THE IMPACT OF EMOTIONAL DISTRACTION ON COGNITION:
FROM BASIC BRAIN RESPONSES TO LARGE-SCALE NETWORK INTERACTIONS

BY

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DISSERTATION

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ABSTRACT

The goal of the current dissertation was to clarify the behavioral and neural mechanisms associated with the impact and control of emotional distraction by investigating the influences of the nature (positive vs. negative) and source (external vs. internal) of emotional distraction, the types of emotion regulation (spontaneous vs. instructed) engaged to cope with it, and the role of sex differences. The present dissertation comprises three studies, with the first two focusing on external emotional distraction, and the third focusing on internal emotional distraction.

Study one investigated the roles of arousal and valence in the impact of external emotional distraction on working memory (WM) performance, and yielded four main findings. First, positive distraction had reduced impact on WM performance, compared with negative distraction. Second, fMRI results identified valence-specific effects in a dorsal executive system (DES) and overlapping arousal and valence effects in a ventral affective system (VAS), suggesting both increased impact of negative distraction and enhanced engagement of coping mechanisms for positive distraction. Third, a valence-related rostro-caudal dissociation was identified in medial frontal regions associated with the default-mode network (DMN). Finally, these DMN regions showed increased functional connectivity with DES regions for negative compared with positive distraction.

Study two investigated sex differences in the response to external emotional distraction and yielded three main findings. First, an increased impact of emotional distraction among women was detected, in trials associated with high-confidence responses, in the context of overall similar WM performance in women and men. Second, regarding the fMRI results, women showed increased sensitivity to emotional distraction in VAS regions, whereas men showed increased sensitivity in DES regions, in the context of overall similar patterns of

response to emotional distraction in women and men. Third, a sex-related dorsal-ventral hemispheric dissociation emerged in the lateral prefrontal cortex (PFC) related to coping with emotional distraction, with women showing a positive correlation with WM performance in left ventral PFC, and men showing similar effects in the right dorsal PFC.

Study three investigated the impact and regulation of internal emotional distraction, and yielded four main findings. First, the instructed engagement of emotion regulation (ER) diminished both the subjective negative experience and the objective WM interference. Second, the overall response to internal emotional distraction was linked to deactivation in DES and increased activity in VAS regions, similar to the response to external emotional distraction, as well as with specific increased activity in DMN regions. Third, ER engagement was associated with both diminished activity in VAS regions part of the salience network, and increased activity in executive and memory-related regions. Finally, ER was also associated with increased functional connectivity between fronto-parietal regions. Supplementary, a behavioral pilot study investigated the role of valence and showed that negative but not positive internal distraction interfered with concurrent WM performance. Also, an exploratory analysis tested for sex differences and showed increased impact of internal emotional distraction in women for high-confidence WM performance, linked to increased sensitivity in a medial frontal region associated with the salience network.

These findings contribute to a better understanding of healthy functioning under transient emotional distraction. In addition, they have implications for understanding factors linked to increased susceptibility to mood and anxiety disorders, which are afflictions characterized by increased distractibility and altered processing of negative and positive stimuli originating from the external and internal environments, and are more prevalent in women compared to men.

ACKNOWLEDGMENTS

CONTENTS

CHAPTER 1:

GENERAL INTRODUCTION

The systematic investigation of the impairing effect of emotion on cognition is a relatively new addition to the more general area of study of emotion-cognition interactions. However, it has rapidly proven to be important for advancing our understanding of human brain function and dysfunction. While a significant corpus of research has focused lately on the detrimental impact of negative emotional distraction originating from the external environment, important questions remain. The goal of the current dissertation was to clarify aspects concerning influences of the nature (positive vs. negative) and source (external vs. internal) of emotional distraction, the types of emotion regulation (spontaneous vs. instructed) engaged in order to cope with it, and the role of sex differences, in order to advance our understanding of the neural mechanisms associated with the impact and control of emotional distraction.

It is largely accepted today that the processing of emotional information typically benefits from a certain degree of prioritization, possibly due to its enhanced evolutionary value (e.g., finding food, avoiding predators) (Anderson & Phelps, 2001; Hansen & Hansen, 1988; LeDoux, 1996; Ohman, Flykt, & Esteves, 2001; Ohman, Flykt, & Ludqvist, 2000; Whalen et al., 1998). Although such prioritization is adaptive in many circumstances, it may also lead to impairing effects, particularly in situations where emotional information is irrelevant for the on-going task. For instance, we may experience enhanced memory for emotional events, but could also be more distracted by emotional stimuli that interfere with our goals. While the enhancing effects of emotion on cognitive functions such as episodic memory, where emotion tends to be task-relevant, have been the focus of extensive research [see (Dolcos, Denkova, & Dolcos, 2012; Dolcos, Iordan, & Dolcos, 2011) for comprehensive reviews], the detrimental effects of task-irrelevant emotion on cognitive functions have started to be investigated relatively more recently (Dolcos & McCarthy, 2006; Johnson et al., 2005; Most, Chun, Widders, & Zald, 2005;

Shackman et al., 2006) (but see Oaksford, Grainger, Morris, & Williams, 1996; Seibert & Ellis, 1991).

The present research builds on recent progress in elucidating the neural correlates of emotional distraction. Previous investigations (Anticevic, Repovs, & Barch, 2010; Denkova et al., 2010; Diaz et al., 2011; Dolcos, Diaz-Granados, Wang, & McCarthy, 2008; Dolcos et al., 2013; Dolcos, Kragel, Wang, & McCarthy, 2006; Dolcos & McCarthy, 2006; Oei et al., 2012) provided initial evidence regarding the detrimental impact of emotional distraction on cognitive performance and the associated neural correlates of this phenomenon. For instance, Dolcos & McCarthy (2006) showed that negative pictures presented during the delay interval of a working memory (WM) task impair cognitive performance, and that this behavioral effect is linked to increased activity in ventral brain regions involved in emotion processing (e.g., amygdala [AMY] and ventro-lateral prefrontal cortex [vlPFC]), and simultaneous decreased activity in dorsal brain regions involved in executive control (e.g., dorso-lateral prefrontal cortex [dlPFC] and lateral parietal cortex [LPC]). Follow-up studies (Anticevic et al., 2010; Denkova et al., 2010; Diaz et al., 2011; Dolcos et al., 2008; Dolcos et al., 2013; Oei et al., 2012) demonstrated that this is a robust pattern of response, which is specific for emotional distraction. Importantly, this pattern has also been replicated by tasks that have as a common denominator the clear perceptual and temporal segregation of goal-relevant and distracting information (see Banich et al., 2009), including emotional odd-ball tasks (Wang, McCarthy, Song, & Labar, 2005; Yamasaki, LaBar, & McCarthy, 2002) and emotional interrupt tasks (Mitchell et al., 2008). This evidence led to a model of the response to emotional distraction (reviewed in Dolcos et al., 2011; Iordan, Dolcos, & Dolcos, 2013b) according to which emotional stimuli capture attention and

divert processing resources from the main cognitive task, leading to WM impairment (Figure 1.1).

At the neural level, this is reflected by an opposing pattern of transient *in*creased activity in a ventral affective system (VAS) and *de*creased activity in a dorsal executive system (DES), under emotional distraction. VAS is a large aggregate which includes brain regions involved in basic emotion processing, such as AMY, regions involved in emotion integration and regulation, such as vlPFC, portions of the medial frontal cortex, as well as ventral regions susceptible to emotion modulation, such as the visual cortex (Davidson & Irwin, 1999; Davis & Whalen, 2001; Kober et al., 2008; Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012; Phan, Wager, Taylor, & Liberzon, 2002; Sergerie, Chochol, & Armony, 2008; Vytal & Hamann, 2010). DES includes brain regions typically associated with cognitive control and maintenance of goal-relevant information, such as dlPFC and LPC (D'Esposito, Cooney, Gazzaley, Gibbs, & Postle, 2006; Fuster, 1997; Koenigs, Barbey, Postle, & Grafman, 2009; Nee et al., 2012; Niendam et al., 2012; Smith & Jonides, 1999). Thus, the extant evidence suggest that activity in VAS and DES is interconnected, such that increased activity VAS, in the presence of transient emotional distracters, temporarily takes off-line DES and results in WM impairment (Dolcos & McCarthy, 2006; Iordan et al., 2013b).

Previous investigations of the response to emotional distraction (reviewed in Iordan et al., 2013b) also provided evidence regarding the control mechanisms engaged in order to resist distraction and maintain cognitive performance. For instance, functional connectivity analyses of data from the Dolcos & McCarthy (2006) study showed enhanced positive coupling between AMY and vlPFC/inferior frontal cortex during emotional distraction, and a hemispheric asymmetry in vlPFC involvement. Specifically, left vlPFC showed greater activity for correct vs.

incorrect trials, whereas activity in right vlPFC showed negative correlation with subjective ratings of distractibility, consistent with a left vs. right dissociation in objective vs. subjective coping with emotional distraction. The 'double affiliation' of vlPFC to affective and control systems suggests that the dorsal-ventral functional dissociation is not simply an expression of a 'push-pull' relationship between executive and affective networks (Desimone & Duncan, 1995; Miller & Cohen, 2001). The involvement of vlPFC in coping with emotional distraction is consistent with its role in top-down control (Aron, 2007; Aron, Robbins, & Poldrack, 2004, 2014) and with recent findings identifying this area as a site of convergence between multiple functional networks (Gordon et al., 2014; Power et al., 2011; Warren et al., 2014). Furthermore, this also distinguishes the DES-VAS functional dissociation from the simple antagonism between a bottom-up/ventral and a top-down/dorsal systems (Pfeifer & Allen, 2012), by emphasizing the involvement of prefrontal VAS regions (e.g., vlPFC) in both emotion processing and control operations that enable emotion regulation and coping with distraction (Denkova et al., 2010; Dolcos et al., 2006; Dolcos & McCarthy, 2006; Iordan, Dolcos, Denkova, & Dolcos, 2013a). A recent shift in the cognitive neurosciences has been a departure from a region-based interpretation of brain function to a network-based approach [see (Buckner, Krienen, & Yeo, 2013) for a recent discussion]. According to this approach, complex brain functions are implemented not by discrete areas, but by dissociable networks of functionally connected regions showing correlated activity both during task performance and at rest (Bressler & Menon, 2010; Dosenbach et al., 2006; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Dosenbach et al., 2007; Power & Petersen, 2013; Seeley et al., 2007; Yeo et al., 2011). This networks-based perspective is overall compatible with the model of DES-VAS dissociation. Of note, while we do not treat DES and VAS as equal to brain networks, we emphasize the

possibility of overlaps between these larger neural systems and the large-scale functional networks. For instance, the task-induced dorso-ventral dissociation between DES and VAS resembles the dissociation between the fronto-parietal/central executive network and the salience/ventral-attentional network, as identified by investigations employing resting-state functional connectivity (Dosenbach et al., 2008; Dosenbach et al., 2007; Power & Petersen, 2013; Seeley et al., 2007; Yeo et al., 2011).

Despite this remarkable progress in understanding the mechanisms by which goal-irrelevant emotions impact cognition, the model of the response to emotional distraction is not yet complete, and a number of unsolved issues still remain. Among these less explored issues are aspects related to the influence of the nature and source of emotional distraction, the identity of the control mechanisms engaged in order to cope with distraction, and the role of individual differences in the response to emotional distraction. The present research investigates a number of unsolved issues concerning the role of valence in the distracting effect of emotion, the response to internal emotional distraction, the consequences of engaging focused attention as an emotion regulation strategy to cope with internal distraction, and the role of sex differences in the response to emotional distraction. Methodologically, these investigations involve functional magnetic resonance imaging (fMRI) recordings in conjunction with novel adaptations of a delayed-response WM task with emotional distraction (Dolcos & McCarthy, 2006). The rationale for using this methodological approach is that fMRI is the best available noninvasive tool that allows localization of brain activity, and the delayed-response WM task with emotional distraction has been a highly effective and versatile paradigm for examining the behavioral and neural correlates of emotion-cognition interactions. In the next section, I will introduce these tools, and provide details about the main issues identified and addressed in the present research.

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Brain Imaging and Behavioral Methods Employed

I. Functional Magnetic Resonance Imaging

Functional magnetic resonance imaging (fMRI) is a technique which enables the noninvasive imaging of brain activity and provides excellent spatial resolution and relatively good temporal resolution, compared to other methods such as electroencephalography and positron emotion tomography, respectively. The basic principle behind fMRI is neurovascular coupling, i.e. the relationship between neuronal activity and changes in blood flow in an area of brain tissue. Simply stated, when neurons in a particular area of the brain become active, there is also an increase in the amount of oxygenated blood flowing through that area. However, this increase temporarily exceeds the need, leading to a relative local surplus in oxygenated blood. This blood oxygenation level dependent (BOLD) response can be measured using fMRI. It is important to note that whereas neuronal activity occurs at the scale of milliseconds, the increase in blood flow that succeeds this activity takes about five seconds, and it is followed by a long undershoot that recovers in approximately 15-20 seconds. This has important consequences regarding the way fMRI analyses are performed and the inferences that can be made using such measurements.

A detailed presentation of the principles of MR physics is beyond the scope of this chapter, hence only the basic principles will be presented here [see (Huettel, Song, & McCarthy, 2009; Wager, Hernandez, Jonides, & Lindquist, 2007) for detailed presentations of this matter]. The human body is largely made of water. When the protons of the hydrogen atoms that are in the composition of water molecules are placed in the strong magnetic field of the MR scanner (called the B_0 field) the spins of a portion of them will align either parallel or antiparallel with the magnetic field. The overall magnetization of the spins in a piece of tissue is called the *net*

magnetization vector. Applying a small oscillating field (also called radio frequency [RF] pulse or B_1) perpendicular to B_0 tips the net magnetization vector from the longitudinal direction into the transverse plane, generating the MR signal. When the RF pulse is switched off, the magnetization vector will gradually relax to its equilibrium position, parallel with B_0. This phenomenon comprises *spin-lattice* relaxation, which is the recovery of the longitudinal magnetization, and *spin-spin* relaxation, which occurs along the transverse component. Pulse sequences sensitive to the rate of relaxation of these two components (called T_1 and T_2 relaxation times, respectively) generate images which are sensitive to the density properties of the water molecules, and hence to different types of tissue (e.g., neural tissue vs. fat). T_1-weighted images are commonly used for the structural scans. Another type of relaxation, called T_2^*, is generated by local inhomogeneities in the magnetic field. In the brain, such sources of inhomogeneities are usually changes in the local concentrations of deoxygenated hemoglobin. Deoxygenated hemoglobin is paramagnetic and alters the T_2^* properties of adjacent tissue, whereas oxygenated hemoglobin is diamagnetic and does not (Ogawa, Lee, Nayak, & Glynn, 1990). Thus, T_2^*-weighted images reflect changes in blood oxygen level linked to brain metabolism, and form the basis of the functional images collected in BOLD fMRI. Spatial reconstruction of fMRI images is an additional step. Because fMRI images are acquired slice-by-slice, usually in the *z* direction, localization in this direction is handled by *slice selection*, i.e. selectively exciting one slice of tissue at a time. Localization in the *x* and *y* directions is acquired by *frequency-encoding* and *phase-encoding*, respectively, which together define the *k-space*, a bidimensional matrix that contains the power in the signal at each frequency. Through a Fourier transform, this information is translated into an image with varying signal intensities at each pixel. Thus, different intensities of the MR signal reflect changes in the ratio of oxy-/deoxygenated hemoglobin and the

assumption concerning this ratio is that more intense neural activity in associated with increased delivery of oxygenated blood to active brain regions. For these reasons, fMRI is considered an *indirect* measure of brain activity.

Relevant questions in this context, regarding the nature of the BOLD signal, concern to what degree it reflects actual increases in neural activity and whether it is an expression of neural excitation or inhibition (Wager et al., 2007). Although these issues are still a matter of active research, tentative answers can be provided. In brief, although animal studies have shown that BOLD activity typically maps the position of local field potentials (Logothetis, Pauls, Augath, Trinath, & Oeltermann, 2001), the vascular response and neural activity may not always be coupled, and hence fMRI may capture only a fraction of the physiological phenomena associated with neural activity (Logothetis, 2008). Also, while evidence suggests that the BOLD signal likely reflects excitatory processes driven by glutamate metabolism (Shulman & Rothman, 1998), some metabolic increases may be determined by increased inhibition in a brain region (Logothetis, 2008).

II. The Working Memory with Emotional Distraction Paradigm

Working memory (WM) is involved in the active maintenance and manipulation of task-relevant information (Baddeley, 1996). The Sternberg delayed recognition task (Sternberg, 1966) is a paradigm frequently used to assess WM. This type of task involves keeping in mind a set of stimuli (the memoranda; e.g., letter, shapes, human faces) for the duration of a short delay, and then answering whether a single stimulus (the probe) was part of the initial set or not. Because it requires the active maintenance of information in order to respond to the probe, it is a good model for on-line cognitive processing. An adaptation of this task (Figure 1.2) involves the presentation of high-arousing negative pictures as task-irrelevant distracters during the delay

interval between the memoranda and the probes (Dolcos & McCarthy, 2006). The subjects are instructed to look at the distracters but maintain focus on the memoranda, and to make quick and accurate responses to the probes. To avoid induction of longer-lasting effects, the trials within each block are typically pseudo-randomized, so that no more than two or three consecutive trials of the same type are presented. Using this task in conjunction with fMRI recordings, Dolcos & McCarthy (2006) showed greater WM interference under negative distraction relative to control, suggesting that emotional distraction challenges the ability to maintain focus on goal-relevant information and impairs cognitive performance.

An important feature of this type of WM task is that it allows a clear segregation of goal-relevant and distracting information (see Banich et al., 2009). The insertion of a secondary task during the delay interval, which involves processing of emotional information (e.g., watching emotional pictures, remembering emotional past events, etc.), renders the WM task into a dual-task with a main (goal-oriented) cognitive component and a secondary emotional (distracting) component. Importantly, the goal-relevant and distracting stimuli can be segregated on both temporal and perceptual grounds, which may allow a better separation between the dorsal-executive and ventral-affective neural systems by focusing the fMRI analyses on the delay interval. Of note, although this dorsal-ventral dissociation can also be elicited by other types of tasks, such as the emotional odd-ball task (Yamasaki et al., 2002), the delayed-response WM task has superior versatility. For instance, the WM task allows the insertion of different types of responses, such as assessments of emotionality or of the level of confidence (LOC) in the answers to the probes, which provide a subjective or experiential assessment in addition to the objective assessments of WM performance, and hence enable finer evaluations.

In the present research, I employed novel adaptations of the delayed-response WM task with emotional distraction to investigate unclear issues concerning influences of the nature and source of emotional distraction, the engagement of specific emotion regulation strategies, and the role of sex differences in the response to emotional distraction. Three studies were conducted. The first study investigated the role of valence in the response to external emotional distraction. The second study investigated sex differences in the response to external emotional distraction expressing social threat. Finally, the third study examined the response to and regulation of internal emotional distraction. In the following paragraphs, I will provide more details concerning the unsolved issues identified and addressed in these studies.

Issues Investigated

<u>**Study I.**</u> **The Role of Valence in the Response to External Emotional Distraction**

Everyday life suggests that both pleasant and unpleasant emotions can distract us from on-going activities. An influential view regarding the defining features of emotions focuses on two orthogonal components: *valence* (or pleasantness) varying from positive to negative and *arousal* (or intensity) varying from high to low (Lang, Greenwald, Bradley, & Hamm, 1993; Larsen & Diener, 1992; Russell, 1980, 2003; Russell & Barrett, 1999). Based on previous investigations of the memory-enhancing effect of emotion (Dolcos, LaBar, & Cabeza, 2004; Murty, Ritchey, Adcock, & LaBar, 2010), showing that both positive and negative stimuli are better remembered than the neutral ones, a default assumption regarding the impairing effect is that it may also be mainly driven by arousal. On the other hand, theories of motivational dispositions (Berntson, Boysen, & Cacioppo, 1993; Bradley & Lang, 2007; Cacioppo, Gardner, & Berntson, 1997) and of positive affect (Ashby, Isen, & Turken, 1999; Fredrickson, 2001; Isen, 2005) suggest that positive emotions may be linked to different processing strategies, compared

to negative ones, and hence they may favorably influence cognition and behavior. Despite recent progress in understanding the mechanisms by which task-irrelevant emotions influence on-line cognitive processing, investigations of the influence exerted by the valence of emotional distraction have provided equivocal results (e.g., Kensinger & Corkin, 2003; Levens & Phelps, 2008; Lindstrom & Bohlin, 2011). Hence, it remains unclear what roles emotional valence and arousal play in influencing WM processing. Thus, the goal of the first study was to compare the impact of external distracters with different valence and arousal properties on WM performance and the associated neural correlates. Clarification of these issues is important because positive stimuli (e.g., food, potential sexual partners) are equally encountered in everyday life and emotional dysfunctions are associated with alteration in the processing of both negative and positive events (Forbes & Dahl, 2005; Gilbert, 2012; Izard, 2002; Watson & Naragon-Gainey, 2010; Waugh & Koster, 2014). These issues will be addressed in Chapter 2.

<u>Study II.</u> Sex Differences in the Response to External Emotional Distraction

Emotional distraction does not impact everybody in the same way, as people vary in their response to and the ability to cope with emotional distraction. Regarding sex differences, recent behavioral and brain imaging evidence suggests that enhanced emotional reactivity in women may also lead to enhanced emotional distractibility. For instance, available behavioral evidence has shown that, in addition to enhanced emotional competence (Barrett, 2000; Kring & Gordon, 1998; Seidlitz & Diener, 1998), women also show enhanced reactivity to emotional stimuli (Hamann & Canli, 2004; Lang et al., 1993; Shields, 1991), and brain imaging studies point to sex differences primarily in brain regions associated with emotion processing, such as the amygdala (AMY) and the orbitofrontal cortex (OFC) (Goldstein et al., 2001; Gur, Gunning-Dixon, Bilker, & Gur, 2002), as well as in the prefrontal cortex (PFC) (Koch et al., 2007; McRae, Ochsner,

Mauss, Gabrieli, & Gross, 2008). Furthermore, results of a recent investigation from our group (Denkova et al., 2010) showed that the opposite patterns of activity in VAS and DES regions, previously observed in the presence of emotional distraction inducing general negative affect (i.e., emotional pictures), were also observed with stimuli conveying social threat (i.e., angry faces), in female participants. However, similar to previous studies of emotional distraction (e.g., Dolcos & McCarthy, 2006), the study by Denkova et al. (2010) involved only female participants, and hence it is not clear whether similar effects are also observed in males. Therefore, the main goal of the second study was to determine whether sex differences in basic emotional reactivity are associated with differences in emotional distractibility, and to identify the neural mechanisms that implement differences in emotional distractibility between women and men. Investigation of these issues in healthy individuals may help better understand the relation between emotional reactivity and distractibility as independent or correlated factors contributing to differential vulnerability to affective disorders in women and men. These issue will be addressed in Chapter 3.

Study III. The Impact and Regulation of Internal Emotional Distraction

Emotional distraction can be elicited not only by external stimuli, but it can also originate from the internal environment, such as when triggered by distressing thoughts or memories. A study in war-veterans diagnosed with PTSD (Morey et al., 2009) suggested the possibility of a link between increased cognitive distraction and spontaneous recollection of memories with enhanced personal significance. More specifically, processing of cues related to traumatic events (e.g., combat-related pictures) may trigger automatic retrieval of traumatic memories and have an impairing effect on ongoing goal-oriented processing. However, it is not clear whether the emotional content per se or the personal significance of such stimuli is the main factor producing

the distracting effects. This phenomenon may involve not only retrieval of explicit/declarative memories for personally-significant events (Cabeza & St Jacques, 2007; Denkova, Dolcos, & Dolcos, 2015), but also automatic retrieval of implicit/nondeclarative negative associations (Mechias, Etkin, & Kalisch, 2010). The focus in this research is on explicit/declarative emotional memories as internal distraction.

Autobiographical memories (AMs) are explicit/declarative memories for personally-significant events, and their recollection has been linked to increased activity in medial temporal lobe and midline brain regions involved in memory, emotion, and self-referential processing (Cabeza & St Jacques, 2007; Denkova et al., 2015). Given the link between excessive focus/rumination on negative memories and impaired cognitive control in clinical groups (Cooney, Joormann, Eugene, Dennis, & Gotlib, 2010; Nolen-Hoeksema, 1991), it is possible that highly emotional AMs may also be distracting in healthy functioning. Previous investigations (reviewed in Iordan et al., 2013b) focused exclusively on external distraction (emotional pictures), and hence it is not known whether distraction originating from 'within' the individual (internal distraction), such as the retrieval of personally-significant memories, produces similar effects and what the neural correlates of internal distraction are. Clarification of these issues is important because distracting phenomena such as mind-wandering, rumination, and intrusive memories are directly related to the subject's internal environment and have been linked to symptoms of attentional and affective dysfunction (Cooney et al., 2010; Morey et al., 2009; Sood & Jones, 2013). Relevant questions regarding internal distraction, such as the role of emotional valence, the effect of engaging cognitive control, and sex differences will be addressed in Chapter 4, and are introduced below.

III.1. The Role of Valence in the Impact of Internal Emotional Distraction: Behavioral Pilot

Study. In everyday life, people spontaneously recollect events that vary in valence, from positive to negative, and this may influence both their momentary ability to perform tasks at hand as well as their longer-lasting moods. Similar to external emotional distraction, an important question regarding the influence of internal emotional distraction on concurrent cognitive processing is whether the recollection of positive and negative AMs is associated with similar or different effects. On the one hand, both positive and negative personal experiences are typically better and more vividly remembered than the neutral events, hence the processing of cues for positive and negative memories may trigger enhanced recollection and possibly impair on-going goal-oriented activity in similar ways. On the other hand, positive and negative AMs may be governed by different mechanisms and lead to different outcomes. Specifically, positive or negative affective biases in AM recollection have been differentially linked to either personal well-being (Bluck & Alea, 2009; Denkova, Dolcos, & Dolcos, 2012; Finnbogadóttir & Berntsen, 2013) or emotional disorders such as depression and PTSD (Brewin, Reynolds, & Tata, 1999; MacLeod & Byrne, 1996; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), and hence only the recollection of negative memories may be distracting, even in healthy individuals.

III.2. The Effect of Emotional Control on Internal Negative Distraction. The ability to deploy cognitive control in order to cope with emotional distraction is essential for adaptive behavior, while reduced control may lead to enhanced emotional distractibility, which is often a hallmark of affective disorders. Although previous investigations (e.g., Dolcos et al., 2006; Dolcos & McCarthy, 2006) provided basic evidence regarding the neural mechanisms involved in coping with emotional distraction, the identity and nature of these mechanisms remains unclear. For instance, functional connectivity analyses of data from the Dolcos & McCarthy (2006) study

showed enhanced positive coupling between AMY and vlPFC/inferior frontal cortex during emotional distraction, and a hemispheric asymmetry in vlPFC involvement, with left vlPFC showing greater activity for correct vs. incorrect trials, and right vlPFC showing negative correlation with subjective ratings of distractibility. However, it is not known whether the same vlPFC regions whose activity has been associated with diminished subjective and objective impact of distraction during task performance are also involved in the deliberate engagement of emotional control, such as deploying emotion regulation strategies (Gross, 1998, 2002). Also, because this evidence has been exclusively based on investigations of external distraction, it is not known what the mechanisms involved in the control of internal distraction are. This is highly relevant because studies of emotional distraction have not included explicit manipulations of emotion regulation (ER) strategies, and ER studies (Goldin, McRae, Ramel, & Gross, 2008; Gross, 1998, 2002; Ochsner & Gross, 2005; Ochsner & Gross, 2008; Ochsner, Silvers, & Buhle, 2012) have not been performed in the context of dual cognitive/emotional tasks, which more closely resemble real-life situation.

A recent investigation from our group (Denkova et al., 2015) showed that manipulating the focus of attention during AM recollection influences the subjective re-experiencing of emotions and the associated neural correlates, and hence can be effectively used as an ER strategy. More specifically, results showed that focusing away from emotion led to decreased experience of emotion, along with increased engagement of ER-related regions (vmPFC), and reduced activity in emotion-related regions (AMY). Because focused attention can be more quickly engaged than other ER strategies, such as reappraisal (Hajcak, Dunning, & Foti, 2009; Thiruchselvam, Blechert, Sheppes, Rydstrom, & Gross, 2011), it is well suited in the context of a distraction task, and hence will be used in the present research. Clarification of these issues is

important because it will identify the specific conditions under which the engagement of ER helps cognitive performance, which has relevance for prevention of and therapeutic interventions in emotional dysfunctions (Gross & John, 2003; Llewellyn, Dolcos, Iordan, Rudolph, & Dolcos, 2013).

