
Left ACC	-2	52	10	1.00	0.15	1.00	0.69	1.00	0.23	1.00	0.81	0.81	1.00
Left Inferior OFL	-32	16	-20	1.00	0.30	1.00	0.04*	1.00	0.04*	0.99	1.00	1.00	0.99
Left AI	-36	20	-10	1.00	0.21	1.00	0.02*	1.00	0.04*	0.94	1.00	1.00	0.97
Superior MFG	0	48	38	1.00	0.77	1.00	0.77	1.00	0.69	1.00	1.00	1.00	1.00
Right ACC	10	40	16	1.00	0.12	1.00	0.46	1.00	0.15	1.00	0.93	0.95	1.00
Right Caudate Nucleus	12	12	-2	1.00	0.15	1.00	0.18	1.00	0.09	1.00	1.00	1.00	1.00
Left IFG	-42	30	10	1.00	0.88	1.00	0.84	1.00	0.81	1.00	1.00	1.00	1.00
Right AI	32	26	8	1.00	0.10	1.00	0.00*	1.00	0.01*	0.92	1.00	1.00	0.96
Left AI	-34	32	-12	1.00	0.24	1.00	0.01*	1.00	0.03*	0.95	1.00	1.00	0.97
dACC 25/32	4	36	-4	1.00	0.02*	1.00	0.11	1.00	0.02*	1.00	0.74	0.78	1.00
dACC 24/32	8	24	24	1.00	0.05*	1.00	0.00*	1.00	0.01*	0.72	1.00	1.00	0.81

*denotes p-values significant at $p<0.05$

Whole-Brain Analyses

In addition to ROI analyses derived from specific social pain paradigms (S. Cacioppo et al., 2013; Eisenberger, 2012b; Eisenberger & Lieberman, 2003; Rotge et al., 2015), we further explored the underlying signal using a whole-brain analysis, given our novel social script imagery paradigm. At the first level within one-sample t-tests, we explored the neural pattern of activation in response to silent imagery of rejection compared to neutral and inclusion compared to neutral memories within each group individually. This is pertinent, given the focus of the literature to date on investigating the neural response to social pain in healthy controls only.

Thus, one-sample t-tests in healthy controls in Appendix 4.10 revealed activity in bilateral post central gyrus ($p<0.001$ uncorrected) during silent imagery of rejection relative to neutral memories. Inclusion memories compared to neutral memories revealed bilateral post central gyrus activity. There were no significant differences for rejection relative to inclusion memories during silent imagery in healthy controls. One-sample t-tests in MDD participants in Appendix 4.11 revealed activations in right amygdala, anterior hippocampus, subgenual PFC, bilateral insula, inferior frontal gyrus (IFG) and ventral striatum (VS) for rejection versus neutral memories during silent imagery. During inclusion compared to neutral silent imagery, we found the same areas as above, except for VS and subgenual PFC. There were no significant activations for rejection relative to inclusion memories during silent imagery.

In line with our ROI analysis, we next sought to explore between-group differences in response to silent imagery of memories in two-sample t-tests. See Appendix 4.12 and Figure 4.3. MDD participants compared to controls showed increased activation in the subgenual PFC, bilateral insula, dACC and inferior frontal lobe for rejection relative to neutral memories. During inclusion, relative to neutral memories MDD participants, relative to controls, showed increased activation in the dACC (2,26,42, $z=3.44$) and bilateral insula. There was no significant difference between groups for social inclusion relative to rejection or vice versa.

Finally, we explored silent imagery more closely with a conjunction analysis of rejection versus neutral imagery and inclusion versus neutral imagery within and across both groups, inclusively masked by a functionally defined pain meta-analytic map derived from neurosynth (Yarkoni, Poldrack, Nichols, Van Essen, & Wager, 2011). This map was used to highlight the heightened sensitivity to pain and to more closely investigate the relationship between physical pain and social pain initially reported in the mainstream literature (Eisenberger et al., 2006; Eisenberger & Lieberman, 2003; Kross et al., 2011; Woo et al., 2014). Conjunction results thresholded at $p<0.05$, uncorrected, for all participants revealed bilateral postcentral gyrus activation (-48,-22,28, z=3.59 & 48,-22,38, z=3.47). For healthy controls only, results showed bilateral activation in postcentral gyrus (-52,-22,28, z=4.22, & 48,-24,30, z=3.87), while for MDD participants, rejection versus neutral and inclusion versus neutral revealed significant activation within left AI (-34,0,8, z=3.17), bilateral thalamus (18, -6, 10, z=2.48 & -14, -12, -4, z=2.32), bilateral putamen (30,4,8, z=3.25 & 20,6,-2, z=1.91), and anterior cingulate gyrus (0, 32, 24, z=2.27). Finally, to investigate the hypothesis that the common neural substrate for inclusion and rejection processing is heightened within MDD, we explored the conjunction of rejection versus neutral and inclusion versus neutral in MDD relative to controls. This revealed greater activity in bilateral AI (28,16,-14, z=2.31 & -34,12,-12, z=2.17), dACC (2,34,22, z=1.93), right IFG (36,34,-4, z=2.49) and middle frontal gyrus/postcentral gyrus (54,12,42, z=2.44).

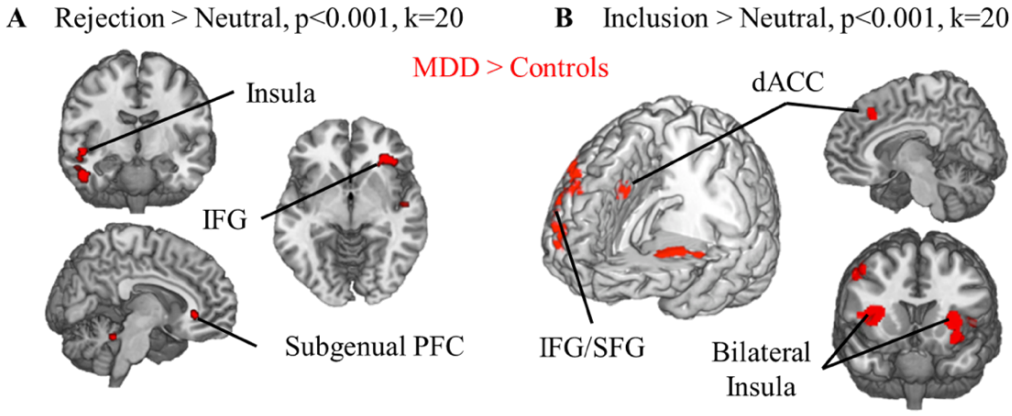


Figure 4.3. **Two-sample whole-brain fMRI analysis results.** (**A**) Silent imagery of rejection>neutral memories and (**B**) inclusion>neutral memories for MDD compared to controls revealed significant activations in bilateral insula, IFG, subgenual PFC and dACC, uncorrected at p<0.001, k=20.

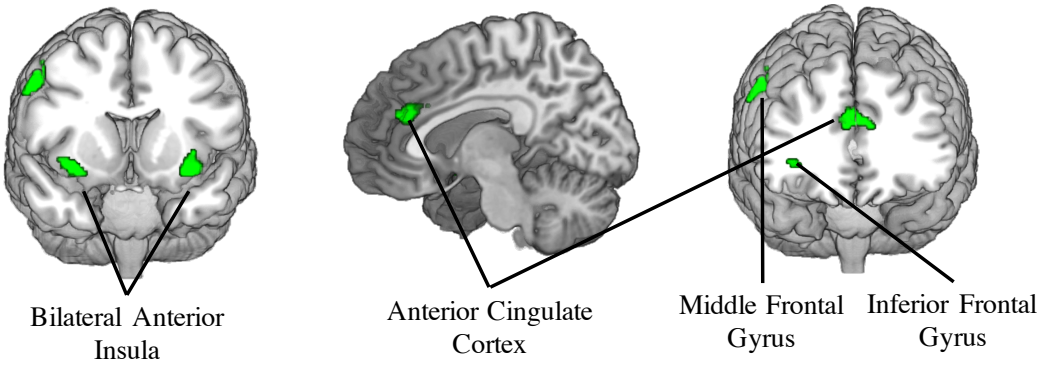


Figure 4.4. **Conjunction analysis results.** A logical 'AND' conjunction analysis of inclusion and rejection (relative to neutral memories) and MDD relative to controls revealed bilateral AI, dACC, MFG and IFG activation. All conjunction analyses were inclusively masked by a FDR thresholded neurosynth pain mask, uncorrected at p<0.01, k=20 (Yarkoni et al., 2011).

4.4 Discussion

This chapter reports a study involving the recall of emotionally salient autobiographical memories of social rejection and social inclusion compared to neutral social memories in depressed participants and healthy controls. Results revealed a common neural substrate for both social inclusion and social rejection (relative to neutral) in affective regions previously associated with social rejection in healthy controls only, in line with our predictions. These results point towards a shared neural architecture for processing social rejection and social inclusion experiences (relative to neutral) in line with recent findings (Dalgleish et al., 2017). In addition, as predicted, this shared pattern of activation in the traditional 'social pain' network, including the dACC and AI, was heightened in depressed individuals relative to healthy controls.

These findings challenge previous suggestions that the dACC-AI social pain network exclusively responds to the psychological experience of social pain, as posited in previous Cyberball paradigms (Eisenberger & Lieberman, 2003). Central to this social pain account is our fundamental need to belong (Baumeister & Leary, 1995), supported by empirical evidence that individuals high in interpersonal rejection sensitivity tend to modify their interpersonal behaviour to avoid social exclusion and maintain social acceptance (Slavich & Irwin, 2014b). As discussed in the main introduction (Chapter 1.6), the sociometer theory provides a compelling explanatory framework reconciling both behavioural and neuroimaging findings investigating the processing of socially relevant information (Baumeister & Leary, 1995; Eisenberger et al., 2011). However, in the social pain account, the sociometer was re-conceptualised as a ‘neural alarm’ system, in which the ‘social pain’ network of activation selectively responds to socially salient cues alerting us to the perceived or actual threat of social exclusion (Eisenberger, 2012a, 2015; Eisenberger et al., 2011).

However, in the context of our findings, we suggest that the 'social pain' network of activation responds more generally to both inclusive and exclusive socially salient cues as a gauge of interpersonal relationships. In other words, a neural sociometer

that continuously monitors and evaluates incoming social information and alerts us to potential changes to our social status. The processing of both positive and negative social signals thus serve to inform and maintain our interpersonal relationships and social standing, as measured by moment to moment fluctuations in our self-esteem (Baumeister & Leary, 1995).

In the social risk hypothesis of depressed mood (Allen & Badcock, 2003), this is further illustrated in the trade-off between social value and social burden estimation, which determines an individual's social investment potential (SIP). Monitoring social cues of both negative and positive information is critical to restoring optimal SIP. This suggests that depressed individuals may exhibit a heightened neural sensitivity to social cues of rejection, or inclusion, relative to healthy controls, alongside attentional and behavioural attunements, described in Chapter 2. Our findings thus extend the existing social pain account, reflected in increased motivation to enhance and maintain social connectedness. They also contribute to the emerging neuroimaging literature pointing towards a common neural substrate for social pain and social gain, underscoring the notion of a more complex representation of social signals in the social pain network (S. Cacioppo et al., 2013; Dalgleish et al., 2017; Eisenberger et al., 2011; Leknes & Tracey, 2008; Woo et al., 2014). This is further complemented by a recent study by Dalgleish et al. (2017), where a novel social evaluation task revealed common activations in the insula and dACC derived from a conjunction analysis of positive versus neutral and negative versus neutral social feedback.

However, the literature on neural and behavioural responses to affective cues of social acceptance remains divided. One line of evidence suggests that greater depressive symptoms are associated with decreased affect in response to positive cues (Feeser et al., 2013). Other findings indicate that social cues and memories involving social acceptance elicit greater positive affect in depressed individuals (Bylsma et al., 2008). This suggests that depressive symptoms may increase sensitivity to experiences of social acceptance (DeWall & Bushman, 2011; DeWall et al., 2009; Steger &

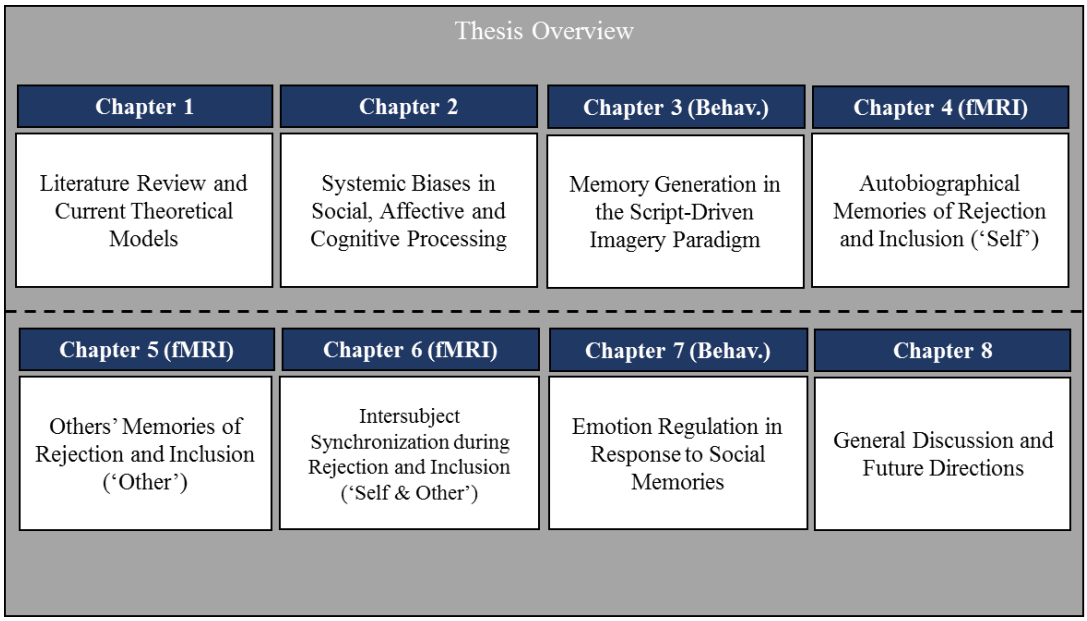
Kashdan, 2009). However, a recent study in a depressed community sample results suggested a dampened affective response to social acceptance using a social evaluation "Chatroom" task (Caouette & Guyer, 2015); modulated by the source of the evaluation (Steger & Kashdan, 2009). This suggested that tasks with an emphasis on social evaluation by a familiar source as opposed to unknown others revealed a heightened sensitivity to positive and negative social cues, in line with our results. In using autobiographical memories to elicit salient social emotions, our design thus employed a highly self-relevant task with sources of rejection stemming from familiar others or at the very least from rehearsed and thereby familiar experiences. This suggests a potential role for familiarity in social processing in depression, which will be further explored in the next chapter. The recollection of these emotionally salient autobiographical memories further provided an ecologically valid measure of social experiences and provided insight into the underlying neural processing of social signals in depressed compared to healthy individuals.

Challenges to this approach include the difficulty in clearly delineating socially inclusive from socially neutral interactions. This limitation extends to previous paradigms, including investigating social rejection in the 'Cyberball' paradigm (Eisenberger & Lieberman, 2003), in which the social inclusion condition may be better conceptualized as a default 'neutral' condition (Somerville et al., 2006). However, as our memories elicited comparably salient emotions, as previously validated in Chapter 3, this argument may not apply in our script-driven imagery paradigm. Firstly, and importantly, despite baseline differences in memory retrieval in depression, we found no difference in the use of spontaneous imagery between groups. This may have accounted for baseline differences in silent imagery and hence brain activation. In addition, comparable changes in affect following each memory lend weight to the notion that both groups were comparably able to imagine salient emotional experiences and that differences in brain activation are not due to difference in imagery or affect. Although accounts of salience cannot be fully discounted, given the prior memory interview, all memories were recalled in depth and rehearsed and therefore comparably salient when presented back to participants

in the scanner in the fixed order as before. Therefore, future study designs should incorporate both social and non-social positive and negative conditions to fully account for sociality as opposed to saliency as the core process driving these common activations. This presents a limitation to the current study, as well as other Cyberball paradigms described previously. Further discussion of the limitations within the current literature are outlined in Chapter 1.

In sum, it remains to be explored whether the current literature has fully addressed the neural and affective response to events explicitly signalling social inclusion, warranting further investigation into existing accounts of social pain processing. However, our conjunction analysis revealed additional affective and physical regions within the traditional social pain network activated by social rejection and inclusion memories. This study further extends existing findings by revealing a heightened response in MDD, thus representing the first of its kind to explicitly address the social pain debate in the context of depression. However, the 'social pain' network may represent a misnomer within the literature and instead represent a more sophisticated index of social processing. Given our findings we firstly argue that the so-called social pain matrix may share common representations at the gross anatomical level with social inclusion. As a result, in our understanding, the social pain network would be more accurately conceptualized as a dedicated social processing network tasked with monitoring and evaluating socially relevant signals in our environment, reflecting the more complex framework being brought forward by emerging research findings (S. Cacioppo et al., 2013; Leknes & Tracey, 2008; Rotge et al., 2015; Woo et al., 2014). Secondly, our findings shed light on the heightened neural response and hypersensitivity to social signals in depression in the absence of behavioural differences in affective responses from controls, which carry important implications for the observed downstream cognitive biases underlying the development and maintenance of depressive symptoms. However, social proximity and self-relevance may have mediating effects on the findings discussed above and warrant further investigation.

CHAPTER 5. PSYCHOLOGICAL AND NEURAL PROCESSING OF OTHERS' MEMORIES OF SOCIAL REJECTION AND INCLUSION



5.1 Introduction

The previous chapter investigated the neural and behavioural responses to listening and imagining emotionally salient personal experiences from the past in currently depressed and healthy control individuals. Recalling autobiographical memories of social rejection and inclusion compared to neutral social memories activated a common neural substrate including affective regions previously uniquely associated with the dACC-AI 'social pain network' (Eisenberger and Lieberman, 2003; Eisenberger, 2015). Further, conjunction analyses of rejection compared to neutral AND inclusion compared to neutral memories revealed a heightened response within the same dACC-AI network in depressed participants compared to healthy controls. This points towards a heightened neural sensitivity towards socially salient information in depression rather than selective neural sensitivity towards negatively valenced social information, as previously assumed. These findings integrate well into recent evidence suggesting a common neural substrate for complex representations of both positive and negative social signals (S. Cacioppo et al., 2013; Dalgleish et al., 2017).

However, important questions remain concerning the personal relevance of a given social context in activating these neural circuits (Steger & Kashdan, 2009). We know that self-referential information is processed differently from other-relevant information in healthy controls and depressed alike (Wisco, 2009). This gives rise to questions regarding the psychological and neural bases of how we process other-relevant social experiences. In healthy controls, the presentation of self-relevant stimuli is associated with better memory recall, greater speed of processing and greater attentional shifts in autobiographical memory specificity (Symons & Johnson, 1997; J. M. G. Williams et al., 2007; N. Wood & Cowan, 1995). This has been conceptualised as the 'self-reference effect' (Klein, 2012). However, heightened self-focused attention can give way to negative self-referential thinking and rumination. Thus, in depression, negative self-coherence is maintained over more adaptive

thinking styles (M. A. Conway & Pleydell-Pearce, 2000), suggesting a detrimental impact of heightened self-referential thinking in depression.

At a neural level, neuroimaging evidence suggests that self-referential processing, including self-evaluation of traits, beliefs and preferences, is associated with increased activity in the prefrontal cortex (PFC), and the medial PFC (Frewen et al., n.d.; Kelley et al., 1989; Schmitz et al., 2004; D'Argembeau, 2013; Kim and Johnson, 2013). In depression, heightened attention to self-referential information revealed conflicting results, with both increased and decreased mPFC activation, compared to healthy controls (Lemogne et al., 2012). Further, a study investigating resting-state activity, argued to reflect self-referential processing, suggested greater activity in ventromedial PFC, ventral striatum, and thalamus with reduced activity in postcentral gyrus, fusiform gyrus, and insula in depression compared to controls, suggestive of resource allocation away from externally-oriented cognitive processes (Kühn & Gallinat, 2013).

These findings warrant a deeper understanding of the atypical neural representation of self- versus other-relevant information in the context of social functioning in depression. To date, limited research has addressed empathy for others' social experiences of rejection and inclusion in healthy controls, with existing studies revealing conflicting results (Eisenberger, 2015; Masten, Morelli, & Eisenberger, 2011b; Nordgren et al., 2011). On the one hand, observing others' social pain of exclusion was associated with increased activation in areas associated with self-referential processing, including the dorsomedial, medial PFC and precuneus (Masten et al., 2011a). On the other hand, empathy for social pain was argued to activate sensory-discriminative areas, including posterior insula cortex and secondary somatosensory cortex (S2) (Lamm et al., 2011). Finally, the subgenual cingulate cortex was recruited during empathic processing of both physical and social pain (Novembre et al., 2013), contrasting with earlier evidence suggesting affective but not sensory activation in response to others' experience of physical pain (Singer et al., 2004).

Moreover, neural networks appear to respond differentially as a function of social proximity and interdependence. Affective areas, including the dACC and insula were recruited during the observation of social exclusion of close others (Beeney et al., 2011; Meyer et al., 2013, 2014). In contrast, observing less proximal social targets', i.e. strangers', social pain of exclusion, was associated with greater activity in the dorso-medial prefrontal cortex (DMPFC), precuneus, and temporal pole, mirroring previous findings (Masten et al., 2011b). In addition, a study investigating the relevance of social hierarchy modulated by incidental performance on a visuo-spatial task revealed that a superior social rank motivated empathy towards inferior social targets' painful stimulation similarly activating the AI and anterior middle cingulate cortex (aMCC). In contrast, this pattern of activity was markedly attenuated when observing painful stimulations to superior ranked social targets (Feng et al., 2016). Thus, differential activation during empathic processing may be modulated by situational and individual factors.

However, these findings are based almost exclusively on healthy control populations and the important question of how depressed individuals will engage in other-relevant social processing involving inclusion and exclusion remains to be examined. As described in Chapter 2, depressed individuals exhibit greater self-perceptions of inferiority, submissiveness and involuntary subordination (Allan & Gilbert, 1997; Sturman, 2011). This might suggest similar neural responses in depression in response to others' social pain as those seen in healthy controls when viewing superior ranked social targets' pain (Feng et al., 2016). As discussed in the introduction in Chapter 1, depression is associated with heightened levels of empathetic stress, but reduced empathic concern or perspective-taking ability (Cusi et al., 2011; Schreiter et al., 2013). Empathic concern encompasses externally-oriented responses to the feelings of others, which may result in prosocial behaviour and social support (Jean Decety, 2010). This is illustrated in depressed mothers' decreased emotional reactivity to their newborns' distress, as well as overall reduced responsiveness compared to healthy mothers (Field et al., 2009; Young et al., 2015), despite other suggestions that depressed individuals display greater empathy in

response to social pain, as a result of prior personal experience (Nordgren et al., 2011).

From a theoretical perspective, the emotion context-insensitivity (ECI) hypothesis (Rottenberg et al., 2005) suggests that lowered emotional reactivity in depression may reflect an evolutionary adaptive overall disengagement with one's environment aimed at reducing exposure to potential threat. This is similar to the social risk (SR) hypothesis of depressed mood (Allen & Badcock, 2003), which suggests that depressed mood is the result of adopting a risk-averse internally-oriented approach to social interactions. Therefore, one's social investment potential, as described in the previous chapter, would only be sensitive to others' currently relevant social experiences, which are personally meaningful or could impact on the likelihood of exclusion. If this is not the case, then the SR hypothesis argues that individuals with depressed mood tend to withdraw from exchange-oriented contexts, in line with behavioural findings. On a neural level, this might be reflected in a distinct neural circuitry involved in processing other's relevant social signals compared to the social evaluative network identified in the previous chapter.

However, as before, the literature to date has focused predominantly on (empathy for) negative (social) experiences, such as social pain, while neglecting the importance of positive experiences, such as social reward or inclusion. Empathic responses to both happy and sad facial expressions have previously revealed shared neural circuitry with activity in right inferior frontal gyrus, and inferior frontal operculum (Jabbi et al., 2007; Harada et al., 2016). However, the strongest support derives from a study suggesting that the anterior insula is actively implicated in the empathetic processing of both negative and positive social processing and social exchanges more generally, including perceived fairness and cooperation (Lamm & Singer, 2010). This suggests, as with the discussion in the previous chapter, that empathy for positive and negative social information may share a common underlying neural representation (Jackson, Rainville, & Decety, 2006; Lamm et al., 2011; Lamm & Singer, 2010; Novembre et al., 2015).

In sum, processing of social information is dependent on situational and individual features, such as the proximity of the social target, as well as differences in self-referential processing. While previous research has found neural overlap when contrasting the personal and vicarious experiences of social pain in healthy controls, no study to date has explored empathy for social pain in depression, let alone empathy for social inclusion. The previous chapter revealed overlapping neural activity in response to self-relevant social signals of rejection and inclusion in depression. However, research suggests altered empathic processing at a behavioural level in response to other relevant signals. This may be due to increased self-focused attention and reduced empathic concern. Given the limited neural evidence to date, this raises the question of how individuals with and without depression process others' negative and positive social experiences at the psychological and neural levels. Thus, this chapter aims to explore the importance of self- versus other-referential processing in response to others' personal memories of social rejection and inclusion in depression, compared to healthy controls, using script driven imagery, as previously described.

Our hypotheses were as follows;

HYPOTHESES

Behavioural Hypotheses

- Ratings of valence and arousal will reveal a dampened response in MDD compared to healthy controls in response to other's social experiences of rejection and inclusion (Cusi et al., 2011).

Neural Hypotheses

- Results will reveal overlapping patterns of activity for rejection and inclusion memories (relative to neutral social experiences) in areas including the MCC, AI, precuneus, and supramarginal gyrus (Lamm et al., 2011; Novembre et al., 2015; Singer et al., 2004),
- Individuals with MDD will show reduced activity compared to healthy controls in the 'empathy regions' of the brain outlined above, including the MCC, AI and somatosensory cortices (Fujino et al., 2014), with greater activity in so-called mentalising areas, including the IFG and prefrontal cortices (Feng et al., 2016; Meyer et al., 2013, 2014).

5.2 Methods and Materials

Participants

Twenty-three participants experiencing a current Major Depressive Episode and meeting criteria for a diagnosis of Major Depressive Disorder (MDD; 18 female; mean age = 34.11, SD = 10.9 years), and 27 healthy controls who had never met criteria for MDD (15 female; 33.21±16.1 years) were recruited from volunteer panels at the MRC Cognition and Brain Sciences Unit and the University of Cambridge. All participants were recruited separately to the samples of healthy controls and MDD participants described in the neuroimaging study in Chapter 4. In this study, all participants completed a single neuroimaging session followed by behavioural post-testing outside of the scanner. All participants were right-handed, with no history of brain injury, normal or corrected-to-normal vision and no hearing impairments. MDD participants previously underwent a structural clinical interview to confirm their diagnosis and presence of a current episode. Full demographics can be found in Table 5.2.

Clinical Interview and Social, Affective and Process Self-Report measures

A comprehensive diagnostic interview and battery of social, affective and process self-report measures was undertaken with respect to all participants. See Chapter 2 for a full description.

Experimental Task

Stimuli

The stimuli for the current neuroimaging task consisted of 10x neutral, 10x inclusion and 10x rejection social memories derived from participants who had previously taken part in the neuroimaging study (Chapter 4) or the behavioural study (Chapter 7), respectively. Hence, there was no initial memory generation session within this study, as participants were listening to another's memories. The methodology of

memory generation implemented is described in Chapter 3. In brief, participants were asked to generate highly emotionally salient autobiographical memories involving social rejection, social inclusion and socially neutral experiences. Each memory had previously been edited into 30-second audio-scripts in the first person, present tense and audio-recorded by a range of research assistants gender-matched to the participant from the original study to be used as stimuli in the fMRI script-driven paradigm. For this study, a subset of these acquired memories was selected as stimuli for use in the modified memory presentation task (see below) in the following way.

Firstly, from the 720 individual audio-scripts obtained (see Chapter 3 for details), we selected memories of social rejection, social inclusion and neutral social experiences that were narrated by the identical male or female speaker. This was done to avoid confounding effects of personality or voice, as the same research assistants involved in the study were not available for all recordings for the duration of the project or had since left the project. This reduced the number of available memories in the first instance to 346, of which 220 had been narrated by the same female speaker and 126 by the same male speaker. Secondly, the reduced subset of memories was independently rated by research assistants on vividness and intensity, and with respect to the same four subjective mood states (distress, rejection, inclusion, positivity) on the same Likert scales as previously rated by the participants who had generated the memories in the first place. Finally, the ten most highly rated memories with respect to social rejection, inclusion and neutrality were selected for each category, with 5 memories within each memory category narrated either by a male or female speaker. See Table 5.1 below.

Table 5.1

Mean Ratings of Final Stimuli Selection for Others' Memory fMRI Study (Chapter 5)

		Distress/ Rejection*		Positivity/ Inclusion*		Imaginability		Intensity	
Condition	N	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Inclusion	10	0.13	0.24	6.38	0.65	6.65	1.29	3.80	1.86
Neutral	10	0.00	0.00	0.58	0.36	6.50	1.05	0.80	0.35
Rejection	10	6.03	1.18	0.00	0.00	6.05	1.14	4.50	1.86

**Distress/Rejection and Positivity/Inclusion were averaged into their respective composite scores (see Chapter 3). N= Number of memories.*

Modifications to 'Self' Memory Presentation Task (see Chapter 4)

At the outset of the current experiment, the aim was to apply a traditional general linear modelling (GLM) approach to the fMRI analysis, as well as a novel intersubject correlation (ISC) analysis method (Hasson et al., 2004a; Kauppi et al., 2014), as described in Chapter 6. To this end, we closely matched our paradigm to a recent study investigating inter-subject synchronicity in an unselected sample in response to watching a series of emotionally salient movies (Nummenmaa et al., 2014). This paradigm implemented both the standard GLM approach alongside an ISC analysis, which required some modifications to the 'self' memory presentation (SEMP) task implemented in the previous chapter.

Firstly, apart from an increase in the number of trials in each block relative to the paradigm used in Chapter 4 (see below), the other-relevant memories were presented in a fixed order to allow for ISC analysis at each time point between individuals. Secondly, in the SEMP task, the auditory presentation or 'listening' period of the memories was previously immediately followed by a silent 'imagery' period. This 'imagery' period represented the contrast of interest for subsequent whole-brain and region of interest analyses in line with previous script-driven imagery paradigms (Lanius et al., 2003). For the purpose of adapting our paradigm to the methodology implemented by Nummenmaa et al. (2014), the contrast of interest in the current experiment consisted of the 'listening' period only, with no additional imagery period between memories. This allowed for a more realistic investigation into on-line processing of socially salient information as the narrative unfolds that is appropriate when listening to and processing another's memory that has not been encountered before. This time-sensitive activity was captured by ISC analysis in contrast to capturing the neural response to self-generated memories as described in Chapter 4 using a traditional GLM approach. Finally, mood ratings previously obtained in a self-timed manner immediately following each memory in Chapter 4 would not allow for subsequent trials to be presented at the same time point. Thus, ratings were obtained following the scanning session with respect to mood and arousal, in line

with Nummenmaa et al. (2014). The resulting modified 'other' memory presentation (OMP) task is presented below.

'Other' Memory Presentation (OMP) Task

The neuroimaging session consisted of a single run block-design with three blocks (neutral, rejection, inclusion) presented in fixed order to facilitate overall mood repair as previously. The paradigm consisted of ten consecutively presented 30-second same-type closed-eye audio scripts within each of the three blocks during which participants were instructed to close their eyes and listen. All 30 memories were presented in the exact same order to allow for the subsequent ISC analysis, in which stimuli need to be presented in a fixed and identical order across participants (Hasson et al., 2004a; Kauppi et al., 2014). A tone cue following each memory prompted participants to press any button using a button box as quickly as possible in a fixed 5 second time window, while keeping their eyes closed, to ensure participants' continued attention to the task. See Figure 5.1 for overview of paradigm in scanner.

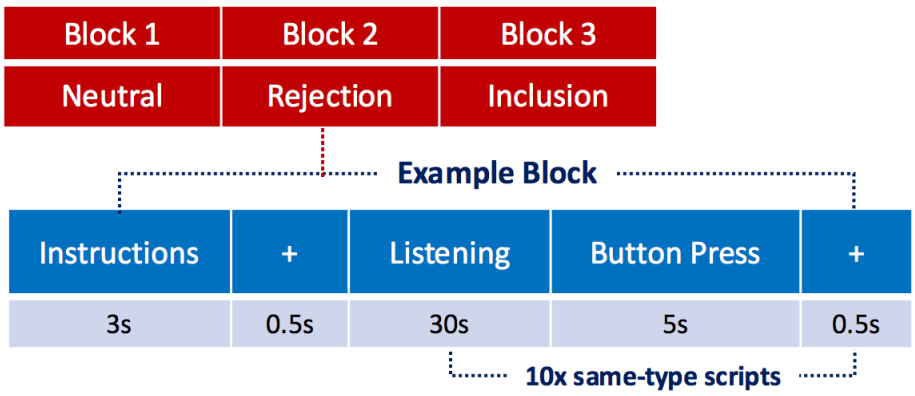


Figure 5.1. Script-driven imagery paradigm for Other' Memory presentation (OMP) task.

Outside the scanner, following the neuroimaging session, participants rated each memory separately in terms of induced mood and level of arousal on 5-point self-assessment manikin (SAM) scales ranging from "Negative" to "Positive" and "Calm" to "Excited", respectively (see Figure 5.2). The SAM scales allow for a non-verbal pictorial assessment of emotion (Bradley & Lang, 1994) and were presented on a computer screen. Ratings were provided using arrow keys prior to each memory category to establish baseline levels and following each memory within categories. The memories were presented in the exact same order as during the neuroimaging session. Auditory and visual presentation of the stimuli inside and outside the scanner was identical to the stimulus presentation in Chapter 4. The total approximate duration was 20 minutes per scanning run, followed by 30 minutes of behavioural ratings.

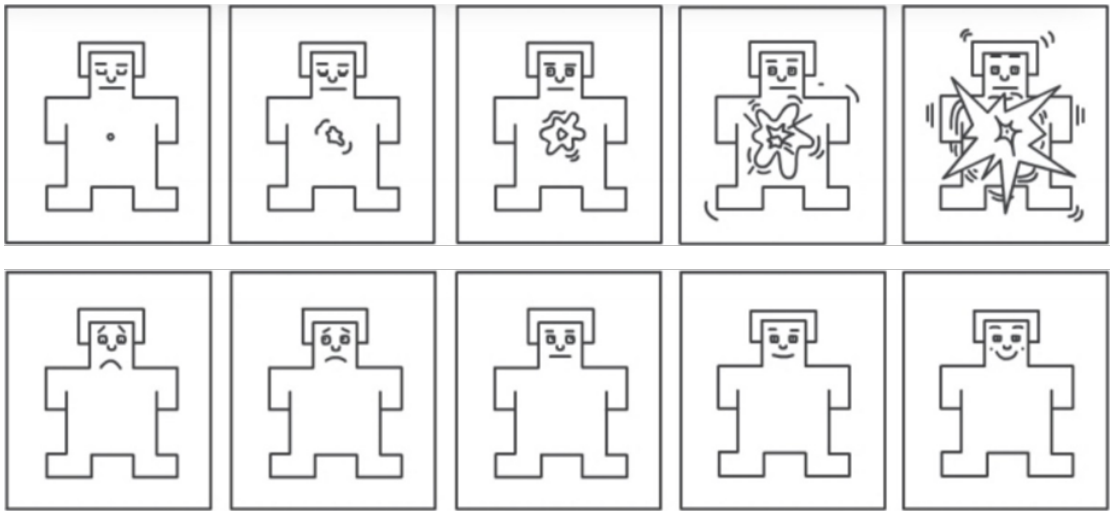


Figure 5.2 SAM scales provided non-verbal pictorial assessment of arousal (top row) and valence (bottom row).

PROCEDURE

Immediately prior to the neuroimaging session, all participants provided informed consent and were then administered the BDI, BAI, and National Adult Reading Test (NART). In the scanner, participants were instructed to keep their eyes closed, to listen and concentrate on a series of brief audio clips describing personal memories of past events. It was emphasised that these were real events. In addition, participants were instructed to press any button as quickly as possible in response to hearing a brief tone cue to ensure participants were still attending to the task. Following the scanning session, participants were given a brief break ($\leq$5min) before providing behavioural ratings outside of the scanner. Participants were instructed to keep their eyes closed while listening to the same personal memories. At the end of the session, participants were provided with a battery of social, affective and process self-report measures to be completed and returned in their own time (see Chapter 2). Finally, participants were thanked for their time and debriefed.

fMRI DATA ACQUISITION

A 3T Siemens Tim Trio MRI scanner with a 32-channel head coil was used to acquire a structural T1-weighted MPRAGE image (1-mm isotropic voxels) and functional data of 555 whole-brain T2*-weighted EPI volumes with 32 oblique axial slices that were 3 mm thick and acquired in descending order, an in-plane 64×64 matrix with 3×3 mm resolution, TR 2 s, and TE 30 ms (single run). fMRI data were pre-processed and analysed using AA (Automatic analysis, Cusack et al., 2015), which uses MATLAB R2013a and SPM12, described in Chapter 4.

STATISTICAL ANALYSIS

Behavioural Ratings

The affective pre- and post-ratings of arousal and mood were averaged within each memory category and analysed in a univariate analyses of variance (ANOVA) with group (controls/MDD) as a between-group factor and memory type (rejection/inclusion/neutral) and time (pre/post) as within-group factors. The affective ratings, as well as self-report measures were analysed as described in Chapter 2 and Chapter 3.

fMRI Pre-processing and analysis

Data was processed and analysed at the first level in the same manner as described in Chapter 4. At the second level, changes from Chapter 4 included separate sets of regressors generated for listening trials only as opposed to listening and imagining. Age and gender were also entered as covariates in all analyses, following significant differences in age and gender between groups (see Table 5.2). Contrasts of these parameters were generated for rejection and inclusion memories relative to neutral social memories, as well as contrasts of rejection relative to inclusion and for each memory individually (neutral, rejection, inclusion), as well as for tone cues for each participant during the closed-eye listening periods. These contrasts were taken to the second level for group level analysis. All whole-brain analyses are thresholded at $k=20$, $p<0.001$ uncorrected, unless otherwise specified.

Regions of Interest Analysis

Having investigated regionally sensitivity patterns of activation in response to social pain based on ROI analysis in Chapter 4, ideally, we would have run similar ROI analyses derived from studies investigating empathy for social pain. However, to date, few studies have explicitly investigated empathy for social pain with significant regional variability in findings. As a result, implementing regions derived from meta-analyses is a more reliable approach (Poldrack, 2007). Therefore, in the absence of such meta-analyses for the present study, we focused our analysis on whole-brain fMRI results.

5.3 Results

Demographic characteristics

Table 5.2 shows the demographic characteristics for the healthy controls and MDD participants, while Appendix 5.1 presents the descriptives and group comparisons of social, affective and process measures for the current sample. All measures revealed significant group differences between MDD and healthy control participants, except for the Spontaneous Use of Imagery Scale ($p=0.20$). Despite efforts to match our groups on demographic characteristics, there was a significant difference in age ($t(48)=2.66$, $p=0.01$), and so age and gender was entered as a co-variate in the subsequent fMRI analysis. However, there was no significant difference in estimated IQ, derived from reading ability as measured by the NART ($t(42)=.33$, $p=0.75$) or in other demographic characteristics, except for marital status ($p=0.03$).

Table 5.2

Demographic Characteristics for Others' Memory fMRI Study for Chapter 5. Numbers are ns unless otherwise stated.

	Controls n=27	MDD n=23	Total N=50	X^2	p
Sex					
Male	12	5	17	3.80	0.07
Female	15	18	33		
Age, years					
Mean	28.96	39.48	33.80		0.01
SD	12.67	15.25	14.75		
National Adult Reading Test					
Mean	12.67	11.00	11.93		0.75
SD	5.39	6.94	6.10		
Ethnicity					
Caucasian	22	23	45	4.74	0.05
Other	5	0	5		
Marital Status					
Single / Unmarried	22	13	35	7.68*	0.03
Married	4	2	6		
Separated / Divorced	0	2	2		
Other	1	6	7		
Education					
Completed Year 10	1	3	4	8.95*	0.08
Completed Year 12	8	8	16		
Completed Bachelors	10	3	13		
Completed Masters	3	0	3		
Completed PhD	0	2	2		
Other	5	7	12		
Employment Status					
Employed	14	10	24	4.48*	0.22
Unemployed	4	7	11		
Student	7	2	9		
Other	2	4	6		
Employment					
Full Time	9	8	17	4.50	0.34
Part Time	8	3	11		
Other	10	12	22		

Note: * indicates Fisher's exact test

BEHAVIOURAL RATINGS

The behavioural analysis involved all participants providing affective ratings of mood and arousal levels in response to listening to the same memories of social rejection, inclusion and neutral social experiences generated by unknown other individuals. The mean affective ratings for each group and each memory type are presented in Table 5.3-Table 5.5, illustrating the mean mood ('Negative-Positive') and arousal ('Calm-Excited') ratings. Overall, mean ratings revealed that positive mood decreased while listening to rejection memories and improved across all participants following inclusion memories, relative to the baseline, while remaining relatively unchanged following neutral memories, see Figure 5.4 for changes (deltas) in mood and arousal by memory and group. Mean arousal in controls was lower overall compared to MDD participants, with an increase in arousal for rejection and inclusion memories and decrease in arousal for neutral memories. In contrast, MDD participants showed a decrease in arousal in response to neutral and inclusion memories and an increase only for rejection memories (Figure 5.5). An initial data exploration suggested an emotional overspill of the negative affect resulting in a reduced baseline rating at the beginning of the inclusion block. This could not be remedied due to the fixed order of presentation. However, the change in positive affect speaks to the salience of the (positive) memory type in manipulating mood.

Table 5.3

Mean mood and arousal ratings by group (Chapter 5)

Measure	Groups	Mean	Std. Error	95% Confidence Interval	
				Lower	Upper
Mood	Controls	3.58	0.14	3.31	3.86
	MDD	2.80	0.13	2.53	3.06
Arousal	Controls	1.96	0.19	1.58	2.33
	MDD	2.57	0.18	2.21	2.92

Table 5.4

Mean mood and arousal ratings by memory type (Chapter 5)

Measure	Memory Type	Mean	Std. Error	95% Confidence Interval	
				Lower	Upper
Mood	Neutral	3.38	0.10	3.17	3.59
	Rejection	2.83	0.11	2.61	3.05
	Inclusion	3.36	0.10	3.15	3.57
Arousal	Neutral	2.26	0.13	2.00	2.52
	Rejection	2.28	0.14	2.00	2.57
	Inclusion	2.24	0.14	1.95	2.53

Table 5.5

Mean mood and arousal ratings by memory type and group (Chapter 5)

Measure	Groups	Valence	Time	Mean	Std. Error	95% CI	
						Lower	Upper
Mood	Controls	Neutral	Pre	3.85	0.20	3.45	4.25
			Post	3.54	0.14	3.25	3.82
		Rejection	Pre	3.90	0.18	3.54	4.26
			Post	2.58	0.19	2.20	2.96
		Inclusion	Pre	3.40	0.21	2.98	3.82
			Post	4.23	0.15	3.92	4.54
	MDD	Neutral	Pre	3.14	0.19	2.76	3.52
			Post	2.99	0.13	2.72	3.26
		Rejection	Pre	3.05	0.17	2.71	3.38
			Post	1.80	0.18	1.43	2.16
		Inclusion	Pre	2.23	0.20	1.83	2.63
			Post	3.58	0.15	3.28	3.87
Arousal	Controls	Neutral	Pre	2.05	0.22	1.60	2.50
			Post	1.89	0.18	1.51	2.26
		Rejection	Pre	1.75	0.20	1.34	2.16
			Post	2.22	0.24	1.73	2.70
		Inclusion	Pre	1.75	0.26	1.23	2.27
			Post	2.08	0.20	1.68	2.48
	MDD	Neutral	Pre	2.73	0.21	2.30	3.15
			Post	2.37	0.18	2.01	2.72
		Rejection	Pre	2.18	0.19	1.79	2.57
			Post	2.99	0.23	2.53	3.45
		Inclusion	Pre	2.73	0.24	2.24	3.22
			Post	2.40	0.19	2.02	2.79

Mood Ratings

For mood ratings (Figure 5.4), there was a significant main effect for group ($F[1,40]=17.27$, $p<0.001$, $\eta_p^2=0.30$), for time ($F[1,40]=4.69$, $p=0.04$, $\eta_p^2=0.03$) and for memory type ($F[2,80]=26.27$, $p<0.001$, $\eta_p^2=0.34$). There was also a significant interaction between memory and time ($F[2,80]=83.84$, $p<0.001$, $\eta_p^2=0.67$). There was no significant interaction between memory type and group ($F[2,80]=1.42$, $p=0.25$, $\eta_p^2=0.03$), indicating that mood ratings for each memory type did not differ as a function of group; no significant interaction for time and group ($F[1,40]=3.74$, $p=0.06$, $\eta_p^2=0.09$), indicating that changes in ratings over time did not differ as a function of group, and no significant interaction between memory, time and group ($F[2,80]=0.83$, $p=0.44$, $\eta_p^2=0.02$), indicating that change in mood ratings over time with respect to each memory type showed no differential patterns as a function of group (see Figure 5.4).

Planned comparisons revealed significant group differences with greater positive mood in controls compared to MDD (0.78 ± 0.19, $p=0.001$) (see Table 5.4), suggesting a more positive baseline mood for controls compared to MDD irrespective of memory type manipulation or time, as would be expected. In addition, planned comparisons for memory type revealed significant differences between all memories ($p<0.001$) with inclusion memories rated significantly more positively relative to neutral and rejection memories (0.51 ± 0.15), while rejection memories were significantly more negative relative to neutral (0.55 ± 0.09), again as would be expected. Overall, this suggests that on a behavioural level, while overall baseline positive mood was increased in controls, the memory manipulation as a function of time effectively impaired and repaired positive mood across both groups. See Table 5.5.

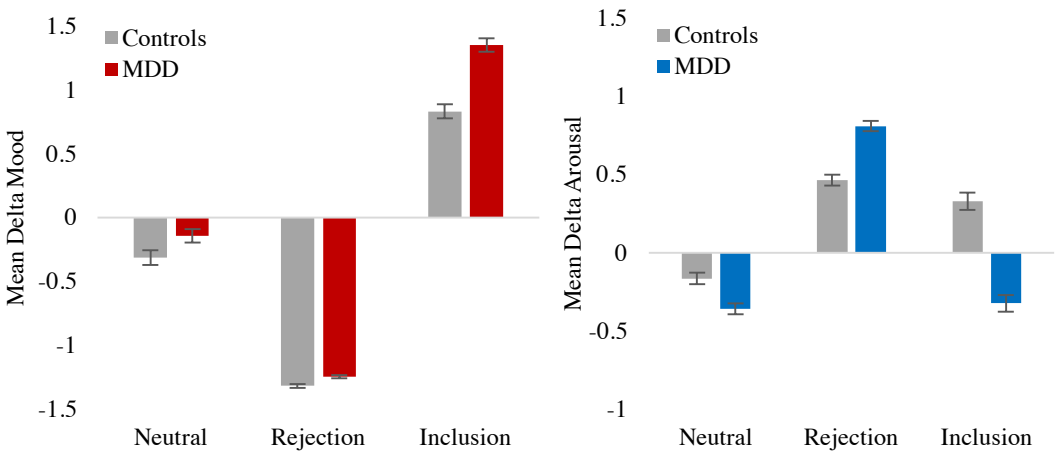


Figure 5.3. Mean changes (deltas) in mood (left) and arousal (right) ± 1SE from baseline to post-memory. Higher scores represent more positive mood and greater arousal, respectively.

Arousal Ratings

For arousal ratings, Mauchly's test of sphericity indicated that the assumption of sphericity was violated for memory type (x^2=7.49, p=0.02) and the interaction of memory type and group (x^2=3.36, p=0.19), and will be reported using the Greenhouse-Geisser correction. There was a significant main effect for group (F[1,40]=5.70, p=0.02, η_p^2=0.13), but not for time (F[1,40]=3.41, p=0.07, η_p^2=0.08) nor for memory type (F[1.71,69.34]=0.13, p=0.85, η_p^2=0.003). There was a significant interaction between memory type and time (F[2,80]=13.21, p<0.001, η_p^2=0.25). There was no significant interaction between memory type and group (F[1.71,68.37]=0.09, p=0.89, η_p^2=0.002) or time and group (F[1,40]=1.50, p=0.23, η_p^2=0.04). Finally, there was a significant three-way interaction between memory type, time and group (F[2,80]=3.85, p=0.03, η_p^2=0.09), suggesting that MDD reported greater change in arousal levels over time with decrease in arousal following the inclusion memory compared to controls, who reported increased arousal following the inclusion memory. Both groups reported increase in arousal in response to the rejection memories and no significant change for neutral.

Planned comparisons revealed significant group differences with diminished arousal in controls compared to MDD (0.62±0.26, p=0.02) overall, suggesting a lowered baseline of arousal in controls (see Table 5.3). There was no significant difference in arousal as a function of memory types. See Table 5.5 for mean pre- and post-mood and arousal ratings by memory type. Overall, this suggests that arousal levels were increased in MDD at baseline, with a differential pattern of response to inclusion memories as a function of group. Decreases in arousal following inclusion memories in MDD may suggest an overspill of arousal following the rejection memories, which saw a significant increase in arousal, not apparent in the control group. Given a similar adjustment to the inclusion baseline as was carried out for the mood ratings, results may suggest similar increases in arousal in MDD in response to inclusion, albeit to a lesser degree than to rejection memories (see Figure 5.5).