III.3. Sex Differences in the Response to Internal Emotional Distraction: Exploratory Analysis. Similar to the response to external emotional distraction, an important issue concerns sex differences in the response to internal emotional distraction, such as recollection of task-irrelevant emotional AMs. Available evidence suggests that affective biases in memory and sex differences in coping strategies may be related to increased incidence of mood and anxiety disorders, particularly in women (Davis, 1999; Nolen-Hoeksema, 2001; Seidlitz & Diener, 1998). Women recall more emotional AMs (Davis, 1999; Seidlitz & Diener, 1998), and are more likely than men to engage in rumination, which may exacerbate depressive symptoms (Nolen-Hoeksema, Larson, & Grayson, 1999). Investigation of these issues is important for understanding affective disorders such as depression, which are associated with a negative bias in remembering AMs, and are more prevalent in women.

Thesis Overview

The goal of the present research is to clarify unsolved issues regarding the influence of the nature and source of emotional distraction, the identity of the control mechanisms engaged in order to cope with distraction, and the role of sex differences in the response to emotional distraction. Three studies were performed to address these uncertainties, involving fMRI recordings in conjunction with novel adaptations of a delayed-response WM task with emotional distraction. The first two studies focused on clarifying issues regarding the response to external emotional distraction. The third study focused on clarifying issues regarding to the impact and

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regulation of internal emotional distraction. The chapter structure of the thesis is as follows. Chapter 2 focuses on the role of valence in the response to external emotional distraction. Chapter 3 focuses on sex differences in the response to external emotional distraction. Chapter 4 focuses on the impact and regulation of internal emotional distraction. This chapter focuses on three aspects related to internal emotional distraction, namely the role of valence in the impact of internal emotional distraction, the effect of emotional control on internal emotional distraction, and sex differences in the response to internal emotional distraction. Finally, Chapter 5 summarizes the key findings of the present research and discusses their contribution and significance. Chapters 2 and 3 are already published. A portion of Chapter 4 is currently in submission for publication. In order to maintain the contents of the chapters as close to the submitted versions, the original manuscripts were only slightly changed when organized as separate chapters.

References

Anderson, A. K., & Phelps, E. A. (2001). Lesions of the human amygdala impair enhanced perception of emotionally salient events. *Nature, 411*(6835), 305-309.

Anticevic, A., Repovs, G., & Barch, D. M. (2010). Resisting emotional interference: brain regions facilitating working memory performance during negative distraction. *Cognitive, Affective, & Behavioral Neuroscience, 10*(2), 159-173.

Aron, A. R. (2007). The neural basis of inhibition in cognitive control. *Neuroscientist, 13*(3), 214-228.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences, 8*(4), 170-177.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: one decade on. *Trends in Cognitive Sciences, 18*(4), 177-185.

Ashby, F. G., Isen, A. M., & Turken, A. U. (1999). A neuropsychological theory of positive affect and its influence on cognition. *Psychological Review, 106*(3), 529-550.

Baddeley, A. (1996). The fractionation of working memory. *Proceedings of the National Academy of Sciences of the United States of America, 93*(24), 13468-13472.

Banich, M. T., Mackiewicz, K. L., Depue, B. E., Whitmer, A. J., Miller, G. A., & Heller, W. (2009). Cognitive control mechanisms, emotion and memory: a neural perspective with implications for psychopathology. *Neuroscience and Biobehavioral Reviews, 33*(5), 613-630.

Barrett, L. F., Lane, R., Sechrest, L., and Schwartz, G. (2000). Sex differences in emotional awareness *Personality and Social Psychology Bulletin, 26*(9), 1027-1035.

Berntson, G. G., Boysen, S. T., & Cacioppo, J. T. (1993). Neurobehavioral organization and the cardinal principle of evaluative bivalence. In F. M. Crinella & J. Yu (Eds.), *Annals of the New York Academy of Sciences: Vol. 702. Brain mechanisms: Papers in memory of Robert Thompson* (pp. 75-102). New York: New York Academy of Sciences.

Bluck, S., & Alea, N. (2009). Characteristics of positive autobiographical memories in adulthood. *International Journal of Aging and Human Development, 69*(4), 247-265.

Bradley, M. M., & Lang, P. J. (2007). Motivation and emotion. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of psychophysiology (2nd edition)*. New York: Cambridge University Press.

Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: emerging methods and principles. *Trends in Cognitive Sciences, 14*(6), 277-290.

Brewin, C. R., Reynolds, M., & Tata, P. (1999). Autobiographical memory processes and the course of depression. *Journal of Abnormal Psychology, 108*(3), 511-517.

Buckner, R. L., Krienen, F. M., & Yeo, B. T. (2013). Opportunities and limitations of intrinsic functional connectivity MRI. *Nature Neuroscience, 16*(7), 832-837.

Cabeza, R., & St Jacques, P. (2007). Functional neuroimaging of autobiographical memory. *Trends in Cognitive Sciences, 11*(5), 219-227.

Cacioppo, J. T., Gardner, W. L., & Berntson, G. G. (1997). Beyond bipolar conceptualizations and measures: The case of attitudes and evaluative space. *Personality and Social Psychology Review, 1*(1), 3-25.

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

D'Esposito, M., Cooney, J. W., Gazzaley, A., Gibbs, S. E., & Postle, B. R. (2006). Is the prefrontal cortex necessary for delay task performance? Evidence from lesion and FMRI data. *Journal of the International Neuropsychological Society, 12*(2), 248-260.

Davidson, R. J., & Irwin, W. (1999). The functional neuroanatomy of emotion and affective style. *Trends in Cognitive Sciences, 3*(1), 11-21.

Davis, M., & Whalen, P. J. (2001). The amygdala: vigilance and emotion. *Molecular Psychiatry, 6*(1), 13-34.

Davis, P. J. (1999). Gender differences in autobiographical memory for childhood emotional experiences. *Journal of Personality and Social Psychology, 76*(3), 498-510.

Denkova, E., Dolcos, S., & Dolcos, F. (2012). Reliving emotional personal memories: affective biases linked to personality and sex-related differences. *Emotion, 12*(3), 515-528.

Denkova, E., Dolcos, S., & Dolcos, F. (2015). Neural correlates of 'distracting' from emotion during autobiographical recollection. *Social Cognitive and Affective Neuroscience, 10*(2), 219-230.

Denkova, E., Wong, G., Dolcos, S., Sung, K., Wang, L., Coupland, N., & Dolcos, F. (2010). The impact of anxiety-inducing distraction on cognitive performance: a combined brain imaging and personality investigation. *PLoS One, 5*(11), e14150. doi 14110.11371/journal.pone.0014150.

Desimone, R., & Duncan, J. (1995). Neural mechanisms of selective visual attention. *Annual Review of Neuroscience, 18*, 193-222.

Diaz, M. T., He, G., Gadde, S., Bellion, C., Belger, A., Voyvodic, J. T., & McCarthy, G. (2011). The influence of emotional distraction on verbal working memory: an fMRI investigation

comparing individuals with schizophrenia and healthy adults. *Journal of Psychiatric Research, 45*(9), 1184-1193.

Dolcos, F., Denkova, E., & Dolcos, S. (2012). Neural correlates of emotional memories: a review of evidence from brain imaging studies. *Psychologia, 55*(2), 80-111.

Dolcos, F., Diaz-Granados, P., Wang, L., & McCarthy, G. (2008). Opposing influences of emotional and non-emotional distracters upon sustained prefrontal cortex activity during a delayed-response working memory task. *Neuropsychologia, 46*(1), 326-335.

Dolcos, F., Iordan, A. D., & Dolcos, S. (2011). Neural correlates of emotion-cognition interactions: A review of evidence from brain imaging investigations. *Journal of Cognitive Psychology, 23*(6), 669-694.

Dolcos, F., Iordan, A. D., Kragel, J., Stokes, J., Campbell, R., McCarthy, G., & Cabeza, R. (2013). Neural correlates of opposing effects of emotional distraction on working memory and episodic memory: An event related fMRI investigation. *Frontiers in Psychology, 4*, 293. doi 210.3389/fpsyg.2013.00293.

Dolcos, F., Kragel, P., Wang, L., & McCarthy, G. (2006). Role of the inferior frontal cortex in coping with distracting emotions. *Neuroreport, 17*(15), 1591-1594.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron, 42*(5), 855-863.

Dolcos, F., & McCarthy, G. (2006). Brain systems mediating cognitive interference by emotional distraction. *The Journal of Neuroscience, 26*(7), 2072-2079.

Dosenbach, N., Visscher, K., Palmer, E., Miezin, F., Wenger, K., Kang, H., Burgund, E., Grimes, A., Schlaggar, B., & Petersen, S. (2006). A core system for the implementation of task sets. *Neuron, 50*(5), 799-812.

Dosenbach, N. U., Fair, D. A., Cohen, A. L., Schlaggar, B. L., & Petersen, S. E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences, 12*(3), 99-105.

Dosenbach, N. U., Fair, D. A., Miezin, F. M., Cohen, A. L., Wenger, K. K., Dosenbach, R. A., Fox, M. D., Snyder, A. Z., Vincent, J. L., Raichle, M. E., Schlaggar, B. L., & Petersen, S. E. (2007). Distinct brain networks for adaptive and stable task control in humans. *Proceedings of the National Academy of Sciences USA, 104*(26), 11073-11078.

Finnbogadóttir, H., & Berntsen, D. (2013). Involuntary future projections are as frequent as involuntary memories, but more positive. *Consciousness and Cognition, 22*(1), 272-280.

Forbes, E. E., & Dahl, R. E. (2005). Neural systems of positive affect: relevance to understanding child and adolescent depression? *Development and Psychopathology, 17*(3), 827-850.

Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *American Psychologist, 56*(3), 218-226.

Fuster, J. M. (1997). Network memory. *Trends in Neurosciences, 20*(10), 451-459.

Gilbert, K. E. (2012). The neglected role of positive emotion in adolescent psychopathology. *Clinical Psychology Review, 32*(6), 467-481.

Goldin, P. R., McRae, K., Ramel, W., & Gross, J. J. (2008). The neural bases of emotion regulation: reappraisal and suppression of negative emotion. *Biological Psychiatry, 63*(6), 577-586.

Goldstein, J. M., Seidman, L. J., Horton, N. J., Makris, N., Kennedy, D. N., Caviness, V. S., Jr., Faraone, S. V., & Tsuang, M. T. (2001). Normal sexual dimorphism of the adult human brain assessed by in vivo magnetic resonance imaging. *Cerebral Cortex, 11*(6), 490-497.

Gordon, E. M., Laumann, T. O., Adeyemo, B., Huckins, J. F., Kelley, W. M., & Petersen, S. E. (2014). Generation and evaluation of a cortical area parcellation from resting-state correlations. *Cerebral cortex*, doi 10.1093/cercor/bhu1239.

Gross, J. J. (1998). Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. *Journal of Personality and Social Psychology, 74*(1), 224-237.

Gross, J. J. (2002). Emotion regulation: affective, cognitive, and social consequences. *Psychophysiology, 39*(3), 281-291.

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology, 85*(2), 348-362.

Gur, R. C., Gunning-Dixon, F., Bilker, W. B., & Gur, R. E. (2002). Sex differences in temporo-limbic and frontal brain volumes of healthy adults. *Cerebral Cortex, 12*(9), 998-1003.

Hajcak, G., Dunning, J. P., & Foti, D. (2009). Motivated and controlled attention to emotion: time-course of the late positive potential. *Clinical Neurophysiology, 120*(3), 505-510.

Hamann, S., & Canli, T. (2004). Individual differences in emotion processing. *Current Opinion in Neurobiology, 14*(2), 233-238.

Hansen, C. H., & Hansen, R. D. (1988). Finding the face in the crowd: an anger superiority effect. *Journal of Personality and Social Psychology, 54*(6), 917-924.

Huettel, S. A., Song, A. W., & McCarthy, G. (2009). *Functional Magnetic Resonance Imaging, 2nd edition*. Sunderland, MA: Sinauer Associates, Inc.

Iordan, A. D., Dolcos, S., Denkova, E., & Dolcos, F. (2013a). Sex differences in the response to emotional distraction: an event-related fMRI investigation. *Cognitive, Affective & Behavioral Neuroscience, 13*(1), 116-134.

Iordan, A. D., Dolcos, S., & Dolcos, F. (2013b). Neural signatures of the response to emotional distraction: A review of evidence from brain imaging investigations. *Frontiers in Human Neuroscience, 7*, 200. doi 210.3389/fnhum.2013.00200.

Isen, A. M. (2005). Positive affect. In T. Dalgleish & M. J. Power (Eds.), *Handbook of Cognition and Emotion* (pp. 521-539): John Wiley & Sons, Ltd.

Izard, C. E. (2002). Translating emotion theory and research into preventive interventions. *Psychological Bulletin, 128*(5), 796-824.

Johnson, M. K., Raye, C. L., Mitchell, K. J., Greene, E. J., Cunningham, W. A., & Sanislow, C. A. (2005). Using fMRI to investigate a component process of reflection: prefrontal correlates of refreshing a just-activated representation. *Cognitive, Affective, & Behavioral Neuroscience, 5*(3), 339-361.

Kensinger, E. A., & Corkin, S. (2003). Effect of negative emotional content on working memory and long-term memory. *Emotion, 3*(4), 378-393.

Kober, H., Barrett, L. F., Joseph, J., Bliss-Moreau, E., Lindquist, K., & Wager, T. D. (2008). Functional grouping and cortical-subcortical interactions in emotion: a meta-analysis of neuroimaging studies. *Neuroimage, 42*(2), 998-1031.

Koch, K., Pauly, K., Kellermann, T., Seiferth, N. Y., Reske, M., Backes, V., Stöcker, T., Shah, N. J., Amunts, K., Kircher, T., Schneider, F., & Habel, U. (2007). Gender differences in the cognitive control of emotion: An fMRI study. *Neuropsychologia, 45*(12), 2744-2754.

Koenigs, M., Barbey, A. K., Postle, B. R., & Grafman, J. (2009). Superior parietal cortex is critical for the manipulation of information in working memory. *The Journal of Neuroscience, 29*(47), 14980-14986.

Kring, A. M., & Gordon, A. H. (1998). Sex differences in emotion: expression, experience, and physiology. *Journal of Personality and Social Psychology, 74*(3), 686-703.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology, 30*(3), 261-273.

Larsen, R. J., & Diener, E. (1992). Promises and problems with the circumplex model of emotion. In M. S. Clark (Ed.), *Review of personality and social psychology: Emotion* (Vol. 13, pp. 22-59). Newbury Park, CA: Sage.

LeDoux, J. (1996). *The emotional brain: The mysterious underpinnings of emotional life*. New York: Simon and Schuster.

Levens, S. M., & Phelps, E. A. (2008). Emotion processing effects on interference resolution in working memory. *Emotion, 8*(2), 267-280.

Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E., & Barrett, L. F. (2012). The brain basis of emotion: a meta-analytic review. *Behavioral and Brain Sciences, 35*(3), 121-143.

Lindstrom, B. R., & Bohlin, G. (2011). Emotion processing facilitates working memory performance. *Cognition & Emotion, 25*(7), 1196-1204.

Llewellyn, N., Dolcos, S., Iordan, A. D., Rudolph, K. D., & Dolcos, F. (2013). Reappraisal and suppression mediate the contribution of regulatory focus to anxiety in healthy adults. *Emotion, 13*(4), 610-615.

Logothetis, N. K. (2008). What we can do and what we cannot do with fMRI. *Nature, 453*(7197), 869-878.

Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, A. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature, 412*(6843), 150-157.

MacLeod, A. K., & Byrne, A. (1996). Anxiety, depression, and the anticipation of future positive and negative experiences. *Journal of Abnormal Psychology, 105*(2), 286-289.

McRae, K., Ochsner, K. N., Mauss, I. B., Gabrieli, J. J. D., & Gross, J. J. (2008). Gender differences in emotion regulation: An fMRI study of cognitive reappraisal. *Group Processes and Intergroup Relations, 11*(2), 143-163.

Mechias, M. L., Etkin, A., & Kalisch, R. (2010). A meta-analysis of instructed fear studies: implications for conscious appraisal of threat. *Neuroimage, 49*(2), 1760-1768.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*(1), 167-202.

Mitchell, D. G., Luo, Q., Mondillo, K., Vythilingam, M., Finger, E. C., & Blair, R. J. (2008). The interference of operant task performance by emotional distracters: an antagonistic relationship between the amygdala and frontoparietal cortices. *Neuroimage, 40*(2), 859-868.

Morey, R. A., Dolcos, F., Petty, C. M., Cooper, D. A., Hayes, J. P., LaBar, K. S., & McCarthy, G. (2009). The role of trauma-related distractors on neural systems for working memory

and emotion processing in posttraumatic stress disorder. *Journal of Psychiatric Research,
43*(8), 809-817.

Most, S. B., Chun, M. M., Widders, D. M., & Zald, D. H. (2005). Attentional rubbernecking:
cognitive control and personality in emotion-induced blindness. *Psychonomic Bulletin
and Review, 12*(4), 654-661.

Murty, V. P., Ritchey, M., Adcock, R. A., & LaBar, K. S. (2010). fMRI studies of successful
emotional memory encoding: A quantitative meta-analysis. *Neuropsychologia, 48*(12),
3459-3469.

Nee, D. E., Brown, J. W., Askren, M. K., Berman, M. G., Demiralp, E., Krawitz, A., & Jonides,
J. (2012). A meta-analysis of executive components of working memory. *Cerebral
Cortex, 23*(2), 264-282.

Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012).
Meta-analytic evidence for a superordinate cognitive control network subserving diverse
executive functions. *Cognitive, Affective & Behavioral Neurosience, 12*(2), 241-268.

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of
depressive episodes. *Journal of Abnormal Psychology, 100*(4), 569-582.

Nolen-Hoeksema, S. (2001). Gender differences in depression. *Current Directions in
Psychological Science, 10*, 173-176.

Nolen-Hoeksema, S., Larson, J., & Grayson, C. (1999). Explaining the gender difference in
depressive symptoms. *Journal of Personality and Social Psychology, 77*(5), 1061-1072.

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination.
Perspectives on Psychological Science, 3(5), 400-424.

Oaksford, M., Grainger, B., Morris, F., & Williams, J. M. G. (1996). Mood, reasoning, and central executive processes. *Journal of Experimental Psychology: Learning, Memory, and Cognition 22*(2), 476-492.

Ochsner, K., & Gross, J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences, 9*(5), 242-249.

Ochsner, K. N., & Gross, J. J. (2008). Cognitive emotion regulation: Insights from social cognitive and affective neuroscience. *Current Directions in Psychological Science, 17*(2), 153-158.

Ochsner, K. N., Silvers, J. A., & Buhle, J. T. (2012). Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences, 1251*, E1-24.

Oei, N. Y., Veer, I. M., Wolf, O. T., Spinhoven, P., Rombouts, S. A., & Elzinga, B. M. (2012). Stress shifts brain activation towards ventral 'affective' areas during emotional distraction. *Social Cognitive and Affective Neuroscience, 7*(4), 403-412.

Ogawa, S., Lee, T. M., Nayak, A. S., & Glynn, P. (1990). Oxygenation-sensitive contrast in magnetic resonance image of rodent brain at high magnetic fields. *Magnetic Resonance in Medicine, 14*(1), 68-78.

Ohman, A., Flykt, A., & Esteves, F. (2001). Emotion drives attention: detecting the snake in the grass. *Journal of Experimental Psychology. General, 130*(3), 466-478.

Ohman, A., Flykt, A., & Ludqvist, D. (2000). Unconscious emotion: evolutionary perspectives, psychophysiological data and neuropsychological mechanisms. In R. D. Lane & L. Nadel (Eds.), *Cognitive Neuroscience of Emotion* (pp. 296-327). New York: Oxford University Press, Inc.

Pfeifer, J. H., & Allen, N. B. (2012). Arrested development? Reconsidering dual-systems models of brain function in adolescence and disorders. *Trends in Cognitive Sciences, 16*(6), 322-329.

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage, 16*(2), 331-348.

Power, J. D., Cohen, A. L., Nelson, S. M., Wig, G. S., Barnes, K. A., Church, J. A., Vogel, A. C., Laumann, T. O., Miezin, F. M., Schlaggar, B. L., & Petersen, S. E. (2011). Functional network organization of the human brain. *Neuron, 72*(4), 665-678.

Power, J. D., & Petersen, S. E. (2013). Control-related systems in the human brain. *Current Opinion in Neurobiology, 23*(2), 223-228.

Russell, J. A. (1980). A circumplex model of affect. *Journal of Personality and Social Psychology, 39*(6), 1161-1178.

Russell, J. A. (2003). Core affect and the psychological construction of emotion. *Psychological Review, 110*(1), 145-172.

Russell, J. A., & Barrett, L. F. (1999). Core affect, prototypical emotional episodes, and other things called emotion: Dissecting the elephant. *Journal of Personality and Social Psychology, 76*(5), 805-819.

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., Reiss, A. L., & Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *The Journal of Neuroscience, 27*(9), 2349-2356.

Seibert, P. S., & Ellis, H. C. (1991). Irrelevant thoughts, emotional mood states, and cognitive task performance. *Memory & Cognition, 19*(5), 507-513.

Seidlitz, L., & Diener, E. (1998). Sex differences in the recall of affective experiences. *Journal of Personality and Social Psychology, 74*(1), 262-271.

Sergerie, K., Chochol, C., & Armony, J. L. (2008). The role of the amygdala in emotional processing: a quantitative meta-analysis of functional neuroimaging studies. *Neuroscience and Biobehavioral Reviews, 32*(4), 811-830.

Shackman, A. J., Sarinopoulos, I., Maxwell, J. S., Pizzagalli, D. A., Lavric, A., & Davidson, R. J. (2006). Anxiety selectively disrupts visuospatial working memory. *Emotion, 6*(1), 40-61.

Shields, S. A. (1991). Gender in the psychology of emotion: A selective research review. In K. T. Strongman (Ed.), *International review of studies on emotion* (pp. 227-245). New York: Wiley.

Shulman, R. G., & Rothman, D. L. (1998). Interpreting functional imaging studies in terms of neurotransmitter cycling. *Proceedings of the National Academy of Sciences of the United States of America, 95*(20), 11993-11998.

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283*(5408), 1657-1661.

Sood, A., & Jones, D. T. (2013). On mind wandering, attention, brain networks, and meditation. *Explore (NY), 9*(3), 136-141.

Sternberg, S. (1966). High-speed scanning in human memory. *Science, 153*(3736), 652-654.

Thiruchselvam, R., Blechert, J., Sheppes, G., Rydstrom, A., & Gross, J. J. (2011). The temporal dynamics of emotion regulation: an EEG study of distraction and reappraisal. *Biological Psychology, 87*(1), 84-92.

Vytal, K., & Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: a voxel-based meta-analysis. *Journal of Cognitive Neuroscience, 22*(12), 2864-2885.

Wager, T., Hernandez, L., Jonides, J., & Lindquist, M. (2007). Elements of functional neuroimaging. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of Psychophysiology* (pp. 19-55). Cambridge: Cambridge University Press.

Wang, L., McCarthy, G., Song, A. W., & Labar, K. S. (2005). Amygdala activation to sad pictures during high-field (4 tesla) functional magnetic resonance imaging. *Emotion, 5*(1), 12-22.

Warren, D. E., Power, J. D., Bruss, J., Denburg, N. L., Waldron, E. J., Sun, H., Petersen, S. E., & Tranel, D. (2014). Network measures predict neuropsychological outcome after brain injury. *Proceedings of the National Academy of Sciences of the USA, 111*(39), 14247-14252.

Watson, D., & Naragon-Gainey, K. (2010). On the specificity of positive emotional dysfunction in psychopathology: Evidence from the mood and anxiety disorders and schizophrenia/schizotypy. *Clinical Psychology Review, 30*(7), 839-848.

Waugh, C. E., & Koster, E. H. (2014). A resilience framework for promoting stable remission from depression. *Clinical Psychology Review, 41*(2015), 49-60.

Whalen, P. J., Rauch, S. L., Etcoff, N. L., McInerney, S. C., Lee, M. B., & Jenike, M. A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *Journal of Neuroscience, 18*(1), 411-418.

Yamasaki, H., LaBar, K. S., & McCarthy, G. (2002). Dissociable prefrontal brain systems for attention and emotion. *Proceedings of the National Academy of Sciences of the United States of America, 99*(17), 11447-11451.

Yeo, B. T., Krienen, F., Sepulcre, J., Sabuncu, M., Lashkari, D., Hollinshead, M., Roffman, J., Smoller, J., Zöllei, L., Polimeni, J., Fischl, B., Liu, H., & Buckner, R. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*(3), 1125-1165.

Figures
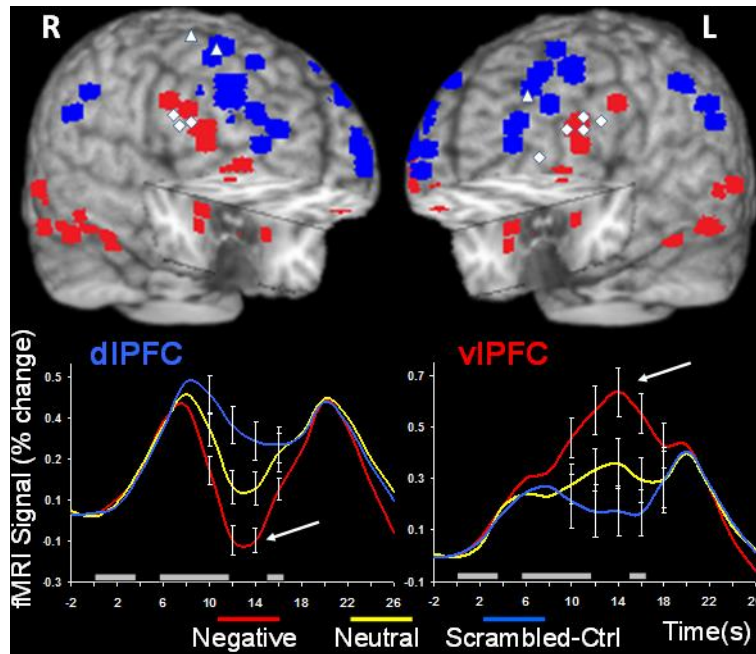
Figure 1.1. Summary of activations in brain regions of the *dorsal executive* and *ventral affective* neural systems. Upper panel displays peak activation voxels form ventral areas showing increased (red) and dorsal areas showing decreased (blue) activity in response to negative emotional distraction from studies employing WM and other similar tasks reviewed in Iordan et al. (2013b). The white diamonds and triangles identify peak voxels from areas involved in coping with emotional distraction. Line graphs depict activity time courses from two typical dorsal (dlPFC) and ventral (vlPFC) regions involved in working memory and emotion processing, respectively. The white arrows point to specific decreased (dlPFC) vs. increased (vlPFC) delay activity in these regions in response to emotional distraction. dlPFC, dorsolateral prefrontal cortex; vlPFC, ventrolateral PFC; R, right; L, Left. Reproduced from Iordan et al. (2013b), with permission.
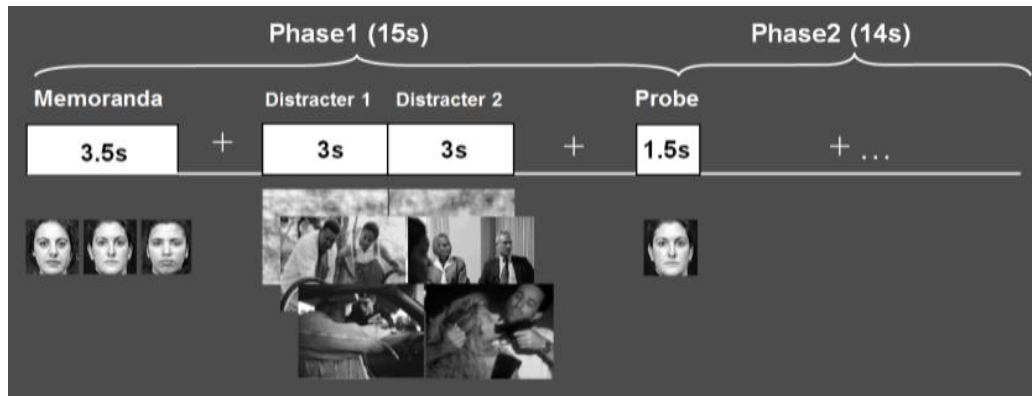
Figure 1.2. Diagram of the original WM task with negative distraction. Three distracter types (Negative, Neutral, or Scrambled-Control) were presented during the delay interval between the memoranda and the probes. Subjects were instructed to remain focused on the WM task, while paying attention to the novel pictures, and then to answer whether the probes were part of the memoranda (*Old*; 50%) or not (*New*; 50%). Reproduced from Dolcos & McCarthy (2006), with permission.