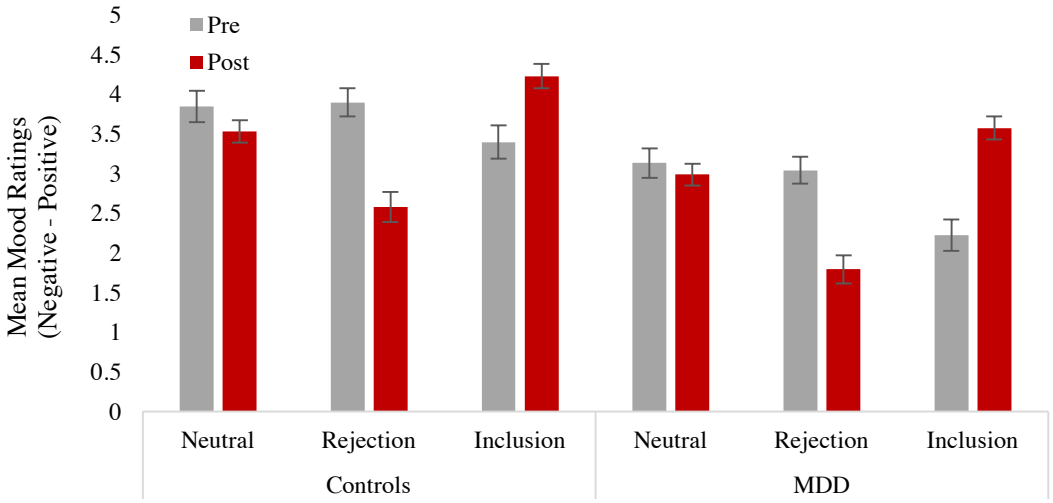


Figure 5.4. Mean mood ratings ± 1SE of the mean by group and memory type over time.

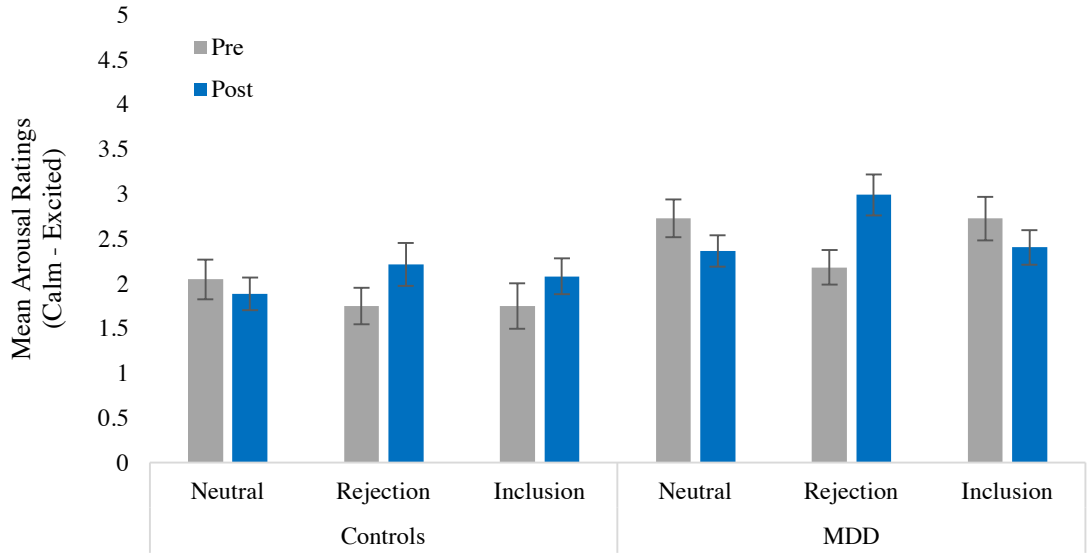


Figure 5.5. Mean arousal ratings ± 1SE of the mean by group and memory type over time.

fMRI Results

Four healthy controls, and one MDD participant were excluded from the final fMRI group analysis due to acquisition difficulties. As noted, all whole-brain analyses are thresholded at $k=20$, $p<0.001$ uncorrected. The first level of analysis consisted of carrying out one-sample t-tests to investigate the neural pattern of activation in response to listening to rejection and inclusion memories within each group.

In control participants, one-sample t-tests of rejection > neutral memories are presented in Appendix 5.1. Results revealed activations in bilateral angular gyrus (AnG), left precuneus, left postcentral gyrus, right superior frontal gyrus medial segment (MSFG), left precentral gyrus, right caudate, right supramarginal gyrus (SMG) and right middle frontal gyrus (MFG). Inclusion > neutral revealed activations in bilateral SMG, right middle and anterior cingulate cortex (MCC/ACC), right AnG, right precuneus, left precentral gyrus, left parietal operculum (PO), right superior and middle frontal gyrus and right AI. For inclusion > rejection, results revealed a large cluster in bilateral superior occipital gyrus, bilateral precentral gyrus, bilateral posterior insula, bilateral superior parietal lobule (SPL), left superior frontal gyrus (SFG), left ACC, and posterior cingulate cortex (PCC). Finally, rejection > inclusion revealed bilateral AnG, bilateral MTG, and right MFG.

In MDD participants, one-sample t-test results for rejection > neutral memories are presented in Appendix 5.3. Results revealed activations in right middle temporal gyrus (MTG), right MFG, right precuneus, left thalamus, left caudate and bilateral AnG. During inclusion > neutral memories, we found left supplementary motor cortex (SMC), left postcentral gyrus (PoG) and precentral gyrus (PrG). For inclusion > rejection, we found bilateral Anterior Insula (AI), left middle cingulate gyrus (MCgG), bilateral posterior orbital gyrus (POrG), right precuneus and the right triangular part of the inferior frontal gyrus (TrIFG). In reverse, rejection > inclusion revealed activations in bilateral MTG, bilateral AnG, and right precuneus.

Next, we sought to explore the differential pattern of activity as a function of group in two-sample t-tests (see Appendix 5.4). Two sample t-tests in controls compared to MDD revealed increased activation in controls in right AnG during rejection > neutral, right middle occipital gyrus (MOG) during inclusion > neutral, and left AI, right PrG, and left MCC for rejection > inclusion memories (see Figure 5.6). MDD compared to controls revealed activity in PoG during rejection > inclusion only.

Finally, as in Chapter 4 we explored neural activity in response to listening to other's memories more closely with a conjunction analysis of rejection versus neutral and inclusion versus neutral within and across both groups. Results revealed bilateral PoG activation in controls only, but not for MDD, thresholded at $p<0.05$, uncorrected, $k=20$. Conjunction analyses of controls compared to MDD, for rejection versus neutral and inclusion versus neutral, revealed no significant activations.

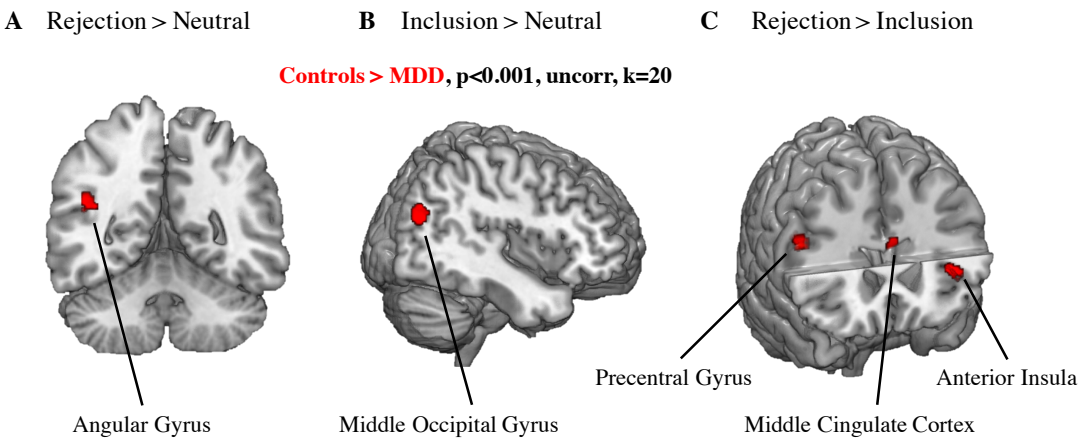


Figure 5.6. **Two-sample whole-brain analysis results. (A)** Listening to rejection>neutral memories, **(B)** inclusion>neutral memories and **(C)** rejection>inclusion memories for controls compared to MDD revealed significant activations in emotion regulation areas, such as the angular gyrus, and affective areas including precentral gyrus, anterior insula and MCC, uncorrected at p<0.001, k=20.

5.4 Discussion

In this chapter, we aimed to assess the psychological and neural responses to listening to others' personal experiences of social rejection and inclusion relative to neutral experiences in currently depressed and healthy control individuals. We measured the change in mood and arousal in response to the individual memories presented, as well as brain activity at the whole-brain level. On a behavioural level, we predicted that behavioural ratings of mood and arousal would reveal a dampened response in *mood* and *arousal* in MDD compared to healthy controls in response to others' social experiences of rejection and inclusion. Our findings revealed that MDD individuals reported lower overall mood compared to healthy controls, irrespective of memory type, in line with our prediction. However, our findings of arousal went against our prediction; rather than overall lowered arousal, we found increased levels of arousals in response to rejection and decreased arousal in response to inclusion memories in MDD, relative to controls.

Overall, reduced affective responses to others' experiences of social rejection and inclusion are in line with meta-analytic findings suggesting reduced emotional reactivity in MDD in response to both positively and negatively valenced stimuli (Bylsma et al., 2008). The emotion context-insensitivity (ECI) hypothesis (Rottenberg et al., 2005) argues that this reduced affect in depression represents an active disengagement with the environment, while the SR hypothesis (Allen & Badcock, 2003, 2006) suggests withdrawal from exchange-oriented contexts. However, this argument remains contentious with previous studies highlighting a discrepancy between behavioural and neural responses to positive and negative sources of information. For instance, depressed individuals require greater intensity of stimuli to correctly identify positive emotions, such as happy facial expressions compared to sad facial expressions (Joormann & Gotlib, 2006). This suggests a negative response bias, alongside reduced sensitivity to positive cues, correlated with depression severity (Gollan et al., 2010). This bias is further illustrated in our arousal findings, which suggest differential reactivity as a function of memory type. In

response to inclusion memories, arousal decreased in depressed compared to controls. This is in line with previous findings suggesting reduced emotional reactivity to anticipated reward (such as the social inclusion event) (McFarland & Klein, 2009) and reduced arousal in response to non-autobiographical positive stimuli (Sloan et al., 2001). In contrast, increased arousal in response to social rejection events may reflect heightened (empathic) stress in MDD, characterised by heightened inward directed attention (Derntl, Seidel, Schneider, & Habel, 2012; Schreiter et al., 2013). Thus, our findings of heightened arousal in depression in response to other' negative social experiences may be driven by such heightened self-focused attention (Schreiter et al., 2013) directed towards prior personal rejection experiences and identification consistent with their negative mood state (Batson, 2009).

On a neural level, we predicted that imagining others' personal experiences of social rejection and social inclusion would reveal common activity for rejection and inclusion experiences (relative to neutral social experiences), in affective and empathetic processing areas (Lamm et al., 2011; Novembre et al., 2015; Singer et al., 2004). We further predicted that individuals with MDD will show reduced activity compared to healthy controls in empathy and somatosensory regions (Fujino et al., 2014), with greater activity in areas associated with self-referential processing (Feng et al., 2016; Meyer et al., 2013, 2014). These predictions were met. Comparing groups, the neural response to other's rejection (relative to neutral) in healthy controls was associated with activation in the angular gyrus, supramarginal gyrus, and medial frontal gyrus, bordering on the MCC. This is consistent with previous findings on observing other's social and physical pain (Lamm et al., 2011; Masten et al., 2011a; Novembre et al., 2015), revealing activity for social pain in MCC, insula, supramarginal gyrus, postcentral gyrus, superior temporal gyrus, and inferior parietal gyrus (Novembre et al., 2015). This suggests a unique role for empathising with social experiences, drawing on higher-level cognitive processes, including mentalisation and Theory of Mind to facilitate social interaction (Baron-Cohen, Leslie, & Frith, 1985; Bird et al., 2010; Jean Decety, 2010). However, the literature has been largely limited to investigations of empathy for negative social emotional

experiences, as opposed to empathy for positive experiences, such as social inclusion. Our findings therefore suggest that the experience of other's inclusion similarly activates areas involved in affective and empathic processing, in AI and MCC, in line with previous suggestions (Lamm and Singer, 2010). This contributes to the growing evidence-base regarding a shared neural circuitry underlying empathy for positive and negative social information (Jackson et al., 2006; Lamm et al., 2011; Lamm & Singer, 2010; Novembre et al., 2015).

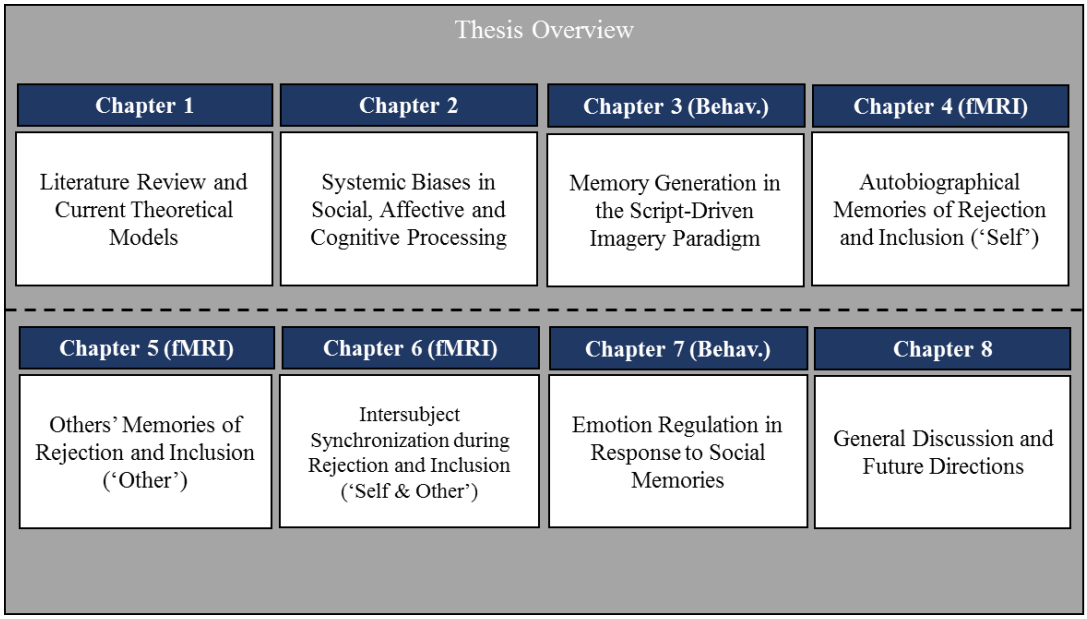
In addition, as highlighted in Chapter 4, the personal relevance and social proximity derived from a social interaction may be key to understanding the functional correlates presented above. Self-relevance as a determinant in empathic processing is evident in the observation that the 'dACC-insula' network preferentially responds to the exclusion of close others but not to strangers (Beeney et al., 2011; Meyer et al., 2013, 2014). In fact, observing less proximal social targets, i.e. stranger's social pain, evoked greater activity in the dorsal medial prefrontal cortex (DMPFC), precuneus, and temporal pole (Meyer et al., 2013, 2014). Similarly, our study uses socially distant targets, i.e. stranger's personal experiences, which may account for heightened activity in medial frontal, precuneus and midline cingulate cortices, involved in mentalising. Thus, in the context of social hierarchy, our findings complement a previous study on empathic responses to inferior and superior target's physical pain (Feng et al., 2016). Differences in self-perceptions of social rank identified in Chapter 2 may thus impact the emphatic processing of social rejection, modulating empathy towards social targets viewed as more superior and reflected in attenuated responses within the AI and MCC in depressed relative to healthy controls.

However, this remains to be fully explored, as in depression, only one study to date has explicitly compared healthy controls and depressed individuals empathic processing of others' physical pain (Fujino et al., 2014). The visual presentation of human hands in painful situations activated the MCC, AI, somatosensory related cortices (SRC) and prefrontal cortices in healthy controls, consistent with previous meta-analytic findings of empathy for physical pain in healthy controls (Lamm et al.,

2011). In contrast, MDD individuals exhibited reduced activation in the left MCC and right SRC, and greater activation in the left IFG. Interestingly, depressed individuals in our study similarly revealed reduced activation in MCC and AI in response to rejection over inclusion, and MCC and posterior insula activation in response to rejection over neutral memories. The attenuated response in MDD relative to controls thus aligns with previously identified deficits in evaluating physical pain (Jackson et al., 2006), reduced empathic concern (Schreiter et al., 2013), reduced awareness of other's emotions (Donges et al., 2005) and difficulty in interpreting externally derived social cues (Kupferberg et al., 2016).

In sum, this chapter aimed to investigate the neural and psychological response in response to listening to others' personal experiences of social rejection and inclusion in individuals with and without depression. This work builds on the previous chapter, which investigated self-relevant processing of autobiographical memories of social rejection and inclusion. Findings suggested that the subjective evaluation of others' rejection and inclusion experiences results in reduced emotional reactivity in depression on a neural and behavioural level, while ratings of arousing differed as a function of memory type. In healthy controls, findings support the existing knowledge base regarding empathic processing of negative social experiences, but extend this to the processing of social inclusion. Here we provide a first investigation of empathy for others' social negative and positive experiences comparing healthy and depressed individuals. Nonetheless, more research is needed, with a focus on the distinction between self- versus other- relevant social contexts. To this end, the next chapter will aim to present an extended narrative of social rejection and inclusion within an elicited dyadic social interaction, allowing us to further investigate self- versus other social processing.

CHAPTER 6. INTERSUBJECT SYNCHRONIZATION DURING REJECTION AND INCLUSION



6.1 Introduction

The findings from the previous two neuroimaging chapters ('self' and 'other' relevant processing of social rejection and inclusion) strongly suggest that depressed individuals and healthy controls exhibit altered neural processing of socially salient experiences of rejection and inclusion, depending on the point of origin. Chapter 4 involved imagining memories describing the emotional experience of personal social rejection and inclusion. Results revealed greater activity in somatosensory cortex in controls compared to MDD participants, and greater activity in the 'social pain' dACC-AI network in MDD participants, relative to controls. In contrast, Chapter 5 involved listening to socially salient events narrated from another person's viewpoint. The vicarious experience of another's social rejection and inclusion experiences was associated with an attenuated response in MDD relative to controls in regions commonly associated with affective and empathic processing (J. Decety, 2011; D. P. Kennedy & Adolphs, 2012), including the angular gyrus and AI during rejection and inclusion compared to neutral, and MCC for rejection compared to inclusion experiences. These findings provide important insight into the differential neural representation of socially salient events between depressed and non-depressed individuals.

However, in line with the majority of neuroscience research, the previous two studies investigated the neural processes underlying social processing in depression using a traditional model-driven GLM approach. This model infers brain activity from an averaged signal in response to repeated trial presentations, thus omitting time-sensitive components (Kauppi et al., 2014; Pajula, Kauppi, & Tohka, 2012). Therefore, the interpretation of these events should be treated with caution given the complexity and intricacy of social interactions and their neural representation. In fact, judgements and impressions about others and their personality occur within brief periods of time, and may affect subsequent social interactions (McAleer, Todorov, & Belin, 2014). Interestingly, lesions within the AI cortex are associated with increased reaction times during empathetic pain processing further emphasising a time-

sensitive component in emotional social processing (Gu et al., 2012). A time-locked sensitivity to unfolding social interactions may thus impact upon the neural processing of socially salient emotions, and implicate key regions identified in previous studies. Time sensitive considerations may further be heightened in the presence of depression, given the behavioural impairments in visuospatial attention, delayed reaction times (Hammar & Ardal, 2009), and attentional biases towards negative interpersonal signals (Gotlib, Krasnoperova, Neubauer Yue, & Joormann, 2004). This suggests that the findings from Chapter 4 and Chapter 5 may be complemented by a methodology capable of capturing time-sensitive variability in incoming sensory information, such as MEG or EEG.

An alternative approach, which maintains high spatial and temporal sensitivity, is to investigate the degree to which brain activity measured by fMRI is correlated or 'synchronized' among a group of listeners exposed to the same stimulus at any given time point. The Intersubject Correlation (ISC) approach represents a similarity measure across subjects who are presented with an identical stimulus, and is especially suited to the presentation within naturalistic contexts, which can entail complex and emotionally-engaging stimuli, such as cinematic displays and emotional scenes (Hasson et al., 2008; Hasson, Nir, Levy, Fuhrmann, & Malach, 2004b). Recently, a novel ISC toolbox was introduced to allow for the implementation of this data-driven approach to fMRI analysis during natural viewing or listening conditions (Hasson et al., 2004a; Kauppi et al., 2014; Pajula et al., 2012). The ISC methodology assumes a model-free approach, with no prior assumptions as to the functionality of the areas identified. ISC implements a series of voxel-wise Pearson's correlations between all subject pairs collapsed over time and across different frequency bands (Hasson et al., 2004a; Kauppi et al., 2014; Pajula et al., 2012). Only a few studies to date have implemented this novel analysis in either a mixed group or mixed condition design (Cantlon & Li, 2013; Hasson, Malach, & Heeger, 2010; Herbec, Kauppi, Jola, Tohka, & Pollick, 2015; Kim et al., 2008; Petrini, McAleer, Neary, Gillard, & Pollick, 2014; Salmi et al., 2013). Importantly, the ISC approach and stimulus-model based

traditional GLM analysis have revealed comparable sensitivity, thus further validating the approach (Kauppi et al., 2014; Pajula et al., 2012).

Although still in its infancy, this approach has seen increasing implementation across a variety of areas, including memory (Hasson et al., 2008), emotions (Nummenmaa et al., 2012, 2014), perspective taking (Lahnakoski et al., 2014) and communication (Nummenmaa et al., 2014; Schmalzle, Hacker, Honey, & Hasson, 2015; Stephens, Silbert, & Hasson, 2010). However, only a few studies to date have explicitly investigated group differences in intersubject correlations. These include studies in autism (Hasson et al., 2010; Salmi et al., 2013), schizophrenia (Kim et al., 2008), in development (Cantlon & Li, 2013), and when investigating the effect of expertise on action perception (Petrini et al., 2014). Autism is of particular interest when considering social functioning in depression, given the well-established difficulties in communication and social domains (Hughes, 2008; M. D. Kaiser & Pelphrey, 2012; Shah & Sowden, 2015). Using the ISC approach, individuals with Autism Spectrum Disorder (ASD) were found to exhibit lower ISCs in social and affective brain regions compared to 'neurotypical' controls in response to viewing social interactions (Hasson et al., 2009; Salmi et al., 2013). These findings revealed decreased ISC in regions implicated in empathetic and social evaluation, including the insula, PCC and ACC, caudate, precuneus, lateral occipital cortex, and supramarginal gyrus (Salmi et al., 2013), as well as visual cortical areas and the superior temporal cortex (Hasson et al., 2009). These findings are intriguing when considered alongside the similar broad social impairments observed in the context of depression.

However, the ISC studies described above have tended to use highly edited cinematic displays, such as Hollywood movies (Hasson et al., 2008) or other popular media (Nummenmaa et al., 2012) to explore the association between ISC and subjective emotional experience of movie-watching. More recently, studies have moved towards the implementation of more ecologically valid, albeit visually degraded stimuli, such as CCTV footage (Petrini et al., 2014) or unedited dance performances

(Herbec et al., 2015), which retain the natural fluctuations in emotionality and arousal experienced over time. These short-lived, albeit highly arousing salient stimuli more closely resemble the affective environment we live, and more importantly, interact in. However, ideally, the data driven approach requires long visual and/or auditory sequences of 90 seconds or more, thus reliably invoking large ISCs in 'proof-of-concept' auditory and visual cortices involved in processing and imagining vivid visual and/or auditory stimuli (Hasson et al., 2004a). The degree of intersubject synchronization can thus provide a novel quantifiable measure of the level of cortical processing of external sensory stimuli. The presentation of long sequences is thought to reveal greater brain activity compared to viewing short epochs (Bartels & Zeki, 2004), as brain mechanisms are thought to be optimised for natural viewing as opposed to traditional brief stimulus presentation paradigms (Bartels & Zeki, 2005). While promising in their approach, these studies nonetheless suffer from a third-person perspective with limited personal agency within the emotional scenes depicted. More recently, a 'speaker-listener' fMRI paradigm investigated cortical synchrony between a speaker telling an unrehearsed non-emotive real-life story and a group of listeners (Stephens et al. 2010). This revealed temporal coupling and comparable neural response patterns between listeners and speakers in linguistic production areas in the brain, such as the superior temporal gyrus (STG), with greater coupling predicting better overall comprehension of the narrative presented. This study may present an avenue for future research to examine real-time dyadic interactions.

In sum, this chapter aims to prompt depressed and non-depressed participants to listen to and vicariously experience another individual's highly personal memories of social rejection and inclusion. The extended social narrative will afford greater personal agency in the social interaction, as opposed to the presentation of affective stimuli with limited personal relevance. This will serve to more accurately reflect the dynamic nature of social information processing and elucidate differences in social processing in depression. To date, there has been no single investigation into group differences underlying social communication in depressed compared to healthy

controls using the ISC approach. This is despite deficits in social functioning and altered neural processing in MDD participants presenting an obvious target for further investigation. While the ISC toolbox is still in development and suffers from methodological limitations discussed in more detail within the statistical analysis section, this chapter will implement this novel methodology to further investigate the time-sensitive neural patterns underlying intersubject synchrony in response to the real-time experience of social interactions in depressed and non-depressed individuals.

The hypotheses were as follows;

HYPOTHESES

Behavioural Hypothesis

- Listening to another's social positive and social negative narratives will result in overall increased positive mood and increased negative mood, respectively, across groups.
- MDD individuals will exhibit dampened overall mood in response to the others' memories presented, compared to healthy controls, in line with the results presented in Chapter 5.

Neural Hypotheses

- MDD participants will show greater synchronicity in 'affective' brain areas involved in self-relevant processing as identified in previous chapters, including the dACC and AI, relative to healthy controls. This study therefore aims to extend findings from the neuroimaging study described in Chapter 4.
- MDD participants will show reduced synchronicity in response to other relevant emotionally salient information compared to healthy controls in so-called empathic and regulatory brain areas (supramarginal gyrus, posterior cingulate cortex (PCC) and middle cingulate cortex (MCC)), and so-called mentalising areas, including the (medial) PFC. This study therefore aims to extend findings from the neuroimaging study described in Chapter 5.
- There will be overlap in terms of inter-subject synchronicity in response to listening to the social rejection and social inclusion narratives, within the affective and empathic brain regions described above, underscoring the common neural processing of social events irrespective of valence described within previous chapters.

6.2 Methods and Materials

Participants

The participants were those recruited in Chapter 5 with 23 participants with Major Depressive Disorder (MDD; 18 female; 34.11±10.9 years), and 27 healthy controls who had never met criteria for MDD (15 female; 35.30±16.1 years). See Chapter 5 for further details and Table 5.2 for full demographics. Within the healthy control group, an additional female "speaker" (age 29) was recruited as part of the experimental task described below.

Clinical Interview and Social, Affective and Process Self-Report measures

A comprehensive diagnostic interview and battery of social, affective and process self-report measures was undertaken with respect to all participants. See Chapter 2 for a full description.

Experimental Task

Stimuli

The stimuli for the neuroimaging task were derived from an initial recording or 'speaker' session within the fMRI scanner, in which a female speaker from within the research unit was invited to take part in a single neuroimaging session consisting of a single run with two conditions (rejection, inclusion) in a fixed order. The female narrator was instructed to provide two approximately 300-second personal autobiographical memories involving social rejection and social inclusion, respectively (see Appendix 6.1 for the transcript). The audio-recordings of the memories were then used as stimuli for all other participants as described in the task below. In choosing suitable memories, the speaker was instructed to provide memories from her life that she very clearly remembers and that still feel important to her, that involve at least one other person, and which still evoke a strong emotional response. The two memories were recalled in the stated order to facilitate mood repair

in both speaker and listeners. A tone cue preceded each memory indicating to the speaker to commence the narration while keeping her eyes closed, followed by a second tone cue, once the 300-second time period had expired indicating to the speaker that she may open her eyes and stop narrating the memory.

Modified OMP Task

In the present study, the sample population and experimental set up is identical to that described in the previous chapter; however, participants were presented with the second part of the experiment following a brief break outside of the scanner. This part of the session consisted of a single run with two consecutively presented 300-second closed-eye audio scripts (rejection, inclusion) acquired in the initial neuroimaging 'speaker' session with the female speaker. The two memories were presented in the stated fixed order (rejection, inclusion) to facilitate overall mood repair and to allow for the ISC analysis. A tone cue preceded each memory indicating to participants that the memory was about to commence and to listen and keep their eyes closed, followed by a second tone cue, once the memory had finished.

Outside the scanner, following the neuroimaging session, participants listened to the two memories a second time and provided continuous affect ratings throughout the duration of the 300-second memories on a horizontal visual analogue sliding scale ranging from 0 ("Strongly Negative") to 100 ("Strongly Positive") using a mouse to slide the pointer across. The simplified rating dimension was selected to keep the task manageable and to allow participants to focus on the emotional salience of the stimuli while listening. This affective dimension has also been shown to account for the largest variance in emotional judgments (Gottman & Levenson, 1985; Levenson & Gottman, 1985). The memories were presented in the same order as during the neuroimaging session, to allow for the ISC analysis, as described in Chapter 5. Participant's continuous affective responses were recorded in 2s intervals, resulting in a time series with 150 samples per memory. The approximate durations of the neuroimaging and behavioural sessions was 12 minutes each. See Figure 6.1.

Instructions	"Start" Tone Cue	Rejection Narrative	"End" Tone Cue	+	"Start" Tone Cue	Inclusion Narrative	"End" Tone Cue
3s	0.5s	300s	0.5	30	0.5s	300s	0.5

Figure 6.1. Script-driven imagery paradigm for modified 'Other' memory presentation (mOMP) task.

PROCEDURE

Immediately prior to the mOMP task in the neuroimaging session, all participants provided informed consent and were then administered the BDI, BAI, and NART, before performing the fMRI task within the scanner. In the scanner, participants were instructed to keep their eyes closed throughout the scan, and to listen to two personal memories of past events just as they would if they were to have a conversation with someone face-to-face in the present. Participants were further instructed to concentrate on their emotional response while listening. Immediately after the fMRI session, participants were given a brief break (<5min) before providing behavioural ratings by indicating how negative or positive they felt at any given moment in the story using a sliding scale presented on a screen. At the end of the session, participants were provided with a battery of self-report measures to be completed and returned in their own time. Finally, participants were thanked for their time and debriefed.

STIMULUS PRESENTATION

The speaker's two memories were audio-recorded in the scanner via a dual channel MRI Microphone System (© 2007 FOMRI™ II OptoAcoustics - www.optoacoustics.com, version 1.1) with effective noise reduction to reproduce high-quality speech from recordings within an MRI environment. The system uses two pressure gradient optical microphones with low self-noise, high bandwidth, a large dynamic range and a high directivity index of 4.8dB arranged in an orthogonal configuration, matched in phase and amplitude to capture the same input sound field.

The two microphones consist of a reference microphone capturing background noise, and a source microphone capturing both background noise and speech signals. The dual-channel OptiMRI implements a dual channel adaptive filter, followed by a single channel speech enhancement algorithm. The dual-adaptive filter subtracts the reference input from the noisy signal channel assuming the signal in the reference input is roughly similar to the interference in the noisy signal. To achieve optimal subtraction, the reference signal is modified by an adaptive filter, whose gains are learned continuously from the residual signal and the reference input. To prevent divergence of the filter when speech is present a speech detector is integrated into the algorithm. The single channel speech enhancement performs its filtering in the spectral domain, by re-shaping the noisy signal spectrum. The noise estimator is aided by an accurate voice activity detector, which evaluates the speech likelihood in each signal block before applying a single channel speech signal restoration with minimal residual artefacts.

Auditory and visual presentation of the stimuli inside and outside of the scanner were identical to those described in detail in Chapter 5. While listening to the memories outside of the scanner, participants were asked to simultaneously provide continuous affect ratings on a visual analogue sliding scale. The horizontal slider interface occupied the main part of the interface window and was developed using the psychophysics toolbox. The slider presented the audio-clips in two blocks, while recording participants' continuous responses at 2s intervals.

Data Acquisition

Data acquisition was identical to that described in Chapter 5 with functional data limited to 335 whole-brain T2*-weighted EPI volumes. The data acquisition for the speaker and listener imaging session was identical. The speaker's data was acquired to allow for further neuroimaging analysis at a later point of the neural coupling between the speaker and the average listeners in line previous studies (Schmalzle et al., 2015; Stephens et al., 2010).

STATISTICAL ANALYSIS

Behavioural Ratings

Self-report measures of affective, process and social processing were analysed using Pearson's and Spearman's correlation analyses and independent samples t-tests. Continuous affect ratings were averaged over the 300 second duration into simple affective means for each social memory. These simple means, collapsed over time were then analysed in a mixed model ANOVA with group as the between-subject factor (controls/MDD) and social valence (rejection/inclusion) as the within-subject factor. In addition, to more closely investigate the temporal characteristics of the affective ratings, the time series were averaged and collapsed into 30-s time windows and entered into a mixed ANOVA with group as the between-subject factor (controls/MDD) and social valence (rejection/inclusion) and time (segments 1-10) as the within-subject factors.

fMRI Pre-processing and analysis

MRI data were pre-processed as described in Chapter 5, and further analysed in the ISC toolbox (Kauppi et al., 2014). See next section for description.

Intersubject Correlation Analysis (ISC)

Intersubject correlation (ISC) is akin to a similarity measure across subjects in response to an identical stimulus and is particularly useful in contexts involving naturalistic presentations of complex dynamic information, such as social interactions (Hasson et al., 2004a). ISC analysis implements voxel-wise Pearson's correlations between all subject pairs over time and across multiple frequency bands (Hasson et al., 2004a; Kauppi et al., 2014; Pajula et al., 2012). In an initial step, Pearson's correlation coefficients are calculated for each subject pair (1), where the sample correlation coefficient between time series is represented by r_{ij}, N denotes the total number of samples in the time series, and S_i and S_j are the timeseries from the *i*th and *j*th subject. Finally, all subject pairs r_{ij} values are averaged (2) into a single combined ISC statistic, where *m* denotes the overall sample size.

$$r_{ij} = \frac{\sum_{n=1}^{N} [(s_i[n] - \bar{s}_i)(s_j[n] - \bar{s}_j)]}{\sqrt{\sum_{n=1}^{N} (s_i[n] - \bar{s}_i)^2 \sum_{n=1}^{N} (s_j[n] - \bar{s}_j)^2}}, \quad (1)$$

$$\bar{r} = \frac{1}{\frac{m^2 - m}{2}} \sum_{i=1}^{m} \sum_{j=2, j>i}^{m} r_{ij}, \quad (2)$$

This novel analysis technique can be performed using an ISC toolbox, developed for Matlab (Kauppi et al., 2014) (https://www.nitrc.org/projects/isc-toolbox/) over specific frequency bands, within specific time-windows and between both -session and -group comparisons. The analysis within this chapter followed the same principles as presented in previous research (Kauppi et al., 2010; Kauppi, Pajula & Tohka 2014; Pajula, Kauppi & Tohka, 2012). ISC maps will be presented showing the ISC across the subjects during the rejection and inclusion conditions respectively, and maps showing the difference in ISC between the two groups for each condition. To date, the toolbox does not allow for a multivariate analysis of variance and is limited to either paired or unpaired comparisons. The ISC analysis in this chapter was implemented via the ISC toolbox (Kauppi et al., 2014) and performed at the full frequency band both within- and between-groups, separated by condition. All results were thresholded via non-parametric voxel-wise resampling with an approximated resampling distribution of 1,000,000 realisations and corrected p-values using an FDR-based multiple comparison correction with independence or positive dependence assumptions.

ISC Between Group Comparison

To explore group differences between the ISC maps in MDD and healthy controls we used permutation testing based on the Pearson–Filon sum statistics on Fisher's Z-transformed correlation coefficients (ZPF statistics) (Kauppi, 2010; Kauppi et al., 2014; Pajula et al., 2012). This was achieved by applying a Fisher's Z-transform to the r-values, followed by calculating the transformed difference between the two groups for each subject pair and estimating the group-level statistics as the sum of the ZPF statistics over subject pairs (Kauppi, 2010). These statistics reflect the sum of the pairwise differences of ISC strength across groups. The statistical significance of

mean ISC differences across groups was estimated via the ISC toolbox by sampling the maximum and minimum sum statistics with 25,000 random permutations of the group labels of each pair. The toolbox samples the maximum (minimum) statistics to estimate the largest differences that would be observed by chance over the entire brain between randomly shuffled groups, controlling for the family-wise error (FWE) rate.

Time Series Analysis

In the next step, we explored the relationship between the elicited emotion derived from continuous affective ratings in response to the two social narratives collected outside of the scanner and the regional neural synchronicity across the same group. Average ISCs of whole-brain activity were computed at each time frame across the 300-second memories using a TR of 2 seconds and converted to 4-D NIFTI files for further use in SPM. These ISC maps, reflecting the moment-to-moment degree of inter-subject synchronisation across participants, were entered into a traditional GLM with continuous affect ratings as the regressor of interest. Resulting beta values were stored in separate maps, in which voxel intensity reflects the degree of ISC in response to positive or negative mood.

6.3 Results

All participants were administered a battery of social, affective and process measures, as described in Chapter 2. The results of the univariate analyses of between-group differences on these measures, as well as full demographic characteristics are presented in Chapter 5. Exploratory data analysis was conducted to verify that the data met the criteria for parametric statistical analysis. As we planned to conduct both between-groups and repeated-measures analyses, we checked for normality and homogeneity of the data as well as sphericity, the conditions of which were met.

Behavioural Ratings

The behavioural analysis involved all participants providing continuous affective ratings of valence in response to listening to the personal memories of social rejection outside of the scanner. In the first instance, these continuous ratings were averaged over time to generate mean affective ratings for each group and each memory type. These mean affective ratings are presented in Table 6.1, illustrating the mean valence ranging from 0 ('very negative') to 100 ('very positive'). Mean ratings confirmed that the social interaction memories elicited strong emotions with average valence ratings during the social inclusion memory ranging from 71.08 to 85.00 in controls, and 51.39 to 66.36 in MDD. During social rejection, mean valence ratings ranged from 24.05 to 37.97 in controls, and 11.43 to 26.41 in MDD. Mean affective ratings collapsed over time showed a significant main effect for both social valence ($F[1,39]=143.94$, $p<0.001$, $\eta p^2=0.71$) and group ($F[1,39]=0.95$, $p<0.001$, $\eta p^2=0.33$) but no interaction ($p=0.34$). Thus, the inclusion memory revealed significantly elevated mood compared to the rejection memory, with overall significantly heightened mood in controls compared to MDD participants, across memories.

Table 6.1.

Mean affective ratings in response to social rejection and inclusion narratives

Narrative	Group	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Inclusion	Controls	78.04	3.52	71.08	85.00
	MDD	58.88	3.78	51.39	66.36
Rejection	Controls	31.01	3.52	24.05	37.97
	MDD	18.92	3.78	11.43	26.41

Next, we investigated whether the fluctuations in emotionality over time in response to the naturalistic narratives would be reflected in between-group differences in *continuous* affective ratings. These continuous affective ratings were analysed in a mixed model ANOVA with group as the between-subject factor (controls/MDD) and social valence (rejection/inclusion) and time (segments 1-10) as the within-subject factors. See Figure 6.2 and Figure 6.3 below for an illustration of the full timeseries of social inclusion and rejection narratives, respectively.

The ANOVA revealed a significant main effect for social valence ($F[1,39]=143.94$, $p<0.001$, $\eta_p^2=0.79$), time ($F[9,31]=5.31$, $p<0.001$, $\eta_p^2=0.61$), and group ($F[1,39]=18.9$, $p<0.001$, $\eta_p^2=0.33$), in line with the previous mean affective ratings. There was also a significant interaction between time and valence ($F[9,31]=18.10$, $p<0.001$, $\eta_p^2=0.84$), suggesting that, as time progressed, social inclusion memories led to greater increases in positive mood, while social rejection memories led to decreases in mood. There was no significant interaction between time and group ($F[9,31]=2.04$, $p=0.07$, $\eta_p^2=0.37$), with similar effects of change in mood over time observed across both groups, despite greater positive mood overall for controls relative to depressed participants. There was no three-way interaction ($F[9,31]=1.66$, $p=0.14$, $\eta_p^2=0.33$).

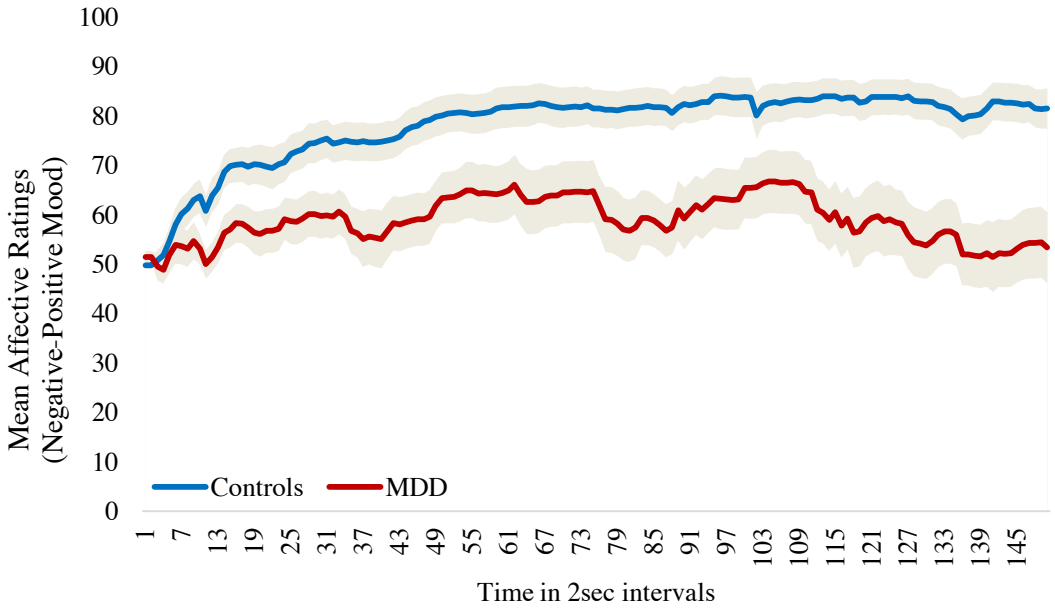


Figure 6.2. Mean continuous affective ratings ± 1SE (in grey) during the social inclusion narrative. MDD (in red) revealed overall dampened affect during social inclusion relative to controls (in blue).

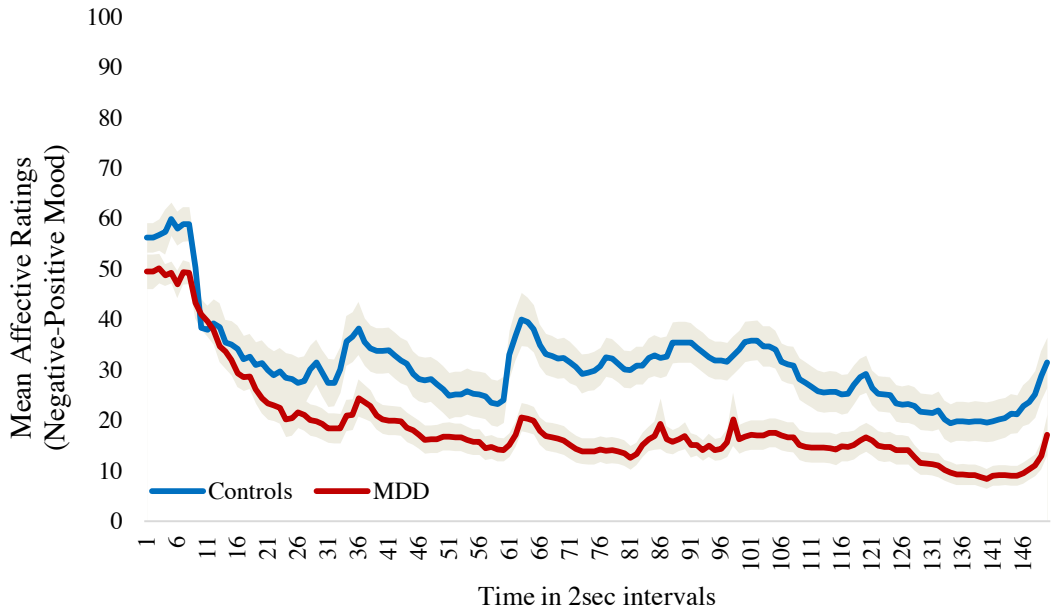


Figure 6.3. Mean continuous affective ratings ± 1SE (in grey) during the social rejection narrative. MDD (in red) revealed greater negative affect during social rejection relative to controls (in blue).

BASIC INTERSUBJECT CORRELATION (ISC) ANALYSIS

At the neural level, we employed ISC analysis to investigate similarity in brain activity across participants, while listening to the social memories. Results revealed that both groups revealed highly time-locked brain activity in key brain regions involved in visual imagery, auditory processing, as well as in affective regions (see Figure 6.4). All statistically significant group-level ISC results are reported at $p<0.001$, FDR corrected (independent/dependent) (Benjamini & Yekutieli, 2001). See Appendix 6.2, Appendix 6.3, and Appendix 6.4 for within- and between-group comparisons.

In MDD participants, during both social rejection (Appendix 6.3) and inclusion (Appendix 6.2), the largest ISCs were observed in the occipital cortex, bilateral auditory cortex and precuneus. Further statistically significant ISC clusters during social inclusion were observed in affective regions, including left ACC (6, 30, -8), left NAcc, (-12, 12, -12) and right amygdala/hippocampus (46, 16, 32) (see Figure 6.5). During social rejection only, additional ISCs were observed in left precentral gyrus, right AI and in the right temporal pole (Figure 6.6).

In healthy controls, the largest ISCs during social inclusion (Figure 6.7 and Appendix 6.2) were observed in bilateral auditory cortex, and visual cortex, with additional significant ISCs in the left precuneus, posterior cingulate cortex (PCC), left AI, left Supra Marginal Gyrus (SMG), and subgenual PFC. During social rejection (Figure 6.8 and Appendix 6.3), large ISCs were observed in auditory cortex and visual cortex, especially the posterior Superior Temporal Gyrus (pSTS) as well as the bilateral precuneus, right precentral and postcentral gyrus, right PCC, bilateral ACC, and bilateral Insula.

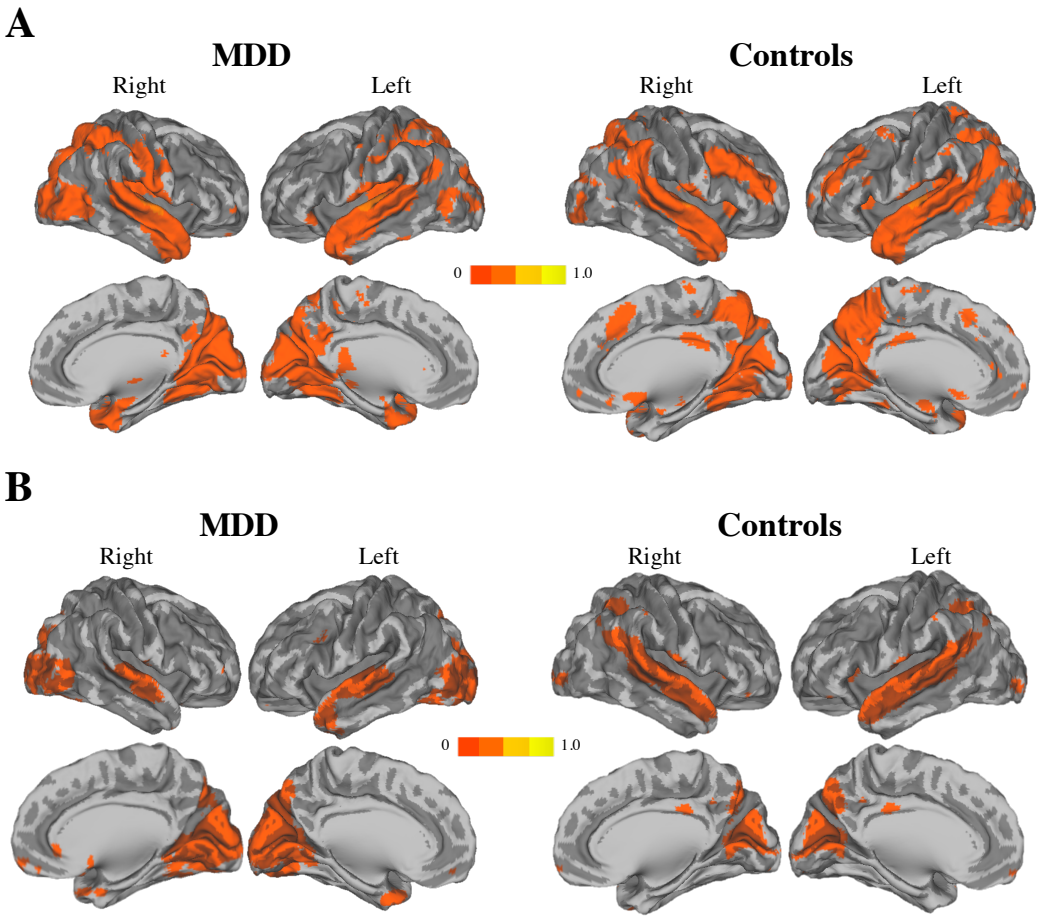


Figure 6.4. Brain regions with significant ISCs during (A) *social rejection* and (B) s*ocial inclusion* across all participants (p<0.001, FDR corrected)

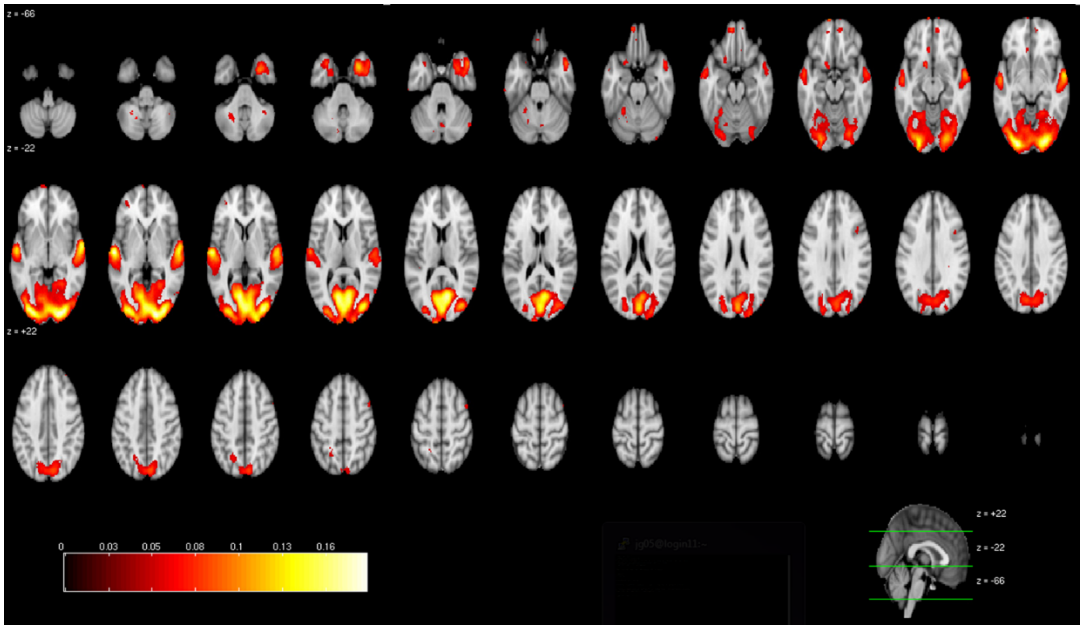


Figure 6.5. Brain regions with significant ISCs during social inclusion in MDD (p<0.001, FDR corrected). From top left to bottom right, axial slices with 4mm inter-slice interval are shown from z = –66 to 62 mm (in MNI-coordinates). Red-yellow colour scales depict lower-higher levels of ISC. See Appendix 6.2 for table of activations.