CHAPTER 2:

THE ROLE OF VALENCE IN THE RESPONSE TO

EXTERNAL EMOTIONAL DISTRACTION

Brain Activity and Network Interactions Linked to Valence-Related Differences in

the Impact of Emotional Distraction

Introduction

Investigations of the enhancing effects of emotion on episodic memory show that both pleasant (positive) and unpleasant (negative) stimuli are better remembered than the neutral ones (e.g., Dolcos, Iordan, & Dolcos, 2011; Dolcos, LaBar, & Cabeza, 2004b; Murty, Ritchey, Adcock, & LaBar, 2010). This evidence suggests that the memory-enhancing effect of emotion is mainly driven by "arousal," although effects of "valence" have also been identified (Kensinger & Corkin, 2004; Mickley Steinmetz, Addis, & Kensinger, 2010; Mickley Steinmetz & Kensinger, 2009; Ritchey, LaBar, & Cabeza, 2011). However, less is known about the roles that arousal and valence play in the impact of emotional stimuli on goal-oriented processing, when emotion is presented as task-irrelevant distraction. Previous investigations provided evidence for arousal- and valence-related effects linked to the emotional content manipulated in working memory (WM) (e.g., Kensinger & Corkin, 2003; Levens & Phelps, 2008; Lindstrom & Bohlin, 2011), but it is not clear how such attributes of the emotional distracters interact with the maintenance of emotionally neutral content in WM. The present study investigated the roles of arousal and valence in the impact of emotional distraction on WM performance and the associated neural mechanisms. Clarification of these issues is relevant for understanding both healthy functioning and alterations in clinical conditions associated with valence-related changes (Forbes & Dahl, 2005; Gilbert, 2012; Izard, 2002; Watson & Naragon-Gainey, 2010; Waugh & Koster, 2014). Altered positive affect is involved in a range of clinical conditions, including depression, social phobia, schizophrenia, and bipolar disorder (Watson & Naragon-Gainey, 2010), and hence can serve as a valid marker for symptoms associated with these disorders (Forbes & Dahl, 2005; Gilbert, 2012).

Valence (pleasantness) and arousal (intensity) are two basic dimensions commonly used to characterize the various forms of affect (Lang, Greenwald, Bradley, & Hamm, 1993; Russell, 1980, 2003; Russell & Barrett, 1999). Although different models proposed over time have emphasized either one (e.g., valence) (Watson & Tellegen, 1985) or the other (e.g., arousal) (Thayer, 1989) of these two dimensions, most current approaches agree with a bidimensional structure, with valence varying from positive to negative and arousal from high to low (Lang et al., 1993; Larsen & Diener, 1992; Russell, 2003; Russell & Barrett, 1999). In the context of experimental manipulations, however, valence and arousal may be more difficult to separate because stimuli used to induce positive and negative emotions typically determine also a change in arousal (Lindquist, Satpute, Wager, Weber, & Barrett, 2015). Hence, it is not only important to employ positive and negative stimuli, but also to dissociate between different levels of arousal within the emotional categories (Shafer, Iordan, Cabeza, & Dolcos, 2011).

Based on previous findings regarding the memory-enhancing effect of emotion (Dolcos et al., 2004b; Murty et al., 2010), a default assumption regarding the impairing effect is that it may also be mainly driven by arousal (the "arousal account"). However, there is also evidence of valence-related differences in these effects (Kensinger & Corkin, 2004; Mickley Steinmetz et al., 2010; Mickley Steinmetz & Kensinger, 2009; Ritchey et al., 2011). Consistent with the existence of differences linked to the valence of emotional information, theories of motivational dispositions (Berntson, Boysen, & Cacioppo, 1993; Bradley & Lang, 2007; Cacioppo, Gardner, & Berntson, 1997) and of positive affect (Ashby, Isen, & Turken, 1999; Fredrickson, 2001; Isen, 2005) suggest that positive emotions and affective states are linked to different processing strategies, compared with negative ones, and hence, they may favorably influence cognition and behavior. Of note, emotional reactions and states are separable phenomena, with emotional

reactions being relatively more intense and short in duration and states being relatively more prolonged, and they may exert different influences on cognition and behavior (Olsson & Öhman, 2009). In the present work, we use "emotions" as referring to emotional reactions.

Although these perspectives jointly predict more favorable influences of positive compared with negative valence on goal-oriented processing, the available evidence so far has been mixed. Investigations focusing on processing emotional content in WM have provided equivocal results, showing either no consistent effects on WM performance (Kensinger & Corkin, 2003), favorable influences on interference resolution (Levens & Phelps, 2008), or performance facilitation irrespective of valence (Lindstrom & Bohlin, 2011). On the other hand, investigations focusing on the impact of emotional distraction on WM maintenance have traditionally focused on negative valence (reviewed in Iordan, Dolcos, & Dolcos, 2013b) and, thus, it is not clear whether positive stimuli may produce similar or different effects.

In contrast to these investigations targeting the effect of emotional reactions, studies examining the influence of affective states on WM performance have more consistently shown that positive affect facilitates controlled processing (Brose, Lovden, & Schmiedek, 2014; Carpenter, Peters, Västfjäll, & Isen, 2013; Nadler, Rabi, & Minda, 2010; Storbeck & Maswood, 2015; Yang, Yang, & Isen, 2013). However, some investigations have identified enhancements only in certain domains, such as verbal WM and cognitive flexibility (Dreisbach, 2006; Dreisbach & Goschke, 2004; Gray, 2001), whereas others have identified deleterious effects, similar to the impact of negative affect (Allen, Schaefer, & Falcon, 2014). Hence, it remains unclear what roles emotional valence and arousal play in influencing WM processing and, thus, the first main goal of the present investigation was to compare the impact of distracters with different valence and arousal properties on WM performance.

At the neural level, brain imaging studies in which emotional information was presented as transient distraction during WM tasks (Anticevic, Repovs, & Barch, 2010; Denkova et al., 2010; Diaz et al., 2011; Dolcos, Diaz-Granados, Wang, & McCarthy, 2008; Dolcos et al., 2013; Dolcos, Kragel, Wang, & McCarthy, 2006; Dolcos & McCarthy, 2006; Iordan, Dolcos, Denkova, & Dolcos, 2013a; Oei et al., 2012) showed that the impairing effect of negative distraction was linked to opposing patterns of activity in two large neural systems: a "dorsal executive system" (DES) involved in cognitive/executive processing, showing decreased/disrupted activity, and a "ventral affective system" (VAS) involved in emotion processing, showing increased activity (reviewed in Dolcos et al., 2011; Iordan et al., 2013b). DES includes brain regions typically associated with cognitive control and maintenance of goal-relevant information, such as the dorsolateral prefrontal cortex (dlPFC) and the lateral parietal cortex (LPC) (D'Esposito, Cooney, Gazzaley, Gibbs, & Postle, 2006; Fuster, 1997; Koenigs, Barbey, Postle, & Grafman, 2009; Nee et al., 2012; Niendam et al., 2012; Smith & Jonides, 1999). VAS is a large aggregate which includes brain regions involved in basic emotion processing, such as the amygdala (AMY), regions involved in emotion integration and regulation, such as the ventro-lateral prefrontal cortex (vlPFC), portions of the medial frontal cortex, as well as ventral regions susceptible to emotion modulation, such as visual cortex (Davidson & Irwin, 1999; Davis & Whalen, 2001; Dolcos et al., 2011; Kober et al., 2008; Lindquist, Wager, Kober, Bliss-Moreau, & Barrett, 2012; Phan, Wager, Taylor, & Liberzon, 2002; Seeley et al., 2007; Sergerie, Chochol, & Armony, 2008; Vytal & Hamann, 2010).

Interestingly, the dorso-ventral dissociation between these two larger neural systems, identified in response to task manipulations with emotional distraction, overlaps with the main functional networks of the brain, identified based on their resting-state intrinsic connectivity.

Specifically, the dlPFC and LPC areas mentioned above as part of DES have been associated with the "fronto-parietal" (FPN) or "central-executive" network (Bressler & Menon, 2010; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Power & Petersen, 2013; Seeley et al., 2007; Yeo et al., 2011). Turning to the VAS regions, the vlPFC is typically considered part of the "salience" (SN) or "ventral-attentional" network (Bressler & Menon, 2010; Corbetta, Patel, & Shulman, 2008; Seeley et al., 2007), and has been associated with both processing of salient information (Bressler & Menon, 2010; Corbetta et al., 2008; Seeley et al., 2007) and response inhibition (Aron, 2007; Aron, Robbins, & Poldrack, 2004, 2014), and affect regulation (Kober et al., 2008; Ochsner, Silvers, & Buhle, 2012; Vytal & Hamann, 2010) (but see Hampshire, Chamberlain, Monti, Duncan, & Owen, 2010). Consistent with these functional associations, empirical evidence from studies of emotional distraction points to vlPFC involvement in both basic emotion processing and coping with distracting emotions (reviewed in Dolcos et al., 2011; Iordan et al., 2013b). The medial frontal areas of VAS, comprising the rostral and ventromedial prefrontal and ventral cingulate cortices (vmPFC/vACC) are an ensemble of subregions that have also been linked to both generation and modulation of emotion (Kober et al., 2008; Lindquist et al., 2015; Ochsner et al., 2012; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008), as well as to self-referential processing (Northoff et al., 2006), and are typically considered part of the "default-mode network" (DMN) (Buckner, Andrews-Hanna, & Schacter, 2008; Fox et al., 2005; Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001). Interestingly, vmPFC/vACC regions have also been reported as being sensitive to different emotional properties of the stimuli linked to emotional arousal and valence (Dolcos, LaBar, & Cabeza, 2004a; Heinzel et al., 2005; Kensinger & Schacter, 2006; Kreplin & Fairclough, 2013; Leclerc & Kensinger, 2010; Lindquist

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et al., 2015; Radua et al., 2014; Schlochtermeier et al., 2013; Straube, Sauer, & Miltner, 2011; Wager et al., 2008; Wager, Phan, Liberzon, & Taylor, 2003).

Importantly, the DES/VAS functional dissociation departs from the simple antagonism between bottom-up/ventral and top-down/dorsal systems (see Pfeifer & Allen, 2012), by emphasizing the involvement of prefrontal VAS regions (e.g., vlPFC) in both emotion processing and control operations that enable emotion regulation and coping with distraction (Denkova et al., 2010; Dolcos et al., 2006; Dolcos & McCarthy, 2006; Iordan et al., 2013b). Such dissociations have been systematically identified in tasks that have as a common denominator the clear perceptual and temporal segregation of goal-relevant and distracting information (see Banich et al., 2009), including emotional odd-ball tasks (Wang, McCarthy, Song, & Labar, 2005; Yamasaki, LaBar, & McCarthy, 2002) and emotional interrupt tasks (Mitchell et al., 2008), in addition to the delayed-response WM tasks employed by us and others. Of note, while we do not treat DES and VAS as equal to brain networks, we emphasize the possibility of overlaps between these larger neural systems sensitive to task-irrelevant emotional information and the large-scale functional networks. For instance, the task-induced dorso-ventral dissociation between DES and VAS resembles the dissociation between FPN/central-executive network and SN/ventral-attentional network, as identified by investigations employing resting-state functional connectivity (Dosenbach et al., 2008; Dosenbach et al., 2007; Power et al., 2011; Seeley et al., 2007; Yeo et al., 2011).

An important emerging issue in the literature concerns identification of network interactions in response to task-related challenges (Barrett & Satpute, 2013; Cole, Bassett, Power, Braver, & Petersen, 2014; Lindquist & Barrett, 2012; Smith et al., 2009). In contrast to FPN and SN, which are considered "task-positive" networks, the DMN has been conceptualized

as a "task-negative network" because it typically deactivates during cognitively demanding tasks (Fox et al., 2005). Increased functional connectivity between "task-positive" cognitive control regions and greater "anticorrelation" (i.e., negative correlation) between "task-negative" and "task-positive" brain regions have been linked to increased performance (Nee & Jonides, 2008) and reduced variability in cognitive tasks (Kelly, Uddin, Biswal, Castellanos, & Milham, 2007). In particular, it has been shown that the FPN is anticorrelated with DMN during the WM maintenance phase (Piccoli et al., 2015). In contrast, increased communication between "task-positive" and "task-negative" brain regions has been associated with performance decrements in cognitive tasks that engage the external environment (van Ast et al., 2014).

Although previous brain imaging investigations of emotional distraction identified specific brain regions involved in coping with emotional distraction (reviewed in Dolcos et al., 2011; Iordan et al., 2013b), they have focused mainly on negative distraction and have not identified network interactions in response to emotional distraction. Thus, the second main goal of the present study was to determine the neural correlates of the response to positive and negative distracters and to clarify whether their possibly differential impact on WM performance is linked to altered interactions between regions of FPN and DMN.

These issues were addressed here by investigating the contributions of emotional arousal and valence in the impact of emotional distraction on cognitive performance and the associated neural correlates. Behavioral assessments involved measures of WM performance in the presence of high- and low-arousing positive and negative distraction. Brain activity was recorded using event-related fMRI, while healthy subjects performed the WM task with distraction. In order to clarify potential interactions between regions associated with the major brain networks, analyses of basic differences in brain activity were supplemented by functional connectivity

analyses investigating task-induced dissociations in functional coupling between these regions. Based on the extant evidence, we made the following conditional predictions. If the distracting effects are mainly driven by arousal (arousal account), increased impact of high- compared with low-arousing stimuli was expected. On the other hand, if the distracting effects are sensitive to valence (valence account), diminished impact of positive compared with the negative distraction was expected (Berntson et al., 1993; Bradley & Lang, 2007; Cacioppo et al., 1997). In the brain, we expected that differential impact of more versus less distracting conditions would be reflected in greater deactivation in DES regions and increased activity in VAS regions involved in emotion processing, for the more distracting condition. Moreover, increased activity in VAS regions involved in coping with emotional distraction was also expected, for the less distracting condition. Of note, the above predictions are not mutually exclusive and, hence, we also considered the possibility of interactions and/or effects consistent with both accounts. Thus, if the distracting effects of emotion are sensitive to both valence and arousal, then more subtle valence-related dissociations are expected in the context of overall arousal-driven responses, in both behavioral and brain imaging results. Finally, regarding interactions between "task-positive" regions associated with the fronto-parietal network and "task-negative" regions associated with the DMN, we expected that the detrimental impact of emotional distraction would be linked to increased functional coupling between "task-positive" and "task-negative" brain regions.

Methods

Subjects

A group of 18 healthy, young, right-handed women (18-34 years of age, average = 21.55, $SD = 3.62$) participated in the study. The rationale for including only female subjects in the

present study was to maintain homogeneity in the subject sample, given previous evidence showing sex differences in the basic response to and coping with emotional distraction (Iordan et al., 2013a). The subjects were screened for neurological and/or psychiatric disorders using a questionnaire developed in consultation with trained clinicians. The data from one participant were excluded from analyses because of large number of nonresponses during the WM task (i.e., more than 10% nonresponses). Hence, the reported behavioral and fMRI analyses are based on data from 17 subjects (average age = 21.65, *SD* = 3.7). The experimental protocol was approved by the Internal Review Board of the University of Illinois at Urbana-Champaign, and all subjects provided written informed consent.

Stimuli

The subjects performed a delayed-response WM task for faces with novel pictures presented as distracters during the delay interval between the memoranda and the probes (Figure 2.1). The memoranda consisted of sets of three human faces (50% females / 50% males) chosen to maximize similarities for increased task difficulty. The distracters consisted of pictures depicting pleasant (positive valence), unpleasant (negative valence), and neutral scenes (e.g., mundane activities) selected from the International Affective Picture System (IAPS, Lang, Bradley, & Cuthbert, 2008) and supplemented from an in-house database for the neutral scenes. Two levels of arousal (high and low) were also considered for both positive and negative stimuli, to allow identification of potentially more subtle arousal effects within the emotional categories. In total, there were five categories of stimuli: negative high (NegHi) and low (NegLo) arousing, positive high (PosHi) and low (PosLo) arousing, and neutral (Neu) (Figure 2.2). High- and low-arousal emotional stimuli were matched for valence and negative and positive stimuli were matched for arousal. The normative IAPS valence scores (mean; SD) for the emotional

categories were as follows: NegHi (3.19; 0.51), NegLo (3.29; 0.37), PosHi (6.83; 0.25); PosLo (6.76; 0.41); Neu (4.99; 0.27). The normative IAPS arousal scores (mean; SD) for the emotional categories were as follows: NegHi (5.97; 0.39), NegLo (4.38; 0.38), PosHi (5.99; 0.48), PosLo (4.38; 0.31), Neu (3.56; 0.40). The valence × arousal separation was confirmed by analyses of variance (ANOVAs). Within the emotional category, positive and negative pictures differed in terms of their valence rating ($p < 0.001$) but not arousal ($p > 0.05$), whereas high- and low-arousing pictures differed in terms of their arousal ratings ($p < 0.001$) but not valence ($p > 0.05$). Furthermore, positive, negative, and neutral pictures differed in terms of their valence ratings (p's < 0.001), and high-arousing, low-arousing, and neutral pictures differed in terms of their arousal ratings (p's < 0.001). All selected stimuli depicted complex scenes, and there were no differences in visual complexity (as assessed by compressed file size, [$F_{(4,235)} = 0.28$, $p = 0.893$] or luminance across the categories [$F_{(4,235)} = 1.17$, $p = 0.326$]. Efforts were also made to match them as closely as possible for human presence and animacy across categories. Each picture was paired with its closest match in terms of arousal and valence properties, resulting in 120 pairs (24 pairs for each category). A total number of 144 trials (120 experimental trials plus 24 no-distraction control trials displaying a fixation cross) were involved. All stimuli were presented in color using E-Prime 1.0 (Psychology Software Tools, Pittsburgh, PA, USA).

Experimental Procedures

The pool of 144 trials was divided into 8 sets of 18 trials (counterbalanced across distracter-type categories), which were randomly assigned to 8 experimental blocks/runs. To avoid induction of longer lasting effects, the trials within each block were pseudo-randomized, so that no more than two consecutive trials of the same type were presented. To prevent possible biases resulted from using the same run order, participants were assigned different run orders; a

total of 8 different run orders were involved. As illustrated in Figure 2.1, each trial started with the presentation of face memoranda (3.5 s), which subjects were instructed to encode and maintain in WM during the delay interval between the offset of the memoranda and the onset of the memory probe (12.5 s). Presentation of novel distracters started 2.5 s after the offset of the memoranda, and occurred for a total time of 6 s (3 s each). Participants were instructed to look at the distracters but maintain focus on the WM task, and then when the single-face probes appeared they had to indicate by a button press whether they were part of the current memorandum (Old) or not (New); 50% of the probes were Old and 50% were New. Subjects were instructed to make quick and accurate responses while the probes were on the screen, and then they also rated the level of confidence (LOC) of their responses, using a 3-point Likert scale (1 = lowest, 3 = highest). The LOC rating was followed by a 10.5-s intertrial interval, to allow the hemodynamic response to return to baseline. During this time, participants were instructed to relax and refrain from doing anything systemically that could potentially affect the intertrial baseline signal (e.g., counting).

Imaging Protocol

Scanning was conducted on a 3-T Siemens Trio scanner. After the sagittal localizer and the 3D magnetization prepared rapid acquisition gradient echo anatomical images [repetition time (TR) = 1800 ms; echo time (TE) = 2.26 ms; flip angle = 9°; field of view (FOV) = 256 × 256 mm^2; matrix size = 256 × 256 mm^2; slice thickness = 1 mm; volume size = 192 slices; voxel size = 1 × 1 × 1 mm^3], 8 blocks of 271 full-brain echo-planar functional images were acquired axially, co-planar with the anterior commissure − posterior commissure line (TR = 2000 ms; TE = 40 ms; flip angle = 90°; FOV = 256 × 256 mm^2; matrix size = 64 × 64 mm^2; slice thickness = 4 mm, no gap; volume size = 28 slices; voxel size = 4 × 4 × 4 mm^3).

Behavioral Data Analyses

Responses in the WM task were classified in one of the four categories derived from signal detection theory (Macmillian & Creelman, 1991): 1) "Hits," corresponding to memorandum faces correctly classified as Old, 2) "Misses," corresponding to memorandum faces incorrectly classified as New, 3) "Correct Rejections" (CRs), corresponding to new faces correctly classified as New, and 4) "False Alarms" (FAs), corresponding to new faces incorrectly classified as Old. Percentages of probes correctly identified as being Old or New were also calculated for each participant (% Correct = [% Hits + % CR] / 2). Normality of % Correct data was assessed using the Shapiro-Wilk test. Differences in WM performance among the trial types were assessed using repeated-measures ANOVAs and follow-up t-tests, using SPSS. First, a 2×2 ANOVA (valence: positive, negative; arousal: high, low) was used to test for differences in WM performance within the emotional category. Then, one-way ANOVAs were used to test for valence and arousal effects individually, in the context of the two control conditions. Specifically, a one-way ANOVA (distraction type: positive, negative, neutral, no-distraction) was used to test for valence effects, and similarly, a one-way ANOVA (distraction type: high-arousal, low-arousal, neutral, no-distraction) was used to test for arousal effects.

fMRI Data Analyses

Statistical analyses were preceded by the following preprocessing steps (performed with SPM8 - Statistical Parametric Mapping): slice timing, realignment, motion correction, co-registration, normalization, and smoothing (8 mm kernel). For the data analysis, we used in-house custom MATLAB scripts involving whole-brain voxel-wise analyses (Dolcos & McCarthy, 2006; Iordan et al., 2013a) to compare the brain activity associated with the conditions of interest (e.g., trials with positive vs. negative distraction). For subject-level

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analyses, the fMRI signal was selectively averaged in each subject's data as a function of trial type (e.g., positive, negative, and control, for analyses concerning valence; and high-arousal, low-arousal, and control, for analyses concerning arousal; see also "Identification of Arousal and Valence-Related Effects" below) and time point (one prestimulus and 13 poststimulus onset time points). Pair-wise t statistics for the contrasts of interest were calculated for each subject. No assumption was made about the shape of the hemodynamic response function because this method allows finer comparisons of the MR signal on a TR-by-TR basis and has been proven effective in dissociating responses produced by the WM task with emotional distraction (Denkova et al., 2010; Dolcos et al., 2008; Dolcos & McCarthy, 2006; Iordan et al., 2013a; Morey et al., 2009). The individual analysis produced whole-brain average and activation t maps for each condition, contrast of interest, and TR/time point.

The outputs of subject-level analyses were used as inputs for second-level random-effects within-group analyses. The analyses focused on effects observed at the peak time point (i.e., covering the 14-16 s period after the memoranda onset - TR 9), when the differential effects of the distracters are most evident (Denkova et al., 2010; Dolcos & McCarthy, 2006; Iordan et al., 2013a). For clarification purposes, in cases where there was a significant effect at TR 9 and the shape of the hemodynamic response suggested that the peak might have been shifted by 1 TR, we also investigated brain activity at ± 1 time point. Analyses were performed on correct trials (Hits and CR collapsed). This more stringent approach ensured that only instances where the subjects were performing the task were included in the analysis. Each random-effects t statistic map was corrected for multiple comparisons using a false discovery rate (FDR) of $q < 0.05$ (Genovese, Lazar, & Nichols, 2002), unless otherwise specified as exception. Then, conjunction analyses were performed in MATLAB using the logical function AND, thus only voxels that met

the threshold criteria in each of the contributing *t* maps survived the masking procedure. This procedure is consistent with the conjunction null hypothesis testing (Nichols, Brett, Andersson, Wager, & Poline, 2005). An extent threshold of 10 contiguous voxels was used in each of the contributing maps (Lieberman & Cunningham, 2009).

A Priori Defined Functional Masks

Based on evidence regarding modulation of activity by emotional distraction in dorsal and ventral brain regions discussed above, on evidence showing differences in mPFC/vACC activity linked to the processing of emotional stimuli (Dolcos et al., 2004a; Heinzel et al., 2005; Kensinger & Schacter, 2006; Kreplin & Fairclough, 2013; Radua et al., 2014), and on evidence identifying the mPFC as part of the DMN (Buckner et al., 2008; Raichle et al., 2001), three a priori functional masks were identified: the DES and VAS and the DMN. The DES and VAS maps were derived from the original study by Dolcos & McCarthy (2006), to identify modulation of activity by emotional distraction. That study used a similar WM task with high-arousing negative pictures as novel distracters, and thus for the purpose of the current study, two functional maps were used: Scrambled > Negative, to identify regions of DES, and Negative > Scrambled, to identify regions of VAS (see Supplementary Figure 2.1). The contrasts between these two conditions were used (Scrambled vs. Negative) because these were the two most dissimilar conditions in terms of their impact on the WM performance (i.e., highest WM performance for scrambled and lowest for negative distraction) in the Dolcos & McCarthy (2006) study. As can be seen from Supplementary Figure 2.1, the brain regions identified for DES, for example (including dlPFC and LPC), map well with the fronto-parietal regions involved in WM processing, as identified by other sources. Furthermore, given that in the present study we also use positive stimuli, it was important to opt for the contrast that allowed

identification of a more comprehensive map. The functional masks were calculated by merging

supra-threshold brain activity in the window from 12 to 16 s (TRs 8-9) after memoranda onset,

which corresponds to the time interval when most of the peak effects reported by Dolcos &

McCarthy (2006) in the two systems occurred, and were thresholded at $q < 0.05$ FDR-corrected.

This ensured that the effects identified in the present study would be confined to regions showing

the typical response to emotional distraction in the dorsal (i.e., increased deactivation) and

ventral (i.e., increased activity) neural systems, based on an independent sample. To identify

modulation of brain activity by emotional distraction in DMN regions, an a priori functional

mask derived by meta-analysis performed with Neurosynth (Yarkoni, Poldrack, Nichols, Van

Essen, & Wager, 2011) was used. The map was derived by an automated meta-analysis

performed on studies indexed by the feature "default mode" (reverse inference map, thresholded

at $q < 0.01$, FDR-corrected, which is the lowest default threshold in Neurosynth). Functional

maps identifying response in the present study within each of these masks were thresholded at q

< 0.05 FDR-corrected and 10 contiguous voxels.

Identification of Arousal- and Valence-Related Effects

The first main goal of the present study was to clarify the impact of emotional distraction

on WM performance, by testing two competing accounts: the *arousal* and the *valence* accounts.

This goal was accomplished by identifying DES, VAS, and DMN brain regions whose activity

was sensitive to distractors with different arousal and valence properties, or their combination,

both within the emotional categories and relative to control. To ensure an equal number of trials

across conditions, both neutral and no-distraction control trials were collapsed into a single

control condition (Ctrl). This was also justified by the absence of differences in WM

performance between the two control conditions (neutral and no-distraction control; $t_{(16)} = 0.68$,

$p = 0.507$; see also Table 2.1). These analyses are described in detail below. To identify brain regions whose activity was consistent with the arousal account, we performed analyses at two different levels, consistent with different conceptualizations of "arousal effects". First, because more generic differences in arousal can be identified by comparing responses to emotionally arousing and neutral/control stimuli (Dolcos et al., 2004a), we tested for overlapping responses to both positive and negative distraction relative to control [i.e., overlapping deactivations in the dorsal system (Pos < Ctrl) ∩ (Neg < Ctrl) and overlapping increased activity in the ventral system (Pos > Ctrl) ∩ (Neg > Ctrl)]. Second, because more specific differences in arousal can be identified by comparing different arousal levels within the emotional category (Shafer et al., 2011), we directly compared brain activity related to high- and low-arousing emotional distraction and further masked with differences relative to control. Specifically, responses to high-arousing distraction were identified by deactivations in the dorsal system (AroHi < AroLo) ∩ (AroHi < Ctrl) and increased activity in the ventral system (AroHi > AroLo) ∩ (AroHi > Ctrl) relative to both low-arousing distraction and control. Similarly, responses to low-arousing distraction were identified by deactivations in the dorsal system (AroLo < AroHi) ∩ (AroLo < Ctrl) and increased activity in the ventral system (AroLo > AroHi) ∩ (AroLo > Ctrl) relative to both high-arousing distraction and control.

To identify brain regions whose activity was consistent with the valence account, we directly compared brain activity related to positive and negative distraction and further masked with differences relative to control. Specifically, responses to positive distraction were identified by deactivations in the dorsal system (Pos < Neg) ∩ (Pos < Ctrl) and increased activity in the ventral system (Pos > Neg) ∩ (Pos > Ctrl) relative to both negative distraction and control. Similarly, responses to negative distraction were identified by deactivations in the dorsal system

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(Neg < Pos) ∩ (Neg < Ctrl) and increased activity in the ventral system (Neg > Pos) ∩ (Neg > Ctrl) relative to both positive distraction and control. Because both the arousal- and valence-related analyses had three conditions, we opted for conjunctions between two separate pair-wise comparisons to test for effects similar to linear trends, but stricter (See http://afni.nimh.nih.gov/sscc/gangc/Trend.html, last accessed October 17, 2015). For instance, the conjunctions (AroHi > AroLo) ∩ (AroLo > Ctrl) and (AroLo > AroHi) ∩ (AroHi > Ctrl) identified linear effects of high and low arousal, respectively, and the conjunctions (Pos > Neg) ∩ (Neg > Ctrl) and (Neg > Pos) ∩ (Pos > Ctrl) identified linear effects of positive and negative valence, respectively. Finally, to identify brain regions whose activity was consistent with an interaction of both accounts, we tested for greater arousal effects for positive than negative distraction (PosHi − PosLo) > (NegHi − NegLo), and greater arousal effects for negative than positive distraction (NegHi − NegLo) > (PosHi − PosLo).