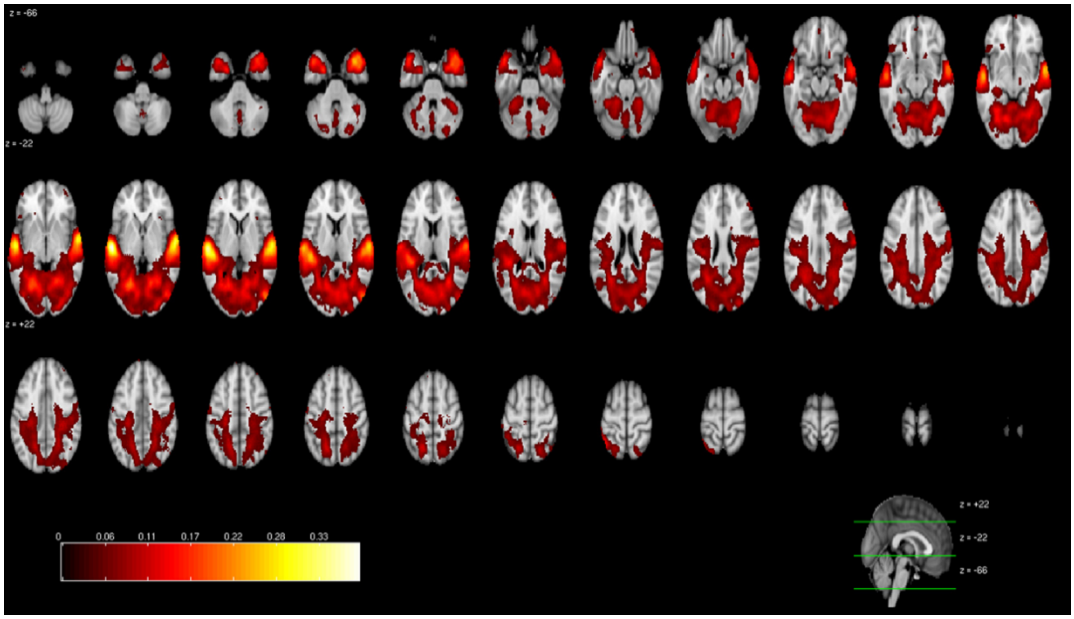


Figure 6.6. Brain regions with significant ISCs during social rejection in MDD (p<0.001, FDR corrected). See Appendix 6.3.

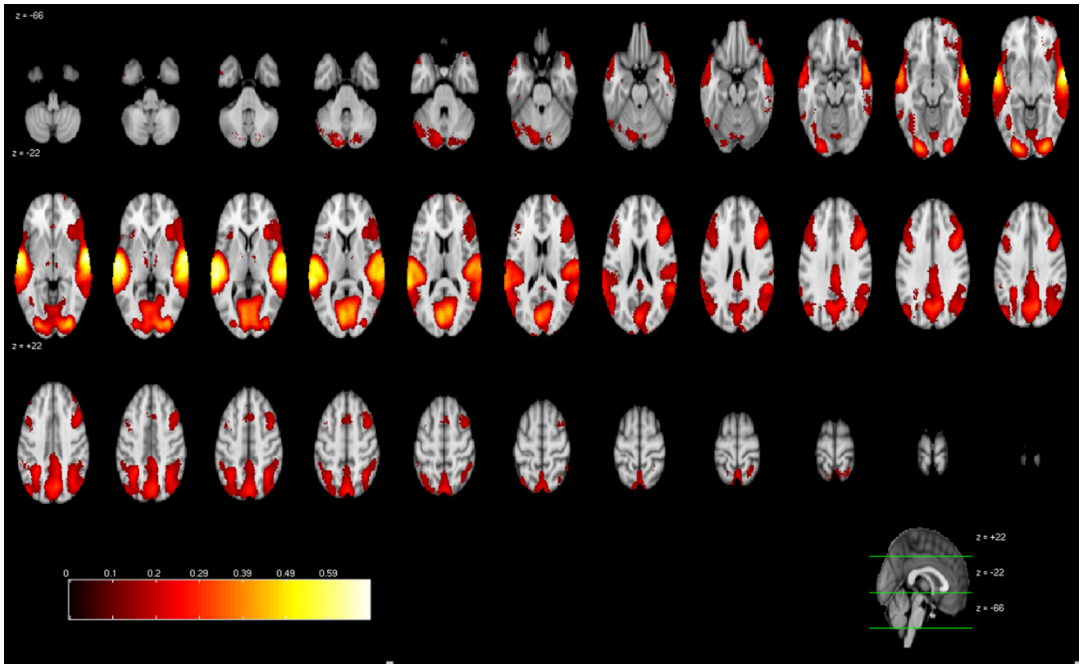


Figure 6.7. Brain regions with significant ISCs during social inclusion in healthy controls (p<0.001, FDR corrected). See Appendix 6.2.

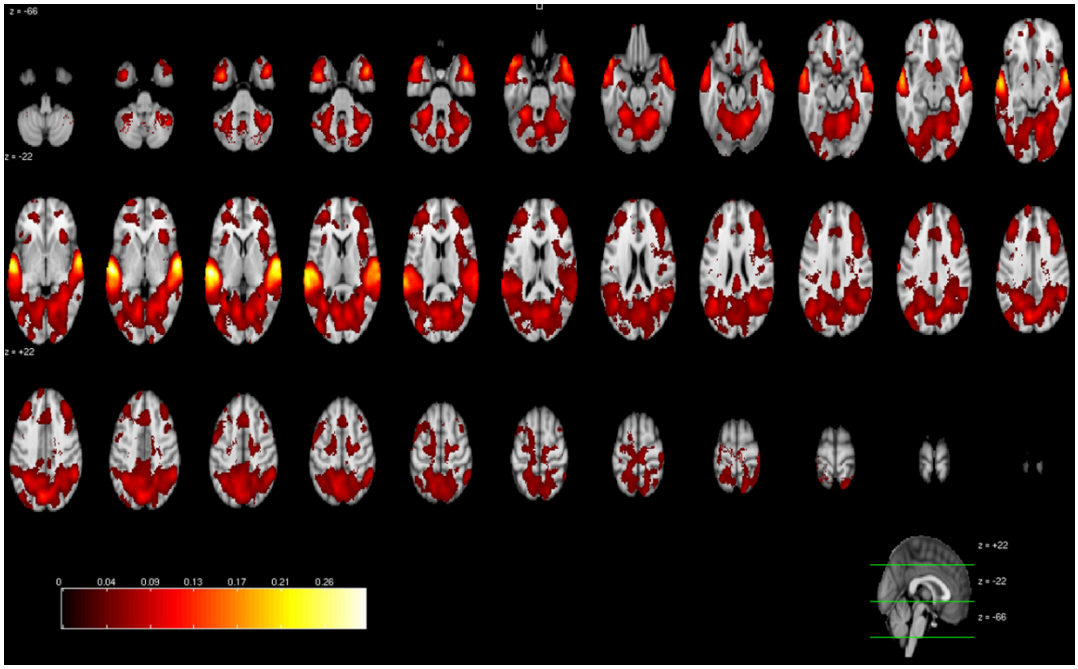


Figure 6.8 Brain regions with significant ISCs during social rejection in healthy controls (p<0.001, FDR corrected). See Appendix 6.3.

ISC Between Group Comparison

We next explored the between-group differences in ISC averaged over time between MDD and healthy controls and calculated summary statistics for each narrative separately (see Appendix 6.4). The summary statistic reflects the sum of the pairwise differences of ISC strength across groups, and is illustrated in Figure 6.9. During social inclusion, healthy controls, relative to MDD participants, exhibited greater ISC in large areas within the frontal cortex, anterior and posterior cingulate cortices, and bilateral posterior superior temporal gyrus (pSTG). In MDD participants, relative to controls, larger ISCs were observed in occipital visual cortex, with additional larger ISCs in inferior frontal gyrus and subgenual PFC. During *social rejection*, results also revealed greater ISC in MDD participants in the visual cortex, while controls exhibited greater ISC in the frontal-parietal cortex, bilateral STG and temporal poles.

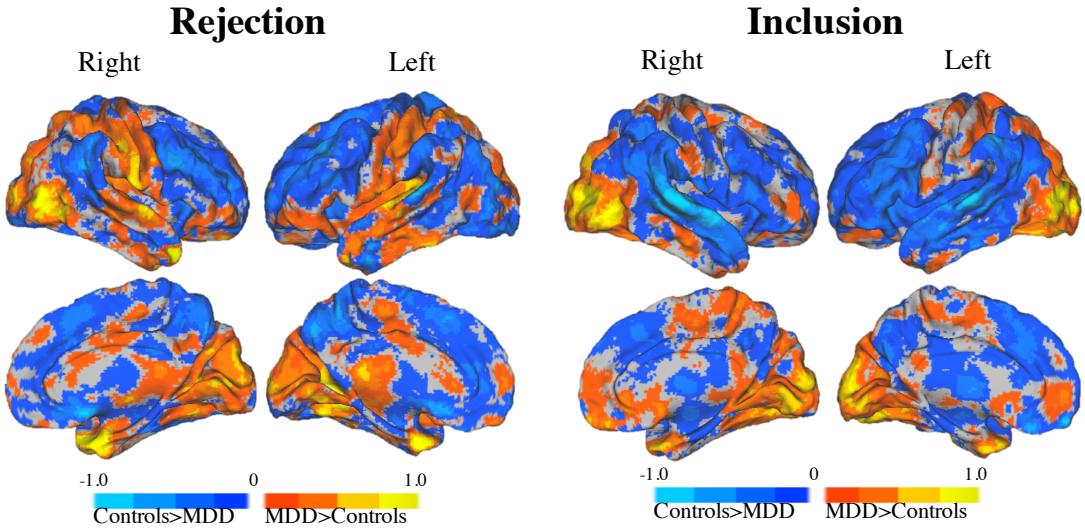


Figure 6.9. Brain regions with greater ISC in MDD compared to healthy controls (on red scale) and healthy controls compared to MDD participants (on blue scale) during s*ocial rejection* and s*ocial inclusion*. Summary ZPF maps have been rescaled from -1 to 1, $p<0.001$, FDR corrected. See Appendix 6.4 for table of brain activation.

Time Series Analysis

Next, we assessed the relationship between mean continuous affect ratings and the degree of inter-subject synchronization over time. Continuous affect ratings were used as regressors to predict voxel-wise ISC time courses in a GLM with voxel intensity reflecting the level of emotional synchronicity. This served to validate that the emotional narratives triggered reliable activity in emotion-related brain regions, in line with previous research on emotional synchronicity using the ISC approach (Nummenmaa et al., 2012). See Appendix 6.5 and Appendix 6.6 for data from healthy controls and MDD participants respectively. See Figure 6.10 for overview of ISC in brain regions correlated with increased negative valence and positive valence during social rejection and inclusion, respectively.

In healthy controls during social rejection, increases in negative valence were associated with greater ISC in in the dACC and bilateral insula. In contrast, increases in positive valence while listening to social rejection were associated with greater ISC in mOFC, ventral striatum, right hippocampus, and bilateral frontal and parietal control regions, including right Angular Gyrus. During social inclusion, positive valence was associated with increased ISC in ventromedial PFC (VMPFC), posterior ACC, ventral striatum and bilateral anterior hippocampus/amygdala, while lower positive mood for social inclusion memories revealed widely distributed heightened synchronicity with large ISCs in bilateral auditory cortex, vmPFC and bilateral inferior frontal gyrus.

In MDD participants, during social rejection, greater negative mood was associated with increased ISCs in bilateral inferior temporal gyrus, bilateral postcentral gyrus, right superior frontal medial gyrus, right fusiform gyrus, bilateral precuneus, and PCC. Greater positive valence during social rejection was associated with increased ISC in bilateral superior temporal gyrus, bilateral insula, bilateral amygdala, left hippocampus, left parahippocampal gyrus, dACC, superior and medial OFC. During social inclusion, as valence increased to positive, ISCs increased in MCC and dACC, right anterior insula, superior frontal (medial) gyrus, supplementary motor area, right

precuneus, bilateral supramarginal gyrus, and bilateral postcentral gyrus. Negative valence was associated with increased ISCs in bilateral caudate, bilateral thalamus, left inferior orbital frontal gyrus, left precentral gyrus, bilateral hippocampus, and large activations across the ventral visual cortex.

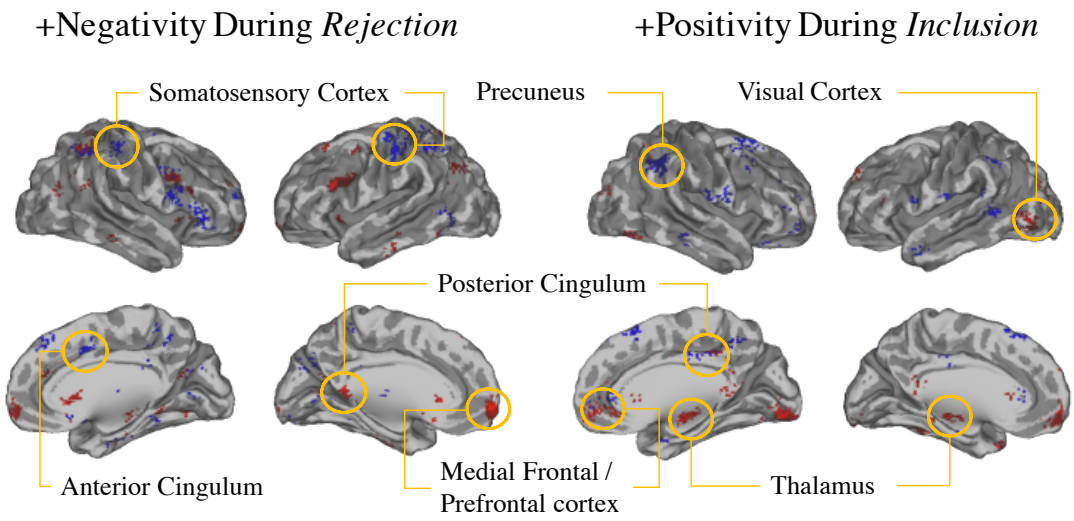


Figure 6.10. Brain regions with ISC correlated with greater *negative* valence in response to *social rejection* and greater *positive* valence in response to *social inclusion* for MDD (in blue) and healthy control participants (in red). All whole-brain results thresholded at $p<0.001$, $k=20$, uncorrected.

6.4 Discussion

This chapter represents the first attempt that we are aware of to investigate the degree of inter-subject synchronization in depressed and non-depressed individuals while listening to another's narratives of positive and negative social interactions. On a behavioural level, we firstly predicted that across groups affect would become more negative in response to the social rejection narrative and improve in response to the social inclusion narrative. This prediction was unsurprisingly met. Secondly, we predicted that the MDD group would exhibit greater decreases in mood in response to the rejection and social inclusion narrative overall, compared to healthy controls. This prediction was also met.

On a behavioural level, while Chapter 5 had presented brief, yet highly salient negative and positive social narratives, the present study involved extended five-minute auditory presentations with natural fluctuations in valence. This raised the question of whether the natural emotional dynamics contained within the narrative would reliably translate into salient overarching negative or positive mood over time. However, our findings suggest that, despite group differences, varying emotional saliency can be reliably elicited, incorporating natural fluctuations in mood as the social dynamic unfolds, with significant differences as a function of valence. This finding adds to the ecological validity of the work presented, in line with the previous chapters. On a neural level, we predicted that MDD participants would show less synchronicity in response to other-relevant emotionally salient information than healthy controls in brain regions associated with processing another's affective memories. This included empathic and regulatory areas, such as the supramarginal gyrus, posterior and middle cingulate cortex and mentalising areas, including the medial (pre)frontal cortex. We further predicted greater synchronicity in MDD in affective areas involved in self-relevant processing. This included areas such as the dACC and AI, relative to healthy controls. These findings would extend the findings reported in the neuroimaging studies in Chapter 4 and Chapter 5. These predictions were partially met. In line with previous ISC studies (Hasson et al., 2004a), our

findings revealed strong ISCs within 'proof-of-concept' regions involved in visual imagery, auditory processing, and also in regions underpinning self and other-relevant affective processing. Greater synchronization in visual and auditory sensory areas across both groups and conditions thus lends weight to the time-locked brain activity identified in key extra-sensory brain regions revealed by our ISC analysis and discussed below.

Healthy controls exhibited affective synchrony in the ACC, bilateral insula and postcentral gyrus when listening and engaging with another's negative social rejection experiences. This mirrors our findings using the traditional GLM approach in Chapter 4, despite being a data-driven approach without stimulus-based modelling. In addition, while listening to the social inclusion narrative, controls revealed increased synchrony in precuneus, PCC and ACC, supramarginal gyrus and subgenual PFC. Similarly, these findings of increased activity in empathic and affective regions mirror those outlined in Chapter 5 in healthy controls relative to MDD. In addition, the finding of increased ISCs in the subgenual PFC provides cross-modal support for the notion that this region is crucial in the integration of social signals and limbic feedback (Drevets et al., 1997; Drevets, Savitz, & Trimble, 2008). Additional ISCs in midline and frontal regions may also indicate greater levels of mentalisation in healthy controls (Feng et al., 2016; Meyer et al., 2013, 2014) and affect sharing, crucial to the empathic response (Hooker, Verosky, Germine, Knight, & D'Esposito, 2010; D. P. Kennedy & Adolphs, 2012; Vrtička et al., 2013).

In depression, listening to the social rejection narrative evoked ISCs in somatosensory cortices, right anterior insula and temporal poles (TP), but not in regions associated with empathic processing, as predicted for healthy controls. However, these findings do fall in line with observing a stranger's social rejection in the Cyberball task (Meyer et al., 2013, 2014), albeit in a healthy control population. While the functionality of the temporal poles (TP) in the context of socio-emotional processing remains to be fully examined (Cabeza & Nyberg, 2000), emerging evidence suggests that this area may integrate dorsal (auditory), medial (olfactory)

and ventral (visual) perceptual streams underlying social and emotional processing (Olson, Plotzker, & Ezzyat, 2007). In addition, during evocative negative emotional processing, the TP may be reactivated even when emotions are merely imagined – in line with our paradigm (Olson et al., 2007). In contrast, the social inclusion narrative evoked ISCs in affective and reward regions - the nucleus accumbens (NAcc) and ACC. Previous functional imaging studies found that activation in reward regions, including the NAcc, was associated with the perception of pleasant emotional stimuli (Sabatinelli et al., 2007). The NAcc activation was found to also extend into the subgenual PFC, thought to be impaired in depression, with early neuroimaging evidence suggesting glial reduction (Ongür, Drevets, & Price, 1998) and abnormalities in gray matter volume (Drevets et al., 1997, 2008). Finally, activity in the ACC mirrors previous findings of positive social processing of autobiographical memories of inclusion (and rejection), described in Chapter 4. Thus, the heightened sensitivity to both self and other relevant social signals in depression highlights a potential role for the ACC in evaluating the socio-emotional state independent of valence.

To further elucidate the time-locked sensitivity to unfolding social interaction, we examined the relationship between the elicited emotion derived from the continuous affective ratings in response to the two social narratives and the regional neural synchronicity within each group. This revealed strong ACC and insula activity across both conditions and both groups in response to changes in mood. This suggests that continuous processing of incoming social signals modulated cingulate cortical activity with strong agreement across groups. Previously, Etkin, Egner, and Kalisch, (2011) suggested that evaluative cognitive control in response to emotional exposure includes the appraisal of positive signals and its evaluation against a negative emotional appraisal within this network. Similarly, a study investigating the relationship between ISC and valence in response to emotional movies revealed that as valence decreased from positive to negative, ISC increased in regions involved in emotional processing, including the medial prefrontal and anterior cingulate cortex, and in the default-mode network, including the precuneus, and ventromedial

prefrontal cortex (Nummenmaa et al., 2012, 2014). This contributes to the growing evidence base that activity in the anterior and posterior cingulate cortices may be associated with a range of higher-order cognitive processes, including mentalising, and self-monitoring, in addition to emotional processing per se (Amodio & Frith, 2006; Mar, 2011). This interpretation is underscored by previous animal models and neuroimaging studies suggesting a social evaluative function in the ACC and medial PFC (Apps et al., 2012, 2016; Apps & Ramnani, 2014). Using the ISC approach, our findings therefore provide further encouraging support for the notion of a neural network sensitive to social evaluation taking into account positive and negative social cues. As described within the discussion of previous chapters, this falls well within the theoretical accounts of social processing, such as the social risk hypothesis of depressed mood, or the social rank hypothesis and sociometer theory.

In addition, the social risk hypothesis of depressed mood suggests a heightened neural sensitivity to social cues in depression, which may be reflected in increased activity within the social evaluative network described above. This assumption was supported by empirical findings in Chapter 4; however, it remains to be explored using the ISC approach. In fact, very few studies to date have investigated differences in the degree of inter-subject synchrony between groups, let alone clinical disorders. Studies investigating differences in social cognition using ISC analyses (Hasson et al., 2004) have focused on socio-emotional deficits in schizophrenia (Kim et al., 2008) and autism (Hasson et al., 2010; Salmi et al., 2013), with the latter revealing less synchronised brain activity across ASD listeners than controls in regions implicated in empathetic and social evaluation processing. These regions included the insula, PCC and ACC, caudate nucleus, precuneus, and supra-marginal gyrus (Salmi et al., 2013). The greater variability in perceptual and sensory processing was attributed to the known deficits in social perception and action recognition in autism, with decreased synchronisation reflecting a more heterogeneous neural response.

Similarly, our results suggest greater ISC activity in healthy controls in areas involved in social and affective cognition across both social narratives when comparing

intersubject correlations between depressed and never-depressed individuals. This includes the superior temporal gyrus (STG), temporal poles, and to some extent ventromedial prefrontal cortices. In contrast, MDD participants exhibited greater activity in primary visual cortices across narratives, and greater activity in the precentral gyrus, associated with physical pain processing during social rejection. Previous studies have proposed a role for mental imagery in cognitive processing, including suppression or distorted appraisals, which may exacerbate and/or maintain depression (Weßlau & Steil, 2014). This is illustrated in a greater proportion of negative (relative to positive) images being generated, characterized further by greater vividness and distress, correlated with depressive symptom severity (Weßlau, Cloos, Höfling, & Steil, 2015). Our findings of elevated visual cortex activity in depressed relative to healthy controls thus begs the question whether mental imagery of dynamic social interactions may elicit a different neural response in MDD, perhaps due to greater perceived 'realness' (Mathews, Ridgeway, & Holmes, 2013). However, large ISCs in visual cortices across groups and narratives overall lend weight to the notion of 'seeing with the mind's eye' when engaging in mental imagery, in line with previous findings (Costa, Lang, Sabatinelli, Versace, & Bradley, 2010; Pearson, Naselaris, Holmes, & Kosslyn, 2015; Sabatinelli et al., 2007).

The results presented in this chapter may be further explained when examining the nature of the task more closely. The STG, activated more strongly in controls relative to MDD, is implicated in language comprehension, and while attending to auditory signals in the presence of background noise within dynamic social contexts (Vander Ghinst et al., 2016). Our task involved attending to an extended auditory social narrative within an inherently noisy environment, as the speaker was being recorded while simultaneously being scanned. While there is limited evidence on how emotional signals in the voice are processed in the human brain as opposed to visual stimuli, it is crucial to detect small fluctuations in prosody, gesture, as well as facial expressions to fully gauge another's intentions, thoughts and actions (Adolphs et al., 2002; D. P. Kennedy & Adolphs, 2012). Greater ISC in the STG may therefore emphasise the ability of healthy controls to extract emotionally salient features within

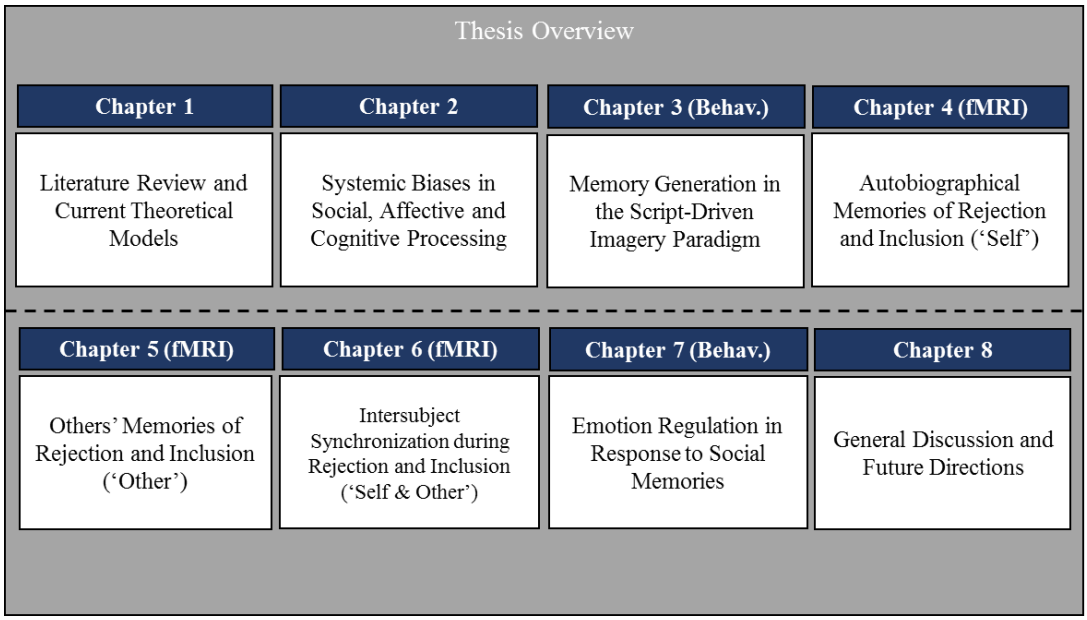
a social narrative, a process that may be disrupted in MDD under the present task conditions.

Curiously, a study investigating ISC in response to rhetorically powerful compared to weaker speeches similarly identified strong and regionally localized ISCs in the STG and medial PFC (Schmalzle et al., 2015). This level of 'resonance' may be mirrored in our findings. Prioritising the most salient features or intent to achieve engagement within a narrative requires a dedicated attentional mechanism, which may be impaired in MDD relative to controls. Instead, attentional resources in MDD appeared to be shifted towards the visual imagery of the scenes presented. Alternatively, decreased regional ISCs in key socio-affective areas may also reflect a more heterogeneous or idiosyncratic response in MDD relative to controls, despite all participants being exposed to the same narratives. This may be due to more inward directed self-referential and ruminative processing, in line with previous notions of heightened self-focused attention in MDD (Gotlib et al., 2004).

In sum, we used a novel approach to study brain mechanisms while listening to another's personal experience of social rejection and inclusion in a naturalistic social context. This has highlighted several important themes. Firstly, the ISC approach can be used to identify primary sensory cortices as well as extra-sensory activation in social, affective and empathic cortical areas. This suggests that social affective stimuli can lead brains to synchronise or 'tick together' in a coherent manner even in the absence of constrained presentations, as revealed by the data-driven approach. Secondly, co-activation of ACC and insula in response to social rejection and inclusion narratives across groups further highlights the social evaluative function posited in previous chapter. However, contrary to the findings described in Chapter 4 and Chapter 5, group comparisons revealed greater synchrony in healthy controls in key social cognitive areas, such as the STG compared to depressed individuals who exhibited greater regional ISCs in the visual cortices. Thus, deficits in social functioning in depression may be in part reflected by more individualistic, heterogeneous neural responses in line with reduced cortical synchrony when

processing other relevant social affective information. Considering these results, implementing the ISC approach to examine the neural basis of social interactions points to exciting lines of future research. However, given its early state of development, results should be interpreted with caution.

CHAPTER 7. EMOTION REGULATION STRATEGIES IN RESPONSE TO SOCIAL MEMORIES



7.1 Introduction

In this chapter, we extend our investigation from emotion elicitation to emotion regulation to address individual differences and cognitive mechanisms in detecting and responding to interpersonal emotional signals. In the previous chapters, our findings revealed that autobiographical memories of social rejection, inclusion and neutral social experiences can reliably elicit salient emotions in the present using the ecologically valid approach of script-driven imagery. The behavioural study presented in this chapter therefore aims to utilise social autobiographical memories to examine emotion activation and regulation in a sample of healthy individuals. It presents an exploratory attempt at implementing this approach to further address pertinent questions within the social affective research context, and with regards to socio-emotional processing.

In responding to salient emotional cues in the environment individuals tend to adopt regulatory goal-directed strategies, characterised by two main processes; (1) the ability to translate a regulatory goal into a behavioural response, and (2) the ability to disengage with a maladaptive regulation strategy once initiated (Gross, 1998). These encompass voluntary and automatic processes that influence the occurrence, magnitude, duration, and expression of a goal-directed emotional response (Gross, 1998; Sheppes, Suri, & Gross, 2015), conceptualised within a dual-process framework (Gyurak, Gross, & Etkin, 2011). Explicit voluntary regulation strategies include the cognitive reappraisal of meaning associated with an emotional context, or the active attentional disengagement from negative stimuli, while implicit regulation strategies include affect labelling or 'putting your feelings into words' with the aim of reducing subjective distress (Gross, 1998; Moyal, Henik, & Anholt, 2014).

Cognitive reappraisal is one of the most widely implemented explicit emotion regulation strategies, which can reduce depressive symptom severity and reduce negative affect by actively reframing a meaning associated with an emotional context (Gross, 1998; Moyal et al., 2014). An alternative to cognitive reappraisal is the active disengagement from a negative stimulus and attentional reallocation (Moyal et al.,

2014). While adaptive in reducing negative affect in response to highly intense stimuli in healthy individuals, in depression, the use of rumination or maladaptive distraction, is intrinsically linked to greater symptom severity (Sheppes et al., 2015). However, the use of adaptive strategies to regulate social emotions has revealed inconsistent results (Aldao, Nolen-Hoeksema, & Schweizer, 2010), although findings from Chapter 2 suggest that difficulty in emotion regulation is significantly associated with a range of social behaviours, such as increased submissive behavior, interpersonal sensitivity, and involuntary subordination in depressed individuals, relative to healthy controls. This suggests that difficulty in emotion regulation may be inherently linked to depressed individuals failing to fulfil regulatory, socially-oriented, goals, as described within the social rank theory (Allan & Gilbert, 1997; Gilbert et al., 2007) and social risk hypothesis of depression (Allen & Badcock, 2003), thus perpetuating the presentation of depressive symptoms.

In addition to the explicit regulation strategies mentioned above, affect labelling, or putting your feelings into words (e.g. 'I am feeling… happy') emerged as an adaptive implicit regulation strategy from within the practice of mindfulness (Moyal et al., 2014). Mindfulness more generally is thought to reduce distress by increasing emotional awareness, thereby reducing the immediate impact of negative self-referential processing, and focusing instead on goal-directed behaviours (Burklund, David Creswell, Irwin, & Lieberman, 2014; Creswell & Lindsay, 2014). Previous studies have found that putting your feelings into words, integral to mindfulness practice, can incidentally downregulate affect in response to emotional faces (Lieberman et al., 2007) and highly distressing negative images on a neural level, when contrasted with passive watching (Lieberman, Inagaki, Tabibnia, & Crockett, 2011), even in the context of exposure therapy for spider phobia (Kircanski, Lieberman, & Craske, 2012).

Importantly, while affect labelling is not considered a more adaptive emotion regulation strategy compared to cognitive reappraisal or distraction, perhaps due to its incidental nature, (Black, 2013; Lieberman et al., 2011), it may have potential

positive carry over effects in other domains, including executive control and working memory (Teper et al., 2013; J. M. G. Williams, 2010; L. E. Williams, Bargh, Nocera, & Gray, 2009). As such, affect labelling may represent a more advantageous emotion regulation strategy, as opposed to explicit regulation strategies constrained in their effect to the regulatory goal at hand. However, self-reported belief in the efficacy of the implicit affect labelling strategy is significantly lower relative to for instance, cognitive reappraisal (Gyurak, Gross, & Etkin, 2011a), with self-report biases potentially limiting the interpretation of behavioural comparisons in the absence of physiological markers (Kircanski et al., 2012). However, investigating the effectiveness of affect labelling nonetheless warrants further investigation, given both the advantages and potential carry-over effects outlined above, and the discrepant findings regarding the adaptive nature of existing emotion regulation strategies to date (Burklund et al., 2014; Gyurak et al., 2011a; Lieberman et al., 2011; Lutz et al., 2014; Opialla et al., 2014).

The latter point is especially pertinent, as a major constraint within the existing emotion regulation literature is the tendency to examine explicit regulation tasks in response to experimentally constrained emotional stimuli, and frequently in the absence of external stressors known to impact the implementation of cognitive control (Raio, Orederu, Palazzolo, Shurick, & Phelps, 2013). Existing 'effortful' emotion regulation strategies may be reduced in their efficacy within realistic affective contexts (Burklund et al., 2014; Gyurak et al., 2011a; Lieberman et al., 2011; Lutz et al., 2014; Opialla et al., 2014), perhaps due to limited attention to the importance of sociality within emotion, despite being an inherent part of the regulatory process (Shuman, 2013). Goal-directed regulatory behaviours are frequently aimed at modifying the current social contexts (Leary, 2004; Vrtička et al., 2013), encompassing others' appraisals. This is demonstrated in amplified positive emotions in the workplace (Wong, Tschan, Messerli, & Semmer, 2013) and social decision-making as a function of anticipated regret about fair and unfair behaviour (Van der Schalk, Bruder, & Manstead, 2012). In these contexts, implicitly labelling affect may offer an 'easier' approach to implement within naturalistic socio-affective

contexts, compared to the more 'effortful' approach required in cognitive appraisal. In addition, our approach addresses the problem of low ecological validity in emotion regulation paradigms by modelling the real-world as closely as possible using autobiographical memories (see Chapter 3 for more detail). This encompasses dynamic affective environments and highly salient negative and positive emotions derived from social interactions. As sociocultural contexts are known to modulate the use of emotion regulation strategies (De Leersnyder, Boiger, & Mesquita, 2013; McRae, Heller, John, & Gross, 2011), script-driven imagery may thus provide a useful paradigm to further explore emotion regulation strategies within distinctly social contexts. Chapter 3 provided the initial validation of this paradigm in the context of memory generation and saliency over time.

This chapter will extend this validation to the memory presentation session, as well as investigating affect labelling as an effective emotion regulation strategy. There are two main aims: i) to further validate the activation of salient emotions in response to autobiographical script-driven memories of social rejection and inclusion and ii) to examine the effectiveness of affect labelling as an implicit emotion regulation strategy in healthy controls in response to autobiographical memories of social rejection and inclusion within a realistic affective context.

Our hypotheses were as follows;

HYPOTHESES

- Memories involving social rejection, social inclusion, and neutral social experiences will reliably modify mood across participants in a script-driven memory presentation session, with the recall of rejection memories resulting in increased negative mood, the recall of inclusion memories resulting in increased positive mood, and neutral memories resulting in relatively unchanged mood.

- Affect labelling will result in greater modification in mood in response to listening to memories of rejection and inclusion relative to a control condition involving describing and attending to memories, only.

7.2 Methods and Materials

Participants

Thirty-four healthy participants (22 female; 39.32±16.73 years) with no history of Major Depressive Disorder or other mental health problems, normal or corrected-to-normal vision and no hearing impairment, were recruited from volunteer panels at the MRC Cognition and Brain Sciences Unit and the University of Cambridge. All participants completed two behavioural research sessions, a memory generation session (described in Chapter 3) and a memory presentation session. Full demographics can be found in the results section in Table 7.2.

Clinical Interview and Social, Affective and Process Self-Report measures

A battery of social, affective and process self-report measures was undertaken with respect to all participants. See Chapter 2 for a full description.

Experimental Task

Memory Generation (Session I)

In the initial behavioural memory-generation session, participants provided 9 autobiographical memories consisting of 3 social rejection memories, 3 social inclusion, memories and 3 neutral social memories (e.g. shopping in the presence of other people) and affective ratings with respect to current mood state at the time of memory recall and mood state at the time of the original experience. See Chapter 3 for detailed information on the memory generation methodology. The generated autobiographical memory scripts represented the stimuli for the following memory presentation session. Audio stimuli of autobiographical memories were recorded and edited using Adobe® Audition® (2009 Adobe Systems, version 3.0).

Emotion Regulation Task (Session II)

In the following behavioural session, the emotion regulation task consisted of three consecutively presented 30-second same-type autobiographical memory scripts

within each of the three blocks (neutral, rejection, inclusion), generated in the previous session. Participants were instructed to listen while imagining experiencing the event in the present and to pay attention to their emotional response during the event and in the brief silence that followed, under three experimental conditions: (1) 'attend', (2) 'describe' and (3) 'label'. In these conditions, participants were instructed, respectively, to (1) only listen and imagine, (2) describe the imagined scene by selecting one of 16 possible neutral descriptive words or (3) label emotions elicited by the scene by selecting one of 16 possible social emotion words. In the (1) 'describe' and (2) 'label' condition, participants were prompted with a wheel displaying either (1) neutral descriptive words or (2) social emotion labels. The wheels were presented at three time segments: mid-script, immediately post-script and after a brief period of silence. For an overview of the paradigm, see Figure 7.1.

After each audio script, there was a 20-second period of silence during which participants were asked to mentally elaborate on the emotionally salient aspects of the previous memory (Lanius et al., 2002). Participants rated their current mood prior to each block following a brief 30-second closed-eye baseline period and following each audio script. Participants rated levels of current subjective distress, rejection, inclusion and positivity on the same 11-point Likert scale as in the initial behavioural session. The positive and negative scores were combined for the analyses into composite mood scores (See Chapter 3). In addition, participants provided ratings of how well they were able to imagine themselves experiencing the event in the present ('imaginability'), as well as of vividness and intensity. An additional 30-second washout clip depicting an ocean sunset was presented between the rejection and inclusion blocks to encourage mood repair. The order of each condition was randomised within a block and indicated by a 3-sec instruction cue immediately preceding each script. The order of individual scripts within each block was randomised. The total approximate task duration was 25 minutes. See Figure 7.1 below.

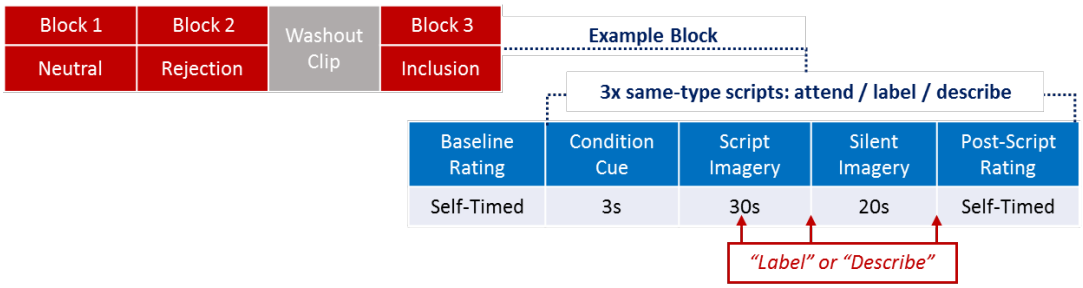


Figure 7.1 Script-driven imagery paradigm for emotion regulation task.

Auditory presentation of the stimuli was delivered via headphones connected to a desktop PC running Matlab (Mathworks) and presented using the psychophysics toolbox (Brainard, 1997; Pelli, 1997). The effective viewing distance was 50 cm with a resolution of 1024 x 768 pixels and a visual angle of 16.7 degrees. Participants were asked to provide affective ratings on the 11-point mood scale using arrow keys. The neutral descriptive and social emotion labels were presented on screen in a circular wheel, from which participants were instructed to select one label as quickly as possible (see Figure 7.2). The 14 social emotion labels were derived from a series of emotions which had been explicitly identified as representing social emotions by a range of authors (see Hareli & Parkinson, 2008, for review). A list of neutral descriptive words for the 'describe' condition was independently generated with the aim of describing scenes. Both lists contained optional labels of 'none' and 'other', in addition to the social emotions or neutral descriptive words. To ensure low emotional valence for descriptive and high emotionality for the social emotion labels, both word lists were cross-referenced with the Affective Norms for English Words (ANEW) database, which provides a set of normative emotional ratings for a large number of words in the English language (M. M. Bradley & Lang, 1999).

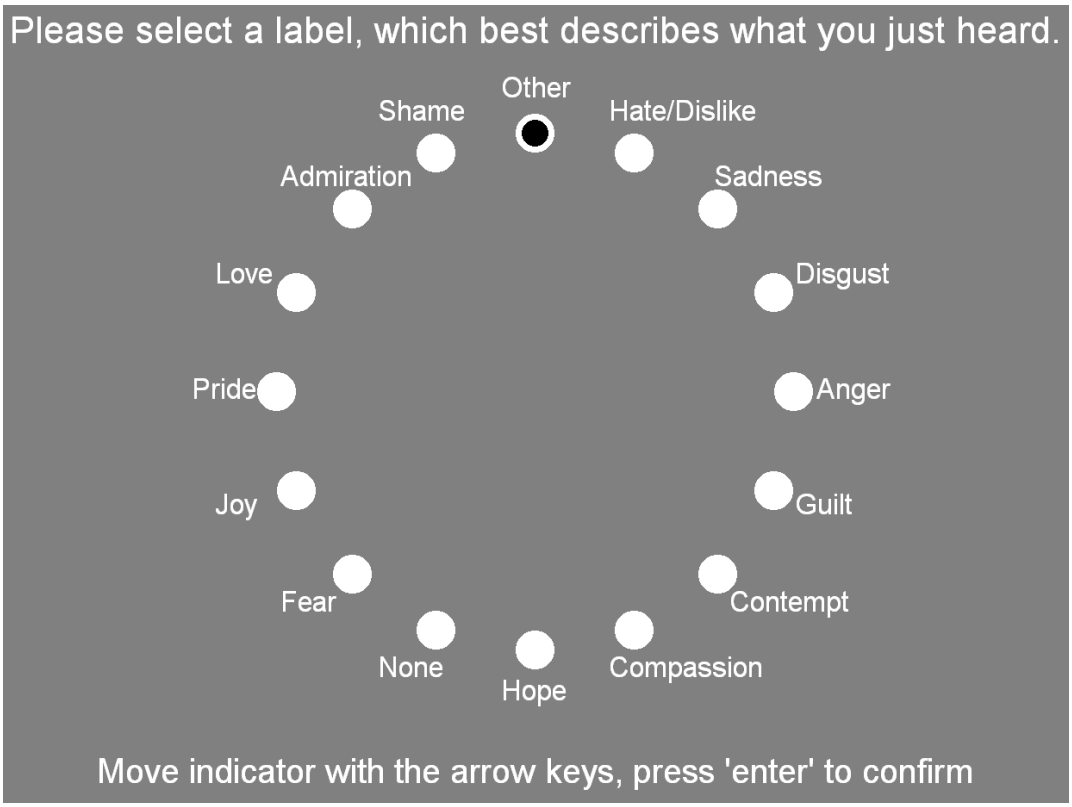


Figure 7.2 Screenshot from the emotion regulation task, depicting a range of emotion labels within the 'label' condition, from which participants are prompted to select one as quickly as possible.

Table 7.1

Social emotion labels ('label') and neutral descriptive words ('describe') used in the emotion regulation task

Number	Social Emotion Labels	Neutral Descriptive Words
1	Hate/Dislike	Large
2	Sadness	Small
3	Disgust	Active
4	Anger	Busy
5	Guilt	Noisy
6	Contempt	Warm
7	Shame	Tall
8	Admiration	Bright
9	Love	Cold
10	Pride	Dark
11	Joy	Cool
12	Fear	Short
13	Hope	Quiet
14	Compassion	Hot

Experimental Procedure

The procedure for the memory generation session is described in Chapter 3. One week later, in this 1.5-hour memory presentation session, participants provided informed consent once more and were then familiarised with the wheels depicting (1) neutral descriptive words or (2) social emotion labels prior to the task, using laminated cue cards. A practice run preceded the experimental block to familiarise participants with the task, in which participants were instructed to listen to brief 30-second audio-scripts consisting of news segments describing neutral events (e.g., a gardening show) under the three experimental conditions described above. Participants then performed the behavioural emotion regulation task described above. Immediately after the main task, participants were administered a battery of social, affective and process measures (see Chapter 2). At the end of the session participants were thanked for their time and debriefed.

Statistical Analysis

Behavioural Appraisal

Affective ratings, vividness and emotional intensity scores acquired in session I were averaged for each memory type and then compared between time of experience and time of recall as described in Chapter 3. Session II change scores in composite mood were calculated from affective ratings acquired in the second session memory presentation task before and following each memory, and analysed using a repeated measures 3x3 ANOVA with condition (affect label/describe/attend) and memory type (rejection/inclusion/neutral) as within-subject factors. Vividness, intensity and imaginability ratings acquired in session II were analysed using a repeated measures ANOVA with memory type (neutral/rejection/inclusion), and condition (affect label, attend, describe) as within-subject factors.

7.3 Results

Demographic characteristics

Table 7.2

Demographic characteristics of the participants.

		N=34
Sex		
	Male	12
	Female	22
Age, years		
	Mean *(SD)*	36.24 *(16.65)*
National Adult Reading Test		
	Mean *(SD)*	7.68 *(6.03)*
Ethnicity		
	Caucasian	33
	Other	1
Marital Status		
	Single / Unmarried	17
	Married	6
	Separated / Divorced	5
	Other	6
Education		
	Completed Year 10	1
	Completed Year 12	10
	Completed Bachelors degree	16
	Completed Masters degree	3
	Completed PhD	0
	Other	4
Employment Status		
	Employed	19
	Unemployed	12
	Student	0
	Other	3
Employment		
	Full Time	6
	Part Time	10
	Other	18

BEHAVIOURAL APPRAISAL

Memory Generation (Session I)

In the first step, we investigated whether the memories recalled in the memory-generation session had maintained their saliency over time since the original event. The results are presented in Chapter 3. Results suggested the memories maintained sufficient emotional saliency over time and were thus deemed appropriate for use in the memory presentation session.

Emotion Regulation Task (Session II)

Six participants' responses to the experimental conditions were excluded from the final analysis where no descriptive or affective label was provided when prompted suggesting lack of engagement with the experimental manipulation. Mean affect change as a function of memory type are presented in Table 7.3, while mean affect change as a function of regulation strategy (condition) is presented in Table 7.4. Results suggest that the affect labelling condition resulted in a marginally greater change in mood numerically, while mean change in mood was lowest for the describe condition. Overall, results suggest that mood was most elevated following inclusion memories, followed by neutral and lastly rejection memories, irrespective of condition (see also Figure 7.3). Mean vividness, intensity and imaginability scores are presented in Table 7.5.

To investigate the response to the emotional memories in the memory presentation session, we compared the change in composite mood scores obtained during the session immediately before and after each memory was presented, as well as vividness, intensity and imaginability ratings. Affective change ratings were analysed using a within-group 3x3 ANOVA with condition (affect label/describe/attend) and memory type (rejection/inclusion/neutral) as the within-group factors. Mauchly's test of sphericity was violated for memory type (x^2=10.96, p=0.004) and the interaction of condition and memory type (x^2=20.04, p=0.02) and results aree reported using a Greenhouse-Geisser correction. For vividness, intensity and imaginability ratings, Mauchly's test of sphericity was not violated, hence sphericity is assumed.

Table 7.3

Mean change in mood by memory type for the emotion regulation task

Memory Type	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Rejection	-6.65	0.64	-7.97	-5.33
Neutral	0.40	0.47	-0.57	1.38
Inclusion	4.43	0.62	3.15	5.71

NB: Lower scores represent more negative mood with a range of -10 to +10 (most positive)

Table 7.4

Mean change in mood by regulation strategy (condition) for the emotion regulation task

Condition	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Affect Label	-.81	.41	-1.66	.04
Attend	-.70	.36	-1.45	.04
Describe	-.31	.29	-.90	.28

NB: Lower scores represent more negative mood with a range of -10 to +10 (most positive)

Table 7.5

Mean vividness, intensity and imaginability ratings for emotion regulation task

Measure	Memory Type	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Vividness	Rejection	7.2	0.38	6.41	7.99
	Neutral	6.77	0.39	5.96	7.57
	Inclusion	7.55	0.35	6.83	8.27
Intensity	Rejection	7.33	0.4	6.51	8.16
	Neutral	6.22	0.45	5.29	7.15
	Inclusion	7.16	0.45	6.22	8.1
Imaginability	Rejection	7.33	0.35	6.61	8.06
	Neutral	7.20	0.36	6.45	7.96
	Inclusion	7.74	0.36	7.00	8.48

Affective change ratings results revealed a main effect for memory type ($F[1.49,40.18]=84.36$, $p<0.001$, $\eta^2=0.76$), but no significant main effect of condition ($F[2,54]=1.28$, $p=0.28$, $\eta^2=0.04$) nor an interaction ($F[3,81.28]=1.43$, $p=0.24$, $\eta^2=0.05$). Bonferroni corrected pairwise comparisons revealed mood change was significantly different between all three memory types (all $p<0.001$) with greatest increases in negative mood in response to rejection memories, followed by a significant improvement in mood following inclusion memories and no significant change in mood following neutral memories. The greatest mean difference in mood was observed for rejection memories compared to inclusion memories (-11.08±1.08), relative to rejection compared to neutral (-7.06±0.79) and inclusion compared to neutral (-4.02±0.67).