Functional Connectivity Analyses

To investigate modulation of functional relationships between targeted DMN and DES/VAS brain regions identified by the above analyses as showing valence-related sensitivity to emotional distraction (see Results section), functional connectivity analyses of delay activity among these regions were performed, using a procedure previously employed by Dolcos et al. (2006). This approach is similar to the "beta-series correlations" procedure described by Rissman, Gazzaley, and D'Esposito (2004), but uses the baseline-subtracted MR signal instead of beta values. For these analyses, at the first level, within-subject voxel-wise correlations were performed on a trial-by-trial basis, using as seeds activity extracted from two mPFC/vACC foci (i.e., peak and neighboring voxels), which were independently identified by the analyses above as showing differential sensitivity to positive and negative distraction (see Results section), and

targeting activity in DES and VAS regions. These trial-based analyses were performed for the time point of interest (TP 9), in each participant, for the two targeted trial types: i.e., trials associated with positive and negative distraction. The resulting correlation maps were normalized using Fisher's z transformation. At the second level, across subject random-effects t comparisons of the individual correlation maps were performed, to identify regions systematically showing greater functional connectivity with the seed regions, for one condition relative to the other (e.g., Neg > Pos). Because we targeted within-subjects differences in correlation strengths (e.g., increased correlations under negative compared with positive distraction), no other pre-processing steps were involved, aside from those performed for the analyses targeting differences in activation. Of note, the selection criterion for the seeds (i.e., differences in activation) did not bias the functional connectivity results because the seeds were selected based on the "average" response to Pos and Neg conditions, whereas the functional connectivity analysis used trial-by-trial estimates, which are independent of the average responses (Kinnison, Padmala, Choi, & Pessoa, 2012). This was confirmed by formal tests assessing whether average differences in brain activation were correlated with differences in functional connectivity (i.e., correlations) between targeted regions based on trial-by-trial data, using a procedure similar to Kinnison et al. (2012). Importantly, our approach was validated by a parallel analysis using "beta-series correlations" using the procedure described by Rissman et al. (2004). In brief, for this, we first created a general linear model in which the distracter phase of each trial was modeled individually by a separate covariate, yielding different parameter estimates for each trial and for each subject; the study (memoranda) and test (probe) phases of each trial, as well as the 6 motion parameters, were modeled as regressors of no interest. Then, seed-based correlations were calculated voxel-wise for each subject and each condition of

interest (e.g., positive and negative distraction) using the same seed ROIs as above, and the resulting correlation maps were normalized using Fisher's *z* transformation. Similar to our procedure described above, random-effects *t* tests were used to detect voxels that showed increased coupling with the seed region for one condition relative to the other (e.g., Neg > Pos). Given our a priori hypotheses, these analyses were limited to activity in the targeted system (i.e., DES) and thresholded at a more liberal but accepted threshold of $p < 0.005$, uncorrected, and 10 contiguous voxels (Lieberman & Cunningham, 2009).

Brain-Behavior Interaction Analyses

To identify brain regions whose activity was sensitive to individual variations in WM performance, brain-behavior relations were also investigated by calculating covariations between the fMRI signals in response to emotional distraction and WM performance. Negative brain-behavior covariations were expected to be indicative of processing leading to detrimental effects on WM performance, whereas positive covariations were presumed to be indicative of processing engaged to cope with distraction. These analyses were restricted within the a priori defined functional masks and involved investigation of covariations between WM performance and brain activity in 1) regions showing sensitivity to positive and/or negative distraction (increased or decreased activity) at the group-level average response, and 2) brain regions not showing differential sensitivity to positive and/or negative distraction at the group level; the latter analyses were justified by the fact that covariations with behavior can also be identified in the absence of significant differences identified at the group level. The analyses performed to investigate brain-behavior relationships were based on calculating correlation maps identifying covariations between brain activity in the presence of distraction and scores indexing WM performance [i.e., % Correct = (% Hits + % CR) / 2]. These analyses were thresholded at a more

liberal but accepted threshold of $p < 0.005$, uncorrected, and 10 contiguous voxels (Lieberman & Cunningham, 2009).

Results

Behavioral Results

Reduced Impact of Positive Distraction on WM Performance

Analyses of the WM data showed increased performance for positive compared with negative distraction, supporting the valence account. A summary of the responses in the WM task is presented in Table 2.1. First, the results of a two-way repeated measures ANOVA (valence: positive, negative × arousal: high, low) on WM performance for emotional distracters yielded a significant main effect of valence [$F_{(1,16)} = 6.74$, $p = 0.019$] with greater performance under positive (80.88%, $SD = 8.69$) than negative (75.65%, $SD = 8.89$) distraction. Because both the main effect of arousal [$F_{(1,16)} = 2.45$, $p = 0.137$] and the arousal × valence interaction [$F_{(1,16)} = 0.004$, $p = 0.952$] were nonsignificant, high- and low-arousing trials were averaged for positive and negative valence, respectively (Table 2.1). Second, the results of a one-way repeated measures ANOVA (distraction type: positive, negative, neutral, and no-distraction control) on WM performance yielded a main effect of Distraction [$F_{(3,48)} = 2.96$, $p = 0.041$], confirming the differential impact of positive and negative distraction also in the context of the two control conditions (neutral distraction and no distraction).

fMRI Results

Behavioral results showed that the impact of emotional distraction on cognitive performance is modulated by the valence of the task-irrelevant distraction. Analyses of fMRI data investigated the responses in brain activity linked to these behavioral findings (valence account), and/or whether it is also consistent with arousal-related responses (arousal account).

Overall, these analyses yielded evidence consistent with both accounts. Consistent with the behavioral differences and the valence account, valence-driven differences were identified in DES and DMN regions and in their functional connectivity, in response to positive versus negative distraction. However, both valence- and arousal-driven effects were identified in VAS regions, in the absence of significant interactions between arousal and valence (Tables 2.2-2.4; see also the Methods section). These results are detailed below.

Dissociable and Overlapping Valence- and Arousal-Driven Effects in DES and VAS Regions

Consistent with both accounts, valence-related effects were identified in DES regions, and overlapping valence- and arousal-driven effects were observed in VAS regions. Consistent with the valence account, brain imaging results identified valence-related dissociations in both DES and VAS systems. Specifically, there was greater deactivation in LPC part of DES [right inferior parietal lobe (IPL), BA 40] under negative distraction, and increased activity in posterior vlPFC part of VAS (right IFG, BA 9, extending into the inferior frontal junction) under positive distraction (Figure 2.3*a*, *b*). Furthermore, brain-behavior covariation analyses identified a more inferior vlPFC region (right IFG, BA 45/13, Talairach coordinates: $x = 40$, $y = 28$, $z = 9$) whose increased activity was linked to better performance for positive compared with negative distraction ($r = 0.78$, $p < 0.001$), in the absence of differences in activation between the two distracter categories at the group level (Figure 2.3*c*). Overall, these findings are consistent with the behavioral results and suggest that the reduced impact of positive distraction on WM performance was associated with both reduced impact on DES regions (LPC) and superior recruitment of VAS regions (vlPFC) involved in coping with distraction, for positive compared with negative stimuli. Also, the findings regarding vlPFC activity and its relation to WM performance suggest both basic recruitment by salient stimuli and a role in coping with

emotional distraction, consistent with its role as a "hub" in integrating emotional and executive processing.

Specific arousal-related effects were identified in both anterior and posterior vlPFC subregions (Table 2.3A), which showed both more generic (i.e., increased activity to both positive and negative distraction relative to control) and more specific arousal-driven effects (i.e., increased responses to high relative to both low-arousing emotional distracters and control). Although the arousal- and valence-related effects in the vlPFC partially overlapped, a relative segregation could also be observed, with valence-related effects being slightly more posterior and lateral than the arousal-driven effects (see Supplementary Figure 2.2). Interestingly, both valence- and arousal-related responses in the right posterior vlPFC also showed patterns of activity consistent with linear effects [i.e., (AroHi > AroLo) ∩ (AroLo > Ctrl) for arousal and (Pos > Neg) ∩ (Neg > Ctrl) for valence] (see also the Methods section). To clarify the brain response in this region, percent signal change for each of the four emotional conditions was inspected individually, and the observed pattern of activity suggested that greater responses to positive valence were mainly driven by the high-arousing positive distracters, in the absence of a significant valence × arousal interaction (see Supplementary Figure 2.2). Finally, other regions showing both valence- and arousal-related effects included the visual areas, extending ventrally to the fusiform gyrus and dorsally to the superior parietal lobule (Table 2.4). Interestingly, only more generic arousal-driven effects were identified in certain DES regions (anterior PFC and posterior LPC) and VAS regions (AMY, hippocampus, and thalamus), which showed similar decreased vs. increased responses, respectively, to both positive and negative distracters (Table 2.3B). These responses occurred in the absence of specific dissociations between high- and low-

arousing distraction, and are consistent with an overall sensitivity to emotional distraction, regardless of valence.

Valence-Related Rostro-Caudal Dissociation in DMN Regions

The results also identified dissociable patterns of response to positive and negative distracters in the mPFC/vACC, a brain region involved in both emotional and self-referential processing, and which is also part of DMN (Buckner et al., 2008; Fox et al., 2005; Raichle et al., 2001). Specifically, a more rostral mPFC area (BA 9), identified as part of both VAS and DMN, showed increased activity for positive distraction, whereas a more caudal mPFC/vACC area (BA 10/32), part of DMN, showed greater deactivation to negative distraction (Figure 2.4). Interestingly, the peak response in the two regions occurred in slightly different time frames, with the deactivation to negative distraction in the more caudal region peaking earlier (TR 8-9) than the increased response to positive distraction in the more rostral region (TR 10). Taken together, these findings suggest an anterior-to-posterior dissociation in mPFC engagement and timing of activity, in response to task-irrelevant stimuli of opposing valence.

Valence-Related Dissociations in the Functional Connectivity of DMN and DES Regions

To further clarify the interactions between "task-positive" and "task-negative" brain regions showing valence-related effects, we performed functional connectivity analyses targeting the DES, VAS, and DMN areas identified above. These analyses were performed at the time point when the maximal impact of distraction on DES and VAS regions was identified (TR 9). Results showed increased functional connectivity between the two mPFC/vACC foci and parietal DES regions for negative compared with positive distraction (Figure 2.5). Specifically, the more caudal mPFC/vACC (BA 10/32) area showing deactivation to negative distraction also showed increased connectivity with the LPC (right IPL, BA 40) for negative compared with positive

distraction. Interestingly, the more rostral mPFC region (BA 9) whose response was strongest to positive stimuli also showed increased connectivity with the LPC for negative compare with positive distraction. Importantly, the parietal DES regions showing increased coupling with the mPFC also showed greater deactivation to negative distraction (see Table 2.2). To ensure that the selection criterion for the functional connectivity seeds (i.e., differences in activation) did not bias the results, we formally tested whether average differences in brain activation were correlated with differences in functional connectivity (i.e., correlations) between targeted regions based on trial-by-trial data, using a procedure similar to Kinnison et al. (2012). Results showed an absence of a relationship between differences in activation and differences in functional connectivity for both rostral mPFC–LPC ($r = -0.08$, $p = 0.77$) and caudal mPFC/vACC–LPC ($r = -0.05$, $p = 0.85$) pairs. Hence, the selection criterion did not bias the functional connectivity results. Additionally, these findings were also replicated by analyses performed with an alternative method, using "beta-series correlations" (Rissman et al., 2004). Overall, these findings suggest increased functional coupling between DMN and FPN for negative distraction, which was also the condition associated with lower WM performance.

Discussion

The goal of the present study was to clarify the roles of arousal and valence in the impact of emotional distraction on WM performance, by testing two competing accounts: the *arousal* and *valence* accounts. There were four main findings. First, consistent with the valence account, behavioral results showed reduced impact of positive compared to negative distraction on WM performance. Second, brain imaging results identified valence-specific effects in DES regions (LPC) and overlapping arousal- and valence-driven effects in VAS regions (vlPFC). Additionally, a valence-related rostro-caudal dissociation was identified in medial frontal regions

(mPFC/vACC) part of DMN, with the rostral sub-region showing increased response to positive and the caudal subregion showing greater deactivation to negative stimuli. Finally, there was a valence-related dissociation in functional coupling, with DMN regions (mPFC/vACC) showing increased functional connectivity with DES regions (LPC) for negative compared to positive distraction. These findings are discussed in turn below.

Reduced Impact of Positive Distraction on WM Performance

The present findings showing reduced impact of positive distraction on WM performance support the valence account, and suggest that subjects were better able to cope with positive compared with negative distraction. Theories of motivational dispositions (Berntson et al., 1993; Bradley & Lang, 2007; Cacioppo et al., 1997) suggest that although both positive and negative stimuli are relevant for survival, positive stimuli have different significance and are usually less imperative than the negative ones. According to these theories, organisms display both a "positivity offset" which encourages approach and exploration at low motivational levels, as well as a "negativity bias" which enables the abrupt engagement of defense systems when a threat signal is detected. Importantly, negative reactions tend to be stronger than the positive ones because the consequences of potential threats typically far exceed those of unpursued opportunities (Berntson et al., 1993; Bradley & Lang, 2007; Cacioppo et al., 1997). For example, the immediate consequences of not readily paying attention to a food source or a potential mating partner are usually less dramatic than the consequences of not paying attention to a predator.

Hence, under conditions of goal-oriented processing, task-irrelevant positive stimuli are better controlled compared with the negative ones, and thus negative distracters are more interfering with on-going cognitive performance, even at similar levels of arousal. Additionally,

positive affect has also been associated with "broadening" the scope of attention and with flexible integration of information (Fredrickson, 2001, 2004; Fredrickson & Branigan, 2005). This is in contrast with the influence of negative affective states on cognitive performance, which have often been associated with deleterious effects (reviewed in Mitchell & Phillips, 2007), probably due to fostering intrusive thoughts and ruminations that detract from goal-oriented processing (Eysenck, Derakshan, Santos, & Calvo, 2007). Although emotional reactions and states are separable phenomena and they may exert different influences on cognition and behavior (Olsson & Öhman, 2009), it is plausible that potential interference from positive distraction may be compensated by facilitatory effects that would allow maintaining the memoranda in WM while still processing the distracters. These results are also in line with recent evidence suggesting facilitation of controlled processing by positive affect (Carpenter et al., 2013; Nadler et al., 2010; Yang et al., 2013).

The present findings extend previous investigations of the impact of emotional distraction on WM maintenance, which have focused on negative valence (Iordan et al., 2013b), and other investigations focusing on arousal- and valence-related effects linked to the emotional content manipulated in WM (Kensinger & Corkin, 2003; Levens & Phelps, 2008; Lindstrom & Bohlin, 2011). It should be noted, however, that findings from these two main types of paradigms may not be directly comparable because of their conceptual and methodological differences. That is, in one case emotional distraction presented during the interval between the memoranda and probes can be perceptually and temporally segregated from the neutral WM content, whereas in the other emotional information is part of the content of information manipulated in WM (see Banich et al., 2009). At any rate, as discussed below, analyses of fMRI data identified for the first time patterns of responses consistent with the behavioral findings, with valence-related

effects in brain activity specific to DES regions and overlaps with arousal-driven effects in VAS regions.

Dissociable and Overlapping Valence and Arousal-Driven Effects in DES and VAS Regions

The findings showing greater deactivation to negative distraction in DES regions (LPC) and increased activation to positive distraction in VAS regions (vlPFC) suggest both greater detrimental impact of negative distraction on mechanisms supporting WM and increased recruitment of coping mechanisms for positive distraction. The present DES results are consistent with previous findings linking greater deactivation in fronto-parietal areas to the interfering effect of emotional distraction on WM performance (Anticevic et al., 2010; Denkova et al., 2010; Diaz et al., 2011; Dolcos et al., 2008; Dolcos et al., 2013; Dolcos et al., 2006; Dolcos & McCarthy, 2006; Iordan et al., 2013a; Oei et al., 2012). Also, the LPC is the posterior "hub" in the fronto-parietal executive network, which also includes the dlPFC (Dosenbach et al., 2006; Dosenbach et al., 2008; Dosenbach et al., 2007; Power et al., 2011; Power & Petersen, 2013; Seeley et al., 2007; Yeo et al., 2011). Increased activity in these regions has been implicated in active maintenance of task-relevant information (Corbetta & Shulman, 2002; D'Esposito et al., 2006; Fuster, 1997; Hopfinger, Buonocore, & Mangun, 2000; Koenigs et al., 2009; Nee et al., 2012; Niendam et al., 2012; Smith & Jonides, 1999). It has been suggested that the role of LPC in WM processing is related to top-down biasing in order to foreground in WM the representation that is the focus of attention (Nee & Jonides, 2008). Given their increased imperativeness (Berntson et al., 1993; Bradley & Lang, 2007; Cacioppo et al., 1997), negative stimuli may interfere more with this process compared to positive stimuli, and hence disrupt WM.

The overlapping arousal and valence-driven responses in the posterior vlPFC, in the absence of significant arousal $\times$ valence interactions, indicate that the contributions of valence and arousal in this region are additive rather than interactive. At the same time, the involvement of this region in processing distracters with different emotional attributes and behavioral outcomes is consistent with its putative role as a "hub" in processing salient information (Bressler & Menon, 2010; Corbetta et al., 2008; Seeley et al., 2007). On the other hand, a relative segregation of responses in the vlPFC, with the valence-related effects being slightly more posterior and lateral than the arousal-driven effects, suggests also potential sub-regional specificity and dissociations within the IFG.

Of note, increased activity in the vlPFC has previously been linked to both increased WM performance and reduced distractibility (Dolcos et al., 2006; Dolcos & McCarthy, 2006; Iordan et al., 2013b). Consistent with this interpretation, the vlPFC has also been proposed as a site of cross-modal inhibition, being generally associated with inhibitory processes (Aron, 2007; Aron et al., 2004; Berkman, Burklund, & Lieberman, 2009) and inhibition of negative emotion (Ochsner et al., 2004; Petrovic, Kalso, Petersson, & Ingvar, 2002). The interpretation that increased vlPFC activity for positive distraction reflects better engagement of coping with distraction mechanisms is further supported by the results of our brain-behavior covariation analyses, showing that subjects who engaged this region more in response to positive than negative distraction also performed better in the WM task. Of note, while these results are consistent with the idea of "functional heterogeneity" in the vlPFC area (Cai, Ryali, Chen, Li, & Menon, 2014; Levy & Wagner, 2011; Warren et al., 2014) (see also Gordon et al., 2014; Power et al., 2011), operational distinctions between "salience" and "inhibition" are not always clear-

cut, as salient or unexpected stimuli may also recruit some form of inhibitory processing (see Aron et al., 2014; Hampshire et al., 2010; Kohn et al., 2014).

Overall, the task-induced dorso-ventral dissociation between DES and VAS resembles the dissociation between FPN/central executive network and SN/ventral-attentional network, as identified in studies assessing resting-state functional connectivity (Dosenbach et al., 2008; Dosenbach et al., 2007; Power et al., 2011; Seeley et al., 2007; Yeo et al., 2011). Although there are important methodological differences between these two approaches (Buckner, Krienen, & Yeo, 2013), the basic configuration of the major brain networks is relatively stable across both task-related recordings and resting-state (Cole et al., 2014). Furthermore, this raises the possibility of overlaps between VAS regions and regions attributed to SN (Lindquist & Barrett, 2012; Lindquist et al., 2015; Seeley et al., 2007; Touroutoglou, Lindquist, Dickerson, & Barrett, 2015). It should be noted, however, that dissociations can also be identified. For instance, both the ventral attention and cingulo-opercular networks converge in the vlPFC, and they have been linked to stimulus-driven orienting of attention and sustained task-set maintenance, respectively (Corbetta et al., 2008; Dosenbach et al., 2008). Whereas a formal testing of this hypothesis was beyond the scope of the present investigation, identification of more subtle networks-based dissociations within these larger neural systems in future research is plausible and important. Given recent evidence for functional heterogeneity in the vlPFC (Cai et al., 2014; Gordon et al., 2014; Levy & Wagner, 2011; Power et al., 2011; Warren et al., 2014), investigation of functional dissociation in this area by combining task manipulations and resting-state recordings seems to be a promising avenue for future research.

Valence-Related Rostro-Caudal Dissociation in DMN Regions

The findings showing overall increased activity to positive distraction in rostral and ventral mPFC/vACC are consistent with the general involvement of this region in encoding positive value (Dolcos et al., 2004a; Kensinger & Schacter, 2006; Kreplin & Fairclough, 2013; Leclerc & Kensinger, 2010; Schlochtermeier et al., 2013; Straube et al., 2011; Wager et al., 2003) and self-referential processing (Cabeza & St Jacques, 2007; Denkova, Dolcos, & Dolcos, 2015; Northoff et al., 2006; Ochsner et al., 2012; Raichle et al., 2001; Schacter, Addis, & Buckner, 2007; Wager et al., 2008), and suggest greater self-engagement in the processing of positive stimuli. The mPFC/vACC region (BA 10/32) has been associated with both DMN (Buckner et al., 2008; Fox et al., 2005; Raichle et al., 2001) and emotion processing (Lindquist et al., 2015; Lindquist et al., 2012; Roy, Shohamy, & Wager, 2012), and in particular shows an overall affinity for positive affect (Lindquist et al., 2015; Lindquist et al., 2012). Although early perspectives (Bush, Luu, & Posner, 2000) have operated a distinction between dorsal-caudal cognitive and ventral-rostral affective mPFC/ACC regions, later evidence has suggested that both regions contribute to emotion processing, with the dorsal-caudal region involved mainly in evaluative operations and the ventral-rostral region involved mainly in regulatory functions (Etkin, Egner, & Kalisch, 2011).

Interestingly, the present findings point to a rostro-caudal dissociation in both sensitivity and timing of the response to positive vs. negative distraction, suggesting differences in functional specialization between the two mPFC/vACC subregions. The differential sensitivity to positive versus negative stimuli suggests differences in encoding the approach versus avoidance value of emotional stimuli (Wager et al., 2003). This finding is also consistent with previous evidence showing valence-related effects in mPFC/vACC (Nielen et al., 2009; Vrtička, Sander,

& Vuilleumier, 2011) and specific deactivations in response to negative (disgusting) images (Radua et al., 2014) and negative words (Richter, Eck, Straube, Miltner, & Weiss, 2010). This valence-related anterior-to-posterior dissociation complements a previously observed dorsal-ventral dissociation in mPFC activity in response to the arousal and valence properties of emotional stimuli, albeit under different task conditions (i.e., using a single, not dual, task) (Dolcos et al., 2004a; Kensinger & Schacter, 2006). Of note, mPFC/vACC is also part of the DMN (Buckner et al., 2008; Fox et al., 2005; Raichle et al., 2001), which comprises so-called task-negative regions whose deactivation is required in order to better perform tasks that require interactions with the external environment (Fox et al., 2005). Hence, it is possible that greater deactivation in this region to negative distraction may reflect increased (though unsuccessful) attempts at re-orienting towards the WM task under increased interference by negative distraction.

The difference in timing along the rostro-caudal axis is consistent with a proposed gradient of processing complexity in the mPFC (Olsson & Ochsner, 2008; Roy et al., 2012). Specifically, the posterior division, including the ventromedial PFC, is thought to be part of the "affect generation" subsystem and involved in more simple operations linked to the processing of "first-order" body state information, whereas the anterior division, including the rostral mPFC, is thought to be part of the "simulation" subsystem, and involved in complex or integrative operations such as re-representation of information and mentalizing (Olsson & Ochsner, 2008; Roy et al., 2012). In this view, the earlier response in the caudal mPFC/vACC region may reflect its involvement in an initial reaction to the sensory qualities of negative information, whereas the delayed response in the rostral mPFC may reflect involvement in the subsequent elaboration of positive information. However, given that the time resolution of fMRI

analyses is typically too coarse for subtle timing-related distinctions, these results should be treated with caution.

Valence-Related Dissociations in Functional Connectivity of DMN and DES Regions

The findings showing increased functional connectivity between mPFC and DES regions for negative distraction suggest task-induced changes in communication between DMN and FPN regions. Increased functional connectivity between mPFC and LPC under higher impact by negative distraction suggests a potential interference of affective information integrated by the mPFC with goal-relevant representations maintained by the fronto-parietal network. Activity in DMN, which includes the mPFC, is typically negatively correlated with activity in the fronto-parietal network (Fox et al., 2005), and in particular during the maintenance phase of WM processing (Piccoli et al., 2015). On the other hand, a reduction in the negative relations between medial prefrontal and parietal regions has been linked to adverse effects of socio-emotional stress (van Ast et al., 2014). Furthermore, the present results suggest that increased DMN-FPN communication occurred independently of the individual selectivity of the more anterior mPFC sub-region for positive distraction. Although the more anterior mPFC region showed specific increased activity to positive distraction, it also showed increased functional connectivity with LPC for negative distraction. Importantly, parietal regions showing increased functional connectivity with the mPFC were also more impacted by negative distraction, as reflected in the patterns of deactivation to negative distraction in LPC (BA 40). Overall, these findings point to increased communication between the DMN and FPN under interference by negative distraction, as a mechanism by which goal-irrelevant negative emotions impact on-going cognitive performance.

Caveats

One limitation of the present study is that only female participants were involved, which reduces the generalizability of our results. However, given sex differences in the response to emotional stimuli and emotional distraction (Domes et al., 2010; Hamann & Canli, 2004; Iordan et al., 2013a; Lang et al., 1993; McRae et al., 2010), this was important for maintaining homogeneity in the subject sample. Another limitation is that the hormonal state of our subjects was not assessed, and this may have potentially influenced their emotional reactivity (see Sundstrom Poromaa & Gingnell, 2014)

Conclusions

In summary, the present findings clarify the roles of arousal and valence in the impact of emotional distraction on WM, by identifying for the first time valence-related dissociations in the response and interactions between brain regions associated with executive and emotion processing. Consistent with the idea of a facilitating effect of positive emotion on controlled processing posited by theories of motivational dispositions (Berntson et al., 1993; Bradley & Lang, 2007; Cacioppo et al., 1997) and of positive affect (Ashby et al., 1999; Fredrickson, 2001; Isen, 2005), our results show that positive distraction is associated with both reduced cognitive interference and better coping compared to negative distraction. The present fMRI findings identified both reduced impact of positive distraction on dorsal brain regions (LPC), part of the fronto-parietal network, and superior recruitment of ventral regions (e.g., vlPFC), part of salience network, as well as valence-related dissociations in medial frontal areas, part of the default mode network (mPFC/vACC). Moreover, there were different patterns of connectivity between regions of the default mode and fronto-parietal networks, for negative vs. positive distraction. Overall, these findings show that, although positive and negative distraction may engage partly similar

arousal-dependent mechanisms, their differential impact on concurrent cognitive performance is linked to valence dissociations in the engagement of and coupling between regions associated with basic emotion processing and higher-lever cognitive control. Collectively, the present study provides initial fMRI evidence regarding the role of valence in the impact of emotional distraction on WM performance, and has implications for understanding affective disorders, which are characterized by increased susceptibility to negatively-valenced distraction and diminished processing of positive emotions (e.g., anhedonia in depression) (Forbes & Dahl, 2005; Gilbert, 2012; Izard, 2002; Watson & Naragon-Gainey, 2010; Waugh & Koster, 2014).

References

Allen, R. J., Schaefer, A., & Falcon, T. (2014). Recollecting positive and negative autobiographical memories disrupts working memory. *Acta Psychologica, 151*, 237-243.

Anticevic, A., Repovs, G., & Barch, D. M. (2010). Resisting emotional interference: brain regions facilitating working memory performance during negative distraction. *Cognitive, Affective, & Behavioral Neuroscience, 10*(2), 159-173.

Aron, A. R. (2007). The neural basis of inhibition in cognitive control. *Neuroscientist, 13*(3), 214-228.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences, 8*(4), 170-177.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: one decade on. *Trends in Cognitive Sciences, 18*(4), 177-185.

Ashby, F. G., Isen, A. M., & Turken, A. U. (1999). A neuropsychological theory of positive affect and its influence on cognition. *Psychological Review, 106*(3), 529-550.