Vividness ratings revealed a significant main effect for memory type ($F[2,44]=5.35$, $p=0.01$, $\eta^2=0.20$), but no main effect for condition ($F[2,44]=1.51$, $p=0.23$, $\eta^2=0.06$) and no significant interaction ($F[4,88]=0.86$, $p=0.49$, $\eta^2=0.04$). Planned comparisons of memory type revealed a significant difference in vividness between neutral and inclusion memories (-0.78±0.24, $p=0.01$), while other comparisons of neutral relative to rejection (-0.43±0.26, $p=0.31$) and inclusion relative to rejection memories (0.35±0.22, $p=0.40$) were not significantly different. However, while not statistically significant, numerically, rejection memories were rated as most vivid, followed by inclusion and then neutral memories (see Table 7.5).

Intensity ratings revealed a significant main effect for memory type ($F[2,44]=8.03$, $p=0.001$, $\eta^2=0.27$), but no main effect for condition ($F[2,44]=0.93$, $p=0.40$, $\eta^2=0.04$) and no significant interaction ($F[4,88]=1.40$, $p=0.45$, $\eta^2=0.04$). Planned comparisons of memory type revealed a significant difference in intensity ratings between neutral and inclusion (-0.94±0.29, $p=0.01$) and rejection memories (-1.12±0.34, $p=0.01$), while rejection memories were not significantly different from inclusion memories (0.17±0.27, $p=1.00$). Overall, inclusion memories were rated as most intense, followed by rejection and then neutral memories (see Table 7.5).

Imaginability ratings revealed no significant main effect for memory type ($F[2,44]=2.57$, $p=0.09$, $\eta^2=0.11$), condition ($F[2,44]=0.34$, $p=0.72$, $\eta^2=0.02$) or interaction ($F[4,88]=1.72$, $p=0.153$, $\eta^2=0.07$) indicating that all memories were comparably imaginable across all memory types and conditions, suggesting the script-driven paradigm was successfully implemented. See Table 7.5.

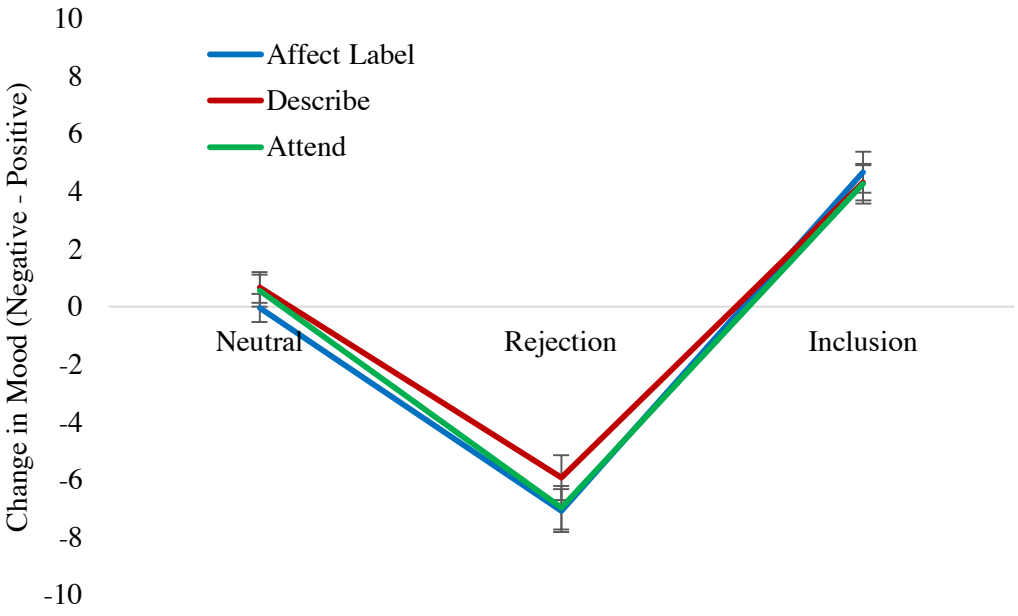


Figure 7.3. Mean change in mood ± 1SE by regulation strategy (condition) and memory type in the emotion regulation task. Results reveal significant change in mood as a function of memory type but not as a function of regulation strategy.

7.4 Discussion

This chapter investigated three emotion regulation strategies for modulating salient emotions of rejection and inclusion elicited using script-driven imagery in a novel implementation. The first aim was to replicate the validation of script-driven imagery as an effective mood induction in eliciting positive and negative social emotions within the memory presentation session, as already demonstrated in Chapter 4. The second aim was to compare the emotional regulatory impact of affective labelling, and descriptive labelling relative to passive listening in response to autobiographical memories of social rejection and inclusion within a naturalistic affective context. The study revealed two main findings. Firstly, we replicated the finding that script-driven imagery used in the emotion regulation task could successfully activate salient social emotions and changes in mood, in line with our predictions. This is further supported by comparable vividness and intensity across inclusion and rejection memories, as well as comparably imaginability across all memories. Secondly, the comparison of emotion regulation strategies revealed no significant differences between affect labelling, describing and passive listening with respect to negative and positive change in mood, in contrast to our predictions.

Successful mood induction in the main experimental task within the memory presentation session underscores the utility of script-driven imagery in eliciting salient emotions from social autobiographical memories. These findings are novel as previous research implemented this paradigm primarily in PTSD populations by eliciting highly arousing memories from a single or limited number of events (Beckham et al., 2007; Frewen et al., 2008, 2010, 2011; Kleim et al., 2010; Lanius et al., 2002, 2003; Lindauer et al., 2004). Thus, this chapter extends the findings from Chapter 3 by further validating the script-driven imagery paradigm in a population of healthy participants, providing support for the implementation of this approach in social affective research contexts and clinical populations, as described in Chapter 4-6.

However, comparing emotion regulation strategies revealed more complicated findings. The contrast of affect labelling compared to describing and attending allowed for an investigation of affect labelling as an adaptive implicit emotion regulation strategy, as opposed to comparing it to more explicit regulation strategies, such as cognitive appraisal. However, studies investigating affect labelling have revealed inconsistent findings (Burklund et al., 2014; Gyurak et al., 2011a; Lieberman et al., 2011; Lutz et al., 2014; Opialla et al., 2014). While previous findings emphasised the importance and utility of 'putting your feelings into words' (Kircanski et al., 2012; Lieberman et al., 2007), our study suggests that labelling with words fails to significantly modulate positive or negative mood beyond passively attending.

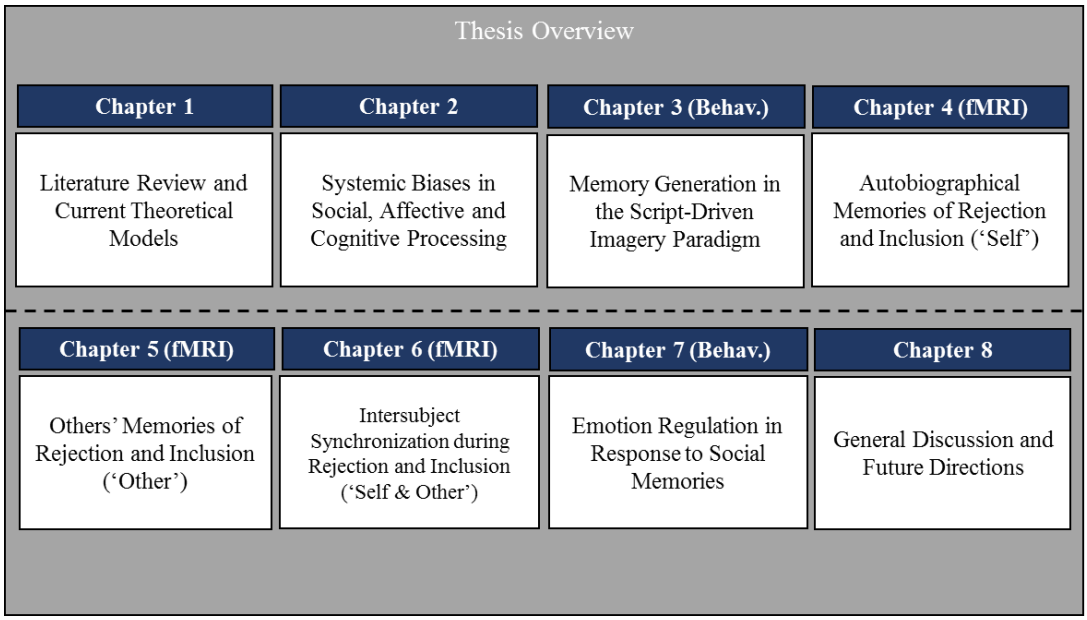
An important consideration at the outset of this study involved the examination of intensity, vividness and imaginability at both the time of experience (as retrospectively rated) and the time of recall to achieve consistency across sessions for the retrieved memories used in the experimental session. This was validated in Chapter 3. It could, however, be the case that although memories recalled within the session were emotionally salient, as demonstrated by the impact on mood, the emotion elicited was insufficiently arousing to the extent that it required regulation. This is reflected in the attenuation in vividness and intensity over time and over sessions. In addition, as previously suggested, affect labelling may reveal implicit changes in physiological states, such as skin conductance rate, in response to intense affective stimuli, but not in subjective self-reported distress (Kircanski et al., 2012). This is aided by findings indicating that subjectively, labelling is considered a less efficient emotion regulation strategy compared to explicitly cognitively reappraising emotional meaning (Lieberman et al., 2011). Our findings may therefore reflect a subjective response bias, in which all three strategies are considered equally effective or ineffective, a limitation that requires attention in subsequent implementations.

Further, previous studies have shown that emotion regulation strategies consider the sociality dimension an important part of the regulatory process (Shuman, 2013), with

distinct sociocultural contexts known to modulate the use of emotion regulation strategies (De Leersnyder, Boiger, & Mesquita, 2013; McRae, Heller, John, & Gross, 2011). While the implementation of the script-driven imagery was aimed at increasing the ecological validity of the emotion regulation task, autobiographical memories involving emotional experiences of social interactions may have already undergone a process of previous regulation, thus attenuating the need for further regulation within the goal-directed regulatory framework. However, incorporating ecologically valid approaches to investigating emotion regulation within realistic socio-affective contexts provides a starting point for further research.

In sum, this chapter aimed at investigating affect labelling as an effective emotion regulation strategy in a novel implementation and further validation of the script-driven imagery. Results revealed that script-driven imagery presents a viable mood induction with the aim of eliciting salient social emotions in response to autobiographical memories of social rejection and inclusion. This is of particular importance in the study of dysfunctional emotion regulation in clinical populations, such as depression, as individual differences in the ability to regulate emotion contribute to the vulnerability and maintenance of affective disorders (Joormann & Gotlib, 2010). However, it is debatable whether the saliency of the elicited emotions was sufficient to warrant regulation, or whether biased self-report ratings may have interfered with the behavioural investigation. Thus, in future investigations, it will be important to implement different methods to investigate the efficacy of affect labelling in realistic socio-affective contexts, either by increasing saliency or incorporating physiological indicators.

CHAPTER 8. GENERAL DISCUSSION AND FUTURE DIRECTIONS



8.1 Thesis Overview

The work described in this thesis aimed at investigating the psychological and neural bases of social processing in Major Depressive Disorder, building on the existing literature. The experimental investigations described in the previous chapters represent an attempt to resolve current conflicts and gaps in the social affective neuroscience literature regarding social functioning in depression. This may inform current theoretical accounts of depression, as well as providing a scientific basis for incorporating functional treatment outcomes from within social domains into existing intervention approaches.

Firstly, this thesis aimed to challenge the long-held view that a dedicated neural network is selective for processing negative social emotions, such as social pain, in healthy individuals in response to being rejected or excluded. Secondly, this thesis was motivated by the importance of this 'social pain' debate to the understanding of social functioning in depression. This included an extension to the above debate to incorporate an experimental investigation of processing positive social emotions both in individuals with and without depression.

This chapter will review the experimental findings from the previous chapters and discuss these with respect to current theoretical frameworks of social processing in depression discussed in more detail in Chapter 1. Personal memories as vehicles for eliciting social emotions were used to investigate the complex psychological and neural mechanisms underlying dynamic social interactions across Chapter 4, Chapter 5, Chapter 6, and Chapter 7. This chapter will therefore further aim to highlight some of the challenges in the social affective neuroscience literature more generally, and discuss the validity and implications of using personal social memories in this context, more specifically. Finally, this chapter will outline the limitations of the experimental investigations, the wider implications for clinical practice and future directions.

In sum, that was the outline; let's review the journey.

8.2 Review of Main Findings by Chapter

Chapter 1 provided a general introduction to the work presented in this thesis, outlining the existing evidence-base on social information processing in depression, highlighting the research questions that arose from the literature and embedding these within the context of current theoretical frameworks.

Chapter 2 aimed at investigating systemic biases using a battery of social, affective and process measures. Replicating previous findings, depressed individuals were more anxious and depressed, and exhibited greater difficulty in emotion regulation and social processing. This included greater negative social comparison, submissive behaviour and involuntary subordination relative to controls. This provides strong support for the notion of social processing as a hallmark symptom of depression. A further important finding relates to persistence of social processing deficits in remission. These findings provide a comprehensive behavioural characterisation of the altered socio-cognitive profile in depression, which can be measured even in the absence of an acute episode. This investigation thus validated and replicated well-established measures, and provided new insights using measures of social processing.

Chapter 3 described the general methodology and initial implementation of autobiographical memories and script-driven imagery as the main approach within this thesis. The use of autobiographical memories and script-driven imagery aimed at implementing an ecologically valid experimental paradigm in the study of naturalistic social interactions. Thus, memories obtained from the initial memory generation sessions that took place prior to the studies described in Chapter 4 and Chapter 7 were examined for comparable emotional saliency, vividness and intensity in healthy controls and depressed. Findings revealed that depressed and healthy controls successfully retrieved and elicited salient emotions in the present, despite time modulation effects. Importantly, mood, affective intensity, and vividness differed as a function of the respective social autobiographical memory, and not as a function of group. This demonstrated its usefulness for the subsequent chapters and validated the script-driven imagery approach.

The next three chapters used functional neuroimaging (fMRI) to investigate the neural basis for social processing with suggestions that depressed and healthy controls exhibit altered neural processing of socially salient experiences of rejection and inclusion depending on the point of origin.

In Chapter 4, imagining personal experiences of social rejection as well as inclusion, revealed a common neural substrate for both social inclusion and social rejection (relative to neutral) in affective regions previously associated with social rejection in healthy controls only. In addition, between group comparisons revealed greater brain activity in somatosensory cortex in controls compared to those with MDD, and greater activity in the affective 'social pain' network in the dACC and AI in those with MDD relative to controls. However, on a behavioural level, both groups' mood was comparably modulated by the valence of the experience. This study, using robust conjunction analyses and focusing on brain regions of interests identified in the literature, thus highlighted two important findings: the notion of a valence-independent 'social pain *and social gain'* or social evaluation network, and a heightened sensitivity in depression compared to healthy controls to socially salient signals, irrespective of valence.

In contrast, Chapter 5 revealed that the vicarious experience of socially salient experiences, narrated from another person's viewpoint, was associated with reduced emotional reactivity in arousal and valence on a behavioural level in depressed participants compared to controls. It also revealed decreased neural activity in so-called affective and empathy brain regions in depression compared to controls, in line with previous findings in the empathy literature. These regions included the affective components of the 'social pain' network in the dACC and AI and empathy regions within the supramarginal gyrus. In comparison, healthy controls engaged in increased empathic processing of another's experiences of social rejection and inclusion, thus pointing towards a potential dissociation between self- and other-relevant neural processing of socially salient emotional experiences.

Then, Chapter 6 used a novel neuroimaging analysis method to investigate intersubject synchronicity in response to naturalistic social experiences. These dynamically unfolding social emotional narratives provided an opportunity to explore the extent of attentional synchronicity within regions across- and between-listeners over time in a naturalistic and thus ecologically valid paradigm. Results revealed heightened intersubject correlations (ISC) in key sensory and extra-sensory regions in social, affective and empathic cortical areas, including the medial frontal cortex ACC and PCC. In depressed individuals, listening to the socially inclusive narrative revealed a more heterogeneous neural response reflected in overall decreased ISC, while the rejection narrative elicited a strong homogenous ISC in key regions identified previously. Thus, suggests greater synchronicity across depressed listeners in response to rejection compared to inclusion narratives. In contrast, healthy controls revealed consistent levels of ISC across valences, while the between-group comparison revealed greater synchrony in key social affective and cognitive areas, such as the superior temporal gyrus. Reduced cortical synchrony in depression in these areas may thus reflect individualistic heterogeneous neural responses in line with the heterogeneous symptom presentation of depression itself (Chapter 1). While this presents an exciting avenue for further research, these chapter findings should nonetheless be interpreted with some caution, given the methodology's early stages.

Finally, Chapter 7 explored emotion regulation strategies in response to autobiographical memories of rejection, inclusion and neutral memories using the script-driven imagery approach in a sample of healthy controls. Script-driven imagery was validated as a viable mood induction technique aimed at eliciting salient social emotions in the present. However, no significant changes in mood were observed as a function of the respective emotion regulation strategy employed. The efficacy of affect labelling and emotion regulation strategies more generally may thus be limited within naturalistic affective contexts and subject to diverging findings. However, this study also highlighted the usefulness of script-driven imagery as a novel approach for investigating emotion regulation strategies and similar research questions within naturalistic affective contexts. These findings are encouraging,

especially as previous chapters additionally validated this approach within a depressed sample, and as part of a neuroimaging investigation, opening up avenues for future investigations.

Thus, following the summary of the work presented in this thesis thus far, this chapter aims to bring together the behavioural and neural findings to provide a clearer understanding of social processing in MDD, guided by the current theoretical frameworks introduced in Chapter 1. The thesis will conclude with an outline of future directions for this fascinating area of research

8.3 Theoretical Implications

The ability to detect and respond to diverse signals of social inclusion and social exclusion is critical to the establishment and maintenance of relationships, groups and social hierarchies (Baumeister & Leary, 1995). Formation of these social attachments affects important aspects of our narrative self, shaping our motivations, goals, behaviours and self-identity (Walton, Cohen, Cwir, & Spencer, 2012). Moreover, increased social connectedness is associated with a range of positive emotions, such as the experiences of joy, love, and friendship, and social support plays a vital role in the maintenance or rehabilitation of positive psychological well-being following adverse life events (Correa-Velez, Gifford, & Barnett, 2010). In contrast, the psychological sequelae of early social deprivation or the severing of existing social bonds detrimentally affects cognition, memory and development and is associated with an increase in psychopathology and functional impairment (Carlson & Earls, 1997; van Ast et al., 2014).

In depression, major life events involving social rejection, loss or failure are found to be the most proximal risk factors and are associated with lowered feelings of self-worth and early-onset depression (DeWall et al., 2009; Slavich & Irwin, 2014b; Slavich et al., 2010). As outlined in Chapter 1, depression has a debilitating effect on day-to-day functioning and severely impairs appetite, sleep, concentration, and energy and is associated with suicidal ideation, feelings of worthlessness, sadness and

loss of interest in previously enjoyed activities (APA, 1994). Deficits across affective, cognitive and social domains are further outlined in Chapter 2. Here, the socio-cognitive profile of healthy controls and individuals with a current depressive episode or a history of depression highlight the systematic biases in emotional processing of social signals. Findings of heightened interpersonal rejection sensitivity, increased submissiveness, feelings of low social rank and striving to avoid inferiority further emphasise the notion of severe impairments in social functioning in depression and underscore the persistent nature of these deficits beyond recovery, with implications for treatment goals and risk of recurrence.

Implications from behavioural findings

On a behavioural level, we have argued that the findings described in Chapter 2 represent a dysfunctional entrenchment of behavioural coping strategies to avoid social exclusion from a group. This assumes that depression, dampened affect and decreased motivation may have presented an evolutionary adaptive condition to conserve energy and resources while engaging in social competition.

The social risk hypothesis (Allen & Badcock, 2003) advocates a risk-averse stance, with downstream behavioural adaptions and cognitive biases in response to critically low social investment potential (SIP). The depressed mood state is thus induced as a function of fluctuations in the ratio of one's respective social value and social burden to the group. For instance, when faced with perceptions of low social rank, and negative social comparison, as described in Chapter 2, the greater perceived social burden relative to an individuals' social value would reduce the ratio and subsequent estimate of SIP (Allan & Gilbert, 1997; Gilbert & Allan, 1998). This theory integrates the previous view on social attention holding power (SAHP) within the hierometer and social rank theories (Gilbert, 2000; Mahadevan et al., 2016), which describe the ability to attract positive attention and social rewards (see Chapter 1 for details). Across theories, adopting a social-risk-averse stance is thus argued to reduce the likelihood for social defeat and expulsion by reducing socially risky behaviours. However, the continued inhibition of socially appetitive behaviour as an 'adaptive'

depressed mood state, once entrenched, prevents the depressed individual from redirecting resources to more beneficial endeavours both in social and non-social contexts in the long-term. This is illustrated in the learned helplessness model, in which the individual 'learns' that outcomes are uncontrollable, thereby continuing to inhibit the appetitive behaviour (Abramson et al., 1978) and potentially resulting in chronic depression.

Underlying these social-risk-averse behavioural adaptions is a proposed capacity to sensitively monitor incoming social information, an evolved 'sociometer', which allows an individual to gauge his or her social value and burden to a group (Baumeister & Leary, 1995; Leary, 2004). Heightened sensitivity in depression to socially salient signals, evidenced in Chapter 2, may thus be designed to optimally respond to social threat or changes in relational value. This interpretation is supported by findings of increased sensitivity to cues of interpersonal rejection in depression and remitted depression (Ayduk et al., 2001; J. C. Butler, Doherty, & Potter, 2007; Liu et al., 2014; Luterek et al., 2004), and the 'depressive realism' effect (Alloy & Abramson, 1988), in which depressed individuals' judgments about self-relevant information can be more accurate than those of non-depressed individuals. These findings are also in line with the generally heightened awareness and attentional orientation towards internally generated or self-relevant information observed in depression (Ingram, 1990), associated with greater negative affect and negative appraisal (Beck & Clark, 1997; David M. Clark, 2001; Mor & Winquist, 2002; Spurr & Stopa, 2002). Thus, previous behavioural investigations have extensively examined the heightened sensitivity to self-relevant social information implied within the previous interpersonal theories. In contrast, the underlying neural mechanisms dedicated to detecting social signals and estimating relational value as proposed by the above theories had yet to be fully investigated.

IMPLICATIONS FROM NEUROIMAGING FINDINGS

So how do our behavioural findings relate to our neuroimaging findings in the context of the above theories? As described in the introduction, one of our main aims was to

challenge the long-held view that a dedicated neural network is selective for processing negative social emotions, such as social pain, in the human brain in response to being rejected or excluded. This was based on previous work by Eisenberger, Inagaki, Muscatell, Byrne Haltom, & Leary (2011), who had conceptualised the 'sociometer' as a 'neural alarm system' geared towards the detection of social cues signalling exclusion in healthy controls. Heightened sensitivity to social threat was thus argued to be reflected in neural activity in the dACC-AI or 'social pain' network, correlated with subjective distress.

However, experimental investigations were limited to the discussion of rejection experiences relative to a fundamentally socially-neutral condition as opposed to incorporating bona fide socially inclusive signals (Eisenberger, 2012b; Eisenberger & Lieberman, 2003). In addition, the Cyberball paradigm suffers from methodological limitations with constrained ecological validity (De Gelder & Bertelson, 2003) and difficulty in establishing a 'true' neutral condition (Somerville et al., 2006). See Chapter 1 and Chapter 4 for a further discussion. The previous assumption of a 'social pain' network therefore deserved further consideration and was examined in Chapter 4. Interestingly, and in line with the theoretical predictions, our neuroimaging study on social rejection and inclusion experiences provided robust evidence for heightened sensitivity to social signals *independent* of valence across both groups and within brain areas formerly attributed exclusively to the processing of social pain (Eisenberger, 2012b; Eisenberger & Lieberman, 2003). Therefore, our findings from Chapter 4 point towards a 'neural sociometer' monitoring incoming signals of both social inclusion and rejection. This interpretation is complemented by other recent findings revealing comparable neural activity in the dACC and AI in response to both positive and negative social evaluation (Dalgleish et al., 2017). In sum, this dedicated neural mechanism may be drawn upon to establish the current relational value, whether that be conceptualised as SAHP, as outlined in the social rank theory (Gilbert, 2000; Mahadevan et al., 2016), or SIP, as described in the SR hypothesis (Allan & Gilbert, 1997; Gilbert & Allan, 1998). Adding to the terminology provided within the theoretical accounts, the 'social pain' network may, however, be

better understood as a 'social pain *and social gain'* or social evaluative network (SEN).

In addition, this thesis aimed to examine the notion of 'social pain' in the context of social functioning in depression. From the above findings, it follows that a heightened sensitivity to *any* incoming social signals may be associated with altered psychological or neural processing in depression, given the propensity to interpret social signals as more threatening relative to healthy controls (Ayduk et al., 2001; J. C. Butler et al., 2007; Liu et al., 2014; Luterek et al., 2004). As discussed with respect to our behavioural findings, the SR hypothesis further argues that monitoring one's SIP serves to protect one from, for instance, 'overinvesting' in social interactions with uncertain or negative outcomes. This adaptive valence-independent socio-cognitive bias is illustrated in a study investigating the neural basis of judging threat from dynamic social interactions in expert CCTV operators (Petrini et al., 2014). Tasked with predicting violent outcomes from confrontational, neutral and playful social interactions, experts, relative to novice controls were more likely to predict a violent outcome following the presentation of both confrontational and playful social interactions. This was attributed to operators judging playful interactions as more likely to unexpectedly result in confrontation, reflected in greater attentional demands on a neural and behavioural level. Thus, CCTV operators exhibited heightened sensitivity to negative and positive social cues when evaluating potentially threatening social interactions. Similarly, in depression, heightened sensitivity to social signals may thus be designed to optimally respond to potential social threat, as a result of prior exposure to negative life events involving social rejection, loss or failure (Heim & Binder, 2012; Luterek et al., 2004; van Harmelen et al., 2010, 2014).

RETHINKING THE IMPORTANCE OF SOCIAL PROXIMITY AND RELEVANCE

Nonetheless, heightened sensitivity and emotional reactivity to social emotional signals independent of valence is seemingly at odds with the mainstream depression literature. It has been well-established that individuals with depression demonstrate negative response biases and reduced reactivity to positive emotional cues, as

described in the introduction (Roiser & Sahakian, 2013). However, the literature on positive emotional processing has revealed divergent findings, with some suggestions that greater levels of depression are associated with both reduced and increased sensitivity to positive cues (DeWall & Bushman, 2011; DeWall et al., 2009; Steger & Kashdan, 2009). It is, therefore, important to highlight the sociality dimension, which may aid in the understanding of the existing literature.

Previously, it has been suggested that emotions should be better understood as interpersonal phenomena, contingent on the social and cultural context within which the occur (Kitayama, Markus, & Kurokawa, 2000). In line with this thinking, evidence suggests that emotional reactivity independent of valence may be enhanced for self-relevant, more proximal elicitors of social emotions (Rottenberg, Joorman, Brozovich, & Gotlib, 2005). As discussed previously, 'depressive realism' suggests potentially greater accuracy in self-relevant judgements in those who are depressed relative to controls (Alloy & Abramson, 1988). However, the majority of (social) affective neuroscience has relied on the use of standardised non-social external emotional cues, and tasks to elicit emotions (Amodio, 2010; Poldrack, 2008). This approach may have fallen short of capturing the essence of realistic socio-affective contexts, as discussed in more detail in Chapter 3. The presentation of brief, normative and other-relevant cues, such as standardised affective images, to individuals with depression may therefore fail to achieve the same level of engagement as that in healthy controls carrying out the same task, either as a function of impairments in attention or motivation, or lack of perceived self-relevance (Hammar & Ardal, 2009; Snyder et al., 2015).

Emotional reactivity to interpersonal and self-relevant elicitors of emotions, such as idiographic emotional memories, may therefore provide a better approach to understanding social emotion functioning in depression. A Chatroom task designed to prompt social evaluation for instance revealed comparable affective responses to positive and negative social interactions when the social context was more personally meaningful and self-relevant (Caouette & Guyer, 2015; Steger & Kashdan, 2009), in

line with our results. Furthermore, individuals with social phobia are also found to shift their attention to detailed monitoring and observation of themselves when expecting negative evaluation by others (D'Argembeau, Van der Linden, D'Acremont, & Mayers, 2006), with greater self-referential information contained within descriptions of past social events in individuals with social phobia relative to controls (D M Clark & Wells, 1995; Rapee & Heimberg, 1997)

On a neural level, metacognitive evaluations about the self suggest further differential processing compared to other-relevant information. This is reflected in increased activity in right dorsolateral medial prefrontal cortex (Schmitz, Kawahara-Baccus, & Johnson, 2004), even when contrasted to 'familiar' or close others as opposed to judgments about strangers (Heatherton et al., 2006). Interestingly, damage to the medial PFC is found to eliminate the self-reference effect, with impaired memory recall in response to self-relevant cues (Philippi et al., 2012). In line with the SR hypothesis, evaluating one's social investment potential may therefore recruit the dACC-AI network, as highlighted in Chapter 4, as a function of the self-relevance of the social cues signalling social value ('social gain') and social burden ('social pain'), respectively.

In contrast, processing others' relevant social signals, which do not contribute as strongly to one's SIP, may recruit a different neural pattern of activity. See Figure 1.3 and Figure 1.4 in the general introduction for hypothesised inputs and outputs. This was examined in Chapter 5, where individuals with and without depression were exposed to another's experiences of social rejection and inclusion. In this context, the SR hypothesis would predict that the personal SIP would not be contingent on another's past social experiences, as these are not personally meaningful or likely to impact on the probability of personal exclusion. Extending this rationale, the dACC-AI network would not be expected to be activated in response to another's experiences. This was indeed the case, with heightened sensitivity to another's experiences instead reducing neural activity in the affective components of dACC and AI network and the brain's so-called empathy regions within the supramarginal

gyrus and angular gyrus, in those with depression compared to controls. This was mirrored by reduced mood at the behavioural level, with the dichotomy perhaps reflecting the notion of personal significance or proximity as a driving force in activating the social evaluation network.

Intriguingly, perceived superiority within a social hierarchy previously motivated empathy towards inferior social targets' painful stimulation within the AI and aMCC, but was attenuated when observing painful stimulations to superior ranked social targets (Feng et al., 2016). Similarly, our study suggested heightened activity in the MCC and AI for healthy controls relative to depressed, who in this context may arguably perceive themselves as having relatively more stable or higher social status, as evidenced by their self-reported more favourable social comparisons (see Chapter 2). Reduced emotional reactivity on behavioural and neural levels in depression thus endorses the SR hypothesis' notion of motivational disengagement and adoption of a risk-averse state, which is focused on internally oriented processes. This interpretation is supported by previous findings of reduced empathic concern and decreased emotional reactivity in response to another's distress in depression (Field, Diego, & Hernandez-reif, 2009; Young, Parsons, Stein, & Kringelbach, 2015). In fact, the SR hypothesis further predicted that individuals with depression would exhibit greater withdrawal in exchange-oriental contexts, while favouring reciprocity-oriented contexts (Allen & Badcock, 2003, 2006). This may be reflected by the differential pattern of neural activation in self- versus other-relevant social contexts, although the two studies examined in Chapter 4 and Chapter 5 are unfortunately not directly comparable, due to the modifications to the task presented.

An interactionist approach to social functioning

In Chapter 6, this notion was more explicitly investigated by considering reciprocity within the social exchange as a function of the task instructions. Using intersubject correlation, listening to long spontaneous social rejection and inclusion narratives aimed at prompting an engaged social experience within depressed, non-depressed, which would potentially activate self-relevant processes within the dACC-AI

network (or SIP network). It further explored the extent of intersubject synchronicity across listeners. Reciprocity, or self-other social interactions, are closely associated with higher social cognitive processes, including mentalisation and theory of mind (Ladegaard et al., 2014; Schilbach, 2015) and commonly associated with heightened activity in medial prefrontal cortex (MPFC), and posterior cingulate cortex (PCC) (Benoit, Gilbert, Volle, & Burgess, 2010; Garrison et al., 2013; Schmitz et al., 2004). Both depressed individuals and healthy controls revealed activity in these areas. However, greater recruitment of superior temporal gyri in healthy controls may point towards differential socio-affective engagement across narratives, compared to depressed individuals who exhibited greater activity in brain areas associated with visual imagery of the social interaction presented. Previously, Schilbach et al. (2013) argued that interpersonal functioning, or social emotional processing could only be understood within the context of self-relevant cues, the social proximity of the agents involved, and the emotional engagement within the social interaction. As a result, the ability to take another's perspective can be viewed as independent from being emotionally engaged or socially invested. The intended reciprocal interaction may therefore have rather been viewed as non-relevant social interaction, which would not impact on the individual's personal value or burden within a group. In the context of the social risk hypothesis and other theoretical frameworks, investigating the neural basis of real-time social interactions may thus require further resolution. However, the novel analysis method applied in Chapter 7 provides a starting point for further investigations, especially as the ISC methodology continues to be developed.

IS BAD STRONGER THAN GOOD?

In sum, in an early sweeping review of the depression and emotion literature it was proclaimed that "bad is stronger than good" (Baumeister et al., 2001). This claim is well supported in many domains of research, with negative emotional stimuli often eliciting powerful reactions that trump the relatively attenuated response to positive emotional stimuli. However, autobiographical memories may represent an exception to this rule. From an evolutionary perspective, it appears intuitive for threatening

highly arousing negative stimuli to trigger such a highly emotive response, at both behavioural and neural levels, to protect the self from perceived danger and threat. However, the findings presented in this thesis suggest that memories containing self- and other-relevant social cues signalling inclusion and rejection prompt at least some reconsiderations of this claim. One way to address the relative strength of positive and negative events is to consider the personal meaning and self-relevance of the stimuli presented. In this case, autobiographical memories of rejection and inclusion, as opposed to listening to another's experiences of social interactions, and to look at the elicited responses at both behavioural and neural levels. In these investigations, negative social interactions appear on a par with positive inclusive interactions, with heightened sensitivity in depression.

In sum, the findings discussed in this section suggest a revision of the previously held view that the social pain network within the dACC-AI matrix responds exclusively to social rejection or exclusion, extending this to the experience of social inclusion. In addition, our findings identified a heightened sensitivity to social signals in depression, as well as exploring the importance of social interactions at the inter-subject level. These findings were then discussed with respect to the current theoretical models of interpersonal processing. The sociometer and social rank theories argue that the altered behavioural and neural patterns of activation function as a neural alarm system designed to monitor current levels of social risk prior to prompting downstream modifications in social behaviour and cognitive biases in social attention. Similarly, the SR hypothesis (Allen & Badcock, 2003) argues that depressed mood represents a risk-averse motivational state which is activated by the threat of social exclusion by others. However, the SR hypothesis assigns greater importance to the notion of reciprocity, as the altered behaviour serves both to minimise the perceived social burden, while simultaneously increasing the potential social value.

In depression, this may be accomplished by sending signals of submission and inferiority (identified in Chapter 2), social withdrawal or reduced affiliation in

exchange-oriented contexts (Chapter 5 and Chapter 6). Modulating this decision-making process may be the extent of social proximity and heightened attention to self-relevant social cues (Chapter 4). However, unanswered questions, and challenges within the field of social affective neuroscience remain to be explored. These will be outlined in the next section.

8.4 Challenges and opportunities in social affective neuroscience

The term "social neuroscience" was first used by Cacioppo and Berntson (1992) to describe an emerging field aimed at examining the interplay of social and physiological levels of analysis. Central to describing these levels of analysis is the ability to make predictions pertaining to the relationship between variables. One of the key assumptions is that activity observed in specific brain regions reflects an underlying psychological process, which can be measured using modern brain imaging tools, including fMRI (Amodio, 2010). Testing hypotheses in this context is strengthened by the presence of prior regions of interest identified within the literature in response to the repeated presentation of experimental stimuli or paradigms similar in nature aiming to elicit a specific psychological process. This can be achieved more readily when an area is selectively activated by a particular process (Poldrack, 2008). A classic illustration of this process is the reliable, selective and localized activation of the fusiform face area (FFA) in response to the visual presentation of faces (Kanwisher, McDermott, & Chun, 1997; Kanwisher & Yovel, 2006). These results have made important contributions to the challenge of functionally mapping the brain, and further developing the necessary methodology to achieve this goal.

Reverse Inference Problem

However, the current constraints in developing the scientific evidence-base of social neuroscience has been the limited generation and application of novel social psychological hypotheses (Amodio, 2010). One of the challenges in generating

hypotheses within the social neuroscience framework has been the targeted investigation of specific psychological processes underlying complex social interactions. These are either subject to ambiguous or inadequate operationalisation of the mental process in question or are limited by the problem of reverse inference. The reverse inference problem is the process of drawing inferences from observed brain activity, without fully taking into account the selectivity of a particular brain area in response to the psychological process in question (Poldrack, 2008); for instance in cases where psychological processes rely on input from multiple or grossly overlapping brain areas or networks, as is frequently the case in social cognition (D. P. Kennedy & Adolphs, 2012) or where a given brain region may be implicated in a wide range of psychological processes, with little or limited specificity. To illustrate, the social neuroscience literature has thus far identified multiple networks involved in complex social processes, such as inferring others' mental states (Spunt, Satpute, & Lieberman, 2011), empathetic processing (J. Decety, 2011; Lamm et al., 2011; Pfeifer, Iacoboni, Mazziotta, & Dapretto, 2008) or indeed social pain processing (S. Cacioppo et al., 2013; Eisenberger et al., 2006; Eisenberger & Lieberman, 2003), with arguably grossly overlapping anatomical brain regions (D. P. Kennedy & Adolphs, 2012; Kross et al., 2011; Woo et al., 2014).

Similarly, as part of the 'social pain debate', the dACC was described as *selective* for pain (Lieberman & Eisenberger, 2015), drawing on results from the automatic meta-analytic software tool 'Neurosynth' (Yarkoni et al., 2011). This led to a strongly-worded exchange (see also http://www.talyarkoni.org/blog/2015/12/05/no-the-dorsal-anterior-cingulate-is-not-selective-for-pain-comment-on-lieberman-and-eisenberger-2015/; (Lieberman, Burns, Torre, & Eisenberger, 2016; Wager et al., 2016) with arguments reiterating previous accounts of the dACC being involved in saliency and conflict monitoring (Somerville et al., 2006) as well as perhaps more nuanced aspects of social pain processing, such as experiencing *envy* or *schadenfreude* (Takahashi et al., 2009). Overall, the conflicting interpretations of regional brain activity in the field of neuroscience have led to the increasing implementation of large-scale multivariate approaches (Haxby, Connolly, &

Guntupalli, 2014). These posit that in order to accurately decode relevant psychological processes, it is important to take into account (multiple) distributions of activation across many regions across the brain *as well as* in response to a range of different tasks and stimuli (Poldrack, 2008). This is argued to result in a greater likelihood of generalising across individuals compared to eliciting idiosyncratic features of individual brains.

The work presented in this thesis has therefore sought to address the challenges described above as much as possible by carefully validating the tasks and stimuli, as well as using mixed method designs to investigate underlying social processing. However, it remains important to consider the notion of reverse inference when interpreting these neuroimaging findings. While currently the ISC toolbox does not allow for mixed-methods analysis; this data-driven approach invites further validation and implementation, alongside the continued need to further develop principled methods to explore information transfer across individuals using alternative analytical approaches. However, script-driven imagery provides one such viable approach to eliciting social emotions, and, in conjunction with intersubject correlation analysis may open up a promising new avenue for understanding the neural signature of socio-emotional processing (Pajula et al., 2012).

Ecological Validity

A further challenge and opportunity in social neuroscience is the implementation of a variety of tasks and stimuli, in order to capture relevant psychological processes occurring naturally within our environment (Amodio, 2010; Poldrack, 2008). To date, the literature has relied heavily on the presentation of experimentally constrained emotional stimuli to investigate underlying psychological processes. For instance, in the emotion regulation literature, the presentations of angry or fearful facial expressions are frequently used as a target for regulation strategies (Gross, 1998). These stimuli allow for the presentation of characteristics deemed crucial to the regulatory process, above and beyond other contextual features contained within our affective environment. However, there is limited evidence as to the reliability and

ecological validity of emotion regulation paradigms within our rich, multifaceted affective environment. Emerging evidence integrating contextual features as part of paradigms investigating specific psychological processes include for instance the impact of affective contexts on working memory (Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish, 2013) or cognitive control under duress (Raio, Orederu, Palazzolo, Shurick, & Phelps, 2013), which provide more ecologically valid paradigms for generalising results to the general population in the real-word.

In addition, conceptualising tasks and stimuli as explicitly social compared to affective non-social tasks, has seen considerably less attention. This is despite social contexts largely informing regulatory goals, and sociocultural contexts modulating the use of emotion regulation strategies (De Leersnyder, Boiger, & Mesquita, 2013; McRae, Heller, John, & Gross, 2011). The use of autobiographical memories in this thesis therefore presents a unique opportunity to investigate neural responses to socially salient emotional events. The evidence-base on the neural correlates of autobiographical memory has grown considerably over recent decades (Cabeza & St. Jacques, 2007). A range of methods for eliciting salient autobiographical memories has emerged within the fMRI context, ranging from generic cues (Martin A. Conway et al., 1999; Graham, Lee, Brett, & Patterson, 2003) and pre-scan interviews (Fink et al., 1996; D. L. Greenberg et al., 2005), to prospective memory tasks (Cabeza et al., 2004; Levine et al., 2004; Steinvorth, Corkin, & Halgren, 2006). However, a concern has been the extent of control over the age and content of retrieved memories (Cabeza & St. Jacques, 2007), especially given the fading affect bias, as discussed in Chapter 3. Nonetheless, the value of using an autobiographical memory approach lies in the rich emotional complexity of the memories, with distinct qualities of vividness and intensity. However, while this thesis aimed to address aspects of the challenges in social affective neuroscience outlined above, methodological limitations remain. These are described in the next section.

LIMITATIONS TO THE PRESENT WORK

Invoking highly social contexts through the means of mental imagery confers advantages in terms of ecological validity, but also presents several limitations. As described in Chapter 2 and Chapter 3, the script-driven imagery approach requires the generation of memories with sufficient affective saliency, as opposed to, for instance, the presentation of standardised arousing emotional pictures or film. In addition, with a memory generation and memory presentation session one week apart, this approach entails logistical issues with respect to time and resources. Furthermore, when recruiting clinical participants, it is important to consider the attentional demands of prolonged sessions. Unlike emotional pictures or films, the validity of idiosyncratic stimuli was also dependent on the extent of social disclosure participants were willing to extend to the researcher.

A further consideration concerns the sociality of the memories. As described in Chapter 3, participants were explicitly instructed to recall social as opposed to non-social memories with cue cards and prompts within the memory generation session. Memories were further required to involve at least one other person, thereby ensuring social encounters as the source of the emotional impact. However, in the absence of an explicit non-social comparison, our behavioural and neuroimaging findings are limited in their interpretation within the context of non-social salience processing (Eisenberger, 2015; Wiech et al., 2010). That said, the strength of the work in this thesis perhaps lies in the juxtaposing of the behavioural and neural responses to imagining highly salient personal memories of social inclusion and social rejection, relative to neutral experiences, with the fixed order accounting for expectancy violation (Kawamoto et al., 2012). With modifiable emotional impact as a function of memory type, our paradigm arguably contrasts favourably against previous paradigms such as Cyberball, in which the inclusion condition may be better understood as a default or neutral state (Somerville et al., 2006). This highlights the difficulty in defining standalone neutral conditions, despite our behavioural findings

underscoring the differential impact of neutral compared to negative and positive memories.

Ultimately, the overarching benefit of our approach lies in the highly self-relevant nature of personal memories, which uniquely 'recreates' the phenomenological experience of being socially rejected or included. While the Cyberball paradigm has shown that being excluded by virtual characters increases levels of self-reported distress (Eisenberger, 2012b; Eisenberger & Lieberman, 2003), it fails to capture changes in distress as a function of socially positive information. Originally, the Cyberball paradigm was aimed at extracting the *essence of the drama* of ostracism (K. D. Williams et al., 2012). However, the question remains as to whether this paradigm has satisfied this aim. With strong dissociable behavioural findings as a function of memory type, our script-driven imagery paradigm appears to more effectively address this question. Nonetheless, it is important to note that the use of ideographical memory stimuli does sacrifice the experimental control conferred as opposed to standardized stimuli to an extent.

8.5 Chapter Summary and Future Directions

In sum, social functioning is contingent on the ability to accurately recognise and respond to emotions, with evidence suggesting that depressed individuals struggle with detecting and responding to salient affective information in their immediate social environment; this is illustrated by a greater difficulty with identification of happy facial expressions (Joormann & Gotlib, 2006), and of affective gestures and body movements (Kaletsch et al., 2014), and a reduced awareness of others' emotions and of the ability to empathise (Donges et al., 2005). These biases in emotion recognition and awareness tend to correlate with depression severity (Gollan et al., 2010), and persist even beyond recovery (Lemoult & Sherdell, 2010). However, the understanding of one's personal emotional experience appears relatively unimpaired in depression (Donges et al., 2005), reflected in comparable behavioural changes in mood between depressed and healthy controls in response to listening to personal

memories of rejection and inclusion described in Chapter 3. On a neural level, the potential dissociation between self-relevant (Chapter 4) and other-relevant (Chapter 5 and Chapter 6) understanding and awareness of (social) emotional experiences were further illustrated in differential neural patterns of activity in healthy controls relative to depressed.

In the future, addressing the challenges in social affective neuroscience, while incorporating the approaches outlined in this thesis, may allow for a richer understanding of the individual differences in social processing in depression. This may be achieved by implementing script-driven imagery and other more naturalistic paradigms capturing the essence of social interactions. Furthermore, identifying a neural socio-affective profile will allow for more focused therapeutic interventions, as poor social functioning may be indicative of future relapse into depressive episodes. This could be incorporated into existing social interventions with a focus on social functioning, such as interpersonal therapy (IPT), and compassion focused CBT, which address current or recent life events and interpersonal difficulties (Feijo De Mello et al., 2005). However, CBT may equally benefit from a more targeted evidence-based approach on challenging and restructuring cognitive distortions in core beliefs and assumptions explicitly from within the social domain (Beck, 1967; Beck et al., 1979; A. Butler et al., 2006).

To conclude, the work presented in this thesis was aimed at investigating individual differences in detecting and responding to interpersonal emotional signals on a behavioural and neural level, as well as differences in cognitive mechanisms involved in emotion recognition and emotion regulation. Results were interpreted within explanatory theoretical frameworks, with an emphasis on the social risk hypothesis of depression, but also encompassing previous theories, including the sociometer, social rank and hierometer theories. Finally, challenges and opportunities in the existing social affective neuroscience literature were outlined, with implications for future directions in both clinical research and clinical practice.

Therefore, I would like to end with a quote - “knowing is not enough; we must apply. Willing is not enough; we must do.”

“Es ist nicht genug, zu wissen, man muß auch anwenden; es ist nicht genug, zu wollen, man muß auch tun.“ (Johan Wolfgang von Goethe, Wilhelm Meisters Wanderjahre).

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APPENDICES

Appendix 1 (Chapter 1)

Appendix 1.1 DSM-5 Criteria for Major Depressive Disorder and Persistent Depressive Disorder

Major Depressive Disorder
In children and adolescents, mood can be irritable.
5 or more of 9 symptoms (including at least 1 of depressed mood and loss of interest or pleasure) in the same 2-week period; each of these symptoms represents a change from previous functioning • Depressed mood (subjective or observed) • Loss or interest or pleasure • Change in weight or appetite • Insomnia or Hypersomnia • Psychomotor retardation or agitation (observed) • Loss of energy or fatigue • Worthlessness or guilt • Impaired concentration or indecisiveness • Thoughts of death or suicidal ideation or suicide attempt
Persistent Depressive Disorder
In children and adolescents, mood can be irritable and duration must be 1 year or longer.

Depressed mood for most of the day, for more days than not, for 2 years or longer. Presence of 2 or more of the following during the same period and never without symptoms for more than 2 months.

- Poor appetite or overeating
- Insomnia or Hypersomnia
- Low energy or fatigue
- Low self-esteem
- Impaired concentration or indecisiveness
- Hopelessness

Appendix 2 (Chapter 2)

Appendix 2.1 Ethics approval letter and application

Karen Douglas
Secretary

Dr T Dalgleish
MRC Cognition and Brain Sciences Unit
15 Chaucer Road
Cambridge
CB2 2EF

UNIVERSITY OF CAMBRIDGE

CAMBRIDGE
PSYCHOLOGY RESEARCH
ETHICS COMMITTEE

7 May 2014

Application No: Pre.2014.43

Dear Dr Dalgleish

An examination of emotion regulation and social information processing in response to autobiographical memories of social rejection and affiliation

The Cambridge Psychology Research Ethics Committee has given ethical approval to your research project: An examination of emotion regulation and social information processing in response to autobiographical memories of social rejection and affiliation, as set out in your revised application dated 28 April 2014.

The Committee attaches certain standard conditions to all ethical approvals. These are:

(a) that if the staff conducting the research should change, any new staff should read the application submitted to the Committee for ethical approval and this letter (and any subsequent letter concerning this application for ethical approval);

(b) that if the procedures used in the research project should change or the project itself should be changed you should consider whether it is necessary to submit a further application for any modified or additional procedures to be approved;

(c) that if the employment or departmental affiliation of the staff should change you should notify us of that fact.

Members of the Committee also ask that you inform them should you encounter any unexpected ethical issues.

If you would let us know that you that you are able to accept these conditions, I will record that you have been given ethical approval.

Yours sincerely

K S Douglas

cc: Ms Julia Gillard

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UNIVERSITY OF CAMBRIDGE

COUNCIL OF THE SCHOOL OF THE BIOLOGICAL SCIENCES

Cambridge Psychology Research Ethics Committee

Question 1: Title of the study

An examination of emotion regulation and social information processing in response to autobiographical memories of social rejection and affiliation

Question 2: Primary applicant

Professor Tim Dalgleish, BA, MA, PhD, MSc, Clinical Psychologist and Cognition & Mental Health Programme Leader, Medical Research Council Cognition & Brain Sciences Unit

Question 3: Co-applicants

Julia Gillard, BSc, MSc, PhD Candidate, Medical Research Council Cognition & Brain Sciences Unit

Question 4: Corresponding applicant

Julia Gillard
Email: Julia.Gillard@mrc-cbu.cam.ac.uk

Question 5: In which Department(s) or Research Unit(s) will the study take place?

Medical Research Council, Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge, CB2 7EF. Data will be stored securely at the same location in a locked filing cabinet and on the imaging data storage server that only investigators have access to.

Question 6: What are the start and end dates of the study?

Start Date: March 2014
End Date: Approximately September 2015 (exact study length will depend on recruitment).

Question 7: Briefly describe the purpose and rationale of the research

The aim of this project is to investigate how information pertaining to social emotions in response to autobiographical scripts describing rejection and inclusion memories of different intensity, is processed at the behavioural and neural level in people with varying degrees of low mood and/or a history of socially adverse life events. Individuals with low mood or a history of adverse life events tend to show altered sensitivity to social rejection and inclusion. Investigating the neural response to interpersonal sensitivity and emotion dysregulation in low mood individuals could identify differential neural signatures that could underpin this aberrant processing. Interpersonal rejection sensitivity is a phenomenon encompassing either enhanced or diminished sensitivity to the behaviour and emotions of others (Boyce and Parker, 1989). This reactivity extends to receiving social feedback, concern about behaviour and verbal statements of others and fears of perceived or actual criticism. This may result in feelings of inadequacy, inferiority and the misinterpretation of social cues signalling rejection and/or affiliation, correlated with low mood (Gilbert & Allan, 1998). Behaviourally, individuals tend to modify their interpersonal behaviour and frequently experience social withdrawal (Slavich & Irwin, 2014). The social signal transduction theory argues that social threat of exclusion can activate an immune response to adversity in the same way as experiencing actual physical threat or injury, thereby protecting the physical and emotional integrity of an individual (Slavich & Irwin, 2014). Interpersonal rejection sensitivity mediates the relationship between early adverse life events, and depressive symptoms in later adult life (Luterek et al, 2004). Thus, major life events involving social rejection, loss or failure are found to be the most proximal risk factors for depression and persistent low mood (Brown & Harris, 1989; Slavich & Irwin, 2014). On a neural level, processing of social rejection in healthy people leads to increased activity in the dorsal anterior cingulate cortex (dACC), anterior insula (AI), and the right ventral prefrontal cortex (vPFC) regions, as well as qualitatively distinct self-reported feelings of "social pain" (Eisenberg et al. 2003, 2012). This suggests a similar underlying neural circuitry as somatosensory pain regions (Kross et al., 2011). In people with low mood, meta-analytical evidence of emotional processing suggests heightened amygdala response and attenuated dorsolateral prefrontal cortex (DLPFC) activation (Hamilton et al., 2012). A novel technique of self-regulation of amygdala activity using real-time functional magnetic resonance imaging neurofeedback (rtfMRI-nf) showed an enhancement in functional connectivity between relevant brain regions in healthy participants (Zotev et al., 2011). In depression, people were able to "train" brain areas, including the ventrolateral prefrontal cortex (VLPFC) and insula, involved in generating positive emotions (Linden et al., 2012). This emotion dysregulation in people with varying levels of low mood and coupled with recent meta-analysis results arguing that the neural correlates of social pain are more complex than previously thought, suggests that a further investigation of social pain in people with inherent emotion regulation difficulties is warranted (Cacioppo et al., 2013). This project aims to use behavioural measures and fMRI to investigate interpersonal rejection sensitivity and self-regulation of social pain and emotion in individuals with varying low mood. It is anticipated that lower mood will be associated with a bias towards a wider range of rejection cues and will have a distinct neuro-affective profile relative to individuals without low mood (on behavioural and neural levels). Identifying the neural basis of this maladaptive behaviour would further the understanding of the neurobiological impact of low mood.

Question 8: Who is funding the costs of the study?

This study will be funded by the Medical Research Council, UK.

Question 9: Describe the methods and procedures of the study

This project will consist of three studies examining social information processing of autobiographical memories in response to social rejection and inclusion.

Study 1 will be a behavioural study, while studies 2 and 3 are fMRI studies in people with varying levels of mood and/or a history of adverse life events. For each study, participants will be assessed in two, 1.5 hour sessions, including refreshment breaks, on separate days. In each study, an experimental second session is preceded by an initial behavioural script-development session, which focuses on the development of personalised scripts based on autobiographical memories for use in a script-driven imagery procedure during the experimental task.

Study 1 is a behavioural study that aims to assess the efficacy of emotion regulation strategies on mood in response to memories of rejection and affiliation. Study 2 is an fMRI study that aims to establish the neuro-affective profile of how such memories are processed. Study 3 aims at implementing an emotion regulation strategy using real-time fMRI neurofeedback training.

Study 1: A Behavioural Study of Emotion Regulation in Response to Memories of Social Rejection and Affiliation

This behavioural study will compare the effect of different emotion regulation strategies on mood ratings in response to memories of rejection and affiliation.

Study 1, METHODS:

Session 1 focuses on developing short personalised scripts based on autobiographical memories for use in a script-driven imagery procedure. See **Appendix 1** for detailed protocol. Session 2 compares the effect of different emotion regulation strategies on mood ratings in response to personalised scripts derived from session 1 using a script-driven imagery experimental procedure.

Study 1, Participants

Participants will have varying mood levels and based on scores from the Beck Depression Inventory II (BDI-II), will be divided into low-mood/euthymic mood groups.

Study 1, Design

In a within-subject design, participants will listen to memory scripts under three experimental conditions, (1) 'attend', (2) 'describe' and (3) 'label', in which participants are instructed to (1) only imagine, (2) describe the imagined scene using neutral descriptors or (3) label social emotions using an emotion wheel. There will be three blocks (social positive, social negative, social neutral) with three trials of same-category scripts each. The primary analysis will be a 3 (memory type) x 3 (emotion regulation strategy) ANOVA. Dependent variables consist of a range of affective responses (see below).

MATERIALS (Self-Report Measures):

Appendix 2; The Beck Depression Inventory-II (BDI-II; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961)

The BDI-II is a 21-question multiple-choice self-report inventory, one of the most widely used instruments for measuring the severity of depression. The BDI-II is widely used as an assessment tool by health care professionals and researchers in a variety of settings. Participants in our sample will be assigned into low-mood/euthymic mood groups based on BDI-II scores. Scores on the BDI-II will indicate any change in mood symptoms over time.

Appendix 3; The Beck Anxiety Inventory (BAI; Beck and Steer, 1993)

The BAI is a 21-item self-report measure of anxiety symptoms. It has strong psychometric properties and participants indicate the extent to which they have experienced anxiety symptoms over the previous week. Scores on the BAI will indicate any change in mood symptoms over time.

Appendix 4; Involuntary Subordination Questionnaire (ISQ; Sturman, 2011)

The ISQ is a 32-item questionnaire designed to interrogate involuntary subordination indexing tendencies of feeling stuck (entrapment), defeated, inferior, and seeing the self as submissive.

Appendix 5; Social Comparison Scale (SCS; Allan and Gilbert, 1995)

This SCS measures self-perceptions of social rank and relative social standing using a semantic differential methodology and consists of 11 bipolar constructs. Participants are required to make a global comparison of themselves in relation to other people and to rate themselves along a ten-point scale. The 11-items cover judgments of rank, attractiveness and how well the person thinks they 'fit in' with others in society. Low scores point to feelings of inferiority and general low rank self-perceptions.

Appendix 6; Strive to Avoid Inferiority Scale (SAIS; Gilbert, Broomhead et al. 2007)

Part one of the SAIS is a 31 item scale designed by Gilbert et al. (2007) to measure a) beliefs about striving to compete to avoid inferiority, feelings of acceptance by others whether one succeeds or fails and not having to compete. The striving element refers to 'insecure striving', while the second element refers to 'secure non-striving'. Participants rate statements describing how they think and feel about the need to strive and compete in life. Each item is answered using a five-point Likert scale of 0 = never to 4 = always. The second part of the SAIS focused on the reasons for people feeling under pressure to compete and avoid inferiority. Participants respond on a 10-point scale (0 = 'don't agree' to 10 = 'completely agree').

Appendix 6; Submissive Behaviour Scale (SBS; Allan and Gilbert, 1997)

The SBS consists of 16 examples of submissive behaviour (e.g. "I agree that I am wrong even though I know I'm not") which people rate as a behavioural frequency (0 = Never to 4 = Always). These social measures in Appendices 4-6 will allow us to compare social traits across individuals with high vs low mood.

Appendix 8; Questions from the Structured Clinical Interview for DSM Axis-IV Disorders (SCID-I; First, Spitzer, Gibbon., & Williams, 1996)

The SCID-I involves a series of questions concerning current and past symptoms of a range of psychological disorders and usually takes between ½ and 1 hour. The SCID is only administered by experienced research staff that has undergone comprehensive SCID training. The mood module will be used to verify whether participants are currently experiencing low mood of clinical severity or not.

Appendix 9: Five Facet Mindfulness Questionnaire (FFMQ; Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006)

The FFMQ is based on a factor analytic study of five independently developed mindfulness questionnaires, encompassing the five facets of observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience. It consists of 39 items and asks people to indicate what 'best describes your own opinion of what is generally true for you' on a 5-point scale (5 = Always or Very Often True to 1 = Never or Very Rarely True).

Appendix 10: Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004)

The DERS is a 36-item self-report measure developed to examine difficulties in the ability to regulate emotions. Participants rate how often statements such as "I feel at ease with my emotions" apply to them on a 5-point scale (1='almost never', to 5='almost always'). Subscales assess six dimensions of difficulties.

Appendix 11: Spontaneous Use of Imagery Scale (SUIS; Reisberg, Pearson, & Kosslyn, 2003).

The SUIS consists of 12 items and asks people to 'indicate the degree to which each is appropriate for them', using a 1–5 scale (5= Completely Appropriate, 1= Never Appropriate). These process measures in Appendices 9-10 will allow us to compare individual's high vs low mood on these measures.

Appendix 12: Positive and Negative Affect Schedule (PANAS; Watson & Clark, 1988)

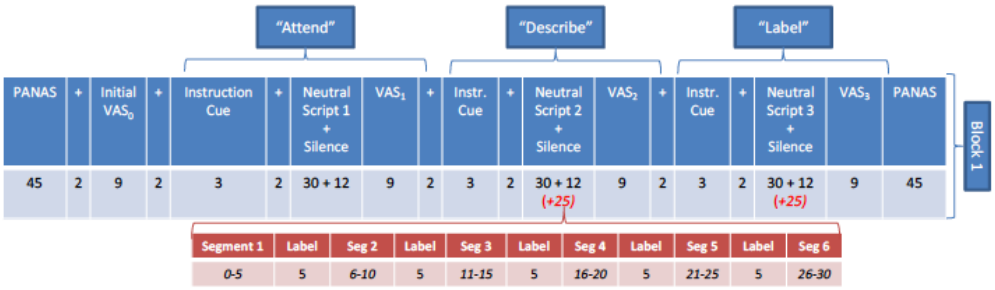
The PANAS assesses current positive and negative affect by asking participants to rate themselves in relation to ten positive (e.g. "attentive") and negative (e.g., "hostile") terms on a 5-point Likert scale. The PANAS will be used to measure state mood.

Appendix 13: Interpersonal Sensitivity Measure (IPSM; Boyce & Parker, 1989)

The IPSM assesses excessive sensitivity to the interpersonal behaviour of others, to social feedback and to (perceived or actual) negative evaluation by others. The 36 items are completed on a 4-point Likert-type scale (1= 'very unlike me', 2='moderately unlike me', 3='moderately like me', 4='very like me').

Study 1, Memory Presentation Task

The experimental task consists of listening to audio-recordings of autobiographical scripts while trying to imagine the event in the present. Participants complete 9-sec mood ratings (VAS_0) before and after listening to the scripts (VAS_1) to assess the change in emotional intensity. Participants rate their mood on three states (distress, rejection and inclusion) using 11-point scales from 0 (not at all) to 10 (extremely) (Davies & Clark, 1998). Scores across the three scales will be averaged (inclusion reverse scored) to provide a single index of mood at each time point (Woud, Postma, Holmes, Dalgleish, Mackintosh 2012). Each condition within a block will be indicated by a 3-sec instruction cue and fixation cross immediately before the script. Pre- and post PANAS ratings for each block will be obtained (Appendix 12). The order of the blocks will be presented in a fixed order (the neutral block, followed by the negative and finishing on the positive block to ensure mood repair before the end of the experiment). The order of the scripts will be randomized within the blocks.



Study 1, Session 1, Procedure:

All participants will complete a memory interview in which they will be asked to recall autobiographical memories of social rejection, social affiliation and neutral social memories of different intensity. To elicit images, participants will be asked to imagine their memory in as much vivid detail as possible and provide a comprehensive narrative. The experimenter will provide examples and cues for common experiences and reactions to social rejection and affiliation to expand individual narratives and/or to include relevant sensory detail (e.g., physical reactions, contextual stimuli, etc). Participants will be asked to rate their autobiographical memories on perceived vividness and intensity on a visual analogue scales ranging from 0 ("Not at all") to 11 ("Extremely"). Participants will be asked to indicate where one meaningful segment of the narrative has ended and another has begun, thereby providing meaningful event boundaries within the narrative. The written narrative will be audio-recorded into 30-second scripts in the first person, present tense and including different visceral, physical reactions and sensory details. Multiple scripts of each memory type provided in this script-development session will be used during the script-driven imagery procedure to avoid repetition effects. Audio recordings will be gender specific to the participants and contain no information that could identify participants. The recordings will be destroyed at the end of the experiment. At the end of the session participants are thanked for their time and fully debriefed. The same procedure from session 1 will precede study 2 and 3. See **Appendix 1** for detailed protocol.

Study 1, Session 2, Procedure:

Participants will be familiarized with the visual analogue scale (VAS) and social emotion wheel prior to the task (see **Appendix 14**). A practice run will precede the experimental block to familiarize participants with the task. In the experiment, participants will listen to audio-recordings of their autobiographical scripts while trying to imagine experiencing the event in the present and are told to pay attention to their emotional response during the event and during a brief silence that follows. Following each script, participants will be asked how well they were able to imagine themselves experiencing the event in the present and how much they had thought about specific labels while listening on a 11-point scale with 0 ("Not at all") to 11 ("Extremely"). Following the experiment, participants will provide ratings of interpersonal rejection sensitivity using the IPSM (**Appendix 13**); provide ratings of spontaneous imagery using the SUIS (**Appendix 11**) and fill in the BDI-II (**Appendix 2**) and BAI (**Appendix 3**) to assess change in mood symptoms over time. At the end of the session participants are thanked for their time and fully debriefed.

Study 2: An fMRI study of emotion processing in response to social memories compared to non-social memories

This is a one-hour neuroimaging session assessing the neural processing of social and non-social emotions in response to autobiographical memories, including refreshment breaks. Study 2 is preceded on a separate day by a one-hour behavioural script-development session, identical to the session 1 in study1 (**Appendix 1**).

Study 2, Session 2, METHODS:

Design

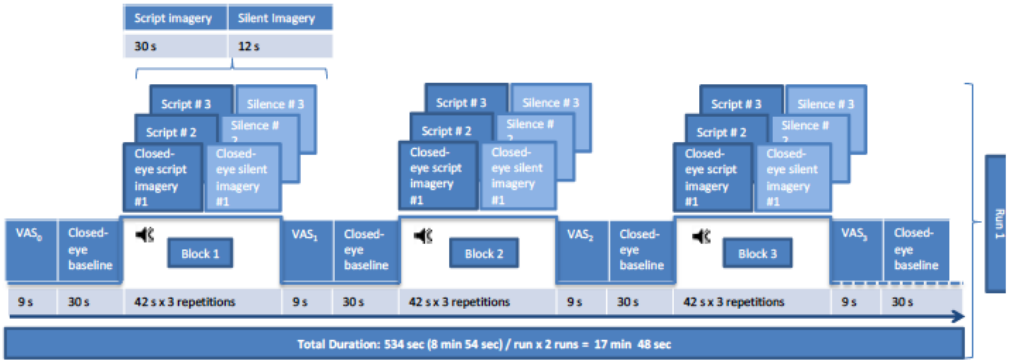
Study 2, session 2 will employ the same memory presentation task used in study 1, session 2. This study is modelled as an epoch-design comprised of two functional runs (social, non-social) of six blocks with three blocks containing socially relevant scripts (run 1), while the other three are non-socially relevant scripts (run 2). Overall, participants will listen to and imagine three consecutive 30-sec scripts (incl. 12 sec silence) of the same category within each block (neutral, negative, positive), resulting in 18 overall scripts with a total duration of ca. 18 min.

Study 2, Session 2, Materials:

The same self-report measures as in study 1 will be used (see **Appendix 2-13**). Auditory stimuli will be presented via headphone using the Etymotic ER3 pneumatic tube presentation system in combination with ear defenders to attenuate scanner noise. Simultaneously, participants are asked to focus on a fixation cross during the open-eye baseline, presented on a custom-built mirror stereoscope, with the participants' heads stabilized by a chin-and-head rest. The effective viewing distance will be 50 cm.

Study 2, Session 2, Memory Presentation Task:

The same memory presentation task as in study 1, session 2 will be used.



Study 2, Session 2, Procedure:

After providing informed consent, participants will perform the memory presentation task described in study 1, session 2. Participants complete VAS and PANAS mood ratings and manipulation checks assessing script intensity, imaginability and use of spontaneous imagery. A practice run will precede the experimental block to familiarize participants with the procedure. A variety of affective measures assess change in mood symptoms. At the end of the session participants are thanked for their time and debriefed.

Study 3: A Real-time fMRI study of self-regulation of brain activity in response to social memories using neurofeedback training

This study consists of 3 neuroimaging sessions of 1.5 hour duration investigating self-regulation of brain activity using real-time neurofeedback (NF), including refreshment breaks. Study 3, session 2 is preceded by a 1.5 hour behavioural script-development session identical to session 1 in studies 1 and 2 (**Appendix 1**).

Study 3, Session 2, METHODS:

Design

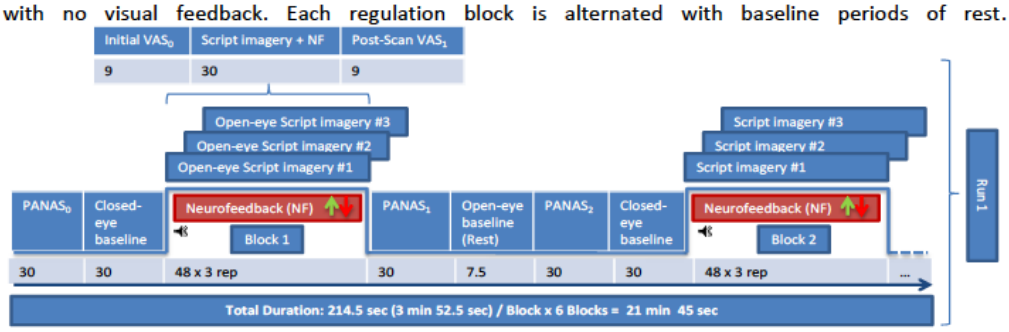
This study is modelled as an epoch-design comprised of six blocks containing socially relevant autobiographical scripts (negative, neutral, positive), and neurofeedback blocks with exclusively negative social memories. Blocks are distributed over two functional runs (localizer, NF) with three conditions, 'neurofeedback', 'sham', and 'attend'. Linear contrasts comparing mean change in activation for regulation in social and non-social blocks and positive vs negative blocks will be calculated for each participant and used in a group level, whole-brain analysis. The same affective measures as in Study 1 will serve as the dependent variables.

Materials

The same self-report measures as in study 1 will be used (see **Appendix 1-12**). Auditory stimuli will be presented in the same way as in study 2.

Experimental Task

Outside the scanner, participants are familiarized with the memory presentation task as used in study 2, followed by the neurofeedback procedure (see below). In the scanner, participants perform the memory presentation task as described in study 2. The localizer task provides a functional target area for social emotion processing and regulation. Localizer blocks will be presented in a fixed order (neutral/negative/positive block). After the localizer scan, participants perform the memory presentation task under three different conditions. In the 'Neurofeedback' (NF) condition, participants down-regulate their brain activity in response to negative scripts. The direction of regulation will be indicated by an on-screen arrow on either side of the feedback signal (↓). The NF is a continuous signal from the target area (updated every TR and thus every 2 seconds) which will be displayed using the picture of a thermometer whose dial indicates the amplitude of the fMRI signal in the target area. Changes in the amplitude indicated the percent of signal change, calculated using the current signal intensity value and comparing it with the average value determined from the rest period immediately preceding each block. In the 'Sham' group, participants down-regulate their brain activity with a continuous signal from a functionally similar area, but not the actual target area. In the 'Attend' group, participants down-regulate their brain activity with no visual feedback. Each regulation block is alternated with baseline periods of rest.



Study 3, Session 2, Procedure:

After providing informed consent, participants are randomly allocated to either the 'Control', 'NF' or 'Sham' group in a case control design. Participants perform the experimental memory presentation task, preceded by a practice run. A variety of affective measures assessing change in mood symptoms will be administered. At the end participants are thanked for their time and debriefed

Question 10: What ethical issues does this study raise and what measures have been taken to address them?

All three studies involve the recall of negative memories, a procedure which may elicit negative emotions. In order to reduce the likelihood that participants may recall a very upsetting personal memory, participants will be asked to identify a memory which feels personally relevant but which they would feel comfortable thinking or talking about in the study context. The recall of negative memories is preceded and followed in fixed order by neutral and positive memories respectively to counteract any negative emotion and ensure mood repair prior to the end of the experiment. The use of questionnaires and measures enquiring about emotions including mood and stress symptoms may also be difficult for some participants, particularly those who are experiencing low mood. Script-driven imagery is a widely used procedure for symptom provocation in PTSD research with no long-term negative outcomes reported in clinical and control populations (Lanius et al., 2006). In the present study, no trauma-related memories will be probed, with social memories being much lower in valence and arousal. This study will be conducted under the supervision of a clinical psychologist (Tim Dalgleish), should any participant become distressed or other clinical issues arise. In the unlikely case that a participant becomes distressed, we have a protocol in place in order to ensure their wellbeing. A full description of our protocol is included in **Appendix 15** but in summary, in case of distress we follow these steps –

1. Provide a safe space

Participants are offered a drink and a peaceful environment in which to relax, to allow any adverse effects to dissipate. A member of the research team will remain with them for as long as needed.

2. Offer a confidential consultation with a Clinical Psychologist

If the participant remains upset or wishes to talk at length then they are offered the chance to speak with a nominated clinical psychologist, at a time that is mutually convenient. This will be followed up with a GP referral if necessary and/or contacting emergency services in case of crisis.

3. Ensure safe transport home and further follow up if necessary

The suitability of participants to drive is assessed, and alternative transport is arranged if necessary. Follow-up telephone calls are offered.

Another potential source of distress or risk may arise from the use of real-time Neurofeedback in study 3. The potential risks of self-regulation of brain activity were thoroughly examined in a recent safety study that directly investigated potential adverse events related to fMRI and Neurofeedback. There was no evidence for any greater rates of adverse effects compared to non-scanning controls, including clinical samples typically susceptible to greater risk of side effects (Hawkinson et al., 2012). The potential motivational effect of unsuccessful regulation will be outlined to the participant prior to the experiment and in the debrief procedure, which is included in **Appendix 16**. The use of sham control will also be outlined to participants during the debrief procedure. Subjects will be provided with the opportunity to ask questions and withdraw consent if desired due to being unhappy or frustrated at having been unsuccessful in self-regulation of brain activity.

In the event of clinical issues arising from the structural MRI data, the following summarised procedure will be put in place (a full description of this protocol is provided in **Appendix 17**):

1. In the event that a significant abnormality is noticed by the Qualified MRI Operator, this will be brought to the attention of the CBSU Medical Monitor, who is responsible for acting on this information.
2. The Medical Monitor will take responsibility for referring the individual concerned for further clinical evaluation where this is appropriate.
3. If a volunteer later contacts a researcher to ask about possible abnormal findings, the researcher should only take their contact details, and then tell the Medical Monitor and Radiographers, one of whom will contact the volunteer.

Question 11: Who will the participants be?

Participants will be aged 18-65, literate and fluent in English. All participants will be recruited from our existing MRC CBSU volunteer panels (specifically, either from our research group's panel of participants with a history of low mood or from the department mainstream participant panel) and will thus have already consented to being approached about taking part in such studies. Participants with a history of low mood (from the research group low mood panel) or no such history (from the main dept. panel) will be invited to participate. Exclusion criteria will be current psychosis, current alcohol or substance abuse, current learning disabilities, organic brain damage. No participants will be directly recruited from the NHS.

We plan to recruit 120 participants, with 24 participants taking part in study 1, and 48 participants taking part in each of study 2 and study 3. Participants in study 2 and study 3 will comprise 2 groups of 24 (in groups of low mood and control participants) per study to allow between-group differences to be detected in the imaging data. A sample size of 24 subjects per group is required to achieve 80% power for single voxel activations corrected for multiple comparisons. Participants will be screened for their suitability for MRI (see **Appendix 18**)

Question 12: Describe the recruitment procedures for the study

Participants with a history of low mood will be recruited from our research group's panel of low mood individuals. Control participants will be recruited from the dept.'s main particpant database. These panels comprise the details of individuals who have previously agreed to take part in research conducted by our group. This is our standard method of recruitment which has been previously approved by CPREC (e.g. 2010.11; 2013.30) and applies to all the studies described above.

Question 13: Describe the procedures to obtain informed consent

Participants will be recruited from existing MRC Cognition and Brain Science Unit participant databases so all participants' will have previously consented to take part in research. Consent for the current study will be obtained from adult participants in writing prior to the commencement of the study.

Specifically, during the recruitment phase, participants will be sent or emailed out an information sheet (**Appendix 19, 20 and 21** for study 1, study 2, and study 3 respectively) that includes relevant study information. Participants have as much time as they like to decide whether or not they would like to participate in the study. This information sheet will also be reviewed and discussed at the session before written consent is taken. The experimenter will verbally confirm that the participant wishes to continue with the study, with a reminder of their right to withdraw at any time without giving a reason.

If at any point during the study participants wish to withdraw consent, they will be able to do this without penalty. Fluency in English and ability to read is a requirement of the study so participants should be able to understand verbal explanations and will have the information sheet thoroughly explained to them if there is any aspect of the material that is unclear.

Question 14: Will consent be written?

x Yes

☐ No

The consent forms are attached at **Appendix 22** for study 1 and **Appendix 23** for study 2 and **Appendix 24** for study 3.

Question 15: What will participants be told about the study? Will any information on procedures or the purpose of study be withheld?

For all studies, participants will be told they are participating in a project investigating the processing of social emotions in response to autobiographical scripts of rejection and inclusion memories. For Studies 2 and 3 participants will be informed that the studies involve fMRI. For study 3, in addition, people will be told that they will attempt to regulate their brain activity in response to negative personal memories of social rejection using real-time fMRI Neurofeedback. No information will be withheld that has not been made available to participants in the information sheets. Participants will be fully debriefed at the conclusion of the study with ample opportunity to ask questions. See **Appendix 16**.

Question 16: Will personally identifiable information be made available beyond the research team?

No. To ensure the confidentiality and anonymity of participants, a participant number will be allocated to each person, and data will be recorded in a database according to this number (i.e., not participants' personal information). The analysis between groups will depend on average differences between numerical scores and statistical parametric maps on the imaging data, as will publication of results, thereby protecting the anonymity of participants.

Question 17: What payments, expenses or other benefits and inducements will participants receive?

For study 1, participants will be given an honorarium to reimburse them for their time at a rate of £6/hour (minimum £12 guaranteed) and £2.50-£3 to cover travel expenses (rate depends on living proximity from the research unit). This is anticipated to amount to a maximum of 2 hours for each subject (£12 per subject) plus travel expenses.

For study 2, participants will be paid £10/hour (minimum £20 guaranteed) and £2.50-£3 to cover travel expenses. This is anticipated to amount to £20 per subject plus travel expenses.

For study 3, participants will be paid £10/hour (minimum £20 guaranteed) and £2.50-£3 to cover travel expenses. This is anticipated to amount to £20 per subject plus travel expenses.

Question 18: At the end of the study, what will participants be told about the investigation?

Each participant will be fully debriefed about the overall aims of each study. The study's theoretical goals and potential eventual clinical applications will be explained fully at the conclusion, with particular regard for the explanation of why Neurofeedback is still a novel technique with idiosyncratic limitations in study 3 in order to manage expectations of therapeutic success. Participants will be encouraged to ask any questions they may have at the end of the training. Participants will also be encouraged to contact the investigator at a later time if any further clarification is needed (contact details of the investigator will be provided). As participants will have varying levels of low mood, any clinical issues that arise during the study will be dealt with immediately. Any participant experiencing distress will be provided appropriate psychological support (TD). Please refer to **Appendix 16** for a sample of a general debriefing protocol and detailed scripts for each study.

Question 19: Has the person carrying out the study had previous experience of the procedures? If not, who will supervise that person?

Yes. All involved researchers have had experience with the experimental procedures including questionnaires and experimental tasks. TD has extensive experience working with individuals with varying levels of low mood and will provide clinical supervision should any issues arise. JG has experience in psychological assessments, functional MRI and neuropsychological evaluation in subjects of varying low mood.

Question 20: What arrangements are there for insurance and/or indemnity to meet the potential legal liability for harm to participants arising from the conduct of the study?

The Medical Research Council has indemnity arrangements in place such that public funding is provided to meet claims. Please see **Appendix 25** for the full MRC Statement of Indemnity.

Question 21: What arrangements are there for data security during and after the study?

All information collected will be held according to ethical and legal practice guidelines. Personal identity on these records will be indicated by an ID number rather than any personal details to protect anonymity.

The data will be stored in a locked filing cabinet and imaging data on the secure server located at the CBU which only the investigators will have access to. The information on the computers will be linked to personal information only via ID number and will be fully encrypted. The data will be retained for a minimum of 5 years. Data collected during the study will be stored and used in compliance with the UK Data Protection Act.

Signatures of the study team (including date)

Prof. Tim Dalgleish Date: 09/02/2014

Julia Gillard Date: 09/02/2014

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Appendix 2.2 Demographics questionnaire used across all studies

Participant ID | Participant Number | Classification | Date

Surname | First Name

DOB (Day / Month / Year) | Age | Gender: Female / Male | Ethnicity (eg Caucasian)

Marital Status

- Single (ie unmarried)
- Married
- De-facto Separated / Divorced
- Other

Educational History

- School Certificate / Yr 10 or equivalent
- Completed HSC / Yr 12 or equivalent
- Completed Bachelor degree
- Completed Masters degree
- Completed PhD
- Other

Current Employment Status

- Unemployed
- Employed

Employed as? (Please write occupation)

If employed, please circle type that best describes your work status:

- Part time
- Casual
- Full time
- Other

Have you ever experienced significant psychological difficulties (e.g., anxiety/depression)?

- Yes
- No

If yes, please provide details and indicate whether you are currently receiving any treatment or taking medication

Appendix 2.3 Blank consent form used across all studies

MRC | Cognition and Brain Sciences Unit

Principal Investigator:	Tim Dalgleish, Jason Stretton, Julia Gillard
Project Reference Number:	MR13015
LREC/CPREC Code:	Pre.2014.43 & Pre.2014.02
Scan ID:	

INFORMED CONSENT
(THIS FORM MUST BE COMPLETED PRIOR TO THE TEST)

Initials of participant

☐ I confirm that I have read the CBSU Guide for Volunteers, understand the Volunteer Information Sheet provided to me for the above study and have had the opportunity to ask questions.

☐ I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason, without my medical care or legal rights being affected.

☐ I understand that this is not a diagnostic scan but that if something abnormal should be noticed, I will be informed, as will my GP if I so wish.

☐ I understand that, where the MRC is the Sponsor, there are volunteer indemnity arrangements to cover negligent harm. Where the MRC is not the sponsor, insurance indemnity arrangements are in place.

☐ I understand that the research data may be accessed by researchers working at or in collaboration with the CBSU in similar ethically approved studies but that at all times my personal data will be kept confidential in accordance with data protection guidelines.

I have initialled the above boxes myself and I agree to take part in the study

SIGNATURE OF VOLUNTEER

Signature: _____

Name in block capitals: _____ **Date:** _____

SIGNATURE OF WITNESS

Name: _____ **Date:** _____

MRC Cognition and Brain Sciences Unit
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Appendix 2.4 Information sheet for fMRI study on autobiographical memories of rejection and inclusion (Chapter 4)

Title of the Project: An examination of emotion regulation and social information processing in response to autobiographical memories of social rejection and affiliation (THE SOCIAL EMOTIONS PROJECT)

Title of Study: An fMRI Study of Autobiographical Memories of Social Rejection and Inclusion

Please read the information below to decide if you would like to take part in The SOCIAL EMOTIONS PROJECT:

We are carrying out a series of studies (The Social Emotions Project) to investigate how people with differing levels of mood process and regulate the emotions elicited by social situations. In particular, the studies look at memories for social rejection and inclusion and the way people respond to and regulate their emotion to these personal events on a behavioural and neural level. We would like to invite you to participate in a neuroimaging study within this project. Please read this information sheet if you wish to find out more detail. Your participation is entirely voluntary.

Purpose of The Social Emotions Project:

As human beings, we are inherently oriented towards social interactions and sensitive to the experience of rejection, as well as inclusion. Social rejection increases anger, anxiety, depression, jealousy and sadness. These experiences can also activate areas of the brain in a similar manner as experiencing physical pain. These "social pain" areas are crucial in regulating emotion and in particular social emotions. People with varying levels of mood differ in their sensitivity to rejection and inclusion and have difficulties in regulating their emotions. We believe that the differences in social emotion processing contribute to people's feelings of depression and anxiety. Neurofeedback training offers a novel technique to improve people's ability to self-regulate their emotions, so we want to find out more about these processes and ways to change them in order to help people suffering from depression and interpersonal trauma to feel better.

What does this particular study involve?

This particular study will consist of two sessions, each of 2 hr duration, including refreshment breaks. In the first session outside the scanner we will ask you to generate a set of social and non-social memories from your past. These memories will include positive, negative and neutral themes and should be personally meaningful to you. We will then ask you to elaborate on these experiences to create a set of audio-scripted personal narratives. We will guide you through this process though a series of prompts and examples. In the second session you will perform a simple task within the scanner.

In the second session, we will ask you to pay attention to your emotions in response to listening to your personal narratives of social rejection and affiliation. Before your scan a member of staff will ask you some questions to ensure that you have no metal within you before you enter the strong magnetic field. You will then be asked to lie in the scanner and the scanning will start. The scanning can be

noisy and so we shall give you ear plugs as well as headphones to reduce this noise. It may not be appropriate for you to be scanned if you are very claustrophobic. During some of the scans we will ask you to perform simple tasks. The main task is to listen to and imagine your personal narratives. We will also ask you to complete a set of questionnaires about your current mood and social processing at the beginning and end of the session, which will take around 25 minutes in total.

You will have ample time before scanning to practice the tasks to ensure you are comfortable with them. The tasks we will be using have been used at the MRC CBSU and usually present volunteers with no significant problems. The scanning session will take about one and a half hours, although you will not actually be scanned for more than 45 minutes of this time.

Why have I been invited to take part?

You have been invited to take part in this study because you are a member of one of our volunteer panels at the MRC Cognition and Brain sciences Unit. We are looking for participants with differing levels of mood and we have used the information on our panels' databases to select individuals with a history of low mood or with no such history.

Do you have to take part?

No, it is up to you to decide. We will describe the study and go through this information sheet, which we then give to you. If you do want to join in we'll ask you to sign a consent form, a copy of which you can keep with this information sheet. You are free to withdraw from the study at any point without giving us a reason. You will not be treated any differently by any NHS/MRC service if you choose not to participate in this study or if you decide to withdraw.

What is the device involved?

We can learn a great deal about how the brain works by looking at the blood flow to different parts of the brain whilst the brain performs different tasks. We need to obtain this information in both health and disease. We measure brain function using images taken with a magnetic resonance imaging scanner. This scanner uses a strong magnetic field to create detailed images of brain structure and function. By taking a series of images whilst you perform a task we can build up a picture of the brain areas activated by this type of function. The scan does not involve any injections or X-rays.

What are the possible risks/side effects of taking part?

The scanner can be loud when it takes images, and you will be given earplugs and ear defenders to block out some of the sound. Also, the MR environment is quite confined, and people who are uncomfortable in small or confined spaces may not be able to participate. If this should be you, remember that you may withdraw from the study at any time without explaining why. Otherwise MRI is generally thought to be a safe, non-invasive imaging technique. There are no known risks or side effects.

All of the tasks and questionnaires in the study have been used safely in previous research. As with any research involving emotional material, there is a chance that you will experience some upset during the study. In our experience this is almost always very mild and short-lived with no lasting ill effects. After participation you will receive a complete and thorough explanation of the study and you will be able to contact a member of the research team (a qualified clinical psychologist) should you feel you are experiencing distress as a result of taking part in the study.

What are the possible benefits of taking part?

We will reimburse you for your time and contribute towards the cost of your travel for both sessions, and you will have the pleasure of knowing that you have made a contribution to our understanding of the relationship between brain and behaviour. We hope that the findings from this research will lead to a better understanding about processes of social emotion regulation and how they contribute to the symptoms of interpersonal trauma and depression.

If you wish you can take away a picture of your brain on the day of your scan.

What if new information becomes available?

If any new information pertains specifically to the health of the volunteer, the volunteer will be informed. Otherwise, new information will be disseminated through traditional scientific channels (journal articles, conference presentations).

What happens at the end of the study?

When data from several volunteers is collected, it will be analyzed and written up for publication in a scientific journal. The results may also be presented at scientific meetings, or in talks at academic institutions. Results will always be presented in such a way that data from individual volunteers cannot be identified.

Confidentiality – who will have access to the data?

All information we collect will be used in the strictest confidence and will be held according to ethical and legal practice guidelines. Your identity on these records will be indicated by an ID number rather than by your name or address, so that you cannot be identified. The audio-recordings from the first session will be destroyed upon completion of the experiment and will not be shared with anyone except the primary researchers and members of the research group. Members of the MRC Cognition and Brain Sciences Unit (CBSU) and members of the research group will have access to the scanning data. It is possible that the scanning data may be used by researchers working with the CBSU for other similar ethically approved research protocols, where the same standards of confidentiality will apply. It may also be disclosed to researchers working outside the CBSU, when that person is working in close collaboration with researchers scanning within the Cognition and Brain Sciences Unit. In that case that person has signed a Code of Conduct guaranteeing that the data will be kept confidential & secure. The MRC complies with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and is committed to upholding the Acts core Data Protection Principles. All enquiries concerning access to data held by the Cognition and Brain Sciences Unit should be addressed to the Freedom of Information Liaison Officer at the Unit in the first instance.

What happens if my scan shows something unusual? Will my GP be informed?

Your GP will not be routinely informed if your participation in this study has been as a normal volunteer. This is not a diagnostic scan but if something abnormal is detected you will be appropriately counselled and referred to an appropriate specialist in consultation with your General Practitioner if that is what you would like. Such early detection of an abnormality has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

Who is running this study?

The study is run by the Medical Research Council Cognition and Brain Sciences Unit. The researchers are all psychologists and clinical psychologists.

What if there is a problem?
For any complaint about the way you have been dealt with during the study or any possible harm you may have suffered you can call Dr. Richard Meiser-Steadman who is independent from the study (01223 273624).

What will happen if I don't want to carry on with the study at any point?
If you take part but change your mind and want to stop, you can leave at any time without explaining why. Also if you lose the capacity to consent during the study then you will be withdrawn from the study without any consequences. If you withdraw from the study you will also have the option to with draw all of the data that we have collected from you up to that point.

What will happen to the results of the research study?
Individual results from this study will not be available to participants. However, it is intended that results from this research will be published. Results will be presented in terms of groups of participants, so individual data will not be identifiable. If you wish we will send you a newsletter updating you on the findings from THE SOCIAL EMOTIONS PROJECT. Also, with your consent, we may contact you after the study about possible future research.

Who has reviewed these studies?
All research in the NHS is looked at by independent group of people (called a Research Ethics Committee) to protect your safety, rights, wellbeing and dignity. This project has received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge (Pre.2014.43).

Further Information & Contact Details:

If you would like any further information about THE SOCIAL EMOTIONS project then please contact Julia Gillard at the MRC Cognition and Brain Sciences Unit who is the research coordinator (tel: 01223 273 707; Email: Julia.Gillard@mrc-cbu.cam.ac.uk; address: MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge, CB2 7EF).

Thank you very much for reading this information sheet

Appendix 2.5 Information sheet for fMRI study on other's memories of rejection and inclusion (Chapter 5 and Chapter 6)

NHS National Institute for Health Research | Cambridgeshire and Peterborough NHS Foundation Trust | MRC Cognition and Brain Sciences Unit

INFORMATION SHEET

Title of the Project: An examination of emotion regulation and social information processing in response to autobiographical memories of social rejection and affiliation (THE SOCIAL EMOTIONS PROJECT)

Title of Study: **An fMRI Study of Social Synchrony to Autobiographical Memories of Social Rejection and Inclusion**

Please read the information below to decide if you would like to take part in The SOCIAL EMOTIONS PROJECT:

We are carrying out a series of studies (The Social Emotions Project) to investigate how people with differing levels of mood process and regulate the emotions elicited by social situations. In particular, the studies look at memories for social rejection and inclusion and the way people respond to and regulate their emotion to these personal events on a behavioural and neural level. We would like to invite you to participate in a neuroimaging study within this project. Please read this information sheet if you wish to find out more detail. Your participation is entirely voluntary.

Purpose of The Social Emotions Project:

As human beings, we are inherently oriented towards social interactions and sensitive to the experience of rejection, as well as inclusion. Social rejection increases anger, anxiety, depression, jealousy and sadness. People with varying levels of mood differ in their sensitivity to rejection and inclusion and have difficulties in regulating their emotions. We believe that these differences in social emotion processing contribute to people's feelings of depression and anxiety. Using neuroimaging, we are interested in how individuals with varying levels of mood experience and engage in social interactions in order to help people suffering from depression to feel better.

What does this particular study involve?

This particular study will consist of one session of 1.5hr duration but will be part of the larger 3hr session in conjunction with another study you are participating in. There will be opportunities for refreshment breaks throughout the session.

Before your scan a member of staff will ask you some questions to ensure that you have no metal within you before you enter the strong magnetic field. You will then be asked to lie in the scanner and the scanning will start. The scanning can be noisy and so we shall give you ear plugs as well as headphones to reduce this noise. It may not be appropriate for you to be scanned if you are very claustrophobic. During some of the scans we will ask you to perform simple tasks. The main task is to listen to a speaker narrating a series of personal memories involving social rejection and social

inclusion. These real-life personal memories may include positive, negative and neutral themes and were generated as part of a previous study on social memory. We are interested in measuring how your brain responds when you are listening to these memories. At the end, and outside of the scanner, we will also ask you to provide mood ratings in response to the memories you hear and to complete a set of questionnaires about your current mood and social processing.

You will have ample time before scanning to practice the tasks to ensure you are comfortable with them. The tasks we will be using have been used at the MRC CBSU and usually present volunteers with no significant problems. The scanning session will take about two hours, although you will not actually be scanned for more than ca 90 minutes of this time. Prior and following the scan you will be asked to carry out some behavioural tasks. Overall, this study should take no more than 3 hours. Note that the tasks described here are in addition to other tasks outlined in a separate information sheet.

Why have I been invited to take part?

You have been invited to take part in this study because you are a member of one of our volunteer panels at the MRC Cognition and Brain sciences Unit or you have responded to an advertisement. We are looking for participants with differing levels of mood and we have used the information on our panels' databases to select individuals with a history of low mood or with no such history.

Do you have to take part?

No, it is up to you to decide. We will describe the study and go through this information sheet, which we then give to you. If you do want to join in we'll ask you to sign a consent form, a copy of which you can keep with this information sheet. You are free to withdraw from the study at any point without giving us a reason. You will not be treated any differently by any NHS/MRC service if you choose not to participate in this study or if you decide to withdraw.

What is the device involved?

We can learn a great deal about how the brain works by looking at the blood flow to different parts of the brain whilst the brain performs different tasks. We need to obtain this information in both health and disease. We measure brain function using images taken with a magnetic resonance imaging scanner. This scanner uses a strong magnetic field to create detailed images of brain structure and function. By taking a series of images whilst you perform a task we can build up a picture of the brain areas activated by this type of function. The scan does not involve any injections or X-rays.

What are the possible risks/side effects of taking part?

The scanner can be loud when it takes images, and you will be given earplugs and ear defenders to block out some of the sound. Also, the MR environment is quite confined, and people who are uncomfortable in small or confined spaces may not be able to participate. If this should be you, remember that you may withdraw from the study at any time without explaining why. Otherwise MRI is generally thought to be a safe, non-invasive imaging technique. There are no known risks or side effects.

All of the tasks and questionnaires in the study have been used safely in previous research. As with any research involving emotional material, there is a chance that you will experience some upset during the

study. In our experience this is almost always very mild and short-lived with no lasting ill effects. After participation you will receive a complete and thorough explanation of the study and you will be able to contact a member of the research team (a qualified clinical psychologist) should you feel you are experiencing distress as a result of taking part in the study.

What are the possible benefits of taking part?

We will reimburse you for your time and contribute towards the cost of your travel for both sessions, and you will have the pleasure of knowing that you have made a contribution to our understanding of the relationship between brain and behaviour. We hope that the findings from this research will lead to a better understanding about processes of social emotion regulation and interaction and how they contribute to the symptoms of depression.

If you wish you can take away a picture of your brain on the day of your scan.

What if new information becomes available?

If any new information pertains specifically to the health of the volunteer, the volunteer will be informed. Otherwise, new information will be disseminated through traditional scientific channels (journal articles, conference presentations).

What happens at the end of the study?

When data from several volunteers is collected, it will be analyzed and written up for publication in a scientific journal. The results may also be presented at scientific meetings, or in talks at academic institutions. Results will always be presented in such a way that data from individual volunteers cannot be identified.

Confidentiality – who will have access to the data?

All information we collect will be used in the strictest confidence and will be held according to ethical and legal practice guidelines. Your identity on these records will be indicated by an ID number rather than by your name or address, so that you cannot be identified. Members of the MRC Cognition and Brain Sciences Unit (CBSU) and members of the research group and any collaborators will have access to the scanning data. It is possible that the scanning data may be used by researchers working with the CBSU for other similar ethically approved research protocols, where the same standards of confidentiality will apply. It may also be disclosed to researchers working outside the CBSU, when that person is working in close collaboration with researchers scanning within the Cognition and Brain Sciences Unit. In that case that person has signed a Code of Conduct guaranteeing that the data will be kept confidential & secure. The MRC complies with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and is committed to upholding the Acts core Data Protection Principles. All enquiries concerning access to data held by the Cognition and Brain Sciences Unit should be addressed to the Freedom of Information Liaison Officer at the Unit in the first instance.

What happens if my scan shows something unusual? Will my GP be informed?

Your GP will not be routinely informed if your participation in this study has been as a normal volunteer. This is not a diagnostic scan but if something abnormal is detected you will be appropriately

counselled and referred to an appropriate specialist in consultation with your General Practitioner if that is what you would like. Such early detection of an abnormality has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

Who is running this study?

The study is run by the Medical Research Council Cognition and Brain Sciences Unit. The researchers are all psychologists and clinical psychologists.

What if there is a problem?
For any complaint about the way you have been dealt with during the study or any possible harm you may have suffered you can call Dr. Caitlin Hitchcock who is independent from the study (+ 44 (0) 1223 273 744).

What will happen if I don't want to carry on with the study at any point?
If you take part but change your mind and want to stop, you can leave at any time without explaining why. Also if you lose the capacity to consent during the study then you will be withdrawn from the study without any consequences. If you withdraw from the study you will also have the option to with draw all of the data that we have collected from you up to that point.

What will happen to the results of the research study?
Individual results from this study will not be available to participants. However, it is intended that results from this research will be published. Results will be presented in terms of groups of participants, so individual data will not be identifiable. If you wish we will send you a newsletter updating you on the findings from THE SOCIAL EMOTIONS PROJECT. Also, with your consent, we may contact you after the study about possible future research.

Who has reviewed these studies?
All research in the NHS is looked at by independent group of people (called a Research Ethics Committee) to protect your safety, rights, wellbeing and dignity. This project has received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge (Pre2014.43)

Further Information & Contact Details:

If you would like any further information about THE SOCIAL EMOTIONS project then please contact Julia Gillard at the MRC Cognition and Brain Sciences Unit who is the research coordinator (tel: 01223 273 707; Email: Julia.Gillard@mrc-cbu.cam.ac.uk; address: MRC Cognition and Brain Sciences Unit, 15 Chaucer Road, Cambridge, CB2 7EF).

Thank you very much for reading this information sheet

Information sheet for behavioural study on Emotion Regulation Strategies in Response to Social Memories (Chapter 7)

Title of the Project: An examination of emotion regulation and social information processing in response to autobiographical memories of social rejection and affiliation (THE SOCIAL EMOTIONS PROJECT)

Title of Study: An fMRI Study of Autobiographical Memories of Social Rejection and Inclusion

Please read the information below to decide if you would like to take part in The SOCIAL EMOTIONS PROJECT:

We are carrying out a series of studies (The Social Emotions Project) to investigate how people with differing levels of mood process and regulate the emotions elicited by social situations. In particular, the studies look at memories for social rejection and inclusion and the way people respond to and regulate their emotion to these personal events on a behavioural and neural level. We would like to invite you to participate in a neuroimaging study within this project. Please read this information sheet if you wish to find out more detail. Your participation is entirely voluntary.

Purpose of The Social Emotions Project:

As human beings, we are inherently oriented towards social interactions and sensitive to the experience of rejection, as well as inclusion. Social rejection increases anger, anxiety, depression, jealousy and sadness. These experiences can also activate areas of the brain in a similar manner as experiencing physical pain. These "social pain" areas are crucial in regulating emotion and in particular social emotions. People with varying levels of mood differ in their sensitivity to rejection and inclusion and have difficulties in regulating their emotions. We believe that the differences in social emotion processing contribute to people's feelings of depression and anxiety. Neurofeedback training offers a novel technique to improve people's ability to self-regulate their emotions, so we want to find out more about these processes and ways to change them in order to help people suffering from depression and interpersonal trauma to feel better.

What does this particular study involve?