Banich, M. T., Mackiewicz, K. L., Depue, B. E., Whitmer, A. J., Miller, G. A., & Heller, W. (2009). Cognitive control mechanisms, emotion and memory: a neural perspective with implications for psychopathology. *Neuroscience and Biobehavioral Reviews, 33*(5), 613-630.

Barrett, L., & Satpute, A. (2013). Large-scale brain networks in affective and social neuroscience: towards an integrative functional architecture of the brain. *Current Opinion in Neurobiology, 23*(3), 361-372.

Berkman, E. T., Burklund, L., & Lieberman, M. D. (2009). Inhibitory spillover: intentional motor inhibition produces incidental limbic inhibition via right inferior frontal cortex. *Neuroimage, 47*(2), 705-712.

Berntson, G. G., Boysen, S. T., & Cacioppo, J. T. (1993). Neurobehavioral organization and the cardinal principle of evaluative bivalence. In F. M. Crinella & J. Yu (Eds.), *Annals of the New York Academy of Sciences: Vol. 702. Brain mechanisms: Papers in memory of Robert Thompson* (pp. 75-102). New York: New York Academy of Sciences.

Bradley, M. M., & Lang, P. J. (2007). Motivation and emotion. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of psychophysiology (2nd edition)*. New York: Cambridge University Press.

Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: emerging methods and principles. *Trends in Cognitive Sciences, 14*(6), 277-290.

Brose, A., Lovden, M., & Schmiedek, F. (2014). Daily fluctuations in positive affect positively co-vary with working memory performance. *Emotion, 14*(1), 1-6.

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network. *Annals of the New York Academy of Sciences, 1124*(1), 1-38.

Buckner, R. L., Krienen, F. M., & Yeo, B. T. (2013). Opportunities and limitations of intrinsic functional connectivity MRI. *Nature Neuroscience, 16*(7), 832-837.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences, 4*(6), 215-222.

Cabeza, R., & St Jacques, P. (2007). Functional neuroimaging of autobiographical memory. *Trends in Cognitive Sciences, 11*(5), 219-227.

Cacioppo, J. T., Gardner, W. L., & Berntson, G. G. (1997). Beyond bipolar conceptualizations and measures: The case of attitudes and evaluative space. *Personality and Social Psychology Review, 1*(1), 3-25.

Cai, W., Ryali, S., Chen, T., Li, C. S., & Menon, V. (2014). Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: evidence from intrinsic and task-related functional parcellation, connectivity, and response profile analyses across multiple datasets. *The Journal of Neuroscience, 34*(44), 14652-14667.

Carpenter, S. M., Peters, E., Västfjäll, D., & Isen, A. M. (2013). Positive feelings facilitate working memory and complex decision making among older adults. *Cognition and Emotion, 27*(1), 184-192.

Cole, M. W., Bassett, D. S., Power, J. D., Braver, T. S., & Petersen, S. E. (2014). Intrinsic and task-evoked network architectures of the human brain. *Neuron, 83*(1), 238-251.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. *Neuron, 58*(3), 306-324.

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews. Neuroscience, 3*(3), 201-215.

D'Esposito, M., Cooney, J. W., Gazzaley, A., Gibbs, S. E., & Postle, B. R. (2006). Is the prefrontal cortex necessary for delay task performance? Evidence from lesion and FMRI data. *Journal of the International Neuropsychological Society, 12*(2), 248-260.

Davidson, R. J., & Irwin, W. (1999). The functional neuroanatomy of emotion and affective style. *Trends in Cognitive Sciences, 3*(1), 11-21.

Davis, M., & Whalen, P. J. (2001). The amygdala: vigilance and emotion. *Molecular Psychiatry, 6*(1), 13-34.

Denkova, E., Dolcos, S., & Dolcos, F. (2015). Neural correlates of 'distracting' from emotion during autobiographical recollection. *Social Cognitive and Affective Neuroscience, 10*(2), 219-230.

Denkova, E., Wong, G., Dolcos, S., Sung, K., Wang, L., Coupland, N., & Dolcos, F. (2010). The impact of anxiety-inducing distraction on cognitive performance: a combined brain imaging and personality investigation. *PLoS One, 5*(11), e14150. doi 14110.11371/journal.pone.0014150.

Diaz, M. T., He, G., Gadde, S., Bellion, C., Belger, A., Voyvodic, J. T., & McCarthy, G. (2011). The influence of emotional distraction on verbal working memory: an fMRI investigation comparing individuals with schizophrenia and healthy adults. *Journal of Psychiatric Research, 45*(9), 1184-1193.

Dolcos, F., Diaz-Granados, P., Wang, L., & McCarthy, G. (2008). Opposing influences of emotional and non-emotional distracters upon sustained prefrontal cortex activity during a delayed-response working memory task. *Neuropsychologia, 46*(1), 326-335.

Dolcos, F., Iordan, A. D., & Dolcos, S. (2011). Neural correlates of emotion-cognition interactions: A review of evidence from brain imaging investigations. *Journal of Cognitive Psychology, 23*(6), 669-694.

Dolcos, F., Iordan, A. D., Kragel, J., Stokes, J., Campbell, R., McCarthy, G., & Cabeza, R. (2013). Neural correlates of opposing effects of emotional distraction on working memory and episodic memory: An event related fMRI investigation. *Frontiers in Psychology, 4*, 293. doi 210.3389/fpsyg.2013.00293.

Dolcos, F., Kragel, P., Wang, L., & McCarthy, G. (2006). Role of the inferior frontal cortex in coping with distracting emotions. *Neuroreport, 17*(15), 1591-1594.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004a). Dissociable effects of arousal and valence on prefrontal activity indexing emotional evaluation and subsequent memory: an event-related fMRI study. *Neuroimage, 23*(1), 64-74.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004b). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron, 42*(5), 855-863.

Dolcos, F., & McCarthy, G. (2006). Brain systems mediating cognitive interference by emotional distraction. *The Journal of Neuroscience, 26*(7), 2072-2079.

Domes, G., Schulze, L., Bottger, M., Grossmann, A., Hauenstein, K., Wirtz, P. H., Heinrichs, M., & Herpertz, S. C. (2010). The neural correlates of sex differences in emotional reactivity and emotion regulation. *Human Brain Mapping, 31*(5), 758-769.

Dosenbach, N., Visscher, K., Palmer, E., Miezin, F., Wenger, K., Kang, H., Burgund, E., Grimes, A., Schlaggar, B., & Petersen, S. (2006). A core system for the implementation of task sets. *Neuron, 50*(5), 799-812.

Dosenbach, N. U., Fair, D. A., Cohen, A. L., Schlaggar, B. L., & Petersen, S. E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences, 12*(3), 99-105.

Dosenbach, N. U., Fair, D. A., Miezin, F. M., Cohen, A. L., Wenger, K. K., Dosenbach, R. A., Fox, M. D., Snyder, A. Z., Vincent, J. L., Raichle, M. E., Schlaggar, B. L., & Petersen, S. E. (2007). Distinct brain networks for adaptive and stable task control in humans. *Proceedings of the National Academy of Sciences USA, 104*(26), 11073-11078.

Dreisbach, G. (2006). How positive affect modulates cognitive control: The costs and benefits of reduced maintenance capability. *Brain and Cognition, 60*(1), 11-19.

Dreisbach, G., & Goschke, T. (2004). How positive affect modulates cognitive control: Reduced perseveration at the cost of increased distractibility. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 30*(2), 343-353.

Etkin, A., Egner, T., & Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences, 15*(2), 85-93.

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: attentional control theory. *Emotion, 7*(2), 336-353.

Forbes, E. E., & Dahl, R. E. (2005). Neural systems of positive affect: relevance to understanding child and adolescent depression? *Development and Psychopathology, 17*(3), 827-850.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences USA, 102*(27), 9673-9678.

Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *American Psychologist, 56*(3), 218-226.

Fredrickson, B. L. (2004). The broaden-and-build theory of positive emotions. *Philosophical Transactions of the Royal Society B: Biological Sciences, 359*(1449), 1367-1378.

Fredrickson, B. L., & Branigan, C. (2005). Positive emotions broaden the scope of attention and thought-action repertoires. *Cognition and Emotion, 19*(3), 313-332.

Fuster, J. M. (1997). Network memory. *Trends in Neurosciences, 20*(10), 451-459.

Genovese, C. R., Lazar, N. A., & Nichols, T. (2002). Thresholding of statistical maps in functional neuroimaging using the false discovery rate. *Neuroimage, 15*(4), 870-878.

Gilbert, K. E. (2012). The neglected role of positive emotion in adolescent psychopathology. *Clinical Psychology Review, 32*(6), 467-481.

Gordon, E. M., Laumann, T. O., Adeyemo, B., Huckins, J. F., Kelley, W. M., & Petersen, S. E. (2014). Generation and evaluation of a cortical area parcellation from resting-state correlations. *Cerebral cortex*, doi 10.1093/cercor/bhu1239.

Gray, J. R. (2001). Emotional modulation of cognitive control: approach-withdrawal states double-dissociate spatial from verbal two-back task performance. *Journal of experimental psychology. General, 130*(3), 436-452.

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences of the USA, 100*(1), 253-258.

Hamann, S., & Canli, T. (2004). Individual differences in emotion processing. *Current Opinion in Neurobiology, 14*(2), 233-238.

Hampshire, A., Chamberlain, S. R., Monti, M. M., Duncan, J., & Owen, A. M. (2010). The role of the right inferior frontal gyrus: inhibition and attentional control. *Neuroimage, 50*(3), 1313-1319.

Heinzel, A., Bermpohl, F., Niese, R., Pfennig, A., Pascual-Leone, A., Schlaug, G., & Northoff, G. (2005). How do we modulate our emotions? Parametric fMRI reveals cortical midline structures as regions specifically involved in the processing of emotional valences. *Cognitive Brain Research, 25*(1), 348-358

Hopfinger, J. B., Buonocore, M. H., & Mangun, G. R. (2000). The neural mechanisms of top-down attentional control. *Nature Neuroscience, 3*(3), 284-291.

Iordan, A. D., Dolcos, S., Denkova, E., & Dolcos, F. (2013a). Sex differences in the response to emotional distraction: an event-related fMRI investigation. *Cognitive, Affective & Behavioral Neuroscience, 13*(1), 116-134.

Iordan, A. D., Dolcos, S., & Dolcos, F. (2013b). Neural signatures of the response to emotional distraction: A review of evidence from brain imaging investigations. *Frontiers in Human Neuroscience, 7*, 200. doi 210.3389/fnhum.2013.00200.

Isen, A. M. (2005). Positive affect. In T. Dalgleish & M. J. Power (Eds.), *Handbook of Cognition and Emotion* (pp. 521-539): John Wiley & Sons, Ltd.

Izard, C. E. (2002). Translating emotion theory and research into preventive interventions. *Psychological Bulletin, 128*(5), 796-824.

Kelly, A. M., Uddin, L. Q., Biswal, B. B., Castellanos, F. X., & Milham, M. P. (2007). Competition between functional brain networks mediates behavioral variability. *NeuroImage, 39*(1), 527-537.

Kensinger, E. A., & Corkin, S. (2003). Effect of negative emotional content on working memory and long-term memory. *Emotion, 3*(4), 378-393.

Kensinger, E. A., & Corkin, S. (2004). Two routes to emotional memory: distinct neural processes for valence and arousal. *Proceedings of the National Academy of Sciences of the USA, 101*(9), 3310-3315.

Kensinger, E. A., & Schacter, D. L. (2006). Processing emotional pictures and words: effects of valence and arousal. *Cognitive, Affective & Behavioral Neuroscience, 6*(2), 110-126.

Kinnison, J., Padmala, S., Choi, J. M., & Pessoa, L. (2012). Network analysis reveals increased integration during emotional and motivational processing. *The Journal of Neuroscience, 32*(24), 8361-8372.

Kober, H., Barrett, L. F., Joseph, J., Bliss-Moreau, E., Lindquist, K., & Wager, T. D. (2008). Functional grouping and cortical-subcortical interactions in emotion: a meta-analysis of neuroimaging studies. *Neuroimage, 42*(2), 998-1031.

Koenigs, M., Barbey, A. K., Postle, B. R., & Grafman, J. (2009). Superior parietal cortex is critical for the manipulation of information in working memory. *The Journal of Neuroscience, 29*(47), 14980-14986.

Kohn, N., Eickhoff, S. B., Scheller, M., Laird, A. R., Fox, P. T., & Habel, U. (2014). Neural network of cognitive emotion regulation--an ALE meta-analysis and MACM analysis. *Neuroimage, 87*, 345-355.

Kreplin, U., & Fairclough, S. H. (2013). Activation of the rostromedial prefrontal cortex during the experience of positive emotion in the context of esthetic experience. An fNIRS study. *Frontiers in Human Neuroscience, 7*, 879. doi 810.3389/fnhum.2013.00879.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2008). *International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8.*: University of Florida, Gainesville, FL.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology, 30*(3), 261-273.

Larsen, R. J., & Diener, E. (1992). Promises and problems with the circumplex model of emotion. In M. S. Clark (Ed.), *Review of personality and social psychology: Emotion* (Vol. 13, pp. 22-59). Newbury Park, CA: Sage.

Leclerc, C. M., & Kensinger, E. A. (2010). Neural processing of emotional pictures and words: a comparison of young and older adults. *Developmental neuropsychology, 36*(4), 519-538.

Levens, S. M., & Phelps, E. A. (2008). Emotion processing effects on interference resolution in working memory. *Emotion, 8*(2), 267-280.

Levy, B. J., & Wagner, A. D. (2011). Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating. *Annals of the New York Academy of Sciences, 1224*, 40-62.

Lieberman, M. D., & Cunningham, W. A. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Social Cognitive and Affective Neuroscience, 4*(4), 423-428.

Lindquist, K., & Barrett, L. (2012). A functional architecture of the human brain: emerging insights from the science of emotion. *Trends in Cognitive Sciences, 16*(11), 533-540.

Lindquist, K. A., Satpute, A. B., Wager, T. D., Weber, J., & Barrett, L. F. (2015). The brain basis of positive and negative affect: Evidence from a meta-analysis of the human neuroimaging literature. *Cerebral Cortex*, doi 10.1093/cercor/bhv1001.

Lindquist, K. A., Wager, T. D., Kober, H., Bliss-Moreau, E., & Barrett, L. F. (2012). The brain basis of emotion: a meta-analytic review. *Behavioral and Brain Sciences, 35*(3), 121-143.

Lindstrom, B. R., & Bohlin, G. (2011). Emotion processing facilitates working memory performance. *Cognition & Emotion, 25*(7), 1196-1204.

Macmillian, N. A., & Creelman, C. D. (1991). *Detection theory: a user's guide*. New York: Cambridge University Press.

McRae, K., Hughes, B., Chopra, S., Gabrieli, J. D., Gross, J. J., & Ochsner, K. N. (2010). The neural bases of distraction and reappraisal. *Journal of Cognitive Neuroscience, 22*(2), 248-262.

Mickley Steinmetz, K. R., Addis, D. R., & Kensinger, E. A. (2010). The effect of arousal on the emotional memory network depends on valence. *Neuroimage, 53*(1), 318-324.

Mickley Steinmetz, K. R., & Kensinger, E. A. (2009). The effects of valence and arousal on the neural activity leading to subsequent memory. *Psychophysiology, 46*(6), 1190-1199.

Mitchell, D. G., Luo, Q., Mondillo, K., Vythilingam, M., Finger, E. C., & Blair, R. J. (2008). The interference of operant task performance by emotional distracters: an antagonistic relationship between the amygdala and frontoparietal cortices. *Neuroimage, 40*(2), 859-868.

Mitchell, R. L., & Phillips, L. H. (2007). The psychological, neurochemical and functional neuroanatomical mediators of the effects of positive and negative mood on executive functions. *Neuropsychologia, 45*(4), 617-629.

Morey, R. A., Dolcos, F., Petty, C. M., Cooper, D. A., Hayes, J. P., LaBar, K. S., & McCarthy, G. (2009). The role of trauma-related distractors on neural systems for working memory and emotion processing in posttraumatic stress disorder. *Journal of Psychiatric Research, 43*(8), 809-817.

Murty, V. P., Ritchey, M., Adcock, R. A., & LaBar, K. S. (2010). fMRI studies of successful emotional memory encoding: A quantitative meta-analysis. *Neuropsychologia, 48*(12), 3459-3469.

Nadler, R. T., Rabi, R., & Minda, J. P. (2010). Better mood and better performance. Learning rule-described categories is enhanced by positive mood. *Psychological Science, 21*(12), 1770-1776.

Nee, D. E., Brown, J. W., Askren, M. K., Berman, M. G., Demiralp, E., Krawitz, A., & Jonides, J. (2012). A meta-analysis of executive components of working memory. *Cerebral Cortex, 23*(2), 264-282.

Nee, D. E., & Jonides, J. (2008). Neural correlates of access to short-term memory. *Proceedings of the National Academy of Sciences of the USA, 105*(37), 14228-14233.

Nichols, T., Brett, M., Andersson, J., Wager, T., & Poline, J. B. (2005). Valid conjunction inference with the minimum statistic. *Neuroimage, 25*(3), 653-660.

Nielen, M. M., Heslenfeld, D. J., Heinen, K., Van Strien, J. W., Witter, M. P., Jonker, C., & Veltman, D. J. (2009). Distinct brain systems underlie the processing of valence and arousal of affective pictures. *Brain and cognition, 71*(3), 387-396.

Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012). Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cognitive, Affective & Behavioral Neurosience, 12*(2), 241-268.

Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., & Panksepp, J. (2006). Self-referential processing in our brain--a meta-analysis of imaging studies on the self. *Neuroimage, 31*(1), 440-457.

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage, 23*(2), 483-499.

Ochsner, K. N., Silvers, J. A., & Buhle, J. T. (2012). Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences, 1251*, E1-24.

Oei, N. Y., Veer, I. M., Wolf, O. T., Spinhoven, P., Rombouts, S. A., & Elzinga, B. M. (2012). Stress shifts brain activation towards ventral 'affective' areas during emotional distraction. *Social Cognitive and Affective Neuroscience, 7*(4), 403-412.

Olsson, A., & Ochsner, K. N. (2008). The role of social cognition in emotion. *Trends in Cognitive Sciences, 12*(2), 65-71.

Olsson, A., & Öhman, A. (2009). The affective neuroscience of emotion: Automatic activation, interoception and emotion regulation. In J. T. Cacioppo & G. G. Berntson (Eds.), *Handbook of neuroscience for behavioral sciences*. Hoboken, NJ: Wiley.

Petrovic, P., Kalso, E., Petersson, K. M., & Ingvar, M. (2002). Placebo and opioid analgesia-- imaging a shared neuronal network. *Science, 295*(5560), 1737-1740.

Pfeifer, J. H., & Allen, N. B. (2012). Arrested development? Reconsidering dual-systems models of brain function in adolescence and disorders. *Trends in Cognitive Sciences, 16*(6), 322-329.

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage, 16*(2), 331-348.

Piccoli, T., Valente, G., Linden, D. E., Re, M., Esposito, F., Sack, A. T., & Di Salle, F. (2015). The default mode network and the working memory network are not anti-correlated during all phases of a working memory task. *PLoS One, 10*(4), e0123354. doi 0123310.0121371/journal.pone.0123354.

Power, J. D., Cohen, A. L., Nelson, S. M., Wig, G. S., Barnes, K. A., Church, J. A., Vogel, A. C., Laumann, T. O., Miezin, F. M., Schlaggar, B. L., & Petersen, S. E. (2011). Functional network organization of the human brain. *Neuron, 72*(4), 665-678.

Power, J. D., & Petersen, S. E. (2013). Control-related systems in the human brain. *Current Opinion in Neurobiology, 23*(2), 223-228.

Radua, J., Sarró, S., Vigo, T., Alonso-Lana, S., Bonnín, M. C., Ortiz-Gil, J., Canales-Rodríguez, E. J., Maristany, T., Vieta, E., Mckenna, P. J., Salvador, R., & Pomarol-Clotet, E. (2014). Common and specific brain responses to scenic emotional stimuli. *Brain structure & function, 219*(4), 1463-1472.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences USA, 98*(2), 676-682.

Richter, M., Eck, J., Straube, T., Miltner, W. H., & Weiss, T. (2010). Do words hurt? Brain activation during the processing of pain-related words. *Pain, 148*(2), 198-205.

Rissman, J., Gazzaley, A., & D'Esposito, M. (2004). Measuring functional connectivity during distinct stages of a cognitive task. *Neuroimage, 23*(2), 752-763.

Ritchey, M., LaBar, K. S., & Cabeza, R. (2011). Level of processing modulates the neural correlates of emotional memory formation. *Journal of Cognitive Neuroscience, 23*(4), 757-771.

Roy, M., Shohamy, D., & Wager, T. D. (2012). Ventromedial prefrontal-subcortical systems and the generation of affective meaning. *Trends in Cognitive Sciences, 16*(3), 147-156.

Russell, J. A. (1980). A circumplex model of affect. *Journal of Personality and Social Psychology, 39*(6), 1161-1178.

Russell, J. A. (2003). Core affect and the psychological construction of emotion. *Psychological Review, 110*(1), 145-172.

Russell, J. A., & Barrett, L. F. (1999). Core affect, prototypical emotional episodes, and other things called emotion: Dissecting the elephant. *Journal of Personality and Social Psychology, 76*(5), 805-819.

Schacter, D., Addis, D., & Buckner, R. (2007). Remembering the past to imagine the future: the prospective brain. *Nature reviews. Neuroscience, 8*(9), 657-661.

Schlochtermeier, L. H., Kuchinke, L., Pehrs, C., Urton, K., Kappelhoff, H., & Jacobs, A. M. (2013). Emotional picture and word processing: an FMRI study on effects of stimulus complexity. *PloS one, 8*(2), e55619. doi 55610.51371/journal.pone.0055619.

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., Reiss, A. L., & Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *The Journal of Neuroscience, 27*(9), 2349-2356.

Sergerie, K., Chochol, C., & Armony, J. L. (2008). The role of the amygdala in emotional processing: a quantitative meta-analysis of functional neuroimaging studies. *Neuroscience and Biobehavioral Reviews, 32*(4), 811-830.

Shafer, A., Iordan, A., Cabeza, R., & Dolcos, F. (2011). Brain imaging investigation of the memory-enhancing effect of emotion. *Journal of Visualized Experiements, 51*, doi 10.3791/2433.

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283*(5408), 1657-1661.

Smith, S., Fox, P., Miller, K., Glahn, D., Fox, P., Mackay, C., Filippini, N., Watkins, K., Toro, R., Laird, A., & Beckmann, C. (2009). Correspondence of the brain's functional architecture during activation and rest. *Proceedings of the National Academy of Sciences USA, 106*(31), 13040-13045.

Storbeck, J., & Maswood, R. (2015). Happiness increases verbal and spatial working memory capacity where sadness does not: Emotion, working memory and executive control. *Cognition & Emotion*, doi 10.1080/02699931.02692015.01034091.

Straube, T., Sauer, A., & Miltner, W. H. R. (2011). Brain activation during direct and indirect processing of positive and negative words. *Behavioural Brain Research, 222*(1), 66-72.

Sundstrom Poromaa, I., & Gingnell, M. (2014). Menstrual cycle influence on cognitive function and emotion processing-from a reproductive perspective. *Frontiers in Neuroscience, 8*, 380. doi 310.3389/fnins.2014.00380.

Thayer, R. E. (1989). *The biopsychology of mood and activation*. New York: Oxford University Press.

Touroutoglou, A., Lindquist, K. A., Dickerson, B. C., & Barrett, L. F. (2015). Intrinsic connectivity in the human brain does not reveal networks for 'basic' emotions. *Social Cognitive and Affective Neuroscience, 10*(9), 1257-1265.

van Ast, V. A., Spicer, J., Smith, E. E., Schmer-Galunder, S., Liberzon, I., Abelson, J. L., & Wager, T. D. (2014). Brain mechanisms of social threat effects on working memory. *Cerebral Cortex, 26*(2), 544-556.

Vrtička, P., Sander, D., & Vuilleumier, P. (2011). Effects of emotion regulation strategy on brain responses to the valence and social content of visual scenes. *Neuropsychologia, 49*(5), 1067-1082.

Vytal, K., & Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: a voxel-based meta-analysis. *Journal of Cognitive Neuroscience, 22*(12), 2864-2885.

Wager, T. D., Davidson, M. L., Hughes, B. L., Lindquist, M. A., & Ochsner, K. N. (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron, 59*(6), 1037-1050.

Wager, T. D., Phan, K. L., Liberzon, I., & Taylor, S. F. (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. *NeuroImage, 19*(3), 513-531.

Wang, L., McCarthy, G., Song, A. W., & Labar, K. S. (2005). Amygdala activation to sad pictures during high-field (4 tesla) functional magnetic resonance imaging. *Emotion, 5*(1), 12-22.

Warren, D. E., Power, J. D., Bruss, J., Denburg, N. L., Waldron, E. J., Sun, H., Petersen, S. E., & Tranel, D. (2014). Network measures predict neuropsychological outcome after brain injury. *Proceedings of the National Academy of Sciences of the USA, 111*(39), 14247-14252.

Watson, D., & Naragon-Gainey, K. (2010). On the specificity of positive emotional dysfunction in psychopathology: Evidence from the mood and anxiety disorders and schizophrenia/schizotypy. *Clinical Psychology Review, 30*(7), 839-848.

Watson, D., & Tellegen, A. (1985). Toward a consensual structure of mood. *Psychological Bulletin, 98*(2), 219-235.

Waugh, C. E., & Koster, E. H. (2014). A resilience framework for promoting stable remission from depression. *Clinical Psychology Review, 41*(2015), 49-60.

Yamasaki, H., LaBar, K. S., & McCarthy, G. (2002). Dissociable prefrontal brain systems for attention and emotion. *Proceedings of the National Academy of Sciences of the United States of America, 99*(17), 11447-11451.

Yang, H., Yang, S., & Isen, A. M. (2013). Positive affect improves working memory: Implications for controlled cognitive processing. *Cognition and Emotion, 27*(3), 474-484.

Yarkoni, T., Poldrack, R. A., Nichols, T. E., Van Essen, D. C., & Wager, T. D. (2011). Large-scale automated synthesis of human functional neuroimaging data. *Nature Methods, 8*(8), 665-670.

Yeo, B. T., Krienen, F., Sepulcre, J., Sabuncu, M., Lashkari, D., Hollinshead, M., Roffman, J., Smoller, J., Zöllei, L., Polimeni, J., Fischl, B., Liu, H., & Buckner, R. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*(3), 1125-1165.

Tables

Table 2.1. Scores for Working Memory Performance.

	% Hits	% Misses	% False Alarms	% Correct Rejections	% Average Correct
Positive	**78.60%**	**21.40%**	**16.84%**	**83.16%**	**80.88%**
Negative	**71.91%**	**28.09%**	**20.61%**	**79.39%**	**75.65%**
Positive & High Arousal	78.65%	21.35%	13.46%	86.54%	82.60%
Positive & Low Arousal	78.55%	21.45%	20.23%	79.77%	79.16%
Negative & High Arousal	68.94%	31.06%	14.48%	85.52%	77.23%
Negative & Low Arousal	74.88%	25.12%	26.74%	73.26%	74.07%
Neutral	79.28%	20.72%	24.87%	75.13%	77.21%
No Distraction	69.25%	30.75%	16.67%	83.33%	76.29%

The text in bold font denotes the average WM scores in the presence of positive and negative distraction, regardless of arousal.

Table 2.2. Brain Regions Showing Valence-Driven Effects.