This particular study will consist of two sessions, each of 2 hr duration, including refreshment breaks. In the first session outside the scanner we will ask you to generate a set of social and non-social memories from your past. These memories will include positive, negative and neutral themes and should be personally meaningful to you. We will then ask you to elaborate on these experiences to create a set of audio-scripted personal narratives. We will guide you through this process though a series of prompts and examples. In the second session you will perform a simple task within the scanner.

In the second session, we will ask you to pay attention to your emotions in response to listening to your personal narratives of social rejection and affiliation. Before your scan a member of staff will ask you some questions to ensure that you have no metal within you before you enter the strong magnetic field. You will then be asked to lie in the scanner and the scanning will start. The scanning can be

noisy and so we shall give you ear plugs as well as headphones to reduce this noise. It may not be appropriate for you to be scanned if you are very claustrophobic. During some of the scans we will ask you to perform simple tasks. The main task is to listen to and imagine your personal narratives. We will also ask you to complete a set of questionnaires about your current mood and social processing at the beginning and end of the session, which will take around 25 minutes in total.

You will have ample time before scanning to practice the tasks to ensure you are comfortable with them. The tasks we will be using have been used at the MRC CBSU and usually present volunteers with no significant problems. The scanning session will take about one and a half hours, although you will not actually be scanned for more than 45 minutes of this time.

Why have I been invited to take part?

You have been invited to take part in this study because you are a member of one of our volunteer panels at the MRC Cognition and Brain sciences Unit. We are looking for participants with differing levels of mood and we have used the information on our panels' databases to select individuals with a history of low mood or with no such history.

Do you have to take part?

No, it is up to you to decide. We will describe the study and go through this information sheet, which we then give to you. If you do want to join in we'll ask you to sign a consent form, a copy of which you can keep with this information sheet. You are free to withdraw from the study at any point without giving us a reason. You will not be treated any differently by any NHS/MRC service if you choose not to participate in this study or if you decide to withdraw.

What is the device involved?

We can learn a great deal about how the brain works by looking at the blood flow to different parts of the brain whilst the brain performs different tasks. We need to obtain this information in both health and disease. We measure brain function using images taken with a magnetic resonance imaging scanner. This scanner uses a strong magnetic field to create detailed images of brain structure and function. By taking a series of images whilst you perform a task we can build up a picture of the brain areas activated by this type of function. The scan does not involve any injections or X-rays.

What are the possible risks/side effects of taking part?

The scanner can be loud when it takes images, and you will be given earplugs and ear defenders to block out some of the sound. Also, the MR environment is quite confined, and people who are uncomfortable in small or confined spaces may not be able to participate. If this should be you, remember that you may withdraw from the study at any time without explaining why. Otherwise MRI is generally thought to be a safe, non-invasive imaging technique. There are no known risks or side effects.

All of the tasks and questionnaires in the study have been used safely in previous research. As with any research involving emotional material, there is a chance that you will experience some upset during the study. In our experience this is almost always very mild and short-lived with no lasting ill effects. After participation you will receive a complete and thorough explanation of the study and you will be able to contact a member of the research team (a qualified clinical psychologist) should you feel you are experiencing distress as a result of taking part in the study.

What are the possible benefits of taking part?

We will reimburse you for your time and contribute towards the cost of your travel for both sessions, and you will have the pleasure of knowing that you have made a contribution to our understanding of the relationship between brain and behaviour. We hope that the findings from this research will lead to a better understanding about processes of social emotion regulation and how they contribute to the symptoms of interpersonal trauma and depression.

If you wish you can take away a picture of your brain on the day of your scan.

What if new information becomes available?

If any new information pertains specifically to the health of the volunteer, the volunteer will be informed. Otherwise, new information will be disseminated through traditional scientific channels (journal articles, conference presentations).

What happens at the end of the study?

When data from several volunteers is collected, it will be analyzed and written up for publication in a scientific journal. The results may also be presented at scientific meetings, or in talks at academic institutions. Results will always be presented in such a way that data from individual volunteers cannot be identified.

Confidentiality – who will have access to the data?

All information we collect will be used in the strictest confidence and will be held according to ethical and legal practice guidelines. Your identity on these records will be indicated by an ID number rather than by your name or address, so that you cannot be identified. The audio-recordings from the first session will be destroyed upon completion of the experiment and will not be shared with anyone except the primary researchers and members of the research group. Members of the MRC Cognition and Brain Sciences Unit (CBSU) and members of the research group will have access to the scanning data. It is possible that the scanning data may be used by researchers working with the CBSU for other similar ethically approved research protocols, where the same standards of confidentiality will apply. It may also be disclosed to researchers working outside the CBSU, when that person is working in close collaboration with researchers scanning within the Cognition and Brain Sciences Unit. In that case that person has signed a Code of Conduct guaranteeing that the data will be kept confidential & secure. The MRC complies with the requirements of the Data Protection Act 1998 with regard to the collection, storage, processing and disclosure of personal information and is committed to upholding the Acts core Data Protection Principles. All enquiries concerning access to data held by the Cognition and Brain Sciences Unit should be addressed to the Freedom of Information Liaison Officer at the Unit in the first instance.

What happens if my scan shows something unusual? Will my GP be informed?

Your GP will not be routinely informed if your participation in this study has been as a normal volunteer. This is not a diagnostic scan but if something abnormal is detected you will be appropriately counselled and referred to an appropriate specialist in consultation with your General Practitioner if that is what you would like. Such early detection of an abnormality has the benefit of starting treatment early but, in a small number of cases, may have implications for future employment and insurance.

Who is running this study?

The study is run by the Medical Research Council Cognition and Brain Sciences Unit. The researchers are all psychologists and clinical psychologists.

What if there is a problem?
For any complaint about the way you have been dealt with during the study or any possible harm you may have suffered you can call Dr. Richard Meiser-Steadman who is independent from the study (01223 273624).

What will happen if I don't want to carry on with the study at any point?
If you take part but change your mind and want to stop, you can leave at any time without explaining why. Also if you lose the capacity to consent during the study then you will be withdrawn from the study without any consequences. If you withdraw from the study you will also have the option to with draw all of the data that we have collected from you up to that point.

What will happen to the results of the research study?
Individual results from this study will not be available to participants. However, it is intended that results from this research will be published. Results will be presented in terms of groups of participants, so individual data will not be identifiable. If you wish we will send you a newsletter updating you on the findings from THE SOCIAL EMOTIONS PROJECT. Also, with your consent, we may contact you after the study about possible future research.

Who has reviewed these studies?
All research in the NHS is looked at by independent group of people (called a Research Ethics Committee) to protect your safety, rights, wellbeing and dignity. This project has received ethical approval from the Psychology Research Ethics Committee of the University of Cambridge (Pre.2014.43).

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Thank you very much for reading this information sheet

Appendix 2.6 Testing guidelines and adverse events protocol

This is the guidelines followed for general testing procedures at the MRC Cognition and Brain Sciences Unit, Cambridge.

A formal risk assessment should be made prior to testing. A checklist on the next page is provided to assist in the assessment.

Lower risk studies will include those in which:

- healthy volunteers are recruited or volunteers who are deemed fit by the research team to take part in the study without undue distress being caused to participant or tester.
- neutral stimuli are used (e.g. normal range of cue words not all pleasant or unpleasant and none that under normal circumstances would be expected to produce an adverse reaction).

Higher risk studies will include those in which:

- participants are selected because they belong to a potentially vulnerable group (i.e. depressed/ anxious)
- inductions are used with the intention of inducing a potentially vulnerable state (e.g. negative mood induction)
- emotional stimuli are used (e.g. unpleasant IAPS pictures)
- researchers have consistently found that on previous occasions volunteers have become distressed with the tasks.

Special consideration: Inexperienced testers, new graduate students and new placement students should not be asked to run higher risk studies (or studies which could potentially fall into the high-risk category) without adequate training and support.

Training and support: It is the responsibility of supervisors or line managers to ensure that all research staff are fully competent in carrying out the tests and that strategies for dealing with potential problems have been outlined prior to testing.

'Buddy' system: New testers will be assigned a junior member of the cognition and emotion research team to act as a 'buddy'. The aim of the buddy system is to provide extra advice and support.

Contingency plan: If a proposed study falls into the high risk category, and panel members will be involved in the research, a brief contingency plan should be submitted to the panel office at the time the request is made for volunteers. The plan should provide details of what action will be taken to reduce the risk of distress to volunteers and to testers. The contingency plan must be agreed by the researcher and line manager or supervisor and signed by both parties.

Please note:

- All new members of the research group must find out from their supervisor/line manager if the research that they will be conducting is already covered by an existing ethics application.
- If their research is covered by an existing ethics application, then they must read the application and send a letter to the ethics committee stating that they agree to comply with all aspects of the application.
- If the study is not covered by an existing ethics application, then an application must be made under the guidance of the supervisor/line manager.

Risk management checklist

- ❑ Will the experiment use stimuli that could elicit a strong emotional reaction? (e.g. unpleasant IAPS pictures)
- ❑ Will the experiment use a negative mood induction?
- ❑ Will the experiment use any invasive techniques? (e.g. electrophysiology)
- ❑ Will potentially vulnerable (e.g. anxious or depressed) volunteers be asked to take part in tasks that might increase their vulnerable state?

If the answer to any of the items above is yes, you are required to send a letter to all potential volunteers explaining the nature of the experiment. The letter must be sent prior to recruiting volunteers over the telephone.

Pre-test:

- ❑ If you believe that your study might cause undue distress, and your volunteers intend to drive to the unit to take part, you should ask if they would prefer to be collected prior to the study and taken home afterwards in the unit car.
- ❑ In the event of participants becoming distressed as a result of taking part in the research, what plan of action do you intend to take?
- ❑ If a clinical psychologist might be needed to provide back-up support (e.g. following an adverse reaction to a negative autobiographical mood induction), which clinician has agreed to act on your behalf?
- ❑ Have research-relevant assessments been made to check participants' suitability to take part? (e.g. mood check, claustrophobia check)
- ❑ If the study involves repeated use of keyboard or mouse, have any checks been made concerning repetitive strain injury or arthritis?
- ❑ If there is a possibility that participants may become upset during the test, have you got a box of tissues with you in the testing room?

Post-test:

- ❑ Has the nature of the experiment been fully explained and was the participant given the opportunity to have any questions answered.

- What was the participant's reaction to the experiment? Was there anything about the experiment that they did not like? Will participants be given a feedback sheet to allow them to comment on their experience of taking part in the study?
- Is the participant's mood at its normal pre-testing level?
- Are you giving participants an information sheet with a contact telephone number of the researcher on it to take away with? For previous studies using mood induction procedures, contact sheets have included the following wording: *"We always try to ensure that when people leave the experiment, their mood has returned to normal. On rare occasions, people can find that their mood drops again after they have returned home. We do not expect this to happen but it is possible. If your low mood returns and you feel that your distress is due to the mood induction then call us on the telephone number below and we can discuss how best to help you."*

What to do if participants become distressed as a result of taking part in the research:

- Sit and listen, and offer the participant a drink of tea or coffee.
- If necessary offer a confidential talk with a clinical psychologist.
- If the participant is unable to drive home, the unit policy is to drive the person home yourself in the unit car (you must see Anthea to complete the necessary forms). If this is not possible ask Jackie Harper or Pete Williams if they are willing to drive you and your volunteer to the participant's home. If all else fails, take the participant home in a taxi.
- Ask if the participant would mind if you called them later that day/the next day to check that they are OK.

Research using mood inductions, unpleasant IAPS pictures, invasive techniques and training in cognitive bias

The following guidelines have been adapted from the CBU policy on the use of mood inductions:

- Any researcher proposing to carry out research involving mood inductions, unpleasant IAPS pictures, invasive techniques or training in cognitive bias should send an email/letter to the Director prior to testing to obtain consent.
- A covering letter must be sent to prospective volunteers indicating the nature of the research they are being invited to take part in
- A contingency plan must be submitted to the panel office describing what measures will be taken to reduce the risk of distress to volunteers and to testers, and what action will be taken if an individual does suffer as a result of the testing (see description in ethics application question 10).
- Volunteers must sign a written consent form before beginning the experiment.
- If on the day of testing, the participant has changed their mind since agreeing to take part in the study and no longer wants to engage in the mood induction/view the IAPS pictures/be wired to the equipment, an alternative task must be made available for them to complete.

- Volunteers must be reminded that they are free to terminate the experiment at any point.
- Experimenters must ensure that volunteers' mood has returned to 'normal' (pre-testing level) before concluding the experimental session.
- Volunteers should not be asked to take part in other tests immediately following the experiment.
- A clinical psychologist should be approached and asked whether they would be prepared to talk to any participants who suffer an adverse reaction as a result of the experiment. This is not expected to happen but provision should be made in case it does occur. The discussion would take place at a time mutually convenient to the clinician and the volunteer.

Additional recommendations

- Scientists who are not clinically trained, but who wish to do mood induction research, must obtain guidance from someone experienced in the use of this technique. Guidance should cover screening of volunteers, implementation of the procedure and (most important of all) how to assess whether volunteers have returned to normal mood at the end of the experiment.
- The mood-state of volunteers must be screened before experiments using depression induction procedures, unpleasant IAPS pictures, invasive techniques or training in cognitive bias. Great care must be taken when testing volunteers scoring 14 or more on the Beck Depression Inventory, scoring above 8 on the HADS, and scoring 45 or more on the Spielberger Trait Anxiety Questionnaire. Only testers with suitable training should test volunteers with high depression or anxiety scores.
- As autobiographical mood inductions are more likely to lead to longer-term distress once the participant has returned home (compared with musical or film inductions) a negative autobiographical induction should not be used unless it forms an essential aspect of the study.
- Group mood induction should not take place unless a special case is made for it to the Ethical Committee.

Potential problems and advice on what to do

Participant care

Example 1: If a participant becomes distressed during the study….

If during an experiment (e.g. a study using an autobiographical memory task) a participant becomes distressed and begins to cry, testing should be curtailed. Sit tight, listen and make sympathetic noises if appropriate. Try to give the impression that their emotion is absolutely justified, they are normal, and you care that they are currently distressed. Give them time to recover. If it feels 'unfinished', ring the

participant the next day to check they are OK. Provide feedback to the panel about the incident.

Example 2: If the participant's mood has not returned to normal after testing….

If after an experiment (e.g. a study using a negative mood induction) a participant's mood has not returned to pre-testing levels, explain that it is not unit policy to send participant's away from an experiment feeling unhappy. Take them to a quiet room, if possible, play them relaxing music/ a tape of mood enhancing sounds, offer them a drink, and allow them to sit and relax for a while. Give the participant an information sheet with a daytime contact number (see page 2). Should the participant's low mood return and they attribute it directly to the study, they can then telephone and discuss their feelings with the researcher. Provide feedback to the panel about the incident.

Example 3: If a participant reports feeling adverse effects a week or more after testing….

If, after taking part in a high-risk study (e.g. research using unpleasant IAPS pictures), a participant reports having intrusive thoughts about the stimuli they were presented with, listen to the individual's concerns, and talk to them about their experience. If they remain unhappy, invite them to discuss their concerns with the nominated clinician. Provide feedback to the panel about the incident. Follow-up the complaint 2-3 weeks later with a telephone call to see how the participant is feeling.

Example 4: If a participant faints or becomes ill during testing….

Before you begin testing, check which members of staff are first aid qualified, which are situated nearest to your testing space and whether they are willing to be called upon should the need arise. If a volunteer does become ill during testing let the panel managers know about the incident. Follow-up with a telephone call the next day to see how the participant is feeling.

Researcher support

Example 1: Dealing with distressed participants…

If the researcher suspects that a participant is becoming unduly distressed by the experiment, then testing should be curtailed. After measures have been taken to deal with the participant's distress (see above), the tester should discuss the incident with their line manager or supervisor. This debriefing for the tester should aim to provide reassurance and advice about the way the incident was handled, as well as advice on what further action should be taken.

Example 2: If repetitive testing leads to tester-distress….

If repeated testing using emotional stimuli (e.g. unpleasant IAPS) causes distress for the tester, or an incident with a participant has created 'emotional wear-and-tear', the

tester should seek out their 'buddy' or their line manager/supervisor to discuss the problem. This debriefing for the tester should aim to provide reassurance and advice. If it is the material that is causing particular problems, the issue should be raised with the line manager. They should discuss ways in which to alleviate distress to the tester (e.g. by waiting outside the room during critical parts of the experiment) and if necessary, revise the experiment. The tester should be given as much time and emotional support as they require. Testing should only continue when the tester feels confident to do so.

Example 3: Working outside normal hours or working alone outside the unit….

Junior staff/ students should avoid working alone outside the unit, if possible. All staff testing outside the unit should register their whereabouts, contact details and expected return time with their line manager, their 'buddy' or with reception staff before they leave. They should take a unit mobile phone and inform their line manager/'buddy'/reception when they return. Junior staff/ students should also avoid testing participants in the unit outside normal working hours. If testing outside office hours proves essential, arrangements should be made to make sure that an experienced member of the group is present in the building, who can provide assistance should it be needed. All staff working out of hours should sign in to register their presence.

Appendix 2.7 MRI adverse events protocol

Abnormal (Incidental) Findings

The Cognition and Brain Sciences Unit is a cognitive neuroscience research unit and does not provide any diagnostic services. This policy will be clearly stated on the volunteer information sheet.

However, in order to ensure that only participants with appropriately healthy brains are included in our studies, and also to pick up any major abnormalities that do occur, structural T2-weighted scans will be run on all participants if not already run within 2 years. Even though we do not provide a diagnostic service, a Radiologist reviews all structural T2-weighted scans (taking into account their demographic details, e.g., age). In the event that a significant abnormality is noticed by the Qualified MRI Operator, this will be brought to the attention of the CBSU Medical Monitor, who is responsible for acting on this information. It may be necessary to exclude such participants from the study in which case the reasons for the exclusion will not be fed back to the researcher. The Medical Monitor will take responsibility for referring the individual concerned for further clinical evaluation where this is appropriate. Note that, if a volunteer later contacts a researcher to ask about possible abnormal findings, the researcher should only take their contact details, and then tell the Medical Monitor

and Radiographers, one of whom will contact the volunteer. A researcher should not try to give any other feedback to the volunteer.

Appendix 2.8 Sample debriefing protocol

For All Participants

- Ensure the nature of the experiment is explained

Explain the purpose of the study and what the participant's contribution is.

- Ascertain the participant's reaction to the experiment

Questions to be asked:

"What did you think of the experiment?"

"Was there anything about the experiment that you didn't like?"

"Did you experience any adverse effects, for example concerning how you feel?"

- Check current mood status

Ask the participant about their feelings at this moment, whether or not they feel their mood is at / has returned to normal levels. End the session if all is well, otherwise continue with the steps below.

Additional measures, in case of distress

- Provide a safe space

Participant's should be offered a drink and in a peaceful environment in which to relax, to allow any adverse effects to dissipate. A member of the research team should remain with them or in the vicinity for as long as needed.

- Offer a confidential consultation with a clinical psychologist

If the participant remains upset or wishes to talk at length then offer the chance to speak with a nominated clinical psychologist, at a time that is mutually convenient.

- Ensure Safe transport home and further follow up if necessary

Consider participant's suitability to drive and arrange alternative transport (e.g. staff member- see page 2) if necessary. Offer follow-up telephone calls, as appropriate.

Appendix 2.9 Sample questions from Structured Clinical Interview for DSM Axis-I Disorder (SCID-V)

Mood Module

'Now I'm going to ask you some questions about your mood…

Has there even been a time where you lost interest or pleasure in things you usually enjoyed? (If yes: was it nearly every day? How long did it last?)

Has there ever been a period of time when you were feeling so good, "high" excited or hyper that other people thought you were not your normal self or you were so hyper that you got into trouble? (Did anyone say that you were manic?) Was that more than just feeling good?)

Anxiety Module

Have you ever had a panic attack, when you suddenly felt frightened or suddenly developed a lot of physical symptoms (eg. heart racing, sweating, breathing changes)?

Is there anything that you have been afraid to do or felt uncomfortable doing in front of other people, like speaking, eating or writing?

Alcohol and Other Substance Use Module

What are your drinking habits like? How much do you drink? How often? What do you drink?

Was there ever a time in your life when you were drinking a lot more?

Have you ever used street drugs?

Psychosis Module

Have you ever heard things that other people couldn't hear, such as noises, or the voices of people whispering or talking? What did you hear? How often did you hear it? Have you ever had visions or see things that other people couldn't see?

Appendix 2.10 Beck Depression Inventory (BDI-I)

Participant ID

Date

Please read each group of statements carefully, then pick out the one statement in each group which best describes the way you have been feeling during the past 2 weeks, including today. Select the statement you have picked. If several statements in the group seem to apply equally well, simply select the statement which has the largest number. Be sure that you do not select more than one statement for item 16 (change in sleeping pattern) and item 18 (change in appetite).

1

- I do not feel sad
- I feel sad
- I am sad all the time and I can't snap out of it
- I am so sad or unhappy I can't stand still

2

- I am not particularly discouraged about my future
- I feel discouraged about the future
- I feel I have nothing to look forward to
- I feel my future is hopeless and that things cannot improve

3

- I do not feel like a
- I feel I have ed more than the a person
- As I look b on my life, all I can see is a lot of failur
- I feel I am a lete failure as a erson

4

- I get as much satisfaction out of things as I used to
- I don't enjoy things the way I used to
- I don't get real satisfaction out of anything anymore
- I am dissatisfied or bored with everything

5

- I don't feel parti arly guilty
- I feel guilty a go part of the time
- I feel uite guilty ost of the time
- I ty all of e time

- n't feel I am being ished
- el I may be punished
- I expect to be punished
- I feel I am being punished

7

- I don't feel disappointed in myself
- I am disappointed in myself
- I am disgusted with myself
- I hate myself

8

- I don't feel I am any worse than anybody else
- I am critical of myself for my weakness or mistakes
- I blame myself all the time for my faults
- I blame myself for everything bad that happens

9

- I don't have any thoughts of killing myself
- I have thoughts of killing myself, but I would not carry them out
- I would like to kill myself
- I would kill myself if I had the chance

10

- I don't cry any more than usual
- I cry more now than I used to
- I cry all the time now
- I used to be able to cry, but now I can't cry even though I want to

11

- I am no more irritated now than I ever am
- I get annoyed or irritated more easily than I used to
- I feel irritated all the time now
- I don't get irritated at all by the things that used to irritate

12

- I have not lost interest in other people
- I am less interested in other people than I used to be
- I have lost most of my interest in other people
- I have lost all of my interest in other people

13

- I make decisions about as well as I ever could
- I put off making decisions more than I used to
- I have greater difficulty in making decisions than before
- I can't make decisions at all anymore

14

- I don't feel I look any worse than I used to
- I am worried that I am looking old or unattractive
- I feel that there are permanent changes in my appearance that make me look unattractive
- I believe that I look ugly

15

- I can work about as well as before
- It takes an extra effort to get started at doing something
- I have to push myself very hard to do anything
- I can't do any work at all

16

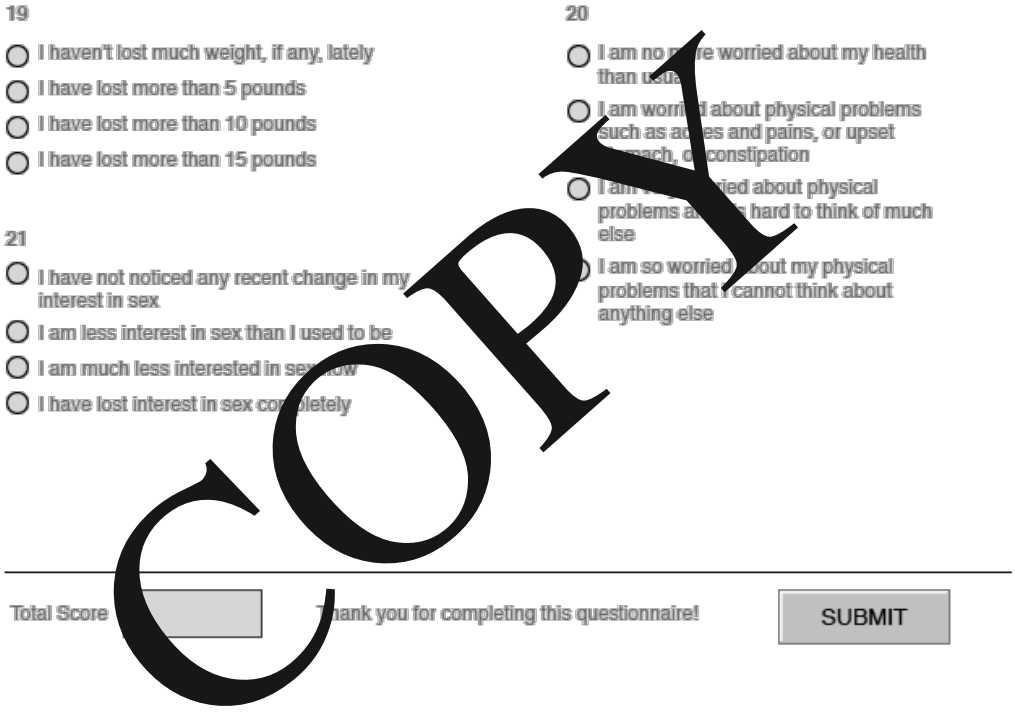
- I can sleep as well as usual
- I don't sleep as well as I used to
- I wake up 1-2 hours earlier than usual and find it hard to get back to sleep
- I wake up several hours earlier than I used to and cannot get back to sleep

17

- I don't get more tired than usual
- I get tired more easily than I used to
- I get tired from doing almost anything
- I am too tired to do anything

18

- My appetite is no worse than usual
- My appetite is not as good as it used to be
- My appetite is much worse now
- I have no appetite at all anymore


19

- I haven't lost much weight, if any, lately
- I have lost more than 5 pounds
- I have lost more than 10 pounds
- I have lost more than 15 pounds

20

- I am no more worried about my health than usual
- I am worried about physical problems such as aches and pains, or upset stomach, or constipation
- I am very worried about physical problems and it's hard to think of much else
- I am so worried about my physical problems that I cannot think about anything else

21

- I have not noticed any recent change in my interest in sex
- I am less interest in sex than I used to be
- I am much less interested in sex now
- I have lost interest in sex completely

Total Score

Thank you for completing this questionnaire!

SUBMIT

Appendix 2.11 Beck's Anxiety Inventory (BAI)

Participant ID

Date

Below is a list of common symptoms of anxiety. Please carefully read each item in the list. Indicate how much you have been bothered by each symptom during the PAST WEEK, INCLUDING TODAY.

	NOT AT ALL	MILDLY It did not bother me much.	MODERATELY It was very unpleasant but I could stand it	SEVERELY I could barely stand it.
1. Numbness or tingling.	☐	☐	☐	☐
2. Feeling hot.	☐	☐	☐	☐
3. Wobbliness in legs.	☐	☐	☐	☐
4. Unable to relax.	☐	☐	☐	☐
5. Fear of the worst happening.	☐	☐	☐	☐
6. Dizzy or lightheaded.	☐	☐	☐	☐
7. Heart pounding or racing.	☐	☐	☐	☐
8. Unsteady.	☐	☐	☐	☐
9. Terrified.	☐	☐	☐	☐
10. Nervous.	☐	☐	☐	☐
11. Feelings of choking.	☐	☐	☐	☐
12. Hands trembling.	☐	☐	☐	☐
13. Shaky.	☐	☐	☐	☐
14. Fear of losing control.	☐	☐	☐	☐
15. Difficulty breathing.	☐	☐	☐	☐
16. Fear of dying.	☐	☐	☐	☐
17. Scared.	☐	☐	☐	☐
18. Indigestion or discomfort in abdomen.	☐	☐	☐	☐
19. Faint.	☐	☐	☐	☐
20. Face flushed.	☐	☐	☐	☐
21. Sweating (not due to heat).	☐	☐	☐	☐

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Appendix 2.12 Positive and Negative Affect Schedule (PANAS)

Participant ID

Date

This scale consists of a number of words that describe different feelings and emotions. Read each item and then list the number from the scale below next to each word. Indicate to what extent you feel this way right now, that is, at the present moment OR indicate the extent you have felt this way over the past week.

	Very Slightly or Not At All	A Little	Moderately	Quite a Bit	Extremely
1. Interested	O	O	O	O	O
2. Distressed	O	O	O	O	O
3. Excited	O	O	O	O	O
4. Upset	O	O	O	O	O
5. Strong	O	O	O	O	O
6. Guilty	O	O	O	O	O
7. Scared	O	O	O	O	O
8. Hostile	O	O	O	O	O
9. Enthusiastic	O	O	O	O	O
10. Proud	O	O	O	O	O
11. Irritable	O	O	O	O	O
12. Alert	O	O	O	O	O
13. Ashame	O	O	O	O	O
14. Inspired	O	O	O	O	O
15. Nervous	O	O	O	O	O
16. Determined	O	O	O	O	O
17. Attentive	O	O	O	O	O
18. Jittery	O	O	O	O	O
19. Active	O	O	O	O	O
20. Afraid	O	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Appendix 2.13 Difficulties in Emotion Regulation Scale (DERS)

Participant ID

Date

Please indicate how often the following 36 statements apply to you by writing the appropriate number from the scale above (1 – 5) in the box alongside each item.

	Almost Never	Sometimes	About Half The Time	Most of The Time	Almost Always
1. I am clear about my feelings (R)	○	○	○	○	○
2. I pay attention to how I feel (R)	○	○	○	○	○
3. I experience my emotions as overwhelming and out of control	○	○	○	○	○
4. I have no idea how I am feeling	○	○	○	○	○
5. I have difficulty making sense out of my feelings	○	○	○	○	○
6. I am attentive to my feelings (R)	○	○	○	○	○
7. I know exactly how I am feeling (R)	○	○	○	○	○
8. I care about what I am feeling (R)	○	○	○	○	○
9. I am confused about how I feel	○	○	○	○	○
10. When I'm upset, I acknowledge my emotions (R)	○	○	○	○	○
11. When I'm upset, I become angry with myself for feeling that way	○	○	○	○	○
12. When I'm upset, I become embarrassed for feeling that way	○	○	○	○	○
13. When I'm upset, I have difficulty getting work done	○	○	○	○	○
14. When I'm upset, I become out of control	○	○	○	○	○
15. When I'm upset, I believe that I will remain that way for a long time	○	○	○	○	○
16. When I'm upset, I believe that I'll end up feeling very depressed	○	○	○	○	○
17. When I'm upset, I believe that my feelings are valid and important (R)	○	○	○	○	○
18. When I'm upset, I have difficulty focusing on other things	○	○	○	○	○
19. When I'm upset, I feel out of control	○	○	○	○	○
20. When I'm upset, I can still get things done (R)	○	○	○	○	○
21. When I'm upset, I feel ashamed with myself for feeling that way	○	○	○	○	○
22. When I'm upset, I know that I can find a way to eventually feel better (R)	○	○	○	○	○
23. When I'm upset, I feel like I am weak	○	○	○	○	○
24. When I'm upset, I feel like I can remain in control of my behaviours (R)	○	○	○	○	○
25. When I'm upset, I feel guilty for feeling that way	○	○	○	○	○
26. When I'm upset, I have difficulty concentrating	○	○	○	○	○
27. When I'm upset, I have difficulty controlling my behaviours	○	○	○	○	○
28. When I'm upset, I believe that there is nothing I can do to make myself feel better	○	○	○	○	○
29. When I'm upset, I become irritated with myself for feeling that way	○	○	○	○	○
30. When I'm upset, I start to feel very bad about myself	○	○	○	○	○
31. When I'm upset, I believe that wallowing in it is all I can do	○	○	○	○	○
32. When I'm upset, I lose control over my behaviours	○	○	○	○	○

Please continue

	Almost Never	Sometimes	About Half The Time	Most of The Time	Almost Always
33. When I'm upset, I have difficulty thinking about anything else	○	○	○	○	○
34. When I'm upset, I take time to figure out what I'm really feeling (R)	○	○	○	○	○
35. When I'm upset, it takes me a long time to feel better	○	○	○	○	○
36. When I'm upset, my emotions feel overwhelming	○	○	○	○	○

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Subscale Scores

Non-acceptance of emotional responses (NONACCEPT)	0
Difficulties engaging in goal directed behaviour (GOALS)	0
Impulse control difficulties (IMPULSE)	0
Lack of emotional awareness (AWARE)	0
Limited access to emotion regulation strategies (STRATEGIES)	0
Lack of emotional clarity (CLARITY)	0

Appendix 2.14 Five Facet Mindfulness Questionnaires (FFMQ)

Participant ID

Date

This instrument is based on a factor analytic study of five independently developed mindfulness questionnaires. The analysis yielded five factors that appear to represent elements of mindfulness as it is currently conceptualized. The five facets are observing, describing, acting with awareness, non-judging of inner experience, and non-reactivity to inner experience.

Please rate each of the following statements using the scale describing your own opinion of what is generally true for you.

	Never Or Very Rarely True	Rarely True	Sometimes True	Often True	Very Often Or Always True
1. When I'm walking, I deliberately notice the sensations of my body moving.	○	○	○	○	○
2. I'm good at finding words to describe my feelings.	○	○	○	○	○
3. I criticize myself for having irrational or inappropriate emotions.	○	○	○	○	○
4. I perceive my feelings and emotions without having to react to them.	○	○	○	○	○
5. When I do things, my mind wanders off and I'm easily distracted.	○	○	○	○	○
6. When I take a shower or bath, I stay alert to the sensations of water on my body.	○	○	○	○	○
7. I can easily put my beliefs, opinions, and expectations into words.	○	○	○	○	○
8. I don't pay attention to what I'm doing because I'm daydreaming, worrying, or otherwise distracted	○	○	○	○	○
9. I watch my feelings without getting lost in them	○	○	○	○	○
10. I tell myself I shouldn't be feeling the way I'm feeling.	○	○	○	○	○
11. I notice how foods and drinks affect my thoughts, bodily sensations, and emotions.	○	○	○	○	○
12. It's hard for me to find the words to describe what I'm thinking	○	○	○	○	○
13. I am easily distracted.	○	○	○	○	○
14. I believe some of my thoughts are abnormal or bad and I shouldn't think that way.	○	○	○	○	○
15. I pay attention to sensations, such as the wind in my hair or sun on my face.	○	○	○	○	○
16. I have trouble thinking of the right words to express how I feel about things	○	○	○	○	○
17. I make judgments about whether my thoughts are good or bad.	○	○	○	○	○
18. I find it difficult to stay focused on what's happening in the present.	○	○	○	○	○
19. When I have distressing thoughts or images, I "step back" and am aware of the thought or image without getting taken over by it.	○	○	○	○	○
20. I pay attention to sounds, such as clocks ticking, birds chirping, or cars passing.	○	○	○	○	○
21. In difficult situations, I can pause without immediately reacting.	○	○	○	○	○
22. When I have a sensation in my body, it's difficult for me to describe it because I can't find the right words.	○	○	○	○	○
23. It seems I am "running on automatic" without much awareness of what I'm doing.	○	○	○	○	○
24. When I have distressing thoughts or images, I feel calm soon after.	○	○	○	○	○
25. I tell myself that I shouldn't be thinking the way I'm thinking.	○	○	○	○	○
26. I notice the smells and aromas of things.	○	○	○	○	○
27. Even when I'm feeling terribly upset, I can find a way to put it into words.	○	○	○	○	○
28. I rush through activities without being really attentive to them.	○	○	○	○	○
29. When I have distressing thoughts or images I am able just to notice them without reacting.	○	○	○	○	○
30. I think some of my emotions are bad or inappropriate and I shouldn't feel them.	○	○	○	○	○
31. I notice visual elements in art or nature, such as colors, shapes, textures, or patterns of light and shadow.	○	○	○	○	○
32. My natural tendency is to put my experiences into words.	○	○	○	○	○

Please continue

	Never Or Very Rarely True	Rarely True	Sometimes True	Often True	Very Often Or Always True
33. When I have distressing thoughts or images, I just notice them and let them go.	O	O	O	O	O
34. I do jobs or tasks automatically without being aware of what I'm doing.	O	O	O	O	O
35. When I have distressing thoughts or images, I judge myself as good or bad, depending what the thought/image is about.	O	O	O	O	O
36. I pay attention to how my emotions affect my thoughts and behavior.	O	O	O	O	O
37. I can usually describe how I feel at the moment in considerable detail.	O	O	O	O	O
38. I find myself doing things without paying attention.	O	O	O	O	O
39. I disapprove of myself when I have irrational ideas.	O	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Subscale Scores

Observe Items (OBSERVE)	0
Describe Items (DESCRIBE)	0
Act with Awareness Items (AWARENESS)	0
Nonjudge Items (NON-JUDGEMENT)	0
Non-react Items (NON-REACTIVITY)	0

Appendix 2.15 Spontaneous Use of Imagery Scale (SUIS)

Participant ID

Date

Please read each of the following descriptions and indicate the degree to which each is appropriate for you. Do not spend a lot of time thinking about each one, but respond based on your thoughts about how you do or do not perform each activity. If a description is always completely appropriate, please write "5"; if it is never appropriate, write "1"; if it is appropriate about half of the time, write "3"; and use the other numbers accordingly.

	1	2	3	4	5
1. When going to a new place, I prefer directions that include detailed descriptions of landmarks (such as the size, shape and color of a gas station) in addition to their names.	O	O	O	O	O
2. If I catch a glance of a car that is partially hidden behind bushes, I automatically "complete it," seeing the entire car in my mind's eye.	O	O	O	O	O
3. If I am looking for new furniture in a store, I always visualize what furniture would look like in particular places in my home.	O	O	O	O	O
4. I prefer to read novels that lead me easily to visualize where the characters are and what they are doing instead of novels that are difficult to visualize.	O	O	O	O	O
5. When I think about visiting a relative, I almost always have a clear mental picture of him or her.	O	O	O	O	O
6. When relatively easy technical material is described clearly in a text, I find illustrations distracting because they interfere with my ability to visualize the material.	O	O	O	O	O
7. If someone were to tell me two single-digit numbers to add (e.g., 24 and 31), I would visualize them in order to add them.	O	O	O	O	O
8. Before I get dressed to go out, I first visualize what I will look like if I wear different combinations of clothes.	O	O	O	O	O
9. When I think about a series of errands I must do, I visualize the stores I will visit.	O	O	O	O	O
10. When I first hear a person's voice, a visual image of him or her almost always springs to mind.	O	O	O	O	O
11. When I hear a radio announcer or DJ I've never actually seen, I usually find myself picturing what they might look like.	O	O	O	O	O
12. If I saw a car accident, I would visualize what had happened when later trying to recall the details.	O	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Appendix 2.16 National Adult Reading Test (NART)

Participant ID _____ Date _____

Experimenter: please indicate reading errors...

☐ CHORD	☐ SUPERFLUOUS
☐ ACHE	☐ SIMILE
☐ DEPOT	☐ [illegible]NAL
☐ AISLE	☐ QUADRUPED
☐ BOUQUET	☐ CE[illegible]LIST
☐ PSALM	☐ [illegible]ADE
☐ CAPON	☐ ZE[illegible]T
☐ DENY	☐ DRAC[illegible]
☐ NAUSEA	☐ AEON
☐ DEBT	☐ PLACEBO
☐ COURTEOU[illegible]	☐ ABSTEMIOUS
☐ RAREFY	☐ DETENTE
☐ EQUIVO[illegible]AL	☐ IDYLL
☐ N[illegible]VE	☐ PUERPERAL
☐ CATACOM[illegible]	☐ AVER
☐ GAOLED	☐ GAUCHE
☐ THYME	☐ TOPIARY
☐ HEIR	☐ LEVIATHAN
☐ [illegible]ADIX	☐ BEATIFY
☐ ASSIGNATE	☐ PRELATE
☐ HIATUS	☐ SIDEREAL
☐ SUBTLE	☐ DEMESNE
☐ PROCREATE	☐ SYNCOPE
☐ GIST	☐ LABILE
☐ GOUGE	☐ CAMPANILE

Total Error Score 0

Thank you for completing the questionnaire!

Appendix 2.17 Interpersonal Sensitivity Measure (IPSM)

Participant ID

Date

A number of statements are listed below which relate to how you might feel about yourself and other people. Please indicate by filling in the appropriate circle showing how each one applies to you (whether it is "very like you", "moderately like you", "moderately unlike you" or "very unlike you"). Respond to each statement in terms of how you are GENERALLY and not necessarily just at present. There are no right or wrong answers.

	Very Like Me	Moderately Like Me	Moderately Unlike Me	Very Unlike Me
1. I feel insecure when I say goodbye to people.	○	○	○	○
2. I worry about the effect I have on other people.	○	○	○	○
3. I avoid saying what I think for fear of being rejected.	○	○	○	○
4. I feel uneasy meeting new people.	○	○	○	○
5. If others knew the real me, they would not like me	○	○	○	○
6. I feel secure when I'm in a close relationship.	○	○	○	○
7. I don't get angry with people for fear that I may hurt them.	○	○	○	○
8. After a fight with a friend, I feel uncomfortable until I have made peace.	○	○	○	○
9. I am always aware of how other people feel.	○	○	○	○
10. I worry about being criticized for things I have said or done.	○	○	○	○
11. I always notice if someone doesn't respond to me.	○	○	○	○
12. I worry about losing someone close to me.	○	○	○	○
13. I feel that people generally like me.	○	○	○	○
14. I will do something I don't want to do rather than offend or upset someone.	○	○	○	○
15. I can only believe that something I have done is good when someone tells me it is.	○	○	○	○
16. I will go out of my way to please someone I am close to.	○	○	○	○
17. I feel anxious when I say goodbye to people.	○	○	○	○
18. I feel happy when someone compliments me.	○	○	○	○
19. I fear that my feelings will upset other people.	○	○	○	○
20. I can make other people feel happy.	○	○	○	○
21. I find it hard to get angry with people.	○	○	○	○
22. I worry about criticizing other people.	○	○	○	○
23. If someone is critical of something I do, I feel bad.	○	○	○	○
24. If other people knew the real me, they really like, they would think less of me.	○	○	○	○
25. I always expect criticism.	○	○	○	○
26. I can never be really sure if someone is pleased with me.	○	○	○	○
27. I don't like people to really know me.	○	○	○	○
28. If someone upsets me, I'm not able to put it easily out of my mind.	○	○	○	○
29. I feel others do not understand me	○	○	○	○
30. I worry about what others think of me.	○	○	○	○
31. I don't feel happy unless people I know admire me.	○	○	○	○
32. I am never rude to anyone.	○	○	○	○

Please continue

	Very Like Me	Moderately Like Me	[illegible] Me	Very Unlike Me
33. I worry about hurting the feelings of other people.	O	O	O	O
34. I feel hurt when someone is angry with me.	O	O	O	O
35. My value as a person depends enormously on what others think of me.	O	O	O	O
36. I care about what people feel about me.	O	O	O	O
37. I can usually describe how I feel at the moment in considerable detail.	O	O	O	O
38. I find myself doing things without paying attention.	O	O	O	O
39. I disapprove of myself when I have irrational ideas.	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Appendix 2.18 Involuntary Subordination Questionnaire (ISQ)

Participant ID

Date

Below are a series of statements that reflect how people may feel about themselves. Please rate the degree to which you agree with each of the statements as they relate to yourself. Please use the following scale:

	Strongly Disagree	Disagree	Neutral - Neither Agree Nor Disagree	Agree	Strongly Agree
1. I feel that I have lost my standing in the world	O	O	O	O	O
2. I feel that I am more confident than other people	O	O	O	O	O
3. I let others criticize me or put me down without defending myself	O	O	O	O	O
4. I feel powerless to change things	O	O	O	O	O
5. I feel completely knocked out of action	O	O	O	O	O
6. I feel that I am more likeable than other people	O	O	O	O	O
7. I do things because other people are doing them rather than because I want to	O	O	O	O	O
8. I feel trapped by my obligations	O	O	O	O	O
9. I feel defeated by life	O	O	O	O	O
10. I feel that I am more desirable than others	O	O	O	O	O
11. At meetings and gatherings I let others monopolize	O	O	O	O	O
12. I can see no way out of my current situation	O	O	O	O	O
13. I feel that life has treated me like a punch-bag	O	O	O	O	O
14. I feel like an outsider in relation to other people	O	O	O	O	O
15. I avoid starting conversations at social gatherings	O	O	O	O	O
16. I want to get away from myself	O	O	O	O	O
17. I feel that I have sunk to the bottom of the ladde	O	O	O	O	O
18. I feel that I am more talented than other people	O	O	O	O	O
19. I am not able to tell my friends	O	O	O	O	O
20. I feel trapped by other pe	O	O	O	O	O
21. I feel that I have lost i	O	O	O	O	O
22. I feel that I am more	O	O	O	O	O
23. If I try to speak and ot	O	O	O	O	O
24. I would like to escape fro	O	O	O	O	O
25. I feel that there is no fight left in	O	O	O	O	O
26. I feel accepted more than other people	O	O	O	O	O
27. I continue to apologize for minor mistakes	O	O	O	O	O
28. I feel trapped inside myself	O	O	O	O	O
29. I feel that my confidence has been knocked out of me	O	O	O	O	O
30. I feel that I am more attractive than others	O	O	O	O	O
31. I listen quietly if people in authority say unpleasant things about me	O	O	O	O	O
32. I would like to get away from who I am and start again	O	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Appendix 2.19 Striving To Avoid Inferiority Scale (SAIS-I and II)

Participant ID _____ Date _____

Sometimes people can see life as something of a competition. For example, we often call it the 'Rat Race'. People can vary in how pressured they feel to strive and compete for things that are important to them. Below are a series of statements, which describe how people may think and feel about the need to strive and compete in life. Please circle a number to the right of the statements which best describes the degree to which a statement is true for you.

	Never	Rarely	Sometimes	Mostly	Always
1. To be valued by others I have to strive to succeed	O	O	O	O	O
2. If I make mistakes, I know other people will still like me	O	O	O	O	O
3. Life is a competition	O	O	O	O	O
4. People don't have to succeed to prove themselves to others	O	O	O	O	O
5. People judge you by how well you perform in comparison to others	O	O	O	O	O
6. Win or lose, people accept me anyway	O	O	O	O	O
7. I never feel my place in society is secure but have to strive to prove myself worthy of it	O	O	O	O	O
8. Others will accept me even if I fail	O	O	O	O	O
9. I need to match what other people achieve	O	O	O	O	O
10. People are accepting of me without comparing me to others	O	O	O	O	O
11. If I don't strive to succeed, I'll be left behind everyone else	O	O	O	O	O
12. Whether I succeed or fail, people value me as a person	O	O	O	O	O
13. People compare me to others to see if I match up	O	O	O	O	O
14. I worry about failure because it means you can't keep up and compete with other people in life	O	O	O	O	O
15. I struggle to achieve things so that other people will not look down on me	O	O	O	O	O
16. If I fail at something, I know others will help me try again	O	O	O	O	O
17. Acceptance is something you have to earn and compete with others for	O	O	O	O	O
18. To get on in the world, you have to compete with others	O	O	O	O	O
19. If you don't keep up in looks or achievements others won't bother with you	O	O	O	O	O
20. If I don't strive to achieve I'll be seen as inferior to other people	O	O	O	O	O
21. I don't feel under pressure to prove myself to others	O	O	O	O	O
22. People who can't compete are seen as weak	O	O	O	O	O
23. Even if I do succeed others will believe it's an illusion	O	O	O	O	O
24. People accept me whether I'm successful or not	O	O	O	O	O
25. Being competitive gives me a right to life	O	O	O	O	O
26. I don't have to be the best in life to feel wanted	O	O	O	O	O
27. Others have to see me succeed otherwise it's worthless	O	O	O	O	O
28. I don't have to prove myself to feel part of a group	O	O	O	O	O
29. You are loved for what you are, not for what you achieve	O	O	O	O	O
30. You earn respect by out-performing others	O	O	O	O	O
31. Unless you can compete and keep up you get left behind	O	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Participant ID

Date

We are interested in the reasons people feel under pressure to compete. Below are a series of questions which tap this, each beginning with 'If you don't compete with others and succeed.....'. Please circle the number which best describes how much you agree or disagree with each statement.

1. LOSING OUT

If you don't compete with others and succeed...	Don't Agree 1	2	3	4	5	6	7	8	9	Completely Agree 10
You will not advance in life	O	O	O	O	O	O	O	O	O	O
You will miss out on opportunities	O	O	O	O	O	O	O	O	O	O
You will fall behind others	O	O	O	O	O	O	O	O	O	O

2. OVERLOOKED

If you don't compete with others and succeed...	Don't Agree 1	2	3	4	5	6	7	8	9	Completely Agree 10
People will overlook you	O	O	O	O	O	O	O	O	O	O
People will not take much interest in you	O	O	O	O	O	O	O	O	O	O
People will pass you over	O	O	O	O	O	O	O	O	O	O

3. ACTIVE REJECTION

If you don't compete with others and succeed...	Don't Agree 1	2	3	4	5	6	7	8	9	Completely Agree 10
Others will actively reject you	O	O	O	O	O	O	O	O	O	O
Others will push you away	O	O	O	O	O	O	O	O	O	O
Others will be critical and shame you	O	O	O	O	O	O	O	O	O	O
Others will go out of their way to actively exclude you	O	O	O	O	O	O	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Subscales

Loosing Out	0
Overlooked	0
Active Rejection	0

Appendix 2.20 Submissive Behaviour Scale (SBS)

Participant ID

Date

Below are a series of statements which describe how people act and feel about social situations. Circle the number to the right of the statements which best describes the degree to which a statement is true for you.