Brain Regions			BA	x	y	z			Cluster size
				x	*y*	*z*			
DES: Greater Deactivation to Neg							Neg < Pos	Neg < Ctrl	
LPC	R	Inferior Parietal Lobule	40	43	-48	53	5.86	4.43	24
	R	Inferior Parietal Lobule	7	35	-59	48	3.34	3.23	
PCC	L/R	Cingulate Gyrus	31	-5	-42	34	3.43	2.85	12
mOC	L/R	Cuneus	7	-2	-68	32	5.19	4.25	45
VAS: Increased Activity to Pos							Pos > Neg	Pos > Ctrl	
mPFC	L/R	Medial Frontal Gyrus	9	-5	56	29	4.43	6.39	83
vlPFC	R	Inferior Frontal Gyrus	9	51	7	26	4.87	3.74	110
PrCG	R	Precentral Gyrus	6/4	50	-10	46	4.93	4.35	
PoCG	R	Postcentral Gyrus	2	54	-25	44	4.52	3.21	20
SPC	R	Superior Parietal Lobule	7	20	-63	54	4.80	5.47	42
	R	Precuneus	7	21	-58	37	3.62	3.44	
TOC	L	Fusiform Gyrus	37	-42	-44	-24	9.82	10.20	997
	L	Fusiform Gyrus	19	-45	-67	-15	7.90	9.88	
	L	Middle Temporal Gyrus	37	-42	-58	3	4.26	5.43	
OC	L	Middle Occipital Gyrus	18	-42	-79	-9	8.19	13.82	
	L	Inferior Occipital Gyrus	18	-23	-87	-6	5.04	13.52	
	L	Cuneus	19	-20	-84	34	5.69	5.25	
Cerebellum	L	Declive		-23	-71	-15	4.60	8.27	
TOC	R	Fusiform Gyrus	37	40	-49	-16	8.58	9.96	1248
	R	Fusiform Gyrus	19	36	-76	-11	5.59	11.60	
	R	Middle Temporal Gyrus	37	43	-55	5	6.40	6.41	
OC	R	Middle Occipital Gyrus	18	28	-77	6	6.01	9.50	
	R	Middle Occipital Gyrus	19	39	-70	4	5.61	7.77	
	R	Cuneus	19	21	-87	31	4.99	6.13	
	R	Lingual Gyrus	18	25	-91	-6	6.30	16.51	
PCC	L/R	Posterior Cingulate	30/23	-5	-63	11	5.33	3.40	
Cerebellum	R	Declive		17	-71	-15	4.95	7.07	
DMN: Greater Deactivation to Neg							Neg < Pos	Neg < Ctrl	
vmPFC/vACC	L/R	Medial Frontal Gyrus/							
		Anterior Cingulate	10/32	3	47	7	6.62	3.68	118
	L/R	Anterior Cingulate	32	-1	39	13	6.68	5.72	
LTC	L	Middle Temporal Gyrus	21	-60	-15	-11	3.46	2.71	12
lPOC	L	Angular Gyrus	39	-42	-68	28	3.93	2.78	19
lPOC	R	Angular Gyrus	39	43	-65	33	3.71	3.55	18
PCC	L/R	Cingulate Gyrus	31	-2	-43	42	3.50	3.13	89
mPOC	L/R	Precuneus	31	-2	-68	28	4.67	3.42	
mOC	L/R	Cuneus	19	-2	-76	35	3.64	3.63	
DMN: Increased Activity to Pos							Pos > Neg	Pos > Ctrl	
mPFC	L	Medial Frontal Gyrus	9	-5	52	29	4.18	4.18	11
TPC	L	Middle Temporal Gyrus	39	-46	-71	20	2.91	2.74	12
	R	Superior Temporal Gyrus	39	47	-60	19	3.86	5.52	27
PCC	L/R	Posterior Cingulate	30/23	-5	-59	11	4.99	3.72	57
PHC	L	Parahippocampal Gyrus	30	-12	-47	5	3.69	2.73	

Table 2.2. (continued). The table identifies brain regions showing valence-driven effects: i.e., specific increased or decreased responses to positive or negative distraction. Effects in the dorsal executive system (i.e., specific *de*activations for negative versus positive distraction), the ventral-affective system (i.e., specific *in*creased activity for positive versus negative distraction), and the default-mode network (i.e., deactivations or increased activity for positive versus negative distraction) were masked with the corresponding *a priori* functional masks for DES, VAS, and DMN (see Methods). *T*-values correspond to TR 9. Cluster size is in voxels. Significance threshold is $q < 0.05$ FDR-corrected. LPC, Lateral Parietal Cortex; PCC, Posterior Cingulate Cortex; mOC, Medial Occipital Cortex; mPFC, Medial Prefrontal Cortex; vlPFC, Ventro-Lateral Prefrontal Cortex; PrCG, Precentral Gyrus; PoCG, Postcentral Gyrus; SPC, Superior Parietal Cortex; TOC, Temporo-Occipital Cortex; vmPFC/vACC, Ventro-Medial Prefrontal/Ventral Anterior Cingulate Cortices; LTC, Lateral Temporal Cortex; lPOC, Lateral Parieto-Occipital Cortex; mPOC, Medial Parieto-Occipital Cortex; TPC, Temporo-Parietal Cortex; PHC, Parahippocampal Cortex; Pos, Positive; Neg, Negative; Ctrl, Control; BA, Brodmann Area; TR, Repetition Time.

Table 2.3. Brain Regions Showing Arousal-Driven Effects.

Brain Regions			BA	Talairach Coordinates			t Values		Cluster size
				x	y	z			
A. Specific Arousal Effects									
DES: None									
VAS: Increased Activity to AroHi							AroHi > AroLo	AroHi > Ctrl	
vlPFC	L	Inferior Frontal Gyrus	9	-38	4	27	4.50	4.97	16
	L	Inferior Frontal Gyrus	44	-49	12	21	3.44	2.47	
	R	Inferior Frontal Gyrus	46	47	31	10	3.34	5.27	8 [a]
		Inferior Frontal Gyrus	45/9	47	15	19	3.96	4.96	38
PCC	L/R	Posterior Cingulate	30/29	-5	-58	4	5.58	4.77	75
	R	Posterior Cingulate	23/30	10	-56	15	3.97	2.32	17
POC	R	Precuneus	7	24	-59	48	3.93	6.32	27
TOC	L	Fusiform Gyrus	20	-38	-41	-13	4.31	9.93	38
	L	Middle Temporal Gyrus	37	-49	-66	6	4.52	9.00	223
	L	Inferior Temporal Gyrus	37	-49	-69	-1	4.53	8.42	
OC	L	Middle Occipital Gyrus	19	-35	-82	19	5.67	7.56	
	L	Cuneus	7	-24	-79	31	5.31	8.87	
POC	R	Precuneus	19	17	-81	42	3.28	4.42	329
	R	Precuneus	31	24	-68	25	6.72	8.47	
TOC	R	Fusiform Gyrus	37	43	-61	-6	4.65	8.35	
	R	Middle Temporal Gyrus	19	39	-75	18	7.70	10.69	
	R	Middle Temporal Gyrus	39	43	-70	11	6.90	10.52	
	R	Middle Temporal Gyrus	37	51	-58	5	5.48	8.13	
	R	Inferior Temporal Gyrus	19	47	-54	2	5.60	6.04	
OC	R	Cuneus	7	21	-72	32	5.45	5.51	
Cerebellum	L	Culmen		-30	-59	-25	4.52	5.49	15
	L	Declive		-16	-71	-22	3.90	3.90	
DMN: None									
B. Generic Arousal Effects [b]									
DES: Overlapping Deactivations to Pos and Neg							Pos < Ctrl	Neg < Ctrl	
aPFC	L	Middle Frontal Gyrus	10	-34	46	13	4.42	4.93	19
	R	Middle Frontal Gyrus	10	40	41	25	4.05	5.87	22
LPC	L	Superior Parietal Lobule	7	-43	-63	50	4.54	6.84	18
	L	Inferior Parietal Lobule	40	-46	-54	36	4.16	8.65	
	R	Superior Parietal Lobule	7	39	-59	48	4.14	7.77	20
	R	Inferior Parietal Lobule	39/40	39	-66	40	4.37	8.17	
VAS: Overlapping Increased Activity to Pos and Neg [c]							Pos > Ctrl	Neg > Ctrl	
MTL	L	Amygdala		-23	1	-19	4.85	4.71	11
	R	Amygdala		21	-8	-9	2.83	4.15	11
	L	Hippocampus		-27	-23	-7	5.90	4.67	87
	R	Hippocampus		25	-11	-16	5.09	2.43	56
Subcortical	L	Thalamus		-16	-32	3	7.34	5.77	18
	R	Thalamus		17	-28	4	6.67	6.24	34
DMN: None									

Table 2.3. (continued). The table identifies (A) brain regions showing specific arousal-driven effects (i.e., specific increased or decreased responses to high or low-arousing distraction, regardless of their valence) and (B) additional brain regions showing only generic arousal-driven effects (i.e., overlapping responses to both positive and negative distraction, regardless of their arousal). Regarding (A), specific arousal-driven effects were targeted in the dorsal executive system (i.e., specific *de*activations for high- versus low-arousing distraction), the ventral-affective system (i.e., specific *in*creased activity for high- versus low-arousing distraction), and the default-mode network (i.e., deactivations or increased activity for high- versus low-arousing distraction). Regarding (B), additional generic arousal-driven effects were identified in specific DES (i.e., overlapping *de*activations to both positive and negative distraction) and VAS (i.e., overlapping *in*creased activity to both positive and negative distraction) regions. Similar to the findings reported in Table 2.2, these effects were masked by their corresponding *a priori* functional masks (see Methods). *T*-values correspond to TR 9. Cluster size is in voxels. Significance threshold is *q* < 0.05 FDR-corrected. vlPFC, Ventrolateral Prefrontal Cortex; PCC, Posterior Cingulate Cortex; POC, Parieto-Occipital Cortex; TOC, Temporo-Occipital Cortex; OC, Occipital Cortex; aPFC, Anterior Prefrontal Cortex; LPC, Lateral Parietal Cortex; MTL, Medial Temporal Lobe; AroHi, High Arousal; AroLo, Low Arousal; Pos, Positive; Neg, Negative; Ctrl, Control; BA, Brodmann Area; TR, Repetition Time.

[a]Exception (cluster size < 10 voxels). [b]Additional regions which show generic but not specific arousal-driven effects; [c]Subcortical clusters were isolated using WFU PickAtlas/AAL (Tzourio-Mazoyer et al., 2002), and their sizes represent the number of active voxels within each anatomical region.

Table 2.4. Brain Regions Showing Overlapping Valence and Arousal-Driven Effects.

Brain Regions			BA	Talairach Coordinates			t Values				Cluster size
				x	y	z					
A. Overlapping Valence and Specific Arousal Effects											
DES: None											
VAS: Overlapping Increased Activity to Pos and AroHi							Pos > Neg	Pos > Ctrl	AroHi > AroLo	AroHi > Ctrl	
vlPFC	R	Inferior Frontal Gyrus	9	47	7	26	4.03	5.07	2.83	5.14	10
SPC	R	Superior Parietal Lobule	7	20	-63	54	4.80	5.47	2.91	4.65	25
PCC	L	Posterior Cingulate	30	-5	-59	11	4.99	3.72	3.42	3.70	22
TOC	L	Fusiform Gyrus	37	-38	-44	-24	9.26	9.63	2.87	9.15	33
	L	Fusiform Gyrus	20	-34	-37	-16	4.87	8.38	3.56	7.50	
	L	Middle Temporal Gyrus	19	-35	-78	20	2.41	5.67	5.16	6.89	178
	L	Middle Occipital Gyrus	19	-42	-74	9	4.27	7.58	3.78	6.70	
OC	L	Cuneus	19	-20	-84	34	5.69	5.25	3.91	5.57	
POC	R	Precuneus	31	24	-68	25	3.20	7.48	6.72	8.47	296
	R	Precuneus	19	17	-81	42	3.99	4.32	3.28	4.42	
TOC	R	Middle Temporal Gyrus	37	43	-55	5	6.40	6.41	5.37	6.67	
	R	Middle Temporal Gyrus	39	47	-70	11	4.45	8.74	6.11	10.46	
	R	Fusiform Gyrus	37	40	-49	-12	6.19	11.47	3.20	9.82	
	R	Fusiform Gyrus	19	40	-64	-10	5.73	10.34	3.09	9.86	
OC	R	Cuneus	7	21	-76	32	4.87	5.52	4.76	5.46	
Cerebellum	L	Culmen		-30	-59	-25	3.18	5.20	4.52	5.49	11
DMN: None											
B. Overlapping Valence and Generic Arousal Effects [a]											
DES: None											
VAS: Overlapping Increased Activity to Pos and Generic Arousal Response [b]							Pos > Neg	Pos > Ctrl	Neg > Ctrl		
MTL	L	Hippocampus		-27	-23	-11	2.63	4.59	3.00		34
	R	Hippocampus		25	-11	-16	3.10	5.09	2.43		10
Subcortical	L	Thalamus		-16	-24	0	2.72	4.18	3.42		13
DMN: None											

The table identifies brain regions showing overlapping valence and arousal effects: i.e., increased or decreased responses to positive versus negative distraction, in regions also showing (A) specific and (B) generic sensitivity to arousal (see Tables 2.2 and 2.3A, B). Also, similar to the findings reported in Tables 2.2 and 2.3, these effects were masked by their corresponding *a priori* functional masks (see Methods). *T*-values correspond to TR 9. Cluster size is in voxels. Significance threshold is $q < 0.05$ FDR-corrected. vlPFC, Ventrolateral Prefrontal Cortex; SPC, Superior Parietal Cortex; PCC, Posterior Cingulate Cortex; TOC, Temporo-Occipital Cortex; POC, Parieto-Occipital Cortex; OC, Occipital Cortex; Pos ,Positive; Neg, Negative; AroHi, High Arousal; AroLo, Low Arousal; Ctrl, Control; BA, Brodmann Area; TR, Repetition Time. [a]Additional regions showing overlaps between valence and generic (i.e., not specific) arousal effects;

Table 2.4. (continued). [b]Subcortical clusters were isolated using WFU PickAtlas/AAL (Tzourio-Mazoyer et al., 2002), and their sizes represent the number of active voxels within each anatomical region.
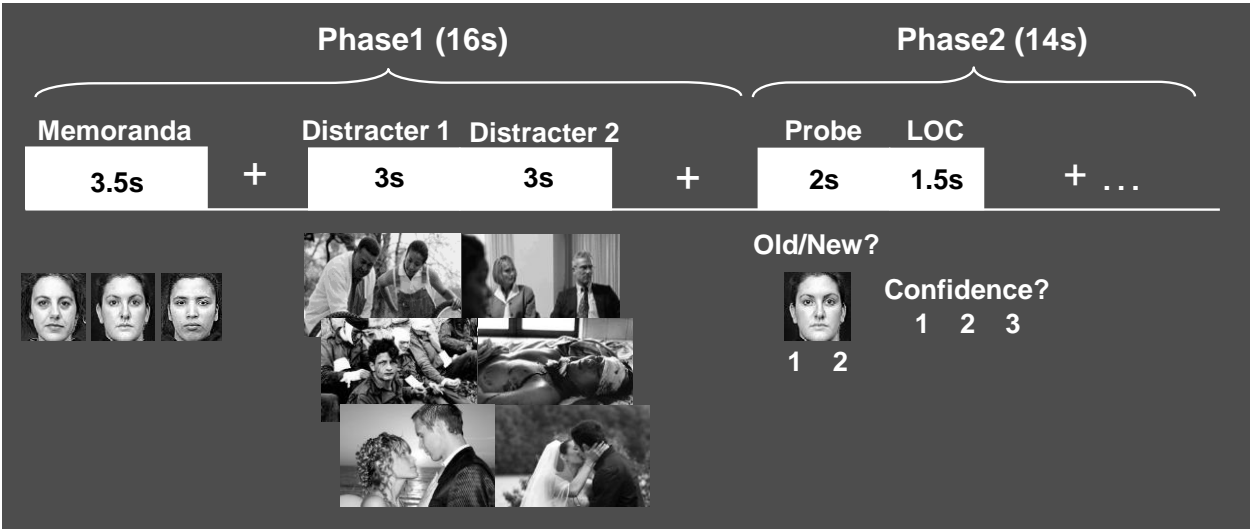
Figures

Figure 2.1. Diagram of the working memory (WM) task with emotional distraction. Functional magnetic resonance imaging (fMRI) data were recorded while subjects performed a WM task for faces, with distracters presented during the delay interval between the memoranda and the probes. The WM performance was measured using a recognition memory task, in which participants indicated by pushing a button whether single-face probes were part of the memoranda (*Old* = 1) or not (*New* = 2), and then they indicated their level of confidence (LOC) in their responses by pushing one of three buttons (1 = low, 2 = medium, 3 = high). All stimuli were presented in color. [Bottom wedding photos credits: Beercha (left) and Steve Evans (right). Licensed under Creative Common Attribution 2.0 Generic license (https://creativecommons.org/licenses/by/2.0/deed.en; last accessed: Oct 17, 2015). Pictures were converted to grayscale.]
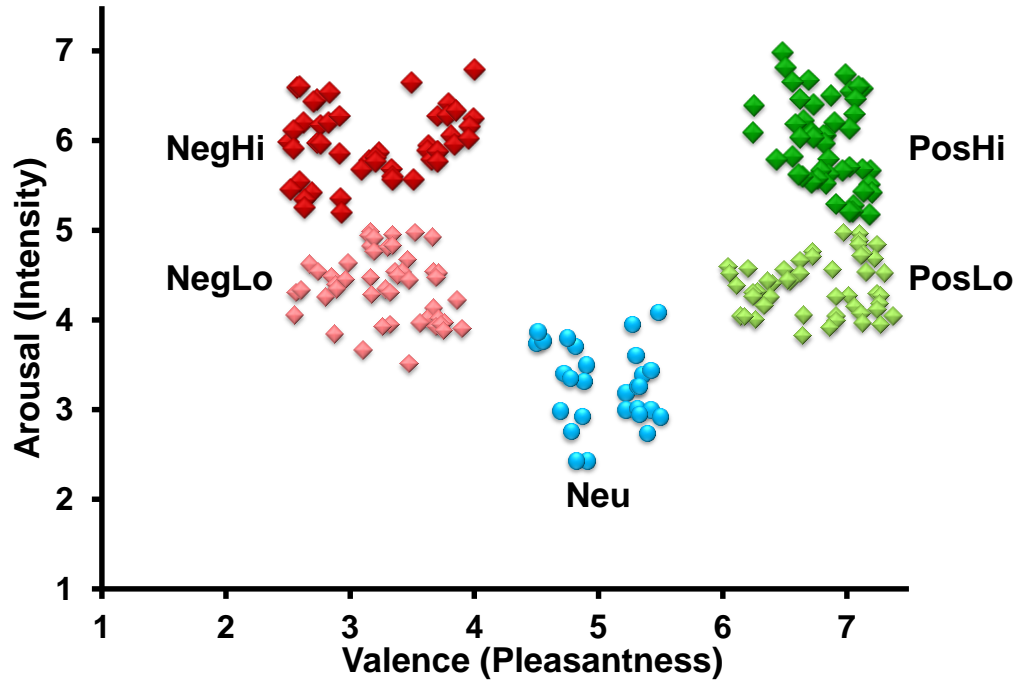
Figure 2.2. **Distracter pictures in the valence × arousal space.** Five non-overlapping categories of stimuli were selected from the International Affective Picture System (IAPS, Lang et al., 2008): negative high (NegHi) and low (NegLo) arousing, positive high (PosHi) and low (PosLo) arousing, and absolute neutral (Neu). High- and low-arousal emotional stimuli were matched for valence and negative and positive stimuli were matched for arousal.
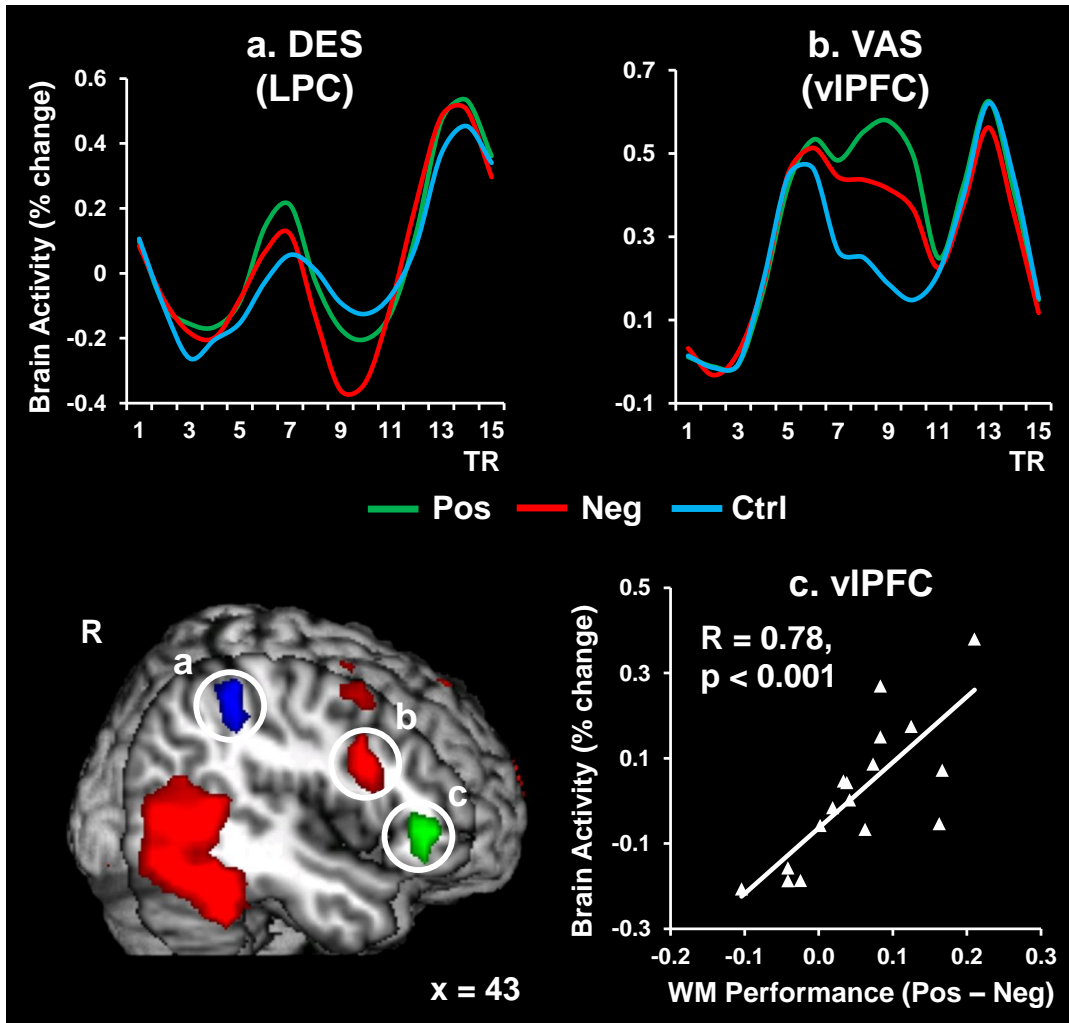
Figure 2.3. Valence-related differences in the activity of DES and VAS regions. Negative distraction was associated with greater deactivation in (a) DES regions (LPC, blue area), whereas positive distraction was associated with increased activity in (b) VAS regions (vlPFC, red area). Also, increased activity in a more inferior vlPFC sub-region (c, green area), was associated with increased WM performance for positive relative to negative distraction. Of note, valence effects overlapped with arousal-driven responses in the vlPFC (b and see Supplementary Figure 2.2). The line graph in (a) displays the time course of brain activity extracted from the peak voxel of the Pos versus Neg comparison (Talairach coordinates: $x = 43$, $y = -48$, $z = 53$).