Please use the following scale:

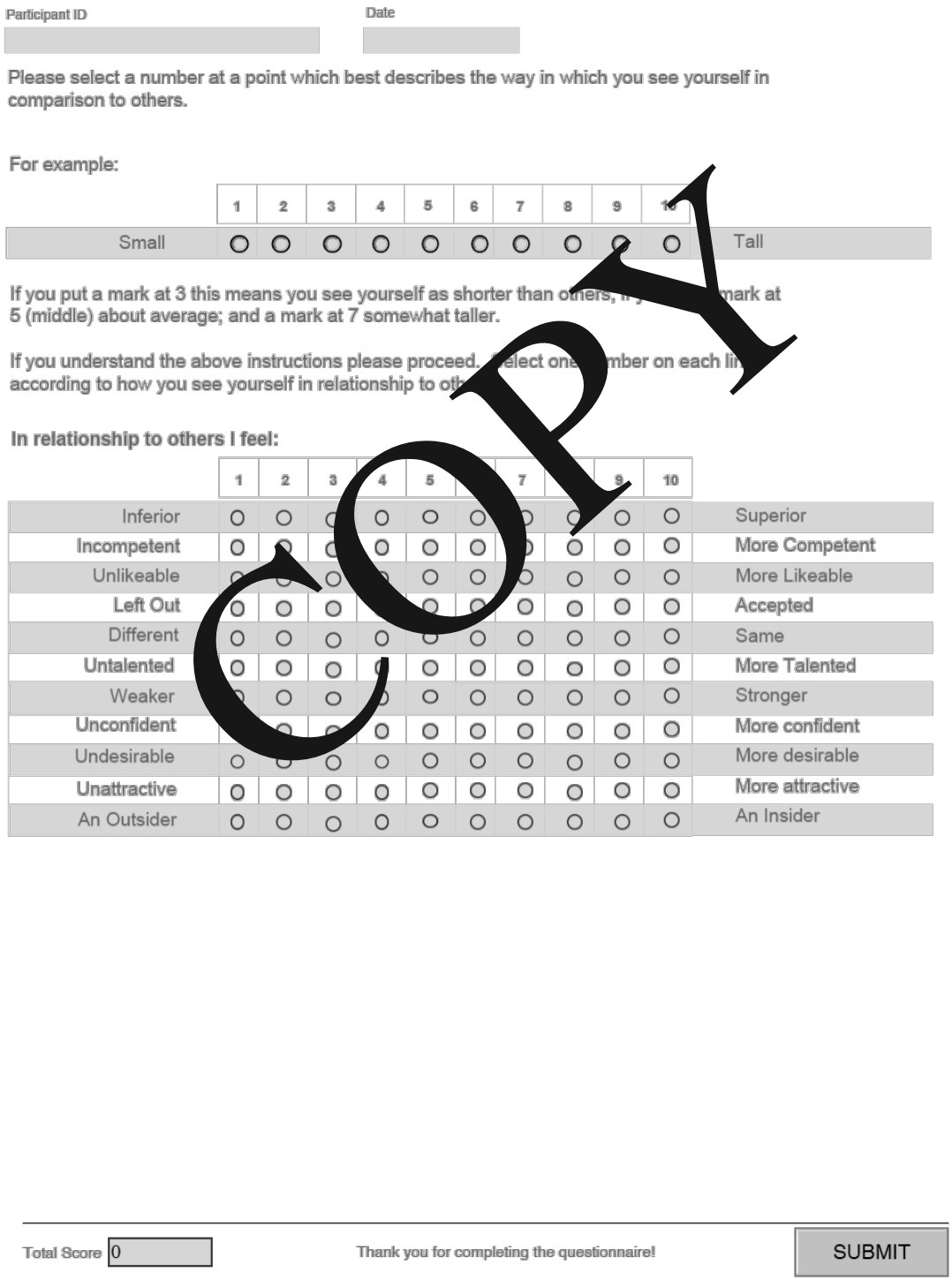
	Never	Rarely	Sometimes	Mostly	Always
1. I agree that I am wrong even though I know I'm not	O	O	O	O	O
2. I do things because other people are doing them, rather than because I want to	O	O	O	O	O
3. I would walk out of a shop without questioning, knowing that I had been short changed	O	O	O	O	O
4.I let others criticise me or put me down without defending myself	O	O	O	O	O
5. I do what is expected of me even when I don't want to	O	O	O	O	O
6. If I try to speak and others continue, I shut up	O	O	O	O	O
7. I continue to apologise for minor mistakes	O	O	O	O	O
8.I listen quietly if people in authority say unpleasa[illegible]hings about me	O	O	O	O	O
9. I am not able to tell my friends when I am angry[illegible] them	O	O	O	O	O
10. At meetings and gatherings, I let o[illegible] monop[illegible]he conversation	O	O	O	O	O
11. I don't like people to look[illegible]aight at me when they a[illegible]	O	O	O	O	O
12. I say 'thank you' enthu[illegible]stically and repeatedly when some[illegible] does a small favour fo[illegible]e	O	O	O	O	O
13. I avoid direct eye cont[illegible]	O	O	O	O	O
14. I avoid starting conversa[illegible] social gatherings	O	O	O	O	O
15. I blush when people stare at [illegible]	O	O	O	O	O
16. I pretend I am ill when declining an invitation	O	O	O	O	O

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Appendix 2.21 Social Comparison Scale (SCS)



Participant ID

Date

Please select a number at a point which best describes the way in which you see yourself in comparison to others.

For example:

	1	2	3	4	5	6	7	8	9	10	
Small	O	O	O	O	O	O	O	O	O	O	Tall

If you put a mark at 3 this means you see yourself as shorter than others, if you put a mark at 5 (middle) about average; and a mark at 7 somewhat taller.

If you understand the above instructions please proceed. Select one number on each line according to how you see yourself in relationship to others.

In relationship to others I feel:

	1	2	3	4	5	6	7	8	9	10	
Inferior	O	O	O	O	O	O	O	O	O	O	Superior
Incompetent	O	O	O	O	O	O	O	O	O	O	More Competent
Unlikeable	O	O	O	O	O	O	O	O	O	O	More Likeable
Left Out	O	O	O	O	O	O	O	O	O	O	Accepted
Different	O	O	O	O	O	O	O	O	O	O	Same
Untalented	O	O	O	O	O	O	O	O	O	O	More Talented
Weaker	O	O	O	O	O	O	O	O	O	O	Stronger
Unconfident	O	O	O	O	O	O	O	O	O	O	More confident
Undesirable	O	O	O	O	O	O	O	O	O	O	More desirable
Unattractive	O	O	O	O	O	O	O	O	O	O	More attractive
An Outsider	O	O	O	O	O	O	O	O	O	O	An Insider

Total Score 0

Thank you for completing the questionnaire!

SUBMIT

Appendix 2.22 Descriptive and sensitivity analysis results for all measures across all studies

Measure	Group	N	Mean	Std. Error	95% CI Lower Bound	95% CI Upper Bound	df	F	Sig.
BAI	Controls	69	5.74	0.56	4.63	6.85	[2,133]	29.66	0.00
	MDD	41	16.94	1.74	13.43	20.46			
	Remitted	24	8.02	1.26	5.42	10.62			
	Total	134	9.58	0.77	8.05	11.10			
BDI-II	Controls	69	7.87	0.60	6.67	9.07	[2,133]	63.72	0.00
	MDD	41	23.69	1.50	20.65	26.73			
	Remitted	24	10.97	1.57	7.73	14.21			
	Total	134	13.26	0.87	11.55	14.98			
DERS	Controls	69	75.31	2.42	70.49	80.13	[2,133]	38.78	0.00
	MDD	41	111.69	3.48	104.66	118.71			
	Remitted	24	102.05	5.39	90.90	113.20			
	Total	134	91.23	2.38	86.53	95.93			
IPSM	Controls	69	100.60	1.74	97.12	104.08	[2,133]	26.72	0.00
	MDD	41	120.23	2.04	116.10	124.36			
	Remitted	24	110.55	2.53	105.32	115.78			
	Total	134	108.39	1.40	105.63	111.15			
ISQ	Controls	69	72.57	2.01	68.56	76.58	[2,133]	48.12	0.00
	MDD	41	102.66	2.50	97.61	107.72			
	Remitted	24	94.02	3.10	87.61	100.43			
	Total	134	85.62	1.83	81.99	89.24			
PANAS	Controls	69	49.19	1.06	47.08	51.30	[2,133]	3.38	0.04
	MDD	41	50.93	1.73	47.44	54.42			
	Remitted	24	44.73	1.54	41.54	47.92			
	Total	134	48.92	0.82	47.30	50.55			
SAIS-I	Controls	69	58.16	1.94	54.28	62.04	[2,133]	2.57	0.08
	MDD	41	65.39	3.42	58.47	72.31			
	Remitted	24	65.00	3.26	58.26	71.74			
	Total	134	61.60	1.58	58.47	64.72			
SAIS-II	Controls	69	43.51	2.10	39.31	47.71	[2,133]	12.97	0.00
	MDD	41	60.38	2.86	54.60	66.17			
	Remitted	24	58.25	4.23	49.51	66.99			
	Total	134	51.31	1.72	47.91	54.72			
SBS	Controls	69	23.05	1.04	20.97	25.14	[2,133]	20.65	0.00
	MDD	41	34.41	1.68	31.02	37.80			
	Remitted	24	29.63	1.44	26.65	32.62			
	Total	134	27.71	0.90	25.94	29.48			
SCS	Controls	69	57.68	2.32	53.05	62.32	[2,133]	13.89	0.00
	MDD	41	40.03	2.17	35.66	44.41			
	Remitted	24	48.40	3.16	41.87	54.93			
	Total	134	50.62	1.62	47.42	53.82			
SUIS	Controls	69	38.88	0.99	36.90	40.87	[2,133]	1.70	0.19
	MDD	41	38.87	1.34	36.15	41.58			
	Remitted	24	35.40	1.68	31.93	38.87			
	Total	134	38.25	0.73	36.82	39.69			
FFMQ	Controls	69	128.10	2.18	123.75	132.45	[2,133]	9.59	0.00
	MDD	41	114.90	2.06	110.73	119.07			
	Remitted	24	122.46	1.60	119.16	125.76			

Total	134	123.05	1.41	120.27	125.83

Note: *. The mean difference is significant at the 0.05 level. BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PA, NA, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups assumed equal.

Appendix 2.23 Planned comparisons in sensitivity analysis for all measures across all studies

Measure	Group		Mean Difference	Std. Error	Sig.	95% CI	
						Lower Bound	Upper Bound
BAI	Controls	MDD	-11.21*	1.47	0	-14.77	-7.64
	Controls	Remitted	-2.28	1.77	0.6	-6.57	2
	MDD	Remitted	8.92*	1.92	0	4.27	13.57
BDI-II	Controls	MDD	-15.81*	1.42	0	-19.25	-12.38
	Controls	Remitted	-3.1	1.7	0.21	-7.23	1.04
	MDD	Remitted	12.72*	1.85	0	8.24	17.2
DERS	Controls	MDD	-36.37*	4.33	0	-46.88	-25.87
	Controls	Remitted	-26.74*	5.21	0	-39.37	-14.11
	MDD	Remitted	9.64	5.65	0.27	-4.06	23.33
IPSM	Controls	MDD	-19.63*	2.7	0	-26.19	-13.07
	Controls	Remitted	-9.95*	3.25	0.01	-17.83	-2.07
	MDD	Remitted	9.68*	3.52	0.02	1.13	18.23
ISQ	Controls	MDD	-30.09*	3.2	0	-37.85	-22.33
	Controls	Remitted	-21.45*	3.85	0	-30.78	-12.12
	MDD	Remitted	8.64	4.17	0.12	-1.48	18.76
PANAS	Controls	MDD	-1.74	1.84	1	-6.21	2.74
	Controls	Remitted	4.46	2.22	0.14	-0.91	9.84
	MDD	Remitted	6.20*	2.4	0.03	0.37	12.03
SAIS-I	Controls	MDD	-7.23	3.57	0.13	-15.88	1.41
	Controls	Remitted	-6.84	4.28	0.34	-17.23	3.55
	MDD	Remitted	0.39	4.65	1	-10.88	11.66
SAIS-II	Controls	MDD	-16.87*	3.62	0	-25.65	-8.1
	Controls	Remitted	-14.74*	4.35	0	-25.28	-4.2
	MDD	Remitted	2.13	4.71	1	-9.3	13.57
SBS	Controls	MDD	-11.36*	1.8	0	-15.71	-7
	Controls	Remitted	-6.58*	2.16	0.01	-11.81	-1.35
	MDD	Remitted	4.78	2.34	0.13	-0.9	10.45
SCS	Controls	MDD	17.65*	3.38	0	9.46	25.85
	Controls	Remitted	9.29	4.06	0.07	-0.56	19.14
	MDD	Remitted	-8.36	4.4	0.18	-19.05	2.32
SUIS	Controls	MDD	0.02	1.65	1	-3.98	4.01
	Controls	Remitted	3.48	1.98	0.24	-1.32	8.29
	MDD	Remitted	3.47	2.15	0.33	-1.74	8.68
FFMQ	Controls	MDD	13.20*	3.02	0	5.88	20.52
	Controls	Remitted	5.64	3.63	0.37	-3.15	14.44
	MDD	Remitted	-7.56	3.93	0.17	-17.09	1.98

Note: * The mean difference is significant at the 0.05 level. BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PA, NA, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups assumed equal.

Appendix 2.24 Principal component analysis: total variance explained (Chapter 2)

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	3.55	59.14	59.14	3.55	59.14	59.14
2	0.89	14.89	74.03			
3	0.58	9.60	83.63			
4	0.44	7.38	91.01			
5	0.36	5.98	96.99			

Extraction Method: Principal Component Analysis.

Component Matrix[a]

IPSM	.81
ISQ	.88
SAIS-I	.63
SAIS-II	.75
SBS	.84

Extraction Method: PCA

Appendix 2.25 Correlation results of social, affective and process measures

In remitted depressed individuals (Appendix 2.26), depressive symptoms were positively correlated with anxiety symptoms, avoiding inferiority, submissive behaviour and negative affect. Depression was negatively correlated with rejection sensitivity and social comparison. Difficulty in emotion regulation was positively correlated with avoiding inferiority and negatively with social comparison. Involuntary subordination was positively associated with avoiding inferiority and submissiveness.

In MDD participants (Appendix 2.27), anxiety scores were positively correlated with depression. Difficulty in emotion regulation was significantly correlated with depression severity, involuntary subordination, submissiveness, comparison and negative affect. Depression scores were also correlated with difficulty in emotion regulation, involuntary subordination, social submission and comparison. Difficulty in emotion regulation was positively associated with rejection sensitivity, subordination, avoiding inferiority, submissive behaviour, social comparison and positive and negative affect.

Correlations in healthy controls (Appendix 2.28) revealed significant correlations predominantly between affective measures assessing depression and anxiety and process measures, including emotion dysregulation and interpersonal rejection sensitivity with greater variability on social measures. Involuntary subordination was positively correlated with interpersonal rejection sensitivity, striving to avoid inferiority, social submissiveness (SBS), and negative, but not positive affect. Avoiding inferiority was correlated with submissive behaviour and negative affect, while increased submissive behaviour was negatively correlated with social comparison and positive affect. Finally, Pearson's correlations for all groups combined revealed significant correlations between all measures, except for the SUIS (Appendix 2.29).

Appendix 2.26 Correlation matrix of social, affective and process measures for remitted depressed participants described in Chapter 2

	BAI	BDI-II	DERS	IPSM	ISQ	SAIS-I	SAIS-II	SBS	SCS	SUIS	PA
BAI											
BDI-II	.553*										
DERS	-.194	.381									
IPSM	-.292	-.476*	.215								
ISQ	.387	.466	.411	.185							
SAIS-I	-.057	.573*	.696**	.208	.328						
SAIS-II	.207	.594**	.388	-.292	.537*	.412					
SBS	.379	.553*	.342	-.054	.575*	.473*	.605**				
SCS	-.287	-.626**	-.578**	-.337	-.413	-.798**	-.412	-.604**			
SUIS	-.079	-.061	-.086	-.199	-.302	-.114	.007	.054	.206		
PA	-.296	-.310	-.335	-.489*	-.302	-.648**	-.134	-.184	.742**	.320	
NA	.367	.600**	.307	-.343	.182	.429	.366	.671**	-.411	.201	.363

Note: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PA, NA, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups assumed equal. **. Correlation is significant at the 0.01 level (2-tailed).*. Correlation is significant at the 0.05 level (2-tailed).

Appendix 2.27 Correlation matrix of social, affective and process measures for MDD participants described in Chapter 2

	BAI	BDI-II	DERS	IPSM	ISQ	SAIS-I	SAIS-II	SBS	SCS	SUIS	FFMQ	PA
BDI-II	.679**											
DERS	.291	.421**										
IPSM	.157	.134	.357*									
ISQ	.517**	.442**	.746**	.537**								
SAIS-I	-.007	.089	.488**	.469**	.386*							
SAIS-II	.163	.185	.372*	.533**	.458**	.694**						
SBS	.452**	.327*	.690**	.521**	.735**	.448**	.453**					
SCS	-.518**	-.589**	-.580**	-.307	-.608**	-.294	-.465**	-.629**				
SUIS	-.060	.087	.171	.009	.013	.103	-.058	-.090	.086			
FFMQ	-.040	-.248	-.363	.089	-.547*	-.201	.024	-.412	.254	-.390		
PA	.157	-.148	-.488**	-.200	-.342*	-.200	-.366*	-.190	.265	.093	.060	
NA	.425**	.288	.357*	.293	.367*	.166	.386*	.274	-.400*	-.001	.217	-.144

Note: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PA, NA, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups assumed equal. **. Correlation is significant at the 0.01 level (2-tailed).*. Correlation is significant at the 0.05 level (2-tailed).

Appendix 2.28 Correlation matrix of social, affective and process measures for healthy control participants described in Chapter 2

	BAI	BDI-II	DERS	IPSM	ISQ	SAIS-I	SAIS-II	SBS	SCS	SUIS	FFMQ	PA
BDI-II	.641**											
DERS	.472**	.645**										
IPSM	.492**	.486**	.597**									
ISQ	.432**	.535**	.661**	.676**								
SAIS-I	.336**	.456**	.273*	.329**	.322**							
SAIS-II	.187	.190	.125	.163	.319**	.462**						
SBS	.149	.273*	.534**	.565**	.641**	.295**	.155					
SCS	-.194	-.061	-.230*	-.346**	-.211	-.096	-.064	-.328**				
SUIS	.084	.101	.098	.204	.025	.128	.112	-.018	.114			
FFMQ	-.364**	-.198	-.095	-.132	-.181	-.012	-.240	.151	.254	.035		
PA	.111	-.254*	-.449**	-.299**	-.493**	-.096	-.099	-.500**	.116	.045	-.165	
NA	.599**	.476**	.400**	.415**	.368**	.239*	.248*	.134	-.354**	.192	-.205	-.099

Note: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PA, NA, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups assumed equal. **. Correlation is significant at the 0.01 level (2-tailed).*. Correlation is significant at the 0.05 level (2-tailed).

Appendix 2.29 Correlation matrix of social, affective and process measures for all subjects described in Chapter 2

	BAI	BDI-II	DERS	IPSM	ISQ	SAIS-I	SAIS-II	SBS	SCS	SUIS	FFMQ	PA
BDI-II	.771**											
DERS	.501**	.682**										
IPSM	.500**	.530**	.672**									
ISQ	.628**	.680**	.801**	.739**								
SAIS-I	.213*	.350**	.462**	.430**	.420**							
SAIS-II	.344**	.404**	.425**	.372**	.532**	.565**						
SBS	.512**	.547**	.686**	.644**	.772**	.432**	.445**					
SCS	-.459**	-.504**	-.534**	-.511**	-.512**	-.314**	-.345**	-.562**				
SUIS	.002	.069	.047	.101	-.024	.070	.026	-.032	.106			
FFMQ	-.321**	-.326**	-.263*	-.216	-.344**	-.015	-.255*	-.121	.322**	-.025		
PA	-.200*	-.423**	-.611**	-.460**	-.583**	-.297**	-.343**	-.512**	.403**	.107	-.022	
NA	.643**	.633**	.580**	.498**	.562**	.307**	.444**	.473**	-.515**	.100	-.166	-.229**

Note: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PA, NA, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups assumed equal. **. Correlation is significant at the 0.01 level (2-tailed).*. Correlation is significant at the 0.05 level (2-tailed).

Appendix 3 (Chapter 3)

Appendix 3.1 Script development protocol for memory generation session across all studies

[Participants complete Informed Consent & Demographics, followed by memory interview and Memory Evaluation Questionnaire.]

Experimenter:

"This study aims at investigating how we are able to regulate our emotional response to memories involving social rejection and affiliation. As we all have had different experiences in social situations – both positive and negative - it is important for us to ask each participant for their personal experience. We would like to ensure that your emotional response is as genuine as possible as regulating your emotion will be different for your own personal memories compared to memories of other people.

We would like you to remember 3/6 negative social memories, involving rejection or exclusion, 3/6 positive social memories, in which you felt particularly included and a greater sense of belonging, and finally, 3/6 neutral social memories, for instance being part of a larger group, without any particular importance to you. To try and help you recall experiences you might have had in the three social situations described above, we will offer examples and cues to retrieve the most sensory and contextual detail as possible. After this session, we will create a personal script that is tailored to your memories and will become relevant in Session II of this study.

Before we start, do you mind if I audio-record this session so that I have as complete a description of the event as possible? Also, as with any research involving emotional material, there is a chance that you will experience some upset during this session. If you feel yourself becoming upset, we can take a break at any time and/or stop the recording and interview. Please just let me know. Ok. Do you have any questions so far? Are you ready to start? Let's start with the [neutral] memories."

[Neutral] Memories

I'd like you to recall a time when you had a [neutral] social experience [see example list below]. It should be a memory you have thought about many times and is still important to you, even as you are recalling it now. Please describe the memory in brief:

_____
_____
_____

[If consent given, audio-record session. Ascertain brief description of event.]. *Once you've got it in mind, close your eyes and get as clear an image as you can.*

"I would now like you to spend some time thinking about the memory you just described briefly and to focus on as much detail as you can. Play the scene over in your head like you are replaying a movie of how the event unfolded. I am going to guide you through a series of questions and prompts to help you do this. Get an image of the event in your mind. Please describe the memory in as much detail as possible."

[Listen and record participant describing memory, make notes as to whether the questions below have been covered. If not, ask the questions and if necessary, provide the prompts below the question.]

- Describe the situation in your own words
- Visualise what you were wearing.
- What kind of day was it? Sunny? Overcast? Bright?
- Imagine what your surroundings looked like. Were you inside or outside?
  [Prompts: Outside / Inside, familiar / unfamiliar place; Public Transport]
- What could you smell? Was the air fresh and crisp [outside]? Had someone been cooking [inside]?
- How long ago was it?
  [Prompts: Up to a week ago; Up to a month ago; Several months ago; Several years ago]
- Were other people there? What where they saying? How were they acting?
  [Prompts: How many? Body language; Voice; Facial Expression]
- What did you say? How did you act?
  [Prompts: Verbal behaviour (silence, expletives, "inner" talk", complete sentences/discussion; Pitch); Facial expression; Gaze; Body/head movement; posture]
- What were the thoughts running through your head at the time?
- What were the sensations going through your body during the event?
  [Prompts: General sensations (un/pleasant, refreshed, tired, tense, harmony, rested); Body temperature (pleasant, blushing, warm, cold, perspiration, goose pimples); Breathing; Heart (Heart pounding chest pain, sense of weight, slower/fast hear beat, "blood boiling"); Muscles (trembling, tense, rested); Stomach (un/pleasant, "butterflies", pressure/churning, feeling sick, hunger)]
- What sounds could you hear?
  [Prompts: Traffic, birds, kids playing, people chatting, absolute silence]
- Did you have any other sensations? [Prompts: taste; touch]
- How long did it last? [Prompt: Under 5 min; Up to 1 hr; Up to a day; Several days and longer]

Thank you very much, that was really helpful! Are you ready to do the same for the next memory or would you like a short break? Ok. Let's continue. *[continue for remaining memories. Take breaks where necessary]*.

Appendix 3.2 Example stimuli derived from memory generation session described in Chapter 5.

Female MDD Rejection Memory

Its early afternoon in the summer. I am in my front room, it has pale green walls and a cast iron fireplace. I get an unexpected phone call from my boyfriend. He tells me the relationship is over. I say "can I come round and talk to you?", but he says his son's at his house so I can't come round. It devastates me. I think you coward for hiding behind your disabled son. I am crying. I feel physically sick and run to the toilet. All my insides feel like jelly. He says "we could have gone on like this for a couple of years" and it makes it worse. I think "what I am supposed to make of that"? Like there is no point in dragging it out. I am shocked, crying and shaking.

Male MDD Neutral Memory

About a month ago I move to Cambridge from London with a man with a van. Its Sunday, the 14th of September. We leave early morning at 8.30. The van is a dark blue people carrier, and we have folded down all the seats in the back and opened up the boot. The driver is about 40, a little bit shorter, chubby, balding, and is wearing glasses. He seems to enjoy his job. I met him when I moved here a week before. I am wearing shorts and just a random loose T-shirt while we are packing. Just before we leave, I change into jeans and a proper shirt, white with lots of small black crosses on it. I sit down in the front passenger seat and we drive off.

Female MDD Inclusion

I'm at my leaving party at the Cambridge Blue with my team at the end of August. Mike gets up on to the table and does a speech. No one is listening at first. It's funny and we are laughing at him. He talks about us being part of their community and how much we've enjoyed it. Our team cheers "waaay". Mike is tall with short brown hair and a large nose. We move on to another pub but there are still a lot of people. My boss Richard is buying everybody shots. Richard is French in his late forties with light brown hair. When we say our goodbyes, everyone gets upset that we are leaving, even Richard. My best friend Jude gets really upset and we hug for quite a while.

Appendix 3.3 Mean descriptives for non-composite affective ratings across memory generation sessions

Measure	Memory Type	Time	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
Positivity	Neutral	Experience	5.10	.26	4.58	5.62
		Recall	5.17	.27	4.62	5.71
	Rejection	Experience	1.19	.16	.86	1.52
		Recall	2.50	.28	1.94	3.07
	Inclusion	Experience	8.86	.13	8.61	9.11
		Recall	8.48	.18	8.12	8.83
Inclusion	Neutral	Experience	3.79	.31	3.16	4.41
		Recall	3.48	.31	2.87	4.10
	Rejection	Experience	1.44	.17	1.10	1.79
		Recall	1.90	.25	1.39	2.40
	Inclusion	Experience	8.82	.14	8.54	9.10
		Recall	8.19	.20	7.80	8.58
Distress	Neutral	Experience	1.50	.21	1.08	1.93
		Recall	.79	.13	.54	1.04
	Rejection	Experience	8.52	.18	8.16	8.88
		Recall	5.91	.25	5.41	6.41
	Inclusion	Experience	1.24	.20	.83	1.65
		Recall	.81	.15	.52	1.10
Rejection	Neutral	Experience	.89	.18	.53	1.25
		Recall	.50	.11	.27	.72
	Rejection	Experience	8.56	.15	8.26	8.86
		Recall	6.20	.30	5.60	6.81
	Inclusion	Experience	.47	.11	.26	.69
		Recall	.50	.10	.29	.71

Appendix 4 (Chapter 4)

Appendix 4.1 Descriptives and group comparison of social, affective and process measures in Chapter 4.

						95% CI			
	Group	N	Mean	SD	SE	Lower	Upper	df	p
BAI	MDD	15	17.53	11.95	3.08	3.53	17.54	18.98	0.01*
	Control	21	7.00	5.95	1.30				
BDI-II	MDD	18	22.33	9.89	2.33	6.37	17.15	25.63	<.001**
	Control	21	10.57	5.48	1.20				
DERS	MDD	18	105.72	20.42	4.81	15.22	42.89	36.80	<.001**
	Control	21	76.67	22.20	4.84				
FFMQ	MDD	18	114.11	18.41	4.34	-25.58	-1.72	35.96	0.03*
	Control	21	127.76	18.20	3.97				
IPSM	MDD	18	119.06	11.59	2.73	8.32	25.79	36.51	<.001**
	Control	21	102.00	15.28	3.33				
ISQ	MDD	18	100.83	11.85	2.79	15.76	36.96	33.07	<.001**
	Control	21	74.48	20.15	4.40				
PANAS	MDD	18	51.72	13.23	3.12	-4.62	10.73	30.60	0.42
	Control	21	48.67	9.64	2.10				
SAIS-I	MDD	18	60.33	10.75	2.53	-12.74	2.93	36.87	0.21
	Control	21	65.24	13.37	2.92				
SAIS-II	MDD	18	58.00	15.70	3.70	-2.65	17.98	36.29	0.14
	Control	21	50.33	16.00	3.49				
SBS	MDD	18	33.78	9.06	2.14	5.01	16.45	35.14	<.001**
	Control	21	23.05	8.43	1.84				
SCS	MDD	18	40.61	15.23	3.59	-32.18	-13.46	33.99	<.001**
	Control	21	63.43	13.22	2.89				
SUIS	MDD	18	36.39	8.48	2.00	-10.09	1.15	36.47	0.12
	Control	21	40.86	8.81	1.92				

Note: BAI, Beck Anxiety Inventory; BDI-II, Beck Depression Inventory; DERS, Difficulties in Emotion Regulation Scale; FFMQ, Five Facet Mindfulness Questionnaire; IPSM, Interpersonal Sensitivity Measure; ISQ, Involuntary Subordination Questionnaire; PANAS, Positive and Negative Affect Scale; SAIS-I/II, Strive to Avoid Inferiority Scale Part I and II; SBS, Submissive Behaviour Scale; SCS, Social Comparison Scale; SUIS, Spontaneous Use of Imagery Scale. All tests, variances of groups not assumed equal. * = $p<0.05$, ** = $p<0.001$. See Chapter 2 for details on measures.

Appendix 4.2 Affective ratings of session I versus session II

We also sought to explore any potential differences as a function of group and memory type between the affective experience in response to recalling the personal memories within the initial memory-generation session ('session I') and the following week, in the fMRI scanning session ('session II') to ensure comparable saliency of memories across session. Results suggest that memories recalled across both sessions elicited comparable positive, negative and neutral affect as a function of memory type (Appendix 4.3); maintained its affective state across sessions, crucial to this paradigm (Appendix 4.4) and exhibited elevated mood in controls compared to MDD (Appendix 4.5). For interactions, see Appendix 4.6 and Appendix 4.7. Affective ratings at time of recall from the session I and during the fMRI session II were entered into an ANOVA with group (MDD/controls) as a between-group factor and memory type (rejection/inclusion/neutral) and time (session I/session II) as the within-group factor. Both memory type (x^2=10.60, p=0.005) and the interaction between memory type and session (x^2=16.53, p<0.001) violated Mauchly's assumption of sphericity and are reported using Greenhouse-Geisser.

Results revealed a significant main effect for memory type (F[1.57,53.35]= 265.33, p<0.001, η_p^2=0.89). Planned comparisons of the main effect of memory type corrected using a Bonferroni adjustment, indicated that affective ratings (p<0.001) derived during rejection, neutral and inclusion memories differed significantly from each other, with greater positive mood in response to inclusion memories, compared to neutral (3.68±0.34) and rejection memories (10.75 ±0.57), which in turn resulted in most impaired positive mood relative to neutral (-7.07±0.49). There was also a main effect of group (F[1,34]= 7.14, p=0.01, η_p^2=0.17), which in planned comparisons revealed significantly elevated mood in control participants compared to MDD (p=0.011) when collapsed across all memories and sessions. Further, there was a significant interaction between session and memory type (F[1.44,48.78]=5.84, p=0.01, η_p^2=0.15), suggesting that while overall there was comparable saliency across sessions and memory types, rejection in particular revealed a slight decrease in

negative mood from session I to session II, while the reverse was observed for inclusion memories, which were rated as slightly less positive in the second session (see Appendix 5.9). However, importantly, there was no main effect for session type ($F[1,34]=0.01$, $p=0.94$, $\eta_p^2=0.00$), interaction between session and group ($F[1,34]=0.39$, $p=0.54$, $\eta_p^2=.01$), or interaction between memory type and group ($F[2,34]=1.10$, $p=0.34$, $\eta_p^2=.03$) or three-way interaction ($F[2,68]=0.46$, $p=0.64$, $\eta_p^2=.01$).

Appendix 4.3 Mean affective ratings for memory type - session I & session II (Chapter 4)

Memory Type	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
Neutral	3.46	0.29	2.87	4.04
Rejection	-3.61	0.42	-4.47	-2.75
Inclusion	7.14	0.31	6.52	7.77

Appendix 4.4 Mean affective ratings for session – session I & session II (Chapter 4)

			95% Confidence Interval	
Session	Mean	Std. Error	Lower Bound	Upper Bound
Session I	2.32	0.20	1.92	2.72
Session II	2.35	0.34	1.65	3.04

Appendix 4.5 Mean affective ratings for group – session I & session II (Chapter 4)

			95% Confidence Interval	
Group	Mean	Std. Error	Lower Bound	Upper Bound
MDD	1.77	.305	1.15	2.39
Controls	2.89	.288	2.31	3.48

Appendix 4.6 Mean mood ratings for group and memory type - session I & II (Chapter 4)

Group	Memory Type	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
MDD	Neutral	3.07	0.42	2.22	3.92
	Rejection	-3.94	0.62	-5.19	-2.68
	Inclusion	6.18	0.45	5.27	7.08
Controls	Neutral	3.85	0.40	3.04	4.65
	Rejection	-3.28	0.58	-4.46	-2.09
	Inclusion	8.11	0.42	7.25	8.96

Appendix 4.7 Mean mood ratings for group, memory type and session - session I & II (Chapter 4)

Group	Memory Type	Session	Mean	Std. Error	95% Confidence Interval	
					Lower Bound	Upper Bound
MDD	Neutral	Session I	3.02	0.44	2.12	3.92
		Session II	3.13	0.58	1.94	4.31
	Rejection	Session I	-4.46	0.70	-5.88	-3.04
		Session II	-3.41	0.86	-5.17	-1.66
	Inclusion	Session I	7.06	0.39	6.27	7.85
		Session II	5.29	0.70	3.87	6.72
Controls	Neutral	Session I	3.49	0.42	2.64	4.34
		Session II	4.20	0.55	3.08	5.32
	Rejection	Session I	-3.69	0.66	-5.03	-2.34
		Session II	-2.87	0.82	-4.53	-1.21
	Inclusion	Session I	8.48	0.37	7.73	9.22
		Session II	7.74	0.66	6.39	9.09

Appendix 4.8 Mean mood ratings for memory type and session - session I & II (Chapter 4)

Memory Type	Session	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
Neutral	Session I	3.26	.31	2.64	3.87
	Session II	3.66	.41	2.85	4.48
Rejection	Session I	-4.07	.48	-5.05	-3.10
	Session II	-3.14	.60	-4.35	-1.93
Inclusion	Session I	7.77	.27	7.23	8.31
	Session II	6.52	.48	5.53	7.50

Appendix 4.9 Mean vividness and intensity ratings for memory type and group in session II (Chapter 4)

Measure	Memory Type	Group	Mean	Std. Deviation	N
Vividness	Rejection	MDD	8.14	1.13	15
		Control	8.06	1.22	16
		Total	8.10	1.16	31
	Neutral	MDD	6.73	1.28	15
		Control	6.39	1.63	16
		Total	6.55	1.46	31
	Inclusion	MDD	8.56	0.83	15
		Control	8.28	0.85	16
		Total	8.41	0.84	31
Intensity	Rejection	MDD	8.29	0.97	15
		Control	8.03	1.10	16
		Total	8.16	1.03	31
	Neutral	MDD	4.28	2.43	15
		Control	3.31	1.65	16
		Total	3.78	2.09	31
	Inclusion	MDD	8.03	1.32	15
		Control	7.68	2.13	16
		Total	7.85	1.77	31

Appendix 4.10 One-sample T-tests in healthy controls (N=21) of brain regions significantly activated during silent imagery of autobiographical memories (Chapter 4)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Inclusion > Neutral						
	L	Lingual Gyrus	-18 -74 -4	175	4.36	0
	L	Postcentral Gyrus	-50 -24 30	214	4.17	0
	R	Postcentral Gyrus	38 -26 38	160	4.07	0
	R	Precentral Gyrus	24 -14 50	25	3.68	0
	L	Angular Gyrus	-42 -54 26	35	3.53	0
Rejection > Neutral						
	L	Secondary Somatosensory Cortex	-52 -26 24	700	4.92	0
	R	Secondary Somatosensory Cortex	50 -24 32	431	4.69	0
	L	Supplementary Motor Cortex	-12 -8 56	103	4.02	0
	L	Caudate	-22 2 18	47	3.92	0
	L	Middle Temporal Gyrus	-48 -64 4	48	3.73	0
Rejection & Inclusion > Neutral						
	L	Postcentral Gyrus	-52 -24 26	405	4.84	0
	R	Postcentral Gyrus	48 -24 32	392	4.71	0
	L	Supplementary Motor Cortex	-12 -8 56	189	4.02	0
	R	Fusiform Gyrus	32 -40 -22	50	3.89	0
	L	Lingual Gyrus	-16 -72 -4	104	3.84	0
	L	Caudate	-22 0 18	47	3.68	0
	L	Postcentral Gyrus	-34 -30 50	86	3.59	0
	L	Middle Frontal Gyrus	-40 -54 2	51	3.42	0

Abbreviations: R; Right, L; Left; Extent threshold: k = 20 voxels; * = p<0.001 uncorrected.

Appendix 4.11 One-sample T-tests in MDD (N=18) of brain regions significantly activated during silent imagery of autobiographical memories (Chapter 4)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Inclusion > Neutral						
	L	Anterior Insula	-30 6 10	644	4.52	0
	R/L	Anterior Cingulate Gyrus	4 30 -2	69	4.46	0
	R	Superior Occipital Gyrus	6 30 -10		3.48	0
	L	Medial Frontal Gyrus	-2 54 -18	120	4.24	0
	R	Inferior Temporal Gyrus	50 -48 -30	53	4.11	0
	R	Cerebellum	18 -64 -38	65	4.1	0
	L	Lingual Gyrus	-12 -82 -8	431	4.05	0
	L	Fusiform Gyrus	-32 -44 -22	37	3.92	0
		Superior Frontal Gyrus				
	L	Medial Segment	-2 58 16	131	3.9	0
	L	Postcentral Gyrus	-50 -24 50	635	3.85	0
	L	Middle Frontal Gyrus	-30 14 28	27	3.83	0
	L	Anterior Cingulate Gyrus	-10 42 12	134	3.8	0
	R	Postcentral Gyrus	46 -22 42	200	3.79	0
	R	Anterior Insula	28 16 8	416	3.78	0
	L	Postcentral Gyrus	-52 4 36	169	3.77	0
	R	Superior Occipital Gyrus	16 -86 40	65	3.76	0
	R	Precentral Gyrus	56 10 24	162	3.73	0
	R	Superior Parietal Lobule	22 -48 54	26	3.65	0
	R	Middle Cingulate Gyrus	8 20 22	36	3.63	0
	R	Fusiform Gyrus	32 -46 -22	73	3.58	0
	L	Superior Temporal Gyrus	-48 -22 -2	42	3.38	0
	R	Anterior Insula	36 -2 -2	21	3.35	0
	R	Lingual Gyrus	8 -74 -4	22	3.32	0
Rejection > Neutral						
	R	Precentral Gyrus	62 6 28	880	4.67	0
	R	Parietal Operculum	38 -30 26	200	4.4	0
	L	Anterior Insula	-32 -4 12	525	4.24	0
		Brain Stem	0 -42 -22	94	4.23	0
	R	Anterior Cingulate Gyrus	8 32 -4	143	4.16	0
		Orbital Part of the Inferior				
	R	Frontal Gyrus	30 36 -2	23	4.01	0
	R	Anterior Insula	28 12 -14	51	3.92	0
	R	Cerebellum	10 -52 -16	516	3.85	0
	R	Thalamus	16 -20 0	248	3.73	0
		Brain Stem	2 -26 -12	114	3.69	0
	R	Middle Temporal Gyrus	44 -28 -8	125	3.66	0
	L	Middle Cingulate Gyrus	-6 -12 34	22	3.63	0
	L	Lingual Gyrus	34 -72 -20	63	3.57	0
	R	Occipital Fusiform Gyrus	-16 -8 8	95	3.56	0
	L	Thalamus	8 -4 -6	67	3.56	0
	R	Thalamus	-4 -78 -6	36	3.46	0
	L	Lingual Gyrus	-10 -46 26		3.34	0
	L	Cerebellum	-28 -78 -36	27	3.39	0
	L	Parietal Operculum	-44 -28 16	21	3.33	0
Rejection & Inclusion > Neutral						
	R	Superior Occipital Gyrus	24 -84 12	482	4.66	0

R	Anterior Cingulate Gyrus	6 30 -2	175	4.53	0
R	Brain Stem	4 -20 -10	144	4.42	0
L	Anterior Insula	-32 6 -6	1292	4.42	0
L	Postcentral Gyrus	-28 -30 38	502	4.11	0
R	Precentral Gyrus	62 8 28	1358	4.03	0
L	Fusiform Gyrus	-32 -44 -24	72	4	0
L	Inferior Temporal Gyrus	-42 -62 -6	270	3.98	0
R	Cerebellum	18 -64 -36	86	3.97	0
L	Gyrus Rectus	-4 54 -20	60	3.95	0
	Brain Stem	2 -42 -24	92	3.94	0
L	Superior Temporal Gyrus	-40 -46 16	163	3.92	0
R	Inferior Temporal Gyrus	52 -62 -18	386	3.87	0
R	Occipital Fusiform Gyrus	26 -76 -20	352	3.87	0
R	Postcentral Gyrus	46 -22 42	358	3.86	0
L	Lingual Gyrus	-14 -64 -10	865	3.83	0
L	Superior Occipital Gyrus	-20 -90 12	182	3.78	0
L	Middle Frontal Gyrus	-30 12 30	31	3.75	0
	Superior Frontal Gyrus				
L	Medial Segment	-2 58 14	101	3.68	0
R	Cuneus	10 -92 18	66	3.65	0
L	Superior Temporal Gyrus	-48 -22 -4	51	3.65	0
R	Anterior Cingulate Gyrus	8 22 18	26	3.62	0
L	Anterior Cingulate Gyrus	-10 30 12	99	3.62	0
R	Inferior Temporal Gyrus	50 -48 -28	26	3.59	0
R	Fusiform Gyrus	30 -48 -20	190	3.57	0
R	Superior Parietal Lobule	28 -50 56	29	3.57	0
R	Thalamus	16 -8 8	44	3.51	0
L	Central Operculum	-44 -6 22	24	3.47	0
R	Postcentral Gyrus	64 -6 22	25	3.45	0
L	Supramarginal Gyrus	-34 -36 30	24	3.43	0

Abbreviations: R; Right, L; Left; Extent threshold: k = 20 voxels; * = p<0.001 uncorrected.

Appendix 4.12 Two-sample T-tests of brain regions significantly activated during silent imagery of autobiographical memories (Chapter 4)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
MDD>Controls, Inclusion > Neutral						
	R	Cerebellum	50 -48 -30	33	4.38	0
	R	Frontal Orbital Cortex	36 30 -4	484	4.63	0
	R	Frontal Pole	36 54 18	316	3.82	0
	L	Frontal Pole	-36 52 18	62	3.77	0
	R	Frontal Pole	26 64 16	31	3.59	0
	R	Inferior Temporal Gyrus	52 -62 -20	74	3.91	0
	L	Inferior Temporal Gyrus	-50 -62 -22	39	3.62	0
	L	Inferior Temporal Gyrus	-48 12 4	26	3.54	0
	L	Insular Cortex	-32 16 6	315	3.79	0
	L	Middle Frontal Gyrus	-46 34 26	37	3.71	0
	R	Paracingulate Gyrus	2 26 42	57	3.44	0
MDD>Controls, Rejection > Neutral						
	R	Cerebellum	2 -44 -24	48	4.07	0
	R	Inferior Temporal Gyrus	48 -8 -30	83	3.99	0
	R	Frontal Orbital Cortex / Inferior Temporal Gyrus	32 36 0	115	3.93	0
	R	Planum Polare / Heschl's Gyrus	50 -8 -6	30	3.43	0
MDD>Controls, Rejection & Inclusion > Neutral						
	R	Frontal Orbital Cortex	36 30 -4	262	4.33	0
	R	Middle Frontal Gyrus	38 30 46	203	3.76	0
	R	Frontal Pole	30 40 42	85	3.72	0
	L	Inferior Temporal Gyrus	-50 -64 -22	27	3.66	0
	R	Frontal Pole	28 56 26	49	3.57	0
	R	Putamen	32 2 -8	27	3.4	0
	R	Posterior Middle Temporal Gyrus	54 -24 -12	22	3.38	0
	R	Inferior Temporal Gyrus	52 -62 -20	25	3.32	0

Abbreviations: R; Right, L; Left; Extent threshold: k = 20 voxels; * = $p<0.001$ uncorrected.

Appendix 4.13 ANOVA (MDD, controls) x memory type (neutral, inclusion, rejection) during silent and script imagery of autobiographical memories (Chapter 4)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Silent Imagery, Main Effect of Group, p<0.05, FEW						
	R	Postcentral Gyrus	50 -4 16	58	5.55	<0.001
	R	Lingual Gyrus	6 -64 0	61	5.29	<0.001
	L	Postcentral Gyrus	-50 -8 16	23	5.28	<0.001
	L	Superior Frontal Gyrus	-16 -8 64	20	5	<0.001
Script Imagery, Main Effect of Group, p<0.05, FEW						
	R	Superior Temporal Gyrus	56 -2 -16	43	5.96	<0.001
	R	Middle Temporal Gyrus	48 -24 -8	175	5.87	<0.001
	R	Hippocampus	16 -16 -24	262	5.73	<0.001
	R	Posterior Insula	40 -10 -16	55	5.42	<0.001
	R	Superior Parietal Lobule	22 -56 40	33	5.31	<0.001
	L	Hippocampus	-36 -24 -18	38	5.26	<0.001
*Rejection>Neutral & Inclusion>Neutral, Controls & MDD**						
	R	Postcentral Gyrus	50 -20 30	60	2.25	0.01
	L	Postcentral Gyrus	-54 -24 32	87	1.99	0.02
*Rejection>Neutral & Inclusion>Neutral, Controls**						
	R	Postcentral Gyrus	50 -20 30	60	2.28	0.01
	L	Postcentral Gyrus	-56 -18 30	98	2.11	0.02
*Rejection>Neutral & Inclusion>Neutral, MDD**						
	R	Putamen	30 4 8	1708	3.25	0.001
	L	Anterior Insula	-34 0 8	1812	3.17	0.001
	R	Thalamus	18 -6 10	259	2.48	0.01
	L	Cerebellum	-12 -28 -32	218	2.44	0.01
	R	Cerebellum	4 -48 -20	40	2.33	0.01
	L	Thalamus	-14 -12 -4	181	2.32	0.01
	L	Anterior Cingulate Gyrus	0 32 24	939	2.27	0.01
	L	Putamen	-16 6 4	31	2.23	0.01
	R	Lingual Gyrus	18 -44 -18	21	2.01	0.02
	R	Putamen	20 6 -2	22	1.91	0.03
Rejection>Neutral & Inclusion>Neutral, MDD>Controls,***						
	R	Inferior Frontal Gyrus	36 34 -4	27	2.49	0.01
	R	Middle Frontal Gyrus/Precentral Gyrus	54 12 42	98	2.44	0.01
	R	Anterior Insula	28 16 -14	84	2.31	0.01
	L	Anterior Insula	-34 12 -12	84	2.17	0.02
	R/L	Anterior Cingulate Gyrus	2 34 22	131	1.93	0.03
		Brain Stem	-4 -42 -24	22	1.91	0.03
	L	Anterior Insula	-30 20 0	29	1.87	0.03

Abbreviations: R; Right, L; Left; Extent threshold: k = 20 voxels;
* = p<0.05, uncorrected. ** = inclusively masked by MDD conjunction of Rejection>Neutral & Inclusion>Neutral at p=0.05.

Appendix 5 (Chapter 5)

Appendix 5.1 Descriptives and group comparison of social, affective and process measures (Chapter 5)

				Std.	95% CI			
		N	Mean	Error	Lower	Upper	F[1,48]	Sig.
BAI	Controls	27	3.02	0.68	1.62	4.42	37.73	<.001*
	MDD	23	17.46	2.42	12.44	22.49		
	Total	50	9.66	1.55	6.55	12.78		
BDI	Controls	27	3.48	0.76	1.91	5.05	114.3	<.001*
	MDD	23	25.09	2.00	20.94	29.23		
	Total	50	13.42	1.83	9.74	17.10		
DERS	Controls	27	67.43	3.77	59.68	75.19	55.30	<.001*
	MDD	23	113.52	5.05	103.04	123.99		
	Total	50	88.63	4.48	79.62	97.64		
IPSM	Controls	27	96.77	2.41	91.82	101.72	35.35	<.001*
	MDD	23	120.32	3.23	113.62	127.03		
	Total	50	107.60	2.57	102.43	112.78		
ISQ	Controls	27	70.08	2.38	65.19	74.97	70.89	<.001*
	MDD	23	105.23	3.56	97.85	112.61		
	Total	50	86.25	3.24	79.74	92.76		
SAIS-I	Controls	27	40.75	2.70	35.20	46.30	19.86	<.001*
	MDD	23	67.22	5.61	55.59	78.85		
	Total	50	52.92	3.48	45.92	59.92		
SAIS-II	Controls	27	42.10	2.63	36.68	47.52	17.29	<.001*
	MDD	23	63.19	4.55	53.76	72.62		
	Total	50	51.80	2.92	45.94	57.66		
SBS	Controls	27	21.27	1.82	17.52	25.01	18.68	<.001*
	MDD	23	34.44	2.52	29.21	39.66		
	Total	50	27.32	1.77	23.76	30.88		
SCS	Controls	27	62.25	2.31	57.50	66.99	41.00	<.001*
	MDD	23	39.49	2.73	33.82	45.17		
	Total	50	51.78	2.39	46.98	56.58		
SUIS	Controls	27	37.46	1.33	34.73	40.19	1.69	.200
	MDD	23	40.39	1.87	36.50	44.27		
	Total	50	38.81	1.13	36.54	41.08		
Positive Affect	Controls	27	33.15	1.51	30.05	36.25	25.93	<.001*
	MDD	23	22.02	1.58	18.75	25.28		
	Total	50	28.03	1.34	25.34	30.72		
Negative Affect	Controls	27	13.39	0.72	11.91	14.88	75.19	<.001*
	MDD	23	27.25	1.51	24.12	30.38		
	Total	50	19.77	1.26	17.23	22.30		

Note: See Chapter 2 for details on measures. All tests, variances of groups assumed equal. *=p<0.001.