Figure 2.3. (continued). The line graph in (b) displays the time course of brain activity extracted from the peak voxel of the overlap between the Pos versus Neg comparison and HiAro versus LoAro comparison in the vlPFC (see main text and Supplementary Figure 2.2; Talairach coordinates: $x = 47$, $y = 7$, $z = 26$). The scatterplot in (c) displays the brain-behavior covariation extracted from the peak voxel of the correlation (Talairach coordinates: $x = 40$, $y = 28$, $z = 9$) (two-tailed). The maps showing differences in activity are displayed at $q < 0.05$ FDR-corrected, and the map showing the brain-behavior covariation is displayed at $p < 0.005$. DES, Dorsal Executive System; VAS, Ventral Affective System; LPC, Lateral Parietal Cortex; vlPFC, Ventro-Lateral Prefrontal Cortex; Pos, Positive; Neg, Negative; Ctrl, Control; WM, Working Memory; TR, Repetition Time (2 s); R, Right.
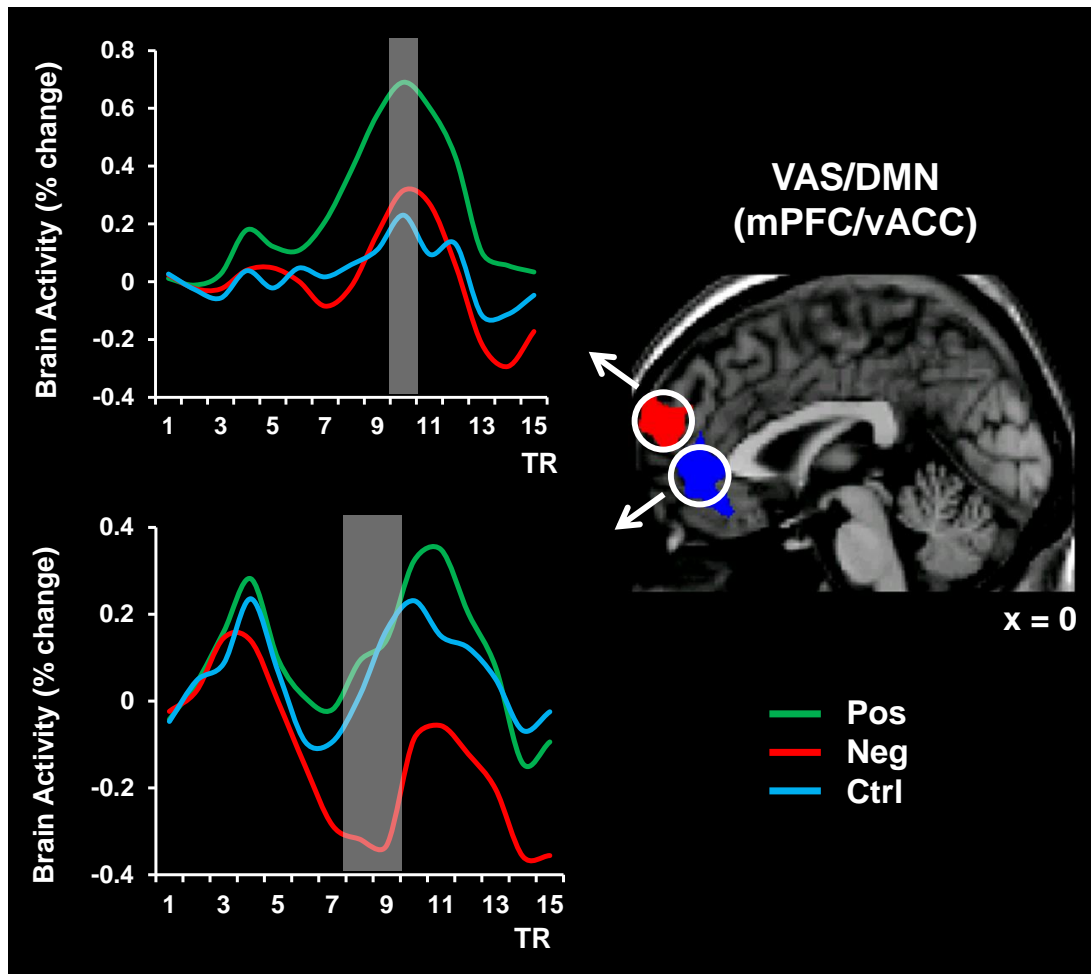
Figure 2.4. Rostro-caudal dissociation in the medial frontal cortex in response to positive and negative distraction. A more rostral mPFC area (BA 9, red area) showed increased activity for positive distraction, whereas a more caudal mPFC/vACC area (BA 10/32, blue area) showed specific deactivation to negative distraction. The line graphs display the time course of brain activity extracted from the peak voxel of the Pos vs. Neg comparison (Talairach coordinates: $x = -5$, $y = 56$, $z = 29$ for the red area, and $x = 3$, $y = 47$, $z = 7$ for the blue area). The grey rectangles highlight the time points (TRs) when the peak difference between Pos and Neg distraction-related activity occurred. All maps are displayed at $q < 0.05$ FDR-corrected. mPFC/vACC, Medial Prefrontal Cortex/Ventral Anterior Cingulate Cortex; Pos, Positive; Neg, Negative; Neu, Neutral; Ctrl, Control; TR, Repetition Time (2 s).
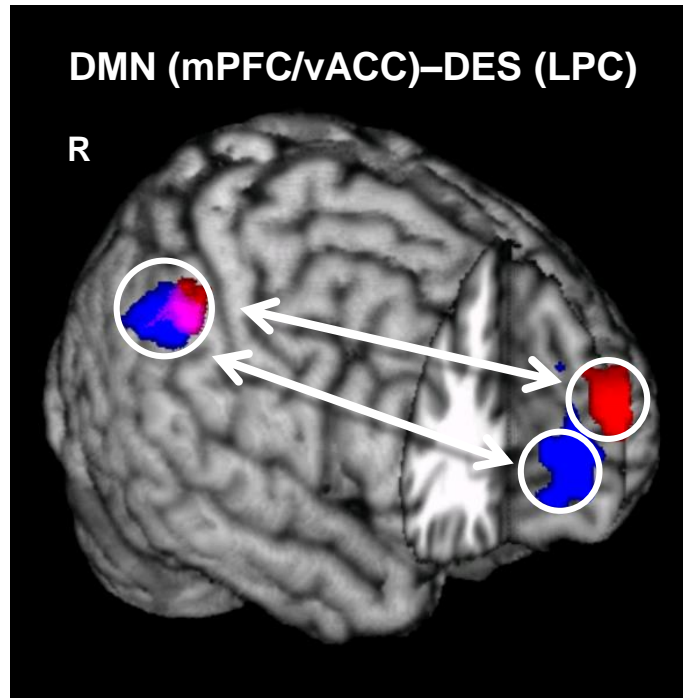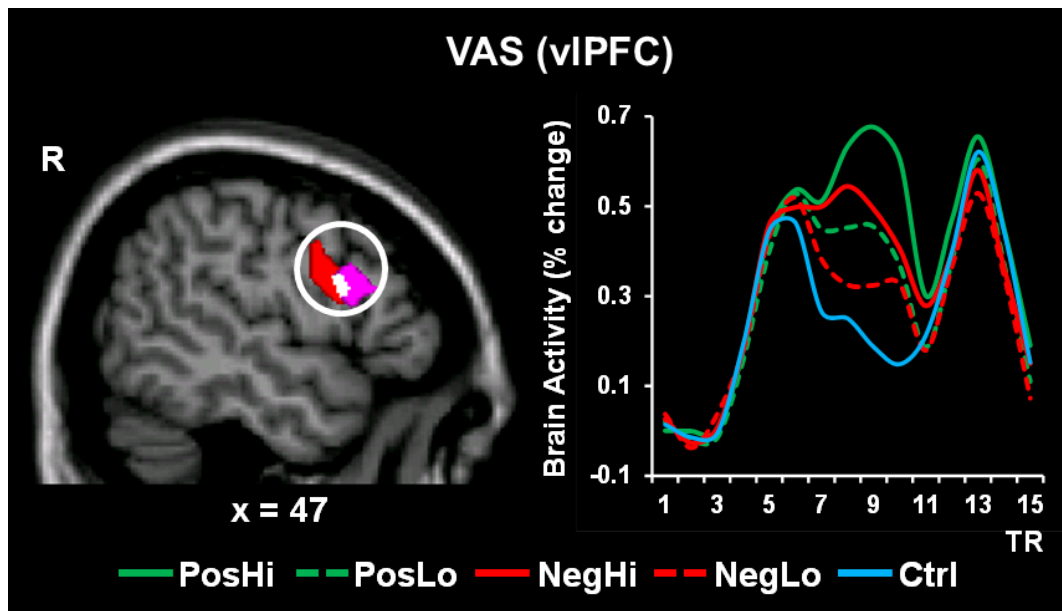
Figure 2.5. Valence-related dissociations in functional connectivity between DMN and DES regions. The two mPFC sub-regions, part of the default mode network (DMN), showing valence-related effects (see Figure 2.4) also showed increased functional connectivity with LPC, part of the dorsal executive system (DES), under negative distraction. Both rostral (red) and caudal (blue) medial frontal sub-regions showed increased connectivity with the LPC areas (red and blue areas, respectively; overlap displayed in magenta), which showed deactivation to negative distraction. The maps showing differences in activation are displayed at $q < 0.05$ FDR-corrected, and the maps showing functional connectivity are displayed at $p < 0.005$. LPC, Lateral Parietal Cortex; mPFC/vACC, Medial Prefrontal Cortex/Ventral Anterior Cingulate Cortex.
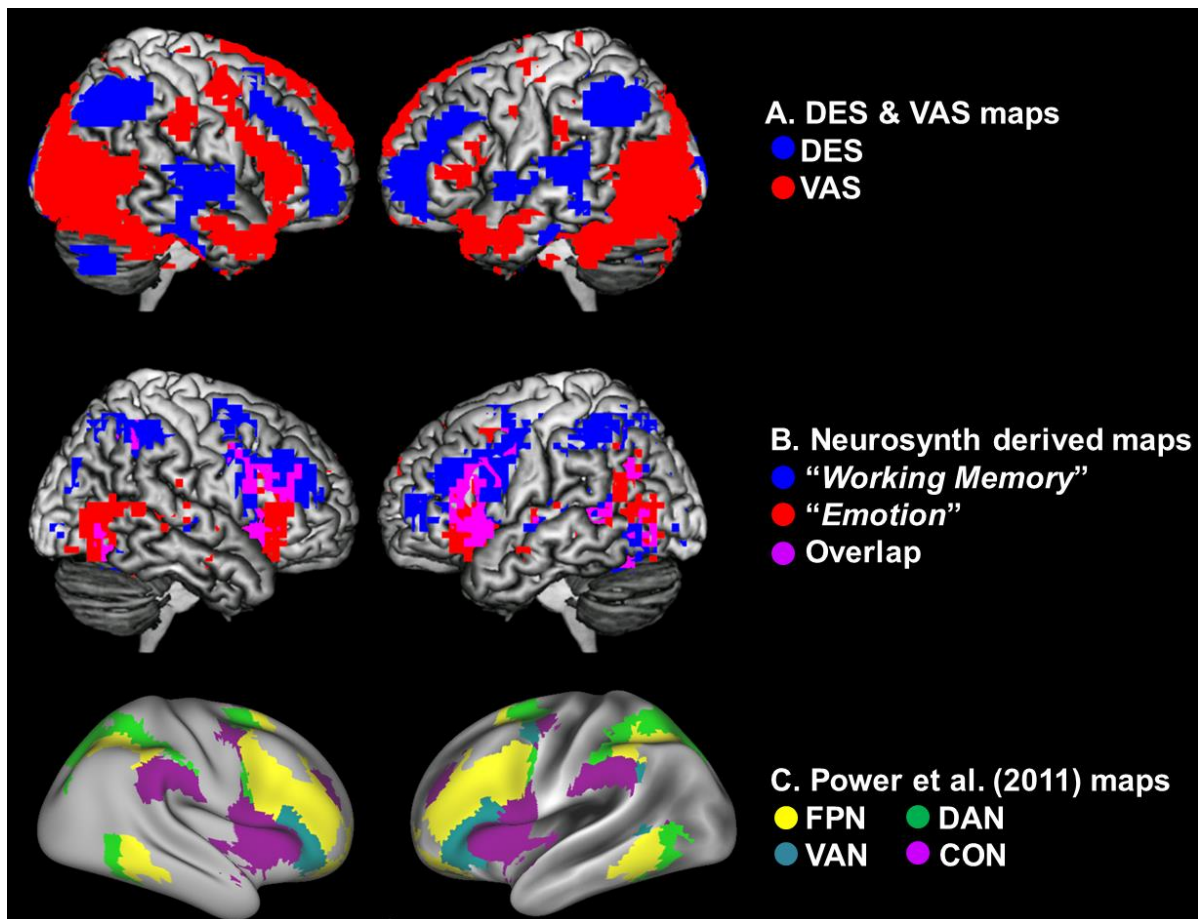
Supplementary Figure 2.1. Similarities among the task-induced DES-VAS dissociation, meta-analytical evidence, and large-scale networks. (A) The top panel displays the employed DES and VAS maps, obtained by contrasting the most dissimilar conditions in the Dolcos and McCarthy (2006) study: i.e., Scrambled > Negative, to identify regions of DES, and Negative > Scrambled, to identify regions of VAS. Both maps were thresholded at $q < 0.05$, FDR-corrected. (B) The middle panel displays the maps derived by meta-analyses performed with Neurosynth (Yarkoni et al., 2011) for "working memory" (blue) and "emotion" (red); the overlap between these two maps is displayed in magenta (forward inference maps, thresholded at $q < 0.01$, FDR-corrected; this threshold is the lowest default with Neurosynth).

Supplementary Figure 2.1. (continued). (C) The bottom panel displays the "dorsal" FPN (yellow) and DAN (green) networks and the "ventral" VAN (teal) and CON (magenta) networks based on the Power et al. (2011) paper. As illustrated, similarities/overlaps are particularly obvious in dlPFC and LPC and anterior vlPFC, across all three displays. Of note, the dissociation between VAN and CON in the PFC portion of VAS is consistent with the idea of subregional specificity within the IFG. DES, Dorsal Executive System; VAS, Ventral Affective System; FPN, Fronto-Parietal Network; DAN, Dorsal Attention Network; VAN, Ventral Attention Network; CON, Cingulo-Opercular Network; dlPFC, Dorso-Lateral Prefrontal Cortex; LPC, Lateral Parietal Cortex; vlPFC, Ventro-Lateral PFC; IFG, Inferior Frontal Gyrus.

Supplementary Figure 2.2. Overlapping and dissociable arousal and valence-related effects in the vlPFC. Although the arousal and valence-related effects in the vlPFC partially overlapped (white area), a relative segregation could also be observed, with valence-related effects (red area) being slightly more posterior and lateral than the arousal-driven effects (magenta area). A more rostral vlPFC area also showed arousal-driven effects, but did not meet the extent threshold (8 voxels). The line graph displays the time course of brain activity extracted from the peak voxel of the overlapping area (white) in the vlPFC (Talairach coordinates: $x = 47$, $y = 7$, $z = 26$; see also main text and Figure 2.3). Of note, these overlapping valence and arousal-driven responses were observed in the absence of significant arousal $\times$ valence interactions (see main text), which indicates that the contributions of valence and arousal in this region are additive rather than interactive. All maps are displayed at $q < 0.05$ FDR-corrected. vlPFC, Ventro-Lateral Prefrontal Cortex; Pos, Positive; Neg, Negative; AroHi, High Arousal; AroLo, Low Arousal; PosHi, Positive and High Arousal; PosLo, Positive and Low Arousal; NegHi, Negative and High Arousal; NegLo, Negative and Low Arousal; Ctrl, Control; TR, Repetition Time (2 s).

CHAPTER 3:

SEX DIFFERENCES IN THE RESPONSE TO

EXTERNAL EMOTIONAL DISTRACTION

Sex Differences in the Response to Emotional Distraction:

An Event-Related fMRI Investigation

Introduction

Probably due to their enhanced relevance for survival, emotional stimuli tend to capture our attention more easily than do neutral ones, and thus they can be powerful distracters, particularly if task-irrelevant. Because people vary in their response to and ability to cope with emotional distraction, goal-irrelevant emotions may impact them differently. The present study focused on sex differences in the response to emotional distraction. Although the available anecdotal and scientific evidence suggests that women and men may respond differently to emotional situations, it is still unclear whether differences in emotional reactivity are also associated with differences in emotional distractibility, and whether men and women engage similar or dissociable mechanisms in their responses to emotional distraction. Previous studies involving dual-task paradigms with emotional distraction that have allowed for clear dissociations of the time courses of response in the ventral-affective and dorsal-cognitive brain systems have included only female subjects (Denkova et al., 2010; Dolcos, Diaz-Granados, Wang, & McCarthy, 2008; Dolcos, Kragel, Wang, & McCarthy, 2006; Dolcos & McCarthy, 2006). Hence, it is not clear whether the observed effects could also be extended to males. For the present investigation, we used functional magnetic resonance imaging (fMRI) in conjunction with behavioral measures to investigate how emotional distraction impairs cognition in women and men, as well as the neutral mechanisms associated with these effects. The main questions concerned the link between emotional reactivity and emotional distraction – specifically, whether the enhanced emotional reactivity observed in female subjects is linked to enhanced emotional distractibility – and identifying the neural mechanisms that implement differences in emotional distractibility between women and men. Investigation of these issues in nonclinical individuals has potential implications for a better understanding of these phenomena as independent or

correlated factors contributing to differential vulnerability to affective disorders in women and men.

Behavioral and brain-imaging evidence has suggested that enhanced emotional reactivity in women may also lead to enhanced emotional distractibility. The available evidence has shown that in addition to enhanced emotional competence (Barrett, 2000; Kring & Gordon, 1998; Seidlitz & Diener, 1998), women also show enhanced reactivity to emotional challenge (Hamann & Canli, 2004; Lang, Greenwald, Bradley, & Hamm, 1993; Shields, 1991), specificity in the deployment of emotion regulation strategies (Denkova, Dolcos, & Dolcos, 2012; Domes et al., 2010; Mak, Hu, Zhang, Xiao, & Lee, 2009; Matud, 2004; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008; Thayer, Rossy, Ruiz-Padial, & Johnsen, 2003), and increased susceptibility to affective disorders (i.e., a lifetime prevalence of mood and anxiety disorders nearly two times higher than that of men) (Bekker & van Mens-Verhulst, 2007; Kessler, 2003). Evidence from brain-imaging studies points to sex-related differences, primarily in the brain regions associated with emotion processing, such as the amygdala (AMY) and the orbitofrontal cortex (OFC) (Goldstein et al., 2001; Gur, Gunning-Dixon, Bilker, & Gur, 2002), but differences in brain regions associated with the cognitive control of emotion, such as the prefrontal cortex (PFC) (Koch et al., 2007; McRae et al., 2008), have also been identified. This evidence raises the possibility that the same mechanisms that help generate the enhanced emotional experience in women could also be partially responsible for enhanced sensitivity to emotional factors. However, in these previous investigations, the emotional stimuli have been task-relevant, and thus it is not known whether similar effects are produced when the emotional information is presented as task-irrelevant distraction.

Brain-imaging studies in which emotional information has been presented as transient distraction have proved informative in identifying the neural circuitry related to the impact of emotional distraction on ongoing cognitive processes, as well as the neural correlates of coping with distracting emotions (reviewed in Dolcos, Iordan, & Dolcos, 2011). In a series of studies by Dolcos and colleagues, the neural correlates that mediate emotion–cognition interactions were investigated using a paradigm in which emotional task-irrelevant distracters were presented during the delay interval of a working memory (WM) task (Dolcos et al., 2008; Dolcos et al., 2006; Dolcos & McCarthy, 2006; Dolcos, Miller, Kragel, Jha, & McCarthy, 2007). The main finding of these studies was that the impairing effect of emotional distraction was linked to opposing patterns of activity in a ventral affective system (VAS), associated with "hot" emotion processing, and a dorsal executive system (DES), associated with "cold" executive processing. Specifically, emotional distracters enhanced activity in emotion-processing regions such as AMY, the ventrolateral prefrontal cortex (vlPFC), and medial PFC, while disrupting delay activity in dorsal executive brain regions such as the dorsolateral PFC (dlPFC) and the lateral parietal cortex (LPC). Given the role of the latter brain regions in attentional processes and active maintenance of goal-relevant information in WM (D'Esposito, Postle, & Rypma, 2000; Hopfinger, Buonocore, & Mangun, 2000; Levy & Goldman-Rakic, 2000; Miller & Cohen, 2001), these findings suggest that activity in the affective and executive neural systems is strongly interconnected, such that increased activity in the ventral affective regions disrupts activity in the dorsal system and results in cognitive impairment.

Evidence from follow-up investigations (Denkova et al., 2010) showed that these opposite patterns of activity in the ventral and dorsal neural systems in the presence of emotional distraction that induces general negative affect (pictures from the International Affective Picture

System) (Lang et al., 1993) were also observed with stimuli that induced specific emotions (i.e., angry faces) in female subjects. Employing an adapted version of the WM task with distraction used by Dolcos & McCarthy (2006), the study of Denkova et al. (2010) provided support for the idea that the impact of angry faces used as distracters is mainly linked to bottom-up effects. These effects were reflected in enhanced activity in brain regions associated with visual and emotional processing (fusiform gyrus [FG] and AMY) and in regions associated with self-referential processing and experiencing of emotion (ventromedial PFC [vmPFC]), which diverts attention from the main WM task and leads to impaired performance.

The vmPFC is part of the so-called default-mode network, which shares common regions with the ventral affective network. Anatomically, the default-mode network comprises mainly midline cortical structures, such as the medial PFC and the posterior parietal cortex (PPC), along with lateral parietal (LPC) and superior temporal cortex (STC) (Buckner, Andrews-Hanna, & Schacter, 2008; Raichle et al., 2001). The default-mode network is involved in self-referential processing (Northoff & Bermpohl, 2004; Northoff et al., 2006), including focus on autobiographical memories (Svoboda, McKinnon, & Levine, 2006), planning for the future (D'Argembeau et al., 2010; Schacter, Addis, & Buckner, 2007), and evaluating the salience of internal and external cues (Phan et al., 2004). In addition, previous evidence has suggested that the default-mode network is also involved in emotion processing (Harrison et al., 2008; Pitroda, Angstadt, McCloskey, Coccaro, & Phan, 2008; Wiebking et al., 2011) and in affective decision making (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Ochsner et al., 2004). Typically, the default-mode network shows increased activity during rest and displays *de*activation from its resting state in response to external attention-demanding tasks (Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001). While the evidence suggests that default-

mode network resting state activity does not differ between women and men (Weissman-Fogel, Moayedi, Taylor, Pope, & Davis, 2010), it is possible that areas of the default-mode network are differentially engaged in the context of transient emotional distraction.

The study by (Denkova et al., 2010) identified changes in VAS and DES regions and in areas of the default-mode network (i.e., vmPFC) in response to emotional distraction, but this study involved only female subjects. Hence, it is not clear whether similar effects would also be observed in males, and whether women and men differ both in the detrimental impact of emotional distraction and in the engagement of the cognitive control mechanisms needed to cope with the presence of emotional distraction. Therefore, the main goals of the present study were to determine whether sex differences in basic emotional reactivity are associated with differences in emotional distractibility, and to identify the neural mechanisms that implement differences in emotional distractibility between women and men. Brain activity was recorded using event-related fMRI while healthy male and female subjects performed a WM task with emotional distraction. The behavioral assessments involved measures of WM performance and subjective ratings of the distracters, along with measures of posttask affective states. To further investigate the significance of possible differences in behavior and brain activity, brain-behavior relationships were also investigated by calculating covariations between the brain responses to transient emotional distraction and WM performance.

From the extant evidence, we made the following three predictions: First, regarding behavioral performance, consistent with evidence of enhanced response in women when emotional information helps cognition (i.e., enhanced memory for emotional events) (Canli, Desmond, Zhao, & Gabrieli, 2002), we expected that women would also be more susceptible to the detrimental impact of emotional information, presented as task-irrelevant distraction

concurrent with a main cognitive task. Second, regarding the brain-imaging results, we expected that sex-related differences in the behavioral impact of emotional distraction would be linked to differences in both brain regions whose engagement reflects a detrimental impact of emotional distraction and brain regions engaged to cope with the presence of emotional distraction. Third, regarding the brain-behavior relationships, we expected that negative covariations between brain activity and WM performance would presumably be indicative of mechanisms whose engagement leads to detrimental effects of emotional distraction on performance, whereas positive covariations would be indicative of mechanisms engaged to counteract the negative impact of emotional distraction.

Methods

Subjects

A group of 36 healthy, young, right-handed adults (18-33 years of age, average = 22.86, SD = 3.89; 18 women, 18 men) participated in the study; the female sample overlapped with that of Denkova et al. (2010). The data from two female and two male subjects were excluded from analyses because of incompleteness (e.g., due to missing runs). Hence, the analyses reported here are based on data from 32 subjects (average age = 23.12, SD = 4.04; 16 women, 16 men). The women and men did not differ in age [$t_{(30)}$ = 0.61, p > 0.5]. The level-of-confidence data from two male subjects and emotional-ratings data from one female subject were not recorded due to technical problems, and hence could not be included in the corresponding analyses. The experimental protocol was approved by the Health Research Ethics Board at the University of Alberta, and all subjects provided written informed consent.

Stimuli

The subjects performed a delayed-response WM task for faces with emotional distraction, which had been used on only female subjects in our previous study (Denkova et al., 2010) (Figure 3.1). This is a modified version of our delayed-response WM task with distraction from Dolcos & McCarthy (2006), adapted to be used with angry-face distracters. The memoranda consisted of sets of three human faces (50 % female, 50 % male) (Chuah et al., 2010; Dolcos et al., 2008; Dolcos & McCarthy, 2006), chosen to maximize similarities, for increased task difficulty. The distracters, selected from the NimStim Face Stimulus Set (http://www.macbrain.org/resources.htm) (Tottenham, Borscheid, Ellertsen, Marcus, & Nelson, 2002), were presented during the delay interval between the memoranda and probes, and consisted of morphed angry faces, neutral faces, and scrambled faces (50 % female, and 50 % male). Morphed facial stimuli were used in order to induce responses closer to those of real-life social interactions; the morphing was performed using Winmorph (http://www.debugmode.com/winmorph/). The scrambled faces had the same average spatial frequency and luminance as the meaningful angry and neutral faces, and served as no-distraction perceptual controls. A total of 90 experimental trials, identified on the basis of types of distracters, were included, as follows: 30 with angry faces, 30 with neutral faces, and 30 with scrambled faces. All of the stimuli were presented in color.

Experimental Procedures

Six sets of 15 trials each were created (five angry, five neutral, and five scrambled faces per set) and randomly assigned to six experimental blocks/runs. To avoid induction of longer-lasting effects, the trials within each block were pseudorandomized, so that no more than two consecutive trials of the same type were presented. To prevent possible biases that could result

from using the same run order, the subjects were assigned different run orders; a total of six different run orders were involved. Each trial started with the presentation of face memoranda (3.5 s), which subjects were instructed to encode and maintain in WM during the delay interval between the offset of the memoranda and the onset of the memory probe (12.5 s). Presentation of novel distracters started 2.5 s after the offset of the memoranda and occurred for a total time of 5 s. All of the distracters started as static stimuli (either neutral or scrambled), and then after a short delay (1 s), they morphed for a 2-s period, which was followed by another static presentation of the final morphed faces (2 s). Half of the initially neutral faces morphed into angry faces, and the other half morphed into neutral faces. Also, to control for motion-related changes, half of the scrambled faces morphed into the corresponding scrambled angry faces, and the other half morphed into the corresponding scrambled neutral faces.

The subjects were instructed to look at the distracters but to maintain focus on the WM task, and when a single face probe appeared, they were to indicate by a button press whether the face was part of the current memorandum (old) or not (new); 50 % of the probes were old and 50 % were new. The subjects were instructed to make quick and accurate responses while the probes were on the screen, and then they also rated the level of confidence (LOC) of their responses, using a three-point Likert scale (1 = *lowest*, 3 = *highest*). The LOC rating was followed by a 10.5-s intertrial interval, so as to allow the hemodynamic response to return to baseline. The total length of each trial was 30 s. Following scanning, subjects performed an emotional-rating task, in which they had to rate how angry they perceived the emotional and neutral distracters to be, using a nine-point Likert scale (1= *not angry at all*, 9 = *very angry*). These ratings were assessed to confirm that the angry faces were perceived as being more emotional than the neutral faces, and to investigate possible sex-related differences in the ratings.

Finally, to assess changes in emotional states as a result of participating in the study, subjects completed the State scales of the Positive and Negative Affective Schedule (PANAS-S) (Watson, Clark, & Tellegen, 1988) and of the State-Trait Anxiety Inventory (STAI-S) (Spielberger, Gorsuch, & Lushene, 1970), at both the beginning and the end of the study.

Imaging Protocol

Scanning was conducted on a 1.5-T Siemens Sonata scanner. After the sagittal localizer and the 3-D MPRAGE anatomical images (TR = 1,600 ms; TE = 3.82 ms; FOV = 256 × 256 mm; volume size = 112 slices; voxel size = $1 \times 1 \times 1$ mm^3), six blocks of full-brain EPI functional images were acquired axially (TR = 2,000 ms; TE = 40 ms; FOV = 256 × 256 mm; volume size = 28 slices; voxel size = $4 \times 4 \times 4$ mm^3).

Behavioral Data Analyses

Responses in the WM task were classified into one of the four categories derived from signal detection theory (Macmillian & Creelman, 1991): (1) *hits* = probes from memoranda (old) correctly classified as "old"*; (2) *misses* = probes from memoranda incorrectly classified as "new"; (3) *correct rejections* (CRs) = new probes correctly classified as "new"; and (4) *false alarms* (FAs) = new faces incorrectly classified as "old". Corrected recognition scores (% Hits – % FAs) were also calculated for each subject. Differences in WM performance among the three trial types (emotional vs. neutral vs. scrambled) and between males and females were assessed using analyses of variance (ANOVAs) and *t* statistics; sex-related differences in emotional ratings and affective state were also assessed.

fMRI Data Analyses

Statistical analyses were preceded by the following preprocessing steps (performed with SPM2 – Statistical Parametric Mapping): slice timing, realignment, motion correction,

coregistration, normalization, and smoothing (8-mm kernel). For the data analysis, we used in-house custom MATLAB scripts involving both whole-brain voxel-wise and region-of-interest (ROI) analyses (Dolcos & McCarthy, 2006) to compare the brain activity associated with the conditions of interest (e.g., trials with angry vs. trials with neutral distracters). For subject-level analyses, the fMRI signal was selectively averaged in each subject's data as a function of trial type (i.e., angry, neutral, or scrambled distracters) and time point (one pre- and 13 post-stimulus-onset time points) using custom MATLAB software, and pair-wise t statistics for the contrast of interest were calculated for each subject; no assumption was made about the shape of the hemodynamic response function (Dolcos & Denkova, 2008; Dolcos & McCarthy, 2006; Morey et al., 2009). The individual analyses produced whole-brain average and activation t maps for each condition, contrast of interest, and TR/time point. The outputs of subject-level analyses were used as inputs for second-level, random-effects within-group and across-groups analyses. The analyses focused on any effects observed at time points within the 14- to 16-s period after the memoranda onset (TR 9), when the differential effects of the distracters were most evident (Denkova et al., 2010; Dolcos & McCarthy, 2006); exceptions are noted in the tables as necessary. Conjunction analyses involved masking procedures performed in MATLAB using the logical function AND; thus, only voxels that met the threshold criteria in each of the contributing t maps survived the masking procedure. This procedure is consistent with the conjunction null hypothesis testing (Nichols, Brett, Andersson, Wager, & Poline, 2005). A joint threshold of $p < 0.0005$ was used in all of the analyses, and an extent threshold of 10 contiguous voxels was used in each of the contributing maps (Lieberman & Cunningham, 2009).

The main goals of the present study were to determine whether sex differences in basic emotional reactivity are associated with differences in emotional distractibility and to identify the

neural mechanisms that implement differences in emotional distractibility between women and men. To accomplish this goal, brain regions part of VAS and DES were first defined as a priori functional ROIs, on the basis of findings from the original study by Dolcos & McCarthy (2006), who used a similar WM task with highly arousing negative pictures as novel distracters. For the purposes of the present study, the following two *t* maps identifying brain areas showing *general* sensitivity to negative distraction were used: Emo > Scr, to identify regions of VAS, and Scr > Emo, to identify regions of DES. The functional ROI masks were calculated by merging suprathreshold brain activity in the window from 12 to18 s (TRs 8 -10) after memoranda onset, which corresponds to the time interval in which the peak effects reported by Dolcos and McCarthy had occurred. This confined the identification of brain areas showing *specific* responses to angry-face distracters, investigated here, to the brain areas showing *general* sensitivity to negative distraction that had been investigated by Dolcos and McCarthy. A threshold of $p < 0.05$ (uncorrected) was used for each of these individual masks. Then, two complementary approaches were used to identify areas showing *specific* sensitivity to the angry-face distracters. The first set of analyses focused on the overall response to angry-face distraction, in order to identify brain areas that are common to women and men in the response to emotional distraction, independent of WM performance. These analyses were performed on the fMRI data for all trials (i.e., 30 per condition), as it was previously reported in the data from female subjects (Denkova et al., 2010). A second set of analyses then focused on the specific impact of angry-face distraction on WM performance, to identify brain activity linked to differences in WM performance between emotional and neutral trials and between male and female subjects. These analyses were performed on the fMRI data from trials in which sex

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differences were identified in WM performance (i.e., LOC 3). Hits and CRs were collapsed together in all analyses, which are described in detail below.

Identification of Common Brain Activity in Response to Emotional distraction in Women and Men

To identify the brain regions whose activity was sensitive to the presence of angry-face distracters in both women and men, an analysis consisting of the following two steps was performed (Denkova et al., 2010). First, the ventral and dorsal brain regions sensitive to angry-face distracters were separately identified in women and men: that is, (Emo > Scr) ∩ (Emo > Neu), for the ventral system, and (Emo < Scr) ∩ (Emo < Neu), for the dorsal system. The joint threshold of the resulting conjunction maps was $p < 0.0005$ (Fisher, 1950), resulting from multiplying the p values of the contributing maps: that is, $p < 0.01$ for the most dissimilar conditions (Emo > Scr and Emo < Scr), and $p < 0.05$ for contrasts between more similar conditions (Emo > Neu and Emo < Neu). This approach also maintained consistency with our previous investigation in women only (Denkova et al., 2010) and allowed for drawing comparable conclusions. Second, conjunction maps identifying the overlapping brain regions sensitive to angry-face distraction in both men and women were calculated for VAS and DES: that is, [women (Emo > Scr) ∩ (Emo > Neu)] ∩ [men (Emo > Scr) ∩ (Emo > Neu)], for VAS, and [women (Emo < Scr) ∩ (Emo < Neu)] ∩ [men (Emo < Scr) ∩ (Emo < Neu)], for DES.

Identification of Brain Activity Linked to Sex Differences in WM Performance

To identify regions of the ventral and dorsal systems showing sex-related differential patterns of responses linked to WM performance, an analysis was performed only for the correct LOC 3 trials in which an emotion effect had been observed in women (Denkova et al., 2010) and sex-related differences in performance were identified. This second approach used a different set

of contrasts than had the first, in order to ensure that the investigation was not limited to areas showing similar effects in women and men. The analysis consisted of the following two steps. First, a between-groups analysis comparing the responses to emotional distraction between females and males was performed using a two-sample t test; for this test, subject-level average signal for the emotional LOC 3 trials was used as the input for second-level between-groups t tests. Second, to make sure that the regions identified by the between-groups analysis were also sensitive to the effect of emotional distraction, the resulting t maps were inclusively masked with statistical maps identifying a main effect of emotion relative to baseline (i.e., *in*creased vs. *de*creased activity in the ventral or dorsal system, respectively). To identify brain areas showing increased response to emotional distraction in women versus men, the following conjunction maps were used: (EmoF > EmoM) ∩ (EmoF > Baseline), for activity in the ventral system, and (EmoF > EmoM) ∩ (EmoM < Baseline), for activity in the dorsal system. Similarly, to identify patterns showing increased response to emotional distraction in men versus women, the following conjunction maps were used: (EmoM > EmoF) ∩ (EmoM > Baseline), for activity in the ventral system, and (EmoM > EmoF) ∩ (EmoF < Baseline), for activity in the dorsal system. The joint threshold of the resulting conjunction maps was $p < 0.0005$ (Fisher, 1950), resulting from multiplying the p values of the contributing maps (0.05×0.01).

Identification of Brain-Behavior Relationships

To further investigate the significance of differences in brain activation, brain-behavior relationships were also investigated by calculating covariations between the fMRI signals in response to transient angry-face distraction and WM performance. These analyses identified brain regions whose activity was sensitive to individual variations in WM performance and was specific to emotional distraction. Negative brain-behavior covariations were expected to be

indicative of processing leading to detrimental effects on WM performance, whereas positive covariations were presumed to be indicative of processing engaged to cope with distraction. These analyses involved the following three strategies: (1) investigation in men of covariations of brain activity with WM performance in the same regions that had been identified in women (Denkova et al., 2010); (2) separate investigation in women and men of covariations of activity in brain regions where sex differences in activation linked to differences in WM performance had been identified by the analyses described in the previous paragraph; and (3) exploratory analyses, in both women and men, to identify covariations between brain activity and WM performance in brain areas showing sensitivity to emotional distraction (*in*creased or *de*crease activity), in the absence of sex differences in activation in the LOC 3 responses, as it is possible that differences in correlations could be observed in the absence of differences in activation. For the latter two strategies, the conjunction analyses performed to investigate brain-behavior relationships consisted of the following two steps. First, correlation maps identifying covariations between brain activity in the presence of distraction and scores indexing WM performance (i.e., corrected recognition scores = % Hits − % False Alarms) were calculated. Then, these correlation maps were inclusively masked with maps identifying a main effect of emotion (increased or decreased) relative to the baseline. The joint threshold of the conjunction map was of $p < 0.0005$ (Fisher, 1950), resulting from multiplying the p values of the contributing maps obtained independently (0.05×0.01).

Confirmatory ROI Investigations

Finally, activity in the main brain regions identified by the whole-brain voxel-wise analyses was subjected to further confirmatory investigations, using a functional ROI approach. This involved extraction of the fMRI signal, for each subject, condition, and time point, from

voxels identified by the group-level conjunction analyses. Then, across-subjects averages of the extracted MR signal (expressed as percentages of signal change) recorded at the delay peak time point (i.e., 14–16 s following memoranda onset) and correlations between the extracted fMRI signal and the individual scores for WM performance were calculated. The signal extracted from the ROIs was also used for illustration purposes (i.e., in the creation of figures) and to check whether some of the effects identified by the voxel-based correlations were driven by outliers.

Results

Behavioral Results

Working Memory – Increased Impact of Emotional Distraction in Women, in the Context of Overall Similar Performance

Analyses of the WM data showed that angry-face distracters had greater impact in women than in men in the trials associated with the highest level of confidence (LOC 3), but not in the overall WM performance (Figure 3.2). The statistical analyses showed that women had lower performance to the LOC 3 trials, although no sex-related differences emerged in the overall WM performance [$t_{(30)} = 1.46$, $p > 0.1$]. LOC 3 trials had the highest proportion (60 %). A mixed-design ANOVA (Sex × Distracter Type × LOC) on corrected recognition scores yielded a significant main effect of LOC [$F_{(2, 56)} = 44.38$, $p < 0.001$], significant Sex × LOC [$F_{(2, 56)} = 4.1$, $p < 0.02$] and Distracter Type × LOC [$F_{(4, 112)} = 6.76$, $p < 0.001$] interactions, and a trend toward the three-way Sex × Distracter Type × LOC [$F_{(4, 112)} = 1.94$, $p = 0.108$] interaction. Further investigation to elucidate this trend – focusing on LOC 3 performance, which was justified by our previous findings in women (Denkova et al., 2010) – showed that the pattern of WM impairment to emotional distraction was only present in females. Also, planned *t* tests showed that women had lower LOC 3 WM performance than did men for trials associated with

the angry-face distracters [$t_{(28)} = 3.14$, $p = 0.004$], but no sex-related differences were apparent in the trials associated with neutral [$t_{(28)} = 1.58$, $p > 0.1$] or scrambled [$t_{(28)} = 1.22$, $p > 0.2$] distracters. Note that analyses performed on the data from pilot subjects ($N = 42$, 24 female, 18 male) − who had performed a similar WM task, but without distraction − identified no sex-related differences in using the confidence scale, for any confidence level (LOC 1, $p > 0.3$; LOC 2, $p > 0.5$; LOC 3, $p > 0.6$). This confirms that the differences between women and men in the LOC 3 ratings were specifically linked to a differential impact of the angry-face distracters on women's ability to make high-confidence ratings in the WM task, rather than to differences in the ways that they performed the LOC ratings in general.

Greater Ratings of Angry Faces and Impact on Affective State in Women

Overall, the angry-face distracters were rated as being more emotional than the neutral-face distracters. The average emotional content scores (1 = *lowest*, 9 = *highest*), as rated by the subjects, were 7.02 (SD = 0.85) for the angry-face distracters and 1.96 (SD = 0.69) for the neutral-face distracters. A mixed-design ANOVA (Sex × Distracter Type) on anger content ratings yielded main effects of sex [$F_{(1, 28)} = 5.58$, $p = 0.025$] and distracter type [$F_{(1, 28)} = 1,144.44$, $p < 0.001$] and a significant Sex × Distracter Type interaction [$F_{(1, 28)} = 7.39$, $p < 0.011$]. Post-hoc analyses showed that, as compared to men, women rated the emotional faces as being more angry [$t_{(28)} = 3.43$, $p < 0.002$]. Regarding the measures of affective states, our previous investigation in women (Denkova et al., 2010) had shown that they had significantly higher levels of state anxiety, and lower levels of state positive affect, as a result of performing the task (as identified by pre- vs. posttask differences in STAI-S and PANAS-S scores, respectively). A mixed-design ANOVA on state anxiety scores (Sex × Time) yielded a marginal effect of time [$F_{(1, 30)} = 3.41$, $p = 0.075$]. Further investigation to elucidate this trend, justified by

our previous findings in women (Denkova et al., 2010), showed that the pattern of increased state anxiety after performing the task was only present in females [women, $t_{(15)} = 2.99$, $p = 0.009$; men, $t_{(15)} = 0.29$, $p > 0.7$]. Similarly, a mixed-design ANOVA on positive affect scores (Sex × Time) yielded a main effect of Time [$F_{(1, 30)} = 23.35$, $p < 0.001$], and post-hoc tests showed that both women and men expressed a similar reduction in levels of state positive affect [women, $t_{(15)} = 2.68$, $p = 0.017$; men, $t_{(15)} = 4.18$, $p < 0.001$]. These results show that, overall, men's levels of state anxiety were less sensitive to the effect of angry-face distraction.

Together, the behavioral results suggest that female subjects were more affected by the presence of the angry-face distracters, as reflected in WM performance, emotional ratings of the distracters, and changes in posttask emotional state. Analyses of the fMRI data investigated whether these behavioral findings were linked to differences in brain activity; these analyses were performed both on all trials, as in (Denkova et al., 2010), regardless of the impact of distraction on WM performance, and on trials in which sex-related differences were identified (i.e., LOC 3).

fMRI Results – Sex Differences in the Response to Emotional Distraction, in the Context of Overall Similar Patterns of Brain Activity

To identify whether women and men show similar patterns of brain activity in response to angry-face distraction, we investigated whether the areas previously identified in women (Denkova et al., 2010) could be generalized to men. For this investigation focusing on the overall response to angry-face distraction (i.e., independent of WM performance), analyses were performed on all trials. The results indicated that, indeed, the overall patterns of activity observed in men were similar to those identified in women using the same task (Denkova et al., 2010). As is illustrated in Table 3.1 and Figure 3.3, men and women showed increased activity in

response to angry-face distraction in a host of common brain regions that are involved in emotion processing (including the AMY and the vmPFC) or are susceptible to emotional modulation (e.g., FG, BA 37). By contrast, angry-face distracters evoked strong *de*activations in brain regions typically involved in cognitive control and attentional processes, including dlPFC (BAs 8/9) and dorsomedial PFC (dmPFC; BA 6). These findings replicate and extend to men the results previously reported in women using similar (Dolcos et al., 2008; Dolcos et al., 2006; Dolcos & McCarthy, 2006) or identical (Denkova et al., 2010) tasks, suggesting that men and women engage overall similar brain areas in response to negative distraction.

Increased Sensitivity in the Ventral Affective System in Women

To identify brain activity specifically linked to differences in WM performance, analyses directly comparing brain activity between women and men were performed on the trials in which sex differences were observed (i.e., LOC 3 trials). Relative to men, women showed increased activity in response to angry-face distraction in a perceptual area susceptible to emotion modulation (i.e., left FG, BA 37; see Figure 3.4 and Table 3.2) and in a region associated with higher-level emotion processing (i.e., subgenual anterior cingulate cortex [sgACC], BA 25; Figure 3.5). Brain-behavior correlations meant to further clarify these differences revealed a negative covariation between brain activity and LOC 3 WM performance in the left FG (BA 37) in women (see Table 3.3). These results complement our previous investigation in women (Denkova et al., 2010), in which a pattern of increased activity and negative covariation with WM performance was observed in the right FG (BA 37). Activity in the same right FG area, however, was not different and did not covary with WM performance in men. It should be noted that the findings regarding the left FG were obtained from slightly different analyses performed in the context of investigating sex differences, as compared to the initial investigation focusing

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on differential behavioral effects of emotional distraction within the female group (Denkova et al., 2010). Specifically, given that within the latter group emotional distracters had a greater impact on WM than did both neutral and scrambled distracters, the covariation analyses in the Denkova et al. (2010) report focused on brain areas showing differential sensitivity for emotional distracters relative to both neural and scrambled distracters. Hence, the negative covariation in the right FG was identified in an area meeting the following conjunction criterion, dictated by the behavioral results: [(Emo > Neu) ∩ (Emo > Scr)]. Similarly, in the present report, the covariation analyses were also guided by behavioral differences, but in the context of the differential effects of emotional distraction in women and men. Specifically, the negative covariation with WM performance in the left FG was identified in an area showing increased activity to emotional distracters in women relative to men, corresponding to the LOC 3 trials in which sex differences in the impact of emotional distraction on WM were identified. Thus, to ensure conceptual consistency across analyses regarding the behavioral effects, a different conjunction mask was used, which met the following criterion: [(EmoF > EmoM) ∩ (EmoF > BaselineF)]. This was also justified by the absence of a differential impact of emotional distraction on WM in men; hence, it was not suitable to employ in men the same masking procedure that had been employed in women by Denkova et al. (2010), whose emotional distracters did differentially impact performance.

Finally, exploratory brain-behavior correlations targeting areas showing sensitivity to emotional distraction (*in*creased or *de*creased activity as compared to baseline), in the absence of differences between women and men, identified negative covariations with WM performance in women in areas linked to both basic emotion processing (AMY) and higher-level emotion integration and control (right ventrolateral PFC [vlPFC], BA 45/47; see Table 3.3). The negative

covariations with LOC 3 WM performance were identified only in female subjects and are likely indicative of impairing effects of angry-face distraction on WM performance.

Increased Sensitivity in the Dorsal Executive System and Increased Deactivation of the Default-Mode Network in Men

Unlike the patterns observed in the ventral emotional system in women, activity in the dorsal systems of men showed patterns of decreased activity in response to angry-face distraction; similar effects were also observed in areas of the default-mode network. Relative to women, men showed greater *de*activations in response to emotional distraction in areas associated with goal-oriented processing and cognitive control, such as polar and lateral PFC (BAs 10, 9, 8, 6; see Table 3.2) and dorsal ACC (dACC, BA 32; see Table 3.2). Brain-behavior correlations meant to further clarify these differences revealed positive covariations between brain activity and LOC 3 WM performance in the presence of emotional distraction in the right dorsal PFC (BA 6/8; Figure 3.6*B*) and in the dorsal ACC (BA 24; see Table 3.3). These positive covariations with LOC 3 WM performance were identified only in male subjects, and are likely indicative of successful engagement of mechanisms for coping with distraction.

Similar effects were also observed in a host of medial (including posterior cingulate cortex, precuneus, and cuneus; BAs 7, 31, 19), lateral parietal (BA 40), and superior temporal (BA 42) areas that partially overlap with regions of the default-mode network (Buckner et al., 2008; Raichle et al., 2001) (see Table 3.2). Also, brain-behavior correlation analyses revealed that some of these areas showed positive covariation between activity in these regions and LOC 3 WM performance in men (see Table 3.3).

Sex-Related Dorso-Ventral Hemispheric Dissociation in Coping with Angry-Face Distraction in PFC

Women and men showed differential patterns of activity in response to angry-face distraction in ventral and dorsal lateral PFC regions, indicative of sex-related differences in engaging PFC mechanisms to cope with emotional distraction. On the one hand, although overall, women showed decreased activity to emotional distraction in a left ventral PFC region (BA 47), activity in this region was also positively correlated with WM performance in the presence of emotional distraction (Denkova et al., 2010) only in women (Figure 3.6*A*). Thus, the same PFC region showing greater response in the female subjects who performed better in the LOC 3 showed "by default" an increased level of activity in males, who overall also had higher levels of performance in these trials. On the other hand, similar patterns of activation and covariation were identified in the right dorsal PFC (BA 6/8) in men, where - although overall they showed decreased activity to emotional distraction - activity was also positively correlated with WM performance in the presence of emotional distraction only in men (Figure 3.6*B*).

Discussion

The goals of the present study were to determine whether sex differences in basic emotional reactivity are associated with differences in emotional distractibility and to identify the neural mechanisms that implement differences in emotional distractibility between women and men. We identified three main findings. First, our behavioral results showed an increased impact of emotional distraction in women. This was reflected in increased impact of angry-face distracters for WM trials associated with a high level of confidence, increased emotional ratings of the distracters, and increased change in negative affect in the posttask emotional states. Second, brain-imaging results identified dissociable patterns of activity in VAS and DES in

women and men, in the context of similar overall patterns of response to emotional distraction in the two sexes. Specifically, women showed increased sensitivity to emotional distraction in VAS regions, including both emotion-processing regions (AMY, vlPFC, and sgACC) and regions susceptible to affective modulation (FG), whereas men showed increased sensitivity in DES regions, including polar and dorsal PFC and dorsal ACC, and in brain regions associated with the default-mode network. Finally, we also found a dorsal-ventral hemispheric dissociation within the lateral PFC linked to the engagement of mechanisms to cope with emotional distraction, with left ventral PFC activity being linked to individual differences in WM performance in women, and right dorsal PFC activity being linked to individual differences in WM performance in men. These findings are discussed in turn below.

Behavioral Results – Increased Impact of Emotional Distraction in Women, in the Context of Overall Similar WM Performance

The present findings showing enhanced overall sensitivity in women in response to emotional distraction are consistent with evidence of increased reactivity among women to emotional stimuli, in general (e.g., Kring & Gordon, 1998), and to emotional facial expressions, in particular (Dimberg & Lundquist, 1990; Orozco & Ehlers, 1998). It should be noted, however, that no differences were observed in the overall WM performance between men and women, but rather in the responses associated with the highest level of confidence. This suggests that sex-related differences in the response to emotional challenge, as induced by our task with distraction, are more subtle and affect only some aspects of behavior – that is, the specific impact on responses requiring a higher level of confidence in the WM task (LOC 3). Although this raises the possibility of sex-related differences in the ways that the LOC ratings were performed by women and men in general, this does not seem to be the case, as shown by analyses

comparing LOC responses in women and men who performed a similar task, but without distraction. These findings confirm that the differences between women and men in the LOC 3 ratings were specifically linked to a differential impact of the angry-face distracters on their ability to make high-confidence ratings in the WM task, and they validate the LOC ratings as being more sensitive than are old/new responses in assessing subtle differences in the impact of emotional distraction.

It may seem somewhat surprising that negative emotional distracters selectively impaired high-confidence responses, given that emotional stimuli often confer a selective benefit on response accuracy (Dolcos, LaBar, & Cabeza, 2005; Ochsner, 2000; Sharot, Delgado, & Phelps, 2004). It should be noted, however, that this effect is typically observed when the emotional information is *task-relevant* and is associated with enhanced episodic memory performance. Instead, in the present study, the emotional information was *task-irrelevant*, so that the typical effect would be impaired performance in the main task (e.g., in WM) (Anticevic, Repovs, & Barch, 2010; Dolcos et al., 2008; Dolcos & McCarthy, 2006). Hence, it is actually expected that this detrimental effect would also impair the ability to make correct responses with increased confidence. This is consistent with the idea presented in the introduction, that activity in the affective and executive neural systems is strongly interconnected, such that increased activity in the ventral affective regions disrupts activity in the dorsal system and results in cognitive impairment. The selective impairment of high-confidence responses, as opposed to the general detrimental effect observed in other studies (e.g., Dolcos & McCarthy, 2006), could be explained by the milder emotional content conveyed by the angry faces used in the present study, as compared to the high-arousing negative pictures from the International Affective Picture System (Lang, Bradley, & Cuthbert, 2008) used in previous studies.

Other potential alternative explanations could be that the observed sex differences are tied to the specific nature of emotional distraction used in the present study. First, because the emotional content conveyed by the angry faces is milder than the one conveyed by the high-arousing negative IAPS pictures used in previous investigations (e.g., Dolcos et al., 2008; Dolcos & McCarthy, 2006), as alluded above, it could be argued that the selective impairment of high-confidence responses in women may reflect the mildness of the employed stimuli, rather than the intrinsic "subtle" quality of the observed sex differences. Hence, it is possible that sex differences in basic (not only in high-confidence) WM performance could be observed when using high-arousing IAPS pictures, instead of angry faces, as distracters. Future investigations should compare the impact of IAPS pictures presented as distracters, in men and women.

Second, it could also be argued that the observed sex differences are due to increased sensitivity to social stimuli, such as angry faces, in women relative to men, rather than to the effects of negative distraction, in general. Some evidence supports the idea that women are more responsive to different types of social cues, including threat signals, such as angry faces (e.g., Dimberg & Lundquist, 1990; Hall, 1978; McClure, 2000; McClure et al., 2004). On the other hand, such differences are not always observed [see, for example, (Grimshaw, Bulman-Fleming, & Ngo, 2004; Seidel, Habel, Kirschner, Gur, & Derntl, 2010)], suggesting that they may be specific instances of more generic sex differences in the emotional response, which have been more consistently supported (e.g., Hamann & Canli, 2004; Lang et al., 1993; Shields, 1991).

Consistent with the idea that the observed sex differences are not limited to angry-face distraction but reflect systematic, albeit subtle, effects, similar results were observed also for another type of emotional distraction (Iordan, Dolcos, & Dolcos, 2015; Study III in the present dissertation). Specifically, similar reduced WM performance in the high-confidence responses

only was also identified in a task using cues for the subjects' most negative autobiographical memories as internal distraction. Thus, this provides additional, albeit indirect, evidence that the sex differences themselves are more subtle and affect only certain aspects of behavior (i.e., high-confidence responses). It should be noted, however, that it is difficult to separate responses to emotional distraction from spontaneous engagements of emotion regulation strategies, because subjects are instructed to try and maximize cognitive performance in tasks with distractions, as discussed in Chapter 4.

Differential sensitivity in women and men was also reflected in higher ratings of angry distracters and increased changes on posttask negative affective state in women, which further confirms that women were more affected overall by the angry faces used as distracters in the present task. Sex differences in ratings of angry faces are consistent with the idea of increased emotional sensitivity in women. However, an alternative way of looking at sex differences in neural responses would be to equate the behavioral performance in women and men, to make sure that eventual differences at the neural level would be observed in the absence of behavioral differences. Thus, one might argue that in such a context, the self-report measure is not a manipulation check, but simply another measure of gender differences that may be viewed as a confound. However, this was not the case in the present investigation, in which, on the basis of established differences between women and men in some aspects of emotion processing (i.e., basic emotional reactivity), we investigated whether these differences "translate" into differences in other related aspects (i.e., emotional distractibility), and whether such possible differences in behavior are associated with similar or different neural correlates. Hence, the higher ratings of angry faces observed in women were not a failed manipulation check, but an expected result. Overall, these behavioral findings warranted analyses of brain-imaging data examining both

common patterns of activation and responses linked to the differential impacts of emotional distraction in women and men, as we will discuss below.

fMRI Results – Sex Differences in the Response to Emotional Distraction, in the Context of Overall Similar Patterns of Brain Activity

Complementing our previous investigation (Denkova et al., 2010), analyses performed on all trials showed that men and women display similar patterns of activation and deactivation in a host of brain regions associated with VAS (e.g., AMY, vmPFC, and FG) and DES (e.g., dlPFC) in response to emotional distracters inducing specific emotions (i.e., anxiety). These findings confirm previous results that have identified this as a robust pattern of activity in response to distracters inducing general negative affect in both healthy (Anticevic et al., 2010; Chuah et al., 2010; Denkova et al., 2010; Dolcos et al., 2008; Dolcos & McCarthy, 2006; Dolcos et al., 2007) and clinical (Anticevic, Repovs, & Barch, 2011; Diaz et al., 2011; Morey et al., 2009) groups. However, unlike previous investigations, which did not investigate sex differences, in the present study we also identified differences in brain activity linked to differential impacts of emotional distraction in women and men.

Increased Sensitivity in the Ventral Affective System in Women

In addition to areas identified in the right FG showing increased activation to and negative covariation with WM performance for emotional distraction, in the present investigation we also identified other brain regions showing increased similar engagement in women. These areas included bilateral FG (BA 37), as well as areas associated with basic emotional response (AMY), higher-level emotion integration (i.e., sgACC, BA 25), and areas associated with top-down control of emotion (i.e., right vlPFC, BA 47). However, the left ventral PFC (BA 47) showed a pattern of positive covariation with WM performance in women, probably reflecting

the engagement of mechanisms to successfully cope with distraction, as we will also discuss in the next section.

Related to the pattern of activity in the FG, it may seem surprising at first that we observed a negative covariation that was selective for angry faces in a perceptual area (left FG), given the possibility that both emotional and neutral distracters could capture attention and lead to WM impairment. It should be noted, however, that this effect was identified in an area specifically showing sensitivity to emotional distraction (i.e., increased activity) and differences in activation between women and men. Therefore, it is more likely that the covariation with WM performance observed in these areas would be identified for the items also producing differential effects in activation (i.e., emotional LOC 3). Although this does not exclude the possibility of also identifying covariations between WM performance and activations for neutral distracters, in the FG or in other areas producing "bottom-up" effects, the absence of such strong covariations for the neutral items may reflect the fact that these distracters did not actually produce an impairment in WM performance in either women or men. Hence, this effect is consistent with the specific impairment observed in women only (Denkova et al., 2010), and with the idea of a "bottom-up" impact of emotional distraction.

Of particular note is the fact that women showed an increased specific response to emotional distraction in the sgACC (BA 25). This region of the ACC is an area closely tied to the autonomic nervous system, which has been linked to the experience of negative emotion in both healthy and clinical samples (Baeken et al., 2010; Ball et al., 2012; Gotlib et al., 2005; Mobbs et al., 2009). Sex-related differences in sgACC have been previously reported, with increased activation in women possibly linked to enhanced emotional reactivity or stronger autonomic reactions to emotional stimuli (Wager, Phan, Liberzon, & Taylor, 2003). For

example, using an instructed fear/anticipatory anxiety paradigm, Butler et al. (2005) reported increased activity in the sgACC in women relative to men during anticipation of mild electric shock. However, to our knowledge, this effect has not been previously studied in relation to transient angry-face distraction.

Altogether, these findings, particularly the patterns of negative covariation in the FG and AMY are consistent with a bottom-up impact of angry-face distraction, and the negative covariation in the right vlPFC is consistent with unsuccessful engagement of top-down control in the face of emotional distraction. These results provide support for the idea that females may be more sensitive to angry-face distraction and offer insight into possible overlapping mechanisms between transient and longer-state moods that may be involved in emotional dysfunctions associated with affective disorders (e.g., Drevets & Raichle, 1998; Mayberg, 1997).

Increased Sensitivity in the Dorsal Executive System and Increased Deactivation of the Default-Mode Network in Men

Consistent with the idea of increased sensitivity in DES regions, men showed reduced activity in the polar (BA 10) and lateral (BAs 9, 8, 6) PFC, in response to angry-face distracters. The pattern of PFC *de*activation in men suggests increased interference with maintenance of goal-relevant information in WM in the presence of emotional distraction (D'Esposito et al., 2000; Levy & Goldman-Rakic, 2000; Miller & Cohen, 2001). Preliminary analyses confirmed that the differential effects of the distracters were most robust 14-16 s after memoranda onset (TR 9) in the present data. Moreover, men also showed a pattern of nonspecific deactivations in the dorsal ACC (BA 32). This suggests a more general impact of distraction on top-down cognitive control mechanisms (Bush, Luu, & Posner, 2000), although this was not reflected in differences in WM performance. However, both right lateral PFC (BA 6/8) and dorsal ACC (BA

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24) also showed a pattern of positive covariation with WM performance, probably reflecting the engagement of mechanisms to successfully cope with distraction.

A similar pattern of increased deactivations was observed in areas of the posterior midline (BAs 7, 31), lateral parietal (BA 40), and superior temporal (BA 42) regions, which are partially overlapping with regions of the default-mode network. The default-mode network is characterized by increased resting-state activity and by deactivation in tasks that require attention to external stimuli (Buckner et al., 2008; Raichle et al., 2001). Thus, the present findings of increased deactivation in men could indicate that men were more successful in disengaging the default-mode network as a result of the demand to perform goal-directed processing, and consequently performed better in the WM task (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003; Raichle et al., 2001). Alternatively, given that these effects were observed for trials associated with increased WM performance in men relative to women, the specific pattern of deactivation may be indicative of sex-related differences in the strategies employed by men and women in response to distraction.

Sex-Related Dorso-Ventral Hemispheric Dissociation in Coping with Angry-Face Distraction in PFC

The present investigation also revealed a dorsal-ventral hemispheric dissociation in the lateral PFC between women and men coping with emotional distraction. Specifically, although the left ventral PFC (BA 47) showed reduced activity in women than in men, it also showed a positive covariation with WM performance in women, suggesting its engagement by women who successfully coped with emotional distraction (Denkova et al., 2010). Consistent with this idea, previous evidence has consistently linked activity in this region to coping with emotional distraction (Banich et al., 2009; Dolcos et al., 2008; Dolcos et al., 2006). By contrast, although

the right dorsal PFC (BA 6/8) showed reduced activity in men relative to women, it also showed a positive covariation with WM performance in men, suggesting its engagement by men who also successfully coped with emotional distraction. Similar effects were also found in the dorsal ACC, indicating that males who maintained an increased level of activity in these areas, despite overall reduced activity as compared to females, also showed better WM performance. These results are consistent with evidence linking activity in lateral BAs 6 and 8 with WM processing, especially in the spatial domain (Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; D'Esposito, 2008; Tanaka, Honda, & Sadato, 2005), and activity in the dorsal ACC with engagement of top-down executive control (Bush et al., 2000).

Interestingly, analyses of brain-behavior relationships in general revealed sex-related opposing patterns of covariation in women and men (i.e., more negative brain-behavior correlations in women and more positive correlations in men). However, this apparently unexpected dissociation could be explained by the fact that these covariations