Appendix 5.2 One sample T-test in healthy control participants (N=21) of brain regions significantly activated during imagery of other's memories (Chapter 5)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Rejection > Neutral						
	R	Angular Gyrus	44 -50 24	1043	4.85	0
	L	Precuneus	0 -54 44	520	4.62	0
	L	Angular Gyrus	-60 -52 26	529	4.43	0
	L	Postcentral	-64 -18 28	191	4.42	0
	R	Superior Frontal Gyrus, medial part	4 52 34	373	4.3	0
	L	Cerebelum	-24 -78 -34	142	4.19	0
	L	Precentral	-62 8 26	23	3.88	0
	R	Middle Temporal Gyrus	64 -16 -18	74	3.86	0
	R	Caudate	12 10 12	52	3.64	0
	R	Superior Frontal Gyrus	28 26 50	62	3.48	0
	R	SupraMarginal	58 -20 38	35	3.43	0
Rejection > Inclusion						
	L	Angular Gyrus	-60 -60 30	515	5.72	0
	R	Angular Gyrus	60 -52 26	876	5.6	0
	R	Middle Temporal Gyrus	62 -22 -10	568	4.4	0
	R	Medial Frontal Gyrus	40 12 32	285	4.35	0
	L	Middle Temporal Gyrus	-50 -30 -12	61	3.86	0
	L	Cerebelum	-20 -90 -32	33	3.77	0
Inclusion > Neutral						
	L	Supramarginal Gyrus	-52 -28 40	3880	5.29	0
	R	Supramarginal Gyrus	56 -18 34	1616	4.41	0
	R	Anterior Cingulate Gyrus	4 42 4	837	4.09	0
	R	Middle Cingulate Gyrus	12 -24 36	37	4.01	0
	R	Angular Gyrus	42 -56 22	193	3.86	0
	R	Middle Cingulate Gyrus	12 -4 40	311	3.81	0
	R	Precuneus	12 -44 66	145	3.8	0
	R	Precuneus	10 -60 30	630	3.77	0
	L	Precentral Gyrus	-60 10 28	81	3.75	0
	L	Parietal Operculum	-38 -24 20	48	3.71	0
	R	Superior Frontal Gyrus	22 38 36	38	3.69	0
	L	Midde Frontal Gyrus	-40 38 24	56	3.52	0
	R	Anterior Insula	44 0 6	37	3.5	0
Inclusion > Rejection						
	R	Superior Occipital Gyrus	20 -82 14	12855	4.92	0

	R	Precentral Gyrus	36 -14 50	2126	4.48	0
	L	Anterior Cingulate Gyrus	-4 42 -10	1240	4.31	0
	L	Precentral Gyrus	-36 -12 54	372	4.18	0
	L	Posterior Insula	-34 -16 12	172	4.14	0
	L	Middle Frontal Gyrus	-42 36 18	104	3.72	0
	L	Superior Frontal Gyrus	-14 38 48	127	3.68	0
	R	Medial Orbital Gyrus	22 30 -16	49	3.66	0
	R	Posterior Insula	38 -6 2	28	3.51	0
	R	Superior Parietal Lobule	20 -62 52	73	3.47	0
	L	Posterior cingulate gyrus	-4 -32 34	26	3.33	0
Neutral > Rejection						
	L	Inferior Frontal Gyrus, pars orbitalis	-32 34 -14	50	3.45	0
Neutral > Inclusion						
	R	Inferior Frontal Gyrus, pars triangularis	38 30 2	61	3.73	0
Rejection & Inclusion > Neutral						
	L	Supramarginal Gyrus	-64 -22 36	956	5.08	0
	R	Angular Gyrus	44 -50 24	666	4.4	0
	R	Superior Frontal Gyrus, medial part	6 48 32	615	4.33	0
	R	Precuneus	2 -58 42	559	4.19	0
	L	Precentral Gyrus	-60 10 26	113	4.17	0
	R	Supramarginal Gyrus	58 -20 38	713	4.17	0
	L	Cerebellum	-24 -80 -32	133	4.16	0
	L	Postcentral Gyrus	-28 -40 52	508	4.03	0
	R	Superior Frontal Gyrus	28 26 50	196	3.64	0
	L	Angular Gyrus	-46 -60 30	53	3.63	0
Neutral						
	L	Superior Temporal Gyrus	-58 -2 -12	6196	6.65	0
	R	Superior Temporal Gyrus	62 -10 -8	4637	6.06	0
	R	Precentral Gyrus	58 -2 46	523	5.61	0
	L	Superior Frontal Gyrus	-12 56 36	208	5	0
	L	Middle Temporal Gyrus	-42 -56 20	566	4.84	0
	R	Cerebelum	26 -78 -36	186	4.37	0
	R	Hippocampus	26 -8 -18	752	4.36	0
	L	Precentral Gyrus	-54 -4 50	140	4.12	0
	L	Inferior Frontal Gyrus, pars triangularis	-54 26 10	123	4	0
	R	Calcarine	16 -54 8	73	3.8	0
	L	Inferior Frontal Gyrus, pars orbitalis	-42 32 -18	91	3.76	0
	L	Lingual	-12 -54 4	51	3.57	0

Rejection						
	L	Middle Temporal Gyrus	-58 -20 0	9762	6.91	0
	R	Superior Temporal Gyrus	66 -12 -8	7625	5.58	0
	L	Superior Frontal Gyrus	-10 54 38	719	5.42	0
	L	Inferior Frontal Gyrus, pars triangularis	-58 26 6	294	5.02	0
	R	Cerebellum	52 2 50	304	4.61	0
	L	Precentral Gyrus	-48 0 56	265	4.37	0
	L	Cerebellum	-22 -82 -34	207	4.24	0
	R	Thalamus	6 -10 0	34	4.07	0
	R	Inferior Frontal Gyrus, pars opercularis	62 22 20	59	3.93	0
	R	Fusiform	30 -34 -14	71	3.87	0
	R	Supplementary Motor Area	12 2 54	84	3.77	0
	L	Rectus	-2 30 -24	89	3.56	0
	L	Thalamus	-12 -16 4	48	3.4	0
Inclusion						
	L	Middle Temporal Gyrus	-58 -20 2	32267	7.25	0
	L	Rectus	-4 34 -20	710	5.53	0
	L	Superior Frontal Gyrus	-12 54 38	821	5.49	0
	L	Precentral Gyrus	-34 -20 50	3756	5.06	0
	L	Precentral Gyrus	-60 8 28	448	4	0
	R	Cerebellum	8 -52 -40	20	3.88	0
	R	Calcarine	24 -104 2	134	3.86	0
	R	Superior Parietal Lobule	14 -44 64	25	3.4	0
	L	Inferior Frontal Gyrus, pars orbitalis	-42 34 -10	53	3.39	0
	L	Calcarine	-16 -102 -4	24	3.22	0.001

*p<0.001 uncorrected unless otherwise stated.

Appendix 5.3 One sample T-test in MDD participants (N=21) of brain regions significantly activated during imagery of other's memories (Chapter 5)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Rejection > Neutral						
	L	Left Calcarine Cortex	-14 -74 10	105	4.52	0
	R	Middle Temporal Gyrus	54 -32 -6	131	4.24	0
	R	Precuneus	6 -56 42	62	4.04	0
	L	Cerebellum	-26 -80 -32	62	4.01	0
	R	Angular Gyrus	46 -56 32	176	3.91	0
	R	Inferior Temporal Lobe	54 10 -36	35	3.86	0
	L	Thalamus	-6 0 -4	74	3.68	0
	L	Angular Gyrus	-42 -56 16	249	3.63	0
	R	Middle Temporal Gyrus	34 24 48	26	3.51	0
Rejection > Inclusion						
	R	Middle Temporal Gyrus	54 -34 -6	352	4.18	0
	L	Cerebellum	-22 -78 -34	111	4.09	0
	L	Angular Gyrus	-50 -54 28	184	3.94	0
	R	Precuneus	6 -58 42	42	3.79	0
	L	Middle Temporal Gyrus	-56 -38 -2	82	3.53	0
	R	Angular Gyrus	56 -58 32	22	3.41	0
Inclusion > Neutral						
	L	SMC	-2 -4 56	237	4.41	0
	L	Postcentral Gyrus	-40 -40 58	61	3.85	0
	L	Precentral Gyrus	-58 10 22	40	3.81	0
	L	Postcentral Gyrus	-60 -18 32	45	3.43	0
Inclusion > Rejection						
	L	Anterior Insula	-42 8 -12	486	4.74	0
	L	Middle Cingulate Cortex	-2 -26 30	569	4.57	0
	L	Middle Cingulate Cortex	-6 12 22	487	4.24	0
	L	Posterior Orbital Gyrus	-26 34 -14	58	3.81	0
	R	Anterior Insula	38 14 4	137	3.76	0
	R	Precuneus	16 -70 44	42	3.67	0
	R	Inferior Frontal Gyrus	44 40 4	141	3.54	0
	L	Posterior Orbital Gyrus	28 34 -14	22	3.52	0
Neutral > Rejection						
	L	Inferior Frontal Gyrus, pars orbitalis (p. o.)	-24 32 -8	457	4.77	0
	R	Inferior Frontal Gyrus, p. o.	26 32 -14	148	4.46	0
	R	Anterior Insula	42 14 -4	465	4.26	0
	R	Occipital Lobe	28 -46 26	146	4.13	0
	L	Precuneus	-18 -56 32	55	3.9	0
	L	Middle Cingulate Cortex	-4 -30 36	221	3.85	0
	R	Hippocampus	36 -36 -4	128	3.8	0
	R	Corpus Callosum	22 -2 34	39	3.74	0
	L	Inferior Frontal Gyrus	-40 24 12	70	3.71	0

	L	Middle Cingulate Cortex	-14 -12 34	24	3.62	0
	L	Fusiform Gyrus	-30 -50 -6	95	3.55	0
	R	Putamen	20 38 16	33	3.52	0
	R	Anterior Cingulate Cortex	6 30 24	22	3.35	0
Neutral > Inclusion						
	R	Anterior Hippocampus	38 -38 -10	95	4.39	0
	L	Inferior Frontal Gyrus	-52 42 -12	29	4.34	0
	L	Calcarine	-18 -56 14	88	3.86	0
	R	Precuneus	18 -50 16	23	3.4	0
Rejection & Inclusion > Neutral						
	L	Precentral Gyrus	-60 10 26	31	4.37	0
	L	Superior Parietal Lobule	-34 -46 70	175	4.03	0
	R	Angular Gyrus	54 -58 26	41	3.51	0
Neutral						
	R	Superior Temporal Gyrus	60 -4 0	5383	6.05	0
	L	Superior Temporal Gyrus	-48 -28 10	8387	5.94	0
	R	Hippocampus	26 -16 -18	436	4.7	0
	L	Calcarine	-18 -50 10	90	4.26	0
	L	Rectus	0 38 -22	137	4.15	0
	R	Cerebellum	28 -80 -34	143	3.89	0
	L	Inferior Orbital Frontal Gyrus	-46 28 -2	133	3.72	0
	L	Superior Medial Frontal Gyrus	-8 56 44	50	3.6	0
	L	Precentral	-54 0 48	22	3.41	0
	L	Inferior Superior Cortex	-32 -86 40	22	3.36	0
Rejection						
	L	Middle Temporal Gyrus	-58 -14 -12	7121	6.37	0
	R	Superior Temporal Gyrus	62 -6 0	4501	6.03	0
	R	Cerebellum	28 -82 -32	185	4.76	0
	L	Inferior Frontal Gyrus	-46 34 -12	265	4.66	0
	L	Rectus	-2 48 -18	81	3.85	0
	R	Medial Frontal Gyrus	54 -74 20	255	3.83	0
	L	Superior Medial Frontal Gyrus	-8 56 44	39	3.81	0
	R	Precentral Gyrus	58 -4 48	46	3.79	0
	L	Cerebellum	-24 -78 -34	34	3.75	0
	L	Precentral Gyrus	-54 -2 48	117	3.7	0
	L	Parahippocampal Gyrus	-28 -8 -26	34	3.65	0
Inclusion						
	R	Superior Temporal Gyrus	56 -14 2	4441	6.49	0
	L	Middle Temporal Gyrus	-58 -14 -10	7151	6.05	0
	R	Precentral Gyrus	58 -4 48	133	4.53	0
	R	Hippocampus	26 -8 -22	129	4.13	0
	L	Rectus	0 36 -24	159	4.08	0
	L	Precentral Gyrus	-52 -2 46	88	3.92	0
	L	Inferior Frontal Gyrus	-58 28 8	111	3.74	0
	R	Corpus Callosum	6 8 22	21	3.63	0

	L	Superior Medial Frontal Gyrus	-10	44	46	50	3.4	0

*p<0.001 uncorrected unless otherwise stated.

Appendix 5.4 Two sample T-tests of brain regions significantly activated during imagery of others' memories in healthy control (N=21) and MDD participants (N=21) (Chapter 5)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Controls > MDD, Rejection > Neutral						
	R	Angular Gyrus	44 -50 22	27	3.78	0
Controls > MDD, Rejection > Inclusion						
	L	Anterior Insula	-38 22 8	55	4.03	0
	R	Precentral Gyrus	48 8 28	55	3.88	0
	L	Middle Cingulate Gyrus	-6 12 22	23	3.82	0
MDD > Controls, Rejection > Inclusion						
	L	Parietal Occipital Gyrus	-18 -96 30	24	3.62	0
Controls > MDD, Inclusion > Neutral						
	R	Middle Occipital Gyrus	44 -72 22	62	3.52	0
Controls > MDD, Rejection & Inclusion > Neutral						
	R	Angular Gyrus	44 -50 22	67	4.18	0
	R	Anterior Cingulate Gyrus	16 48 14	130	3.78	0
Controls > MDD, Neutral						
	R	Supplementary Motor Cortex	12 -2 48	174	4.27	0
	R	Middle Cingulate Gyrus	4 12 34	78	4.01	0
	L	Anterior Insula	-42 10 -16	91	3.81	0
	R	Postcentral Gyrus	46 -28 62	46	3.78	0
	L	Postcentral Gyrus	-14 -32 64	28	3.71	0
	R	Middle Cingulate Gyrus	14 -18 40	37	3.44	0
	L	Hippocampus	-28 -22 -10	20	3.35	0
Controls > MDD, Rejection						
	L	Hippocampus	-26 -18 -6	999	4.82	0
	R	Middle Superior Frontal Gyrus	8 48 30	205	4.26	0
	R	Anterior Cingulate Gyrus	6 22 18	466	4.18	0
	R	Supplementary Motor Cortex	16 -2 48	752	4.17	0
	R	Anterior Insula	36 14 4	314	4.06	0
	R	Posterior Insula	34 -6 -8	181	4.03	0
	R	Cerebellum	10 -26 -32	131	3.94	0
	L	Supramarginal Gyrus	-50 -42 34	87	3.85	0
	L	Middle Cingulate Gyrus	-12 -8 44	73	3.63	0
	L	Precentral Gyrus	-26 -30 48	91	3.6	0
	R	Precuneus	12 -50 58	35	3.58	0
	L	Supramarginal Gyrus	-32 -38 34	38	3.57	0
	L	Brain Stem	-10 -24 -38	35	3.54	0
	R	Angular Gyrus	34 -72 48	26	3.48	0
	R	Anterior Insula	36 16 -16	26	3.48	0
	R	Supramarginal Gyrus	60 -42 38	36	3.45	0
	L	Precentral Gyrus	-34 -18 44	69	3.39	0
	R	Precentral Gyrus	54 12 30	53	3.36	0
Controls > MDD, Inclusion						

R	Posterior Insula	34 -6 -8	413	4.49	0
L	Hippocampus	-26 -22 -6	423	4.35	0
L	Superior Frontal Gyrus	-12 8 58	86	4.14	0
R	Accumbens Area	10 18 -4	102	4.14	0
R	Middle Cingulate Gyrus	8 -26 44	610	3.99	0
L	Middle Frontal Gyrus	-42 42 18	161	3.97	0
L	Lateral Orbital Gyrus	-32 38 -18	112	3.89	0
L	Supramarginal Gyrus	-42 -44 38	198	3.86	0
L	Precentral Gyrus	-28 -24 56	327	3.75	0
L	Precuneus	-10 -56 56	67	3.72	0
R	Superior Frontal Gyrus	10 52 24	67	3.7	0
L	Occipital Fusiform Gyrus	-22 -70 -22	109	3.69	0
L	Caudate	-14 22 -6	35	3.66	0
L	Precuneus	-18 -68 24	54	3.63	0
R	Supplementary Motor Cortex	10 0 50	64	3.61	0
R	Middle Frontal Gyrus	32 0 42	34	3.59	0
L	Inferior Temporal Gyrus	-52 -64 -8	31	3.51	0
L	Anterior Insula	-38 6 -18	79	3.49	0
R	Cerebellum	32 -42 -34	33	3.44	0
R	Superior Parietal Lobule	18 -56 68	33	3.44	0

*p<0.001 uncorrected unless otherwise stated

Appendix 5.5 ANOVA (Group: MDD, controls) x memory type (neutral, inclusion, rejection) during imagery of others' memories (Chapter 5)

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Main Effect of Group, p <0.05, FEW						
	L	Hippocampus	-26 -20 -6	662	6.86	0
	R	Middle Cingulate Cortex	4 12 34	1439	6.7	0
	R	Anterior Insula	34 -6 -8	196	6.19	0
	L	Inferior Parietal Lobule	-50 -42 40	224	5.81	0
	L	Superior Occipital Gyrus	-18 -68 24	57	5.75	0
	L	Posterior Orbital Gyrus	-28 -28 60	356	5.65	0
	L	Inferior Frontal Gyrus, pars orbitalis	-32 42 -16	39	5.33	0.001
	L	Superior Frontal Gyrus	-14 12 56	21	5.24	0.004
	R	Frontal Superior Medial Gyrus	8 52 26	34	5.17	0.002
	R	Middle Temporal Gyrus	56 -52 12	24	5	0.003
Main Effect of Valence						
	L	Posterior Orbital Gyrus	-32 34 -16	146	4.68	0
	R	Angular Gyrus	54 -52 28	175	4.19	0
	L	Postcentral Gyrus	-62 -20 32	210	4.1	0
	R	Postcentral Gyrus	54 -22 42	112	3.83	0
	L	Postcentral Gyrus	-32 -40 60	107	3.69	0
	R	Postcentral Gyrus	32 -40 62	105	3.57	0
All valences all groups						
	L	Middle Temporal Gyrus	-60 -6 -10	40562	Inf	0
	L	Precentral	-54 -2 48	2868	Inf	0
	L	Superior Frontal Gyrus	-10 54 38	1075	Inf	0
	L	Rectus	-2 36 -22	657	Inf	0
	R	Cerebellum	6 -52 -40	129	6.25	0
	R	Superior Occipital Gyrus	20 -106 6	312	5.63	0
	L	Precuneus	-2 -54 36	120	4.1	0
	L	Middle Occipital Gyrus	-16 -104 0	35	3.47	0
Controls > MDD all valences, p <0.05, FEW						
	L	Hippocampus	-26 -20 -6	823	6.96	0
	R	Middle Cingulate Cortex	4 12 34	1768	6.8	0
	R	Putamen	34 -6 -8	299	6.3	0
	R	Insula	34 10 2	188	5.98	0
	L	Inferior Parietal Lobule	-50 -42 40	280	5.92	0
	L	Superior Occipital Gyrus	-18 -68 24	75	5.87	0
	L	Precentral	-28 -28 60	515	5.77	0
	L	Inferior Frontal Gyrus, pars orbitalis	-32 42 -16	54	5.46	0.001
	L	Superior Frontal Gyrus	-14 12 56	32	5.36	0.002
	R	Superior Frontal Gyrus, medial part	8 52 26	55	5.3	0.001
	R	Middle Temporal Gyrus	56 -52 12	51	5.13	0.001
	R	Precentral	40 -10 46	28	5.11	0.003
	R	Superior Parietal Lobule	18 -72 50	32	4.93	0.002
	R	Calcarine	18 -70 10	20	4.92	0.006
	L	Calcarine	-4 -74 12	96	4.92	0

MDD > Controls all valences						
	L	Middle Temporal Gyrus	-62 -24 -4	331	4.88	0
	R	Superior Temporal Gyrus	58 -12 -4	192	4.69	0
	L	Precuneus	-20 -48 12	68	4.25	0
	R	Caudate	6 8 20	129	4.14	0
	R	Middle Temporal Gyrus	46 -24 -10	62	3.97	0
	L	Caudate	-28 10 24	36	3.81	0
	L	Superior Temporal Gyrus	-42 -30 10	45	3.72	0
Neutral > Rejection all groups						
	L	Inferior Frontal Gyrus, orbital part	-34 34 -16	165	4.71	0
	R	Superior Frontal Gyrus, orbital part	22 32 -16	35	3.72	0
	L	Precuneus	-22 -58 18	31	3.62	0

*p<0.001 uncorrected unless otherwise stated

Appendix 6 (Chapter 6)

Appendix 6.1 Transcript of the speaker's social rejection and social inclusion story

Social Rejection Memory

It was very very difficult for me because after my dad passed away I ended up joining a school. And I joined a school a year into when everyone else had already been there. Everyone already had their preformulated friendship groups and I found it very very hard. My best friend was in the other half of the year and I begged and begged to be put in the same half of the year with her and all of her friends. And the school wouldn't let me because they told me that the other half was already too full, but I knew that wasn't true because other people who joined the school after me went into that year. And I couldn't understand why they wouldn't let me join the same year. And so, I stayed in my friendship group or lack thereof and ended up getting teased because everyone already had their friendship groups. And every lunchtime and every break time I hung around with my best friend and those friendship groups. And it was really hard cause I was really popular on that side of the year but really not on my own. I didn't really know what else I could do to try and fit in better with my class but they just weren't very inclusive. So I began to talk in class. Things were hard for me anyway, because things weren't easy at home. So I wasn't sleeping very well and I began to talk more and then the teachers thought I was a bit of a troublemaker and used to put me in detention. And that was really hard because it meant that the time that I was socializing with my friends in the other half of the year, I was in these detentions, which used to take up most of my break time. And it meant that a large part of my school experience was very difficult for me. Because I didn't really feel included, I didn't really have friends that I wanted around me. And then I began to make some friends towards the latter end of my middle school experience. But it was really hard, because there's nothing worse than being surrounded by people who you don't really like very much and you know that there are other people who you really like and you don't have contact with. I felt that the school wasn't listening to me and that it was really unfair that 'why were they allowing other people to be amongst their friends' and not allowing me to be amongst mine. And I could see how happy my friends were and my best friend and they all would hang around together. And have group stories and exchange notes during lessons and I couldn't be a part of that. And sure I tried to kinda get involved in that and I'd send notes in between that they'd open up in their lessons, but it still meant that you'd miss all the inside stories and even when it came to middle school romances, which are obviously not much now that you look back but they all didn't really happen in my half of the year. It was really fragmented. It was like I was living two lives. In one side I was this popular girl and in the other side I wasn't very well liked. So I just continued to try and fit in amongst my year and continued to try and hang around with the friends I had to make in the half I was forced to be in. And they were friends of circumstance really, because they all thought I was a bit of a trouble maker because I was talking.

And I wasn't sleeping very much at home, so they put me with a lot of the troublemakers and I didn't really see eye to eye with them. I didn't really want to be naughty. I just wanted to fit in. And being amongst those people the way to fit in was to be even worse. So it was just the worst thing they could have done. And when they tried to rectify it by putting me with the children who were responding very well and always sitting through class it was even worse, because they were already friends and they weren't liked by the other half of the year either, so I was ostracized even further by that half of the year. So I ended up feeling a bit lonely and it was horrible because not only was I struggling to catch up with the school work because I'd obviously had a year after the loss of my father, and things were really hard at home. But I also wasn't being understood at school either. The teachers didn't really understand that what I was going through and didn't really ask me ever about my home life. They didn't really ask me why I was tired in class. And they never really paid attention to me when I said that I wanted to swap classes and instead spent some time excluding me from seeing the people I wanted to see and the happiest moments I had during my time in middle school which was spending time with the people I did really like.

Social Inclusion Memory

One of my best experiences was my 25th birthday and I'd moved to London. I had set up a life for myself there and I had just come out of a really stressful job and then I took up this other job which was really stress free and I had loads of free time and I was spending it with all of my friends and I had so many friends. I had friends luckily from my work places, I had friends from school, and from my work place, and from all these different pools, from University and I remember I had all this free time to spend with them because I was single and because I was dating. I was having fun. I just met this new guy who I really liked. And I had this 25th birthday party and I had it at this really cool place in London. There were loads of people there and I couldn't believe it when, so I invited like a 125 people and the area could only fit 100 and I had that amount of people come and it was crazy because it was spilling over into other areas of the nightclub. I had people come I hadn't even seen for years from school and they all brought me presents and a guy I had been seeing had come along and I was introducing him to some of my friends. It was just really cool to be amongst all these people that I loved and really cared about and to introduce them to this guy I liked and I was really excited about. And they were telling him these things about me and I could tell they really cared about me. It was lovely. My sister was there and she was giving this speech and so were my friends. And they were all telling me about how happy they were to know me and how humbled they were and how many life experiences I've gone through and how I have come out the other side. And just these amazing things that were really fulfilling friendships and they are people I still know and love and that I still see to this day and I am constantly baffled by the amazing friendships I have and the amazing people I have around me and I've chosen to surround me and the family that I have. I have so much fun with them. We have many memories. And how things haven't changed that much. That 25th birthday sure I had all this time to spend with everyone and I invested all this time to see people and it

meant that the turnout was bigger than anything I'd before and I knew that everyone was shocked at how many people had turned up and I was shocked by how many people had come just for me. It's really flattering and lovely. And to know that some of those friendships, in fact most of them still stood the test of time even though know I'm in a really settled relationship - you know that guy I was seeing, he turned out to be my partner for five years. He was really you know... That night was what really made us. I knew he was really shy but he came and made an amazing effort with everyone I knew. And I was really proud to show him off and I was really proud to show off my friends and still really feel that way. I guess it's one of those things where you look back on everything that's changed and who you are and you can be nothing but proud of the decisions you've made and the love that you conjure up for yourself.

And that night has very happily been one of many that I've experienced that have allowed me to feel that same experience of belonging. And I can't begin to explain how amazing that is that over and over again that you can have this sense of having made the right decisions and at the time I remember while I was in this really stressful job and having just come out of it. I had this freedom and crazy amazing ability to do what I wanted. But I was still obviously worried about where I was going to go, but I don't think you ever lose those things. But having constant support networks, the people around you and are still with you and even on the 25th birthday some of my oldest friends who couldn't make it, they were sending me all these messages about how they wanted to be there and they are people I still know to this day from way when I was 7 years old when I met my best friends. From those days to now.

Appendix 6.2 Brain activations of ISCs during social inclusion in MDD and controls, p<0.001, k=20, FEW

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	p-value*
MDD					
	R	Lingual Gyrus	20 -92 0	17400	0.18
	L	Inferior Occipital Gyrus	-24 -90 -4	17400	0.18
	R	Calcarine Gyrus	12 -70 14	17400	0.17
	L	Superior Temporal Gyrus	-58 -12 2	1552	0.18
	L	Middle Temporal Gyrus	-56 0 -16	1552	0.09
	L	Heschl's Gyrus	-38 -32 14	1552	0.05
	R	Superior Temporal Gyrus	64 -4 0	2744	0.15
	R	Medial Temporal Pole	32 8 -34	2744	0.12
	R	Medial Temporal Pole	56 10 -18	2744	0.07
	L	Frontal Pole	-8 70 -14	52	0.11
	L	Frontal Pole	-6 58 -20	90	0.09
	R	Nucleus Accumbens	-12 12 -12	139	0.09
	L	Medial Temporal Pole	-28 12 -34	191	0.09
	R	Superior Orbital Gyrus	12 56 -12	69	0.08
	R	Cerebellum (Crus 1)	56 -66 -32	23	0.08
	L	Cerebellum (IX)	-20 -56 -40	79	0.08
	L	ACC	-6 30 -8	38	0.07
	R	Cerebellum (VII)	42 -52 -38	28	0.07
	R	Middle Occipital Gyrus	52 -74 30	21	0.06
	R	Middle Frontal Gyrus	50 12 56	62	0.06
	C	Vermis (8)	4 -68 -30	42	0.06
	L	Middle Orbital Gyrus	-34 52 2	51	0.06
	R	Inferior Frontal Gyrus, pars triangularis	46 16 32	51	0.06
	R	Lingual Gyrus	20 -62 -2	17400	0.05
	R	Lateral Superior Occipital Cortex	30 -74 22	17400	0.06
	L	Cerebellum (VI)	-20 -68 -10	17400	0.06
Controls					
	L	Superior Temporal Gyrus	-54 -14 2	5662	0.22
	L	Middle Temporal Gyrus	-54 0 -16	5662	0.13
	L	Inferior Temporal Gyrus	-40 4 -32	5662	0.09
	R	Superior Temporal Gyrus	68 -22 4	22586	0.21
	R	Lingual Gyrus	22 -92 -2	22586	0.17
	L	Lingual Gyrus	-16 -92 -6	22586	0.17
	R	Frontal Pole	6 62 -14	164	0.11
	L	Cerebellum (Crus 2)	-20 -78 -34	623	0.10
	L	Cerebellum (VI)	-26 -60 -24	623	0.06
	R	Cerebellum (Crus 1)	36 -52 -28	1004	0.10
	R	Cerebellum (Crus 2)	28 -74 -34	1004	0.09
	R	Subgenual PFC	12 30 -10	217	0.08
	L	Cerebellum (Crus 1)	-44 -64 -28	67	0.07

L	Fusiform Gyrus	-36 -50 -4	172	0.07
R	Fusiform Gyrus	40 -44 -6	48	0.07
R	Cerebellum	-34 -54 -36	81	0.07
L	Supramarginal Gyrus	-62 -32 46	43	0.07
L	Cerebellum (X)	-22 -42 -38	81	0.06
R	Cerebellum (X)	8 -6 6	73	0.06
C	Vermis (9)	2 -62 -34	40	0.06
L	Anterior Insula	-28 24 -2	77	0.06
R	Superior Temporal Gyrus	54 -48 22	22586	0.05
R	Inferior Frontal Gyrus, pars triangularis	42 32 32	22586	0.05

Appendix 6.3 Brain activations of ISCs during social rejection in MDD and controls, p<0.001, k=20, FEW

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	p-value*
MDD					
	L	Superior Temporal Gyrus	-56 -14 2	64738	0.391
	R	Superior Temporal Gyrus	64 -8 2	64738	0.322
	R	Medial Temporal Pole	38 12 -34	64738	0.257
	R	Frontal Pole	52 42 28	189	0.100
	R	Middle Frontal Gyrus	36 46 40	189	0.056
	R	Superior Orbital Gyrus	20 20 -16	97	0.099
	L	Superior Orbital Gyrus	-20 32 -8	95	0.091
	L	Precentral Gyrus	-54 -8 52	81	0.076
	R	Middle Frontal Gyrus	50 50 12	78	0.070
	L	Frontal Medial Cortex	2 50 -14	47	0.059
	R	Frontal Pole	38 60 -2	35	0.057
	R	Anterior Insula	34 26 0	21	0.055
	R	Fusiform Gyrus	30 -72 4	64738	0.051
	R	Middle Temporal Gyrus	40 -38 0	64738	0.051
	R	Superior Occipital Gyrus	28 -76 24	64738	0.051
Controls					
	L	Superior Temporal Gyrus	-58 -16 4	49316	0.299
	R	Superior Temporal Gyrus	62 -8 4	49316	0.284
	R	Medial Temporal Pole	48 8 -34	49316	0.184
	L	Postcentral Gyrus	-64 -10 34	32	0.108
	L	Frontal Pole	-10 66 -18	234	0.106
	R	Inferior Frontal Gyrus, pars triangularis	40 14 34	4327	0.104
	R	Middle Frontal Gyrus	40 34 40	4327	0.094
	R	Inferior Frontal Gyrus, pars orbitalis	36 28 2	4327	0.092
	R	Rectal Gyrus	8 14 -14	430	0.098
	L	Superior Orbital Gyrus	-12 22 -16	430	0.081
	L	Middle Frontal Gyrus	-30 52 12	1816	0.093
	L	Middle Frontal Gyrus	-34 34 38	1816	0.089
	L	ACC	-12 44 4	1816	0.061
	L	Frontal Pole	-20 68 4	134	0.087
	R	PCC	2 -26 28	308	0.084
	R	Precentral Gyrus	44 -22 68	92	0.080
	R	Frontal Pole	-6 64 38	139	0.076
	R	Rectal Gyrus	10 30 -16	47	0.075
	L	Precentral Gyrus	-48 2 52	289	0.073
	L	Middle Frontal Gyrus	-28 16 58	289	0.052
	R	Superior Medial Gyrus	6 22 50	689	0.073
	R	ACC	8 38 22	689	0.060
	L	Insula	-32 22 6	162	0.072
	R	Frontal Pole	22 72 10	32	0.072

L	Inferior Frontal Gyrus, pars triangularis	-50 22 20	67	0.061
L	Middle Temporal Gyrus	-46 -46 14	49316	0.050
L	Superior Parietal Lobule	-22 -46 52	49316	0.050
L	Supplementary Motor Cortex	-12 -16 58	49316	0.051
R	Middle Frontal Gyrus	44 42 20	4327	0.055
R	Inferior Frontal Gyrus, pars triangularis	46 26 34	4327	0.062

Appendix 6.4 Brain activations of ISCs during social rejection and inclusion between groups, p<0.001, k=20, FEW in Chapter 6

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	p-value*
MDD > Controls Rejection					
	L	Middle Temporal Gyrus	52 -78 8	185322	2.08
	L	Medial Temporal Pole	36 14 -34	185322	2.06
	L	Postcentral Gyrus	-38 -48 68	185322	1.37
Controls > MDD Rejection					
	L	Superior Temporal Gyrus	-66 -28 14	185322	-1.12
	L	Cerebellum (Crus 2)	48 -52 -42	185322	-1.03
	L	Temporal Pole	-50 20 -24	185322	-1.01
MDD>Controls Inclusion					
	L	Middle Occipital Gyrus	-36 -86 2	177386	1.28
	L	Middle Occipital Gyrus	42 -80 8	177386	1.24
	L	Calcarine Gyrus	24 -98 8	177386	1.14
Controls>MDD Inclusion					
	L	Middle Temporal Gyrus	-62 -32 6	177386	-1.20
	L	Superior Temporal Gyrus	72 -24 2	177386	-1.19
	L	Superior Temporal Gyrus	-58 -2 -6	177386	-1.07

Appendix 6.5 Brain activations of statistically significant greater self-reported positivity and negativity during inclusion and rejection in healthy controls

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Greater Positivity During Inclusion						
		Superior Frontal Gyrus				
	L	Medial Segment	0 60 38	203	7.04	0
	L	Temporal Pole	-28 14 -34	59	6.71	0
	R	Hippocampus	22 -14 -10	158	6.51	0
	R	Precuneus	14 -50 10	126	6.39	0
	R	Lingual Gyrus /	8 -86 -12	526	6.28	0
		Superior Frontal Gyrus				
	R	Medial Segment	18 52 6	705	6.17	0
		Middle Frontal Gyrus /				
		Anterior Cingulate				
	L	Gyrus	-18 34 26	70	5.97	0
	L	Middle Occipital Gyrus	-26 -74 22	428	5.91	0
		Triangular Part of the				
	L	Inferior Frontal Gyrus	-38 34 6	35	5.84	0
	R	Cerebellum	42 -48 -44	47	5.82	0
	L	Fusiform Gyrus	-42 -44 -20	190	5.77	0
		Thalamus Proper /				
	L	Hippocampus	-22 -20 -6	117	5.7	0
	R	Inferior Occipital Gyrus	28 -76 2	110	5.65	0
	L	Brain Stem	-2 -36 -22	90	5.63	0
		Superior Occipital				
	R	Gyrus	26 -90 24	92	5.56	0
	L	Middle Frontal Gyrus	-30 42 0	40	5.53	0
		Occipital Fusiform				
	L	Gyrus	-24 -96 -20	101	5.49	0
		Posterior Cingulate				
	R	Gyrus	8 -36 38	60	5.13	0
		Posterior Cingulate				
	L	Gyrus	-14 -32 30	81	4.86	0
		Superior Frontal Gyrus				
	R	Medial Segment	18 38 26	34	4.82	0
	R	Superior Parietal Lobule	28 -56 56	36	4.72	0
		Superior Frontal Gyrus				
		Medial Segment /				
		Anterior Cingulate				
	L	Cortex	-16 46 -4	29	4.61	0
Greater Negativity During Inclusion						
	R	Precuneus	18 -44 16	50293	Inf	0
	L	Frontal Pole	-16 68 -2	757	Inf	0
		Basal Forebrain /				
	L	Amygdala	-12 2 -18	140	Inf	0
	R	Occipital Pole	12 -98 22	446	7.25	0

	R	Inferior Occipital Gyrus	30	-82	-4	121	6.8	0
	R	Brain Stem	10	-18	-24	51	6.44	0
	R	Cerebellum	50	-70	-38	179	6.34	0
	R	Brain Stem	10	-28	-42	210	6.25	0
	L	Amygdala / Hippocampus	-24	-4	-30	106	6.11	0
	L	Fusiform Gyrus / Parahippocampal Gyrus	-24	-10	-40	115	5.94	0
	R	Thalamus Proper	6	-8	-6	61	5.74	0
	R	Inferior Occipital Gyrus	34	-96	-6	43	5.09	0
	R	Temporal Pole	36	22	-24	32	4.85	0
	L	Parahippocampal Gyrus	-14	-22	-18	34	4.51	0
	L	Precuneus	-6	-60	16	38	4.47	0
	R/L	Brain Stem	2	-34	-4	34	4.41	0
	L	Thalamus Proper	-6	-6	-2	20	4.29	0
	R	Thalamus Proper	20	-12	10	30	4.13	0
Greater Positivity During Rejection								
	R	Precentral Gyrus	46	-6	62	14553	Inf	0
	R	Inferior Temporal Gyrus	46	-44	-28	433	Inf	0
	L	Anterior Cingulate Gyrus	-16	48	-4	3398	Inf	0
	L	Middle Cingulate Gyrus	-6	-6	42	1649	7.62	0
	R	Occipital Pole	22	-96	6	497	7.36	0
	R	Medial Orbital Gyrus	24	36	-14	437	7.02	0
	L	Middle Frontal Gyrus	-34	36	18	73	6.43	0
	L	Temporal Pole	-36	2	-42	169	6	0
	R	Hippocampus	38	-18	-10	44	5.82	0
	R	Brain Stem	18	-22	-36	45	5.8	0
	L	Angular Gyrus / Supramarginal Gyrus	-60	-62	30	32	5.34	0
	L	Inferior Occipital Gyrus	-34	-88	6	96	5.11	0
	R	Posterior Cingulate Gyrus / Precentral Gyrus	2	-30	46	63	5.09	0
	R	Inferior Occipital Gyrus	28	-82	4	22	5.08	0
	L	Subcallosal Area	-4	10	-18	53	4.94	0
	R	Triangular Part of the Inferior Frontal Gyrus	50	38	12	61	4.94	0
	L	Temporal Pole	-38	18	-38	21	4.81	0
	L	Middle Frontal Gyrus	-28	30	42	108	4.81	0
	R	Postcentral Gyrus Medial Segment	8	-40	58	50	4.53	0
	L	Frontal Pole	-24	68	6	61	4.41	0
Greater Negativity During Rejection								
	L	Middle Frontal Gyrus	-40	20	22	610	Inf	0
	L	Frontal Pole	-4	64	-8	486	7.54	0
	R	Middle Frontal Gyrus	32	10	26	692	7.48	0
	R	Superior Parietal Lobule	30	-48	48	609	7.25	0
	L	Inferior Temporal Gyrus	-56	-60	-20	158	6.75	0
	R	Thalamus Proper	24	-28	-4	152	6.61	0

	Anterior Cingulate				
L	Gyrus	-10 30 2	234	6.58	0
L	Anterior Insula	-32 20 -6	50	6.27	0
L	Occipital Pole	-4 -100 -10	80	6.15	0
L	Supramarginal Gyrus	-38 -36 40	478	6.14	0
	Anterior Cingulate				
L	Gyrus	-6 20 -16	121	6.03	0
R	Cerebellum	50 -70 -32	71	5.9	0
L	Middle Occipital Gyrus	-44 -84 26	45	5.8	0
	Superior Parietal Lobule				
L	/ Angular Gyrus	-30 -64 26	507	5.77	0
L	Inferior Temporal Gyrus	-44 -24 -30	142	5.75	0
R	Superior Frontal Gyrus	10 66 28	25	5.72	0
	Posterior Cingulate				
L	Gyrus	-4 -48 10	78	5.55	0
L	Cerebellum	-28 -68 -34	57	5.36	0
R	Anterior Insula	38 22 -8	50	5.35	0
L	Superior Frontal Gyrus	-26 2 64	32	5.35	0
	Occipital Fusiform				
R	Gyrus	28 -66 -8	34	5.28	0
L	Brain Stem	-6 -20 -10	58	5.26	0
	Occipital Fusiform				
L	Gyrus	-48 -72 -22	26	5.24	0
L	Middle Frontal Gyrus	-20 40 20	30	5.17	0
R	Cerebellum	8 -78 -30	260	5.16	0
L	Superior Frontal Gyrus	-6 40 54	21	5.12	0
R	Angular Gyrus	50 -60 48	21	4.99	0
R	Middle Frontal Gyrus	30 10 62	21	4.89	0
R	Fusiform Gyrus	36 -18 -34	40	4.83	0
R	Precuneus	16 -68 20	30	4.83	0
R	Middle Occipital Gyrus	42 -66 20	44	4.78	0
R	Angular Gyrus	62 -46 22	36	4.72	0
R	Superior Frontal Gyrus	22 60 28	22	4.59	0
L	Hippocampus	-26 -42 -2	26	4.56	0
L	Middle Occipital Gyrus	-48 -82 12	20	4.37	0
L	Middle Frontal Gyrus	-42 6 54	24	4.3	0
R	Cerebellum	22 -64 -40	21	4.23	0
L	Superior Frontal Gyrus	-20 36 50	28	4.22	0
R	Middle Temporal Gyrus	66 -28 -16	25	4.16	0
R	Angular Gyrus	56 -60 34	33	4.13	0
R	Lingual Gyrus	8 -44 -6	36	3.83	0

Appendix 6.6 Brain activations of statistically significant greater self-reported positivity and negativity during inclusion and rejection in MDD, p<0.001, k=20

Contrast	L/R	MNI Structural Atlas	MNI Coordinates (X,Y,Z)	k-voxels	z-score	p-value*
Greater Positivity During Inclusion						
	R	Supramarginal Gyrus	48 -44 40	382	5.97	0
	L	Cerebellum	-20 -36 -46	81	5.95	0
	L	Posterior Cingulate Gyrus	-4 -32 44	358	5.85	0
	R	Middle Temporal Gyrus	68 -30 -14	47	5.79	0
	R	Superior Frontal Gyrus	18 20 62	451	5.72	0
	L	Middle Temporal Gyrus	-46 -46 -2	260	5.71	0
	L	Supramarginal Gyrus	-62 -38 20	66	5.66	0
	R	Anterior Insula	26 34 2	284	5.54	0
	R	Amygdala	30 0 -28	42	5.54	0
	R	Anterior Cingulate Gyrus	8 42 4	141	5.37	0
	L	Temporal Pole	-56 6 -30	32	5.25	0
	L	Postcentral Gyrus	-66 -16 18	55	5.22	0
	R	Cerebellum	46 -50 -40	48	5.12	0
	R	Precentral Gyrus	64 0 18	81	5.07	0
	L	Cerebellum	-46 -52 -36	78	4.87	0
	L	Supramarginal Gyrus	-50 -48 46	58	4.87	0
	L	Hippocampus	-34 -16 -22	26	4.77	0
	R	Medial Orbital Gyrus	22 32 -20	36	4.69	0
	R	Inferior Temporal Gyrus	56 -26 -24	23	4.55	0
	L	Precuneus	-8 -78 46	40	4.43	0
	R	Middle Frontal Gyrus	28 40 28	28	4.34	0
	L	Inferior Frontal Gyrus	-48 14 16	22	4.03	0
MDD Greater Negativity During Inclusion						
	L	Postcentral Gyrus	-40 -34 64	606	6.21	0
	L	Occipital Fusiform Gyrus	-28 -76 -2	2249	6.12	0
	L	Precentral Gyrus Medial Segment	-6 -26 68	28	5.95	0
	L	Medial Orbital Gyrus	-16 40 -12	54	5.94	0
	L	Posterior Orbital Gyrus	-36 30 -22	241	5.65	0
	L	Gyrus Rectus	-8 50 -18	40	5.54	0
	R	Superior Occipital Gyrus	22 -74 34	20	5.44	0
	R	Superior Occipital Gyrus	20 -88 30	57	5.23	0
	L	Middle Temporal Gyrus	-64 -54 -8	26	5.09	0
	R	Caudate	22 2 18	57	5.08	0
	R	Occipital Pole	8 -96 16	60	4.88	0
	L	Ventral DC	-2 2 -4	119	4.82	0

R	Superior Occipital Gyrus	30 -90 18	25	4.7	0
L	Medial Orbital Gyrus	-14 10 -24	20	4.69	0
R	Middle Occipital Gyrus	50 -78 14	21	4.53	0
L	Precentral Gyrus	-28 -16 54	29	4.52	0
L	Middle Frontal Gyrus	-30 54 32	36	4.47	0
L	Posterior Cingulate Gyrus	-6 -48 26	28	4.46	0
L	Middle Cingulate Gyrus	0 -24 20	30	4.39	0
L	Caudate	-14 20 8	23	4.38	0
R	Middle Occipital Gyrus	48 -78 28	23	4.35	0
R	Superior Parietal Lobule	28 -52 70	20	4.34	0
L	Angular Gyrus	-40 -68 36	50	4.25	0
Greater Positivity During Rejection					
L	Parietal Operculum	-38 -36 22	1333	Inf	0
L	Middle Frontal Gyrus	-34 44 8	6709	7.23	0
L	Cerebellum	-2 -72 -32	69	7.01	0
R	Cerebellum	16 -56 -42	84	6.83	0
R	Angular Gyrus	64 -50 32	120	6.82	0
L	Middle Cingulate Gyrus	-2 -8 26	222	6.71	0
R	Angular Gyrus	52 -54 54	77	6.38	0
R	Middle Occipital Gyrus	42 -74 18	37	5.97	0
R	Calcarine Cortex	28 -58 6	45	5.93	0
R	Calcarine Cortex	8 -70 12	37	5.8	0
R	Angular Gyrus	42 -70 44	256	5.79	0
L	Brain Stem	-12 -18 -30	52	5.63	0
L	Inferior Frontal Gyrus, pars opercularis	-46 20 10	28	5.48	0
R	Occipital Fusiform Gyrus	34 -66 -18	66	5.47	0
L	Middle Occipital Gyrus	-32 -86 24	41	5.39	0
R	Cerebellum	14 -44 -44	28	5.37	0
L	Middle Frontal Gyrus	-32 2 56	41	5.36	0
L	Inferior Temporal Gyrus	-48 -40 -22	37	5.34	0
R	Middle Frontal Gyrus	40 16 52	42	5.33	0
L	Inferior Temporal Gyrus	-50 -22 -22	21	5.1	0
L	Cerebellum	-24 -46 -42	43	5.08	0
R	Entorhinal Area	26 6 -20	92	5.08	0
L	Cerebellum	-32 -34 -32	27	5.07	0
L	Caudate	-10 10 22	52	4.95	0
R	Inferior Occipital Gyrus	42 -76 2	28	4.95	0
R	Caudate	12 12 18	31	4.92	0
R	Parietal Operculum	36 -22 18	35	4.91	0
L	Inferior Temporal Gyrus	-48 0 -38	74	4.87	0
L	Planum Polare/Posterior Insula	-44 -2 -10	97	4.76	0
R	Precentral Gyrus	52 0 42	33	4.67	0

		Occipital Fusiform				
	R	Gyrus	32	-88	-14	22	4.66	0
	R	Fusiform Gyrus	38	-48	-6	23	4.44	0
	R	Superior Parietal Lobule	12	-56	70	34	4.42	0
	R	Superior Frontal Gyrus	24	24	60	20	4.32	0
	L	SMC	-2	26	50	20	4.27	0
	R	STG	60	2	-10	22	3.85	0
Greater Negativity During Rejection								
	R	Middle Cingulate Gyrus	18	12	32	723	7.55	0
	R	Brain Stem	6	-22	-46	199	6.82	0
	L	Postcentral Gyrus	-58	-20	52	480	6.48	0
	R	Superior Frontal Gyrus	24	64	18	117	6.28	0
	L	Precuneus	-12	-64	22	395	6.27	0
	L	Precuneus	-18	-44	54	264	6.26	0
	R	Fusiform Gyrus	44	-14	-26	120	6.25	0
		Triangular Part of the						
	R	Inferior Frontal Gyrus	52	38	-4	211	6.22	0
		Superior Frontal Gyrus						
	R	Medial Segment	2	34	50	104	5.93	0
	L	Precuneus	-20	-50	36	29	5.92	0
	L	Brain Stem	-10	-42	-48	50	5.82	0
		Inferior Frontal Gyrus,						
	R	pars opercularis	44	12	14	287	5.78	0
	R	Anterior Orbital Gyrus	30	40	-6	40	5.75	0
	R	Hippocampus	36	-36	-6	79	5.68	0
	L	Lingual Gyrus	-24	-44	-10	25	5.63	0
	L	Cerebellum	-10	-90	-36	20	5.62	0
	L	Cerebellum	-32	-88	-22	37	5.49	0
	R	Caudate	18	28	14	49	5.47	0
	L	Middle Temporal Gyrus	-46	-62	-2	174	5.44	0
	R	Lingual Gyrus	4	-90	-16	59	5.38	0
	R	Medial Frontal Cortex	8	24	-16	39	5.33	0
	L	Thalamus Proper	0	-16	8	33	5.26	0
		Posterior Cingulate						
	R	Gyrus	20	-46	32	137	5.24	0
	L	Cerebellum	-46	-72	-38	109	5.18	0
	R	Postcentral Gyrus	46	-22	52	128	5.14	0
	L	Angular Gyrus	-26	-66	52	39	5.11	0
	R	Angular Gyrus	40	-42	24	39	4.96	0
	R	Superior Parietal Lobule	34	-58	58	83	4.96	0
		Occipital Fusiform						
	L	Gyrus	-22	-92	-8	28	4.88	0
	R	Parahippocampal Gyrus	24	-8	-34	30	4.87	0
	L	Medial Orbital Gyrus	-16	22	-14	23	4.83	0
	R	Superior Frontal Gyrus	24	2	64	46	4.8	0
	R	Lingual Gyrus	4	-66	4	39	4.76	0
	R	Superior Parietal Lobule	36	-44	48	41	4.54	0
		Posterior Cingulate						
	R	Gyrus	4	-40	24	23	4.41	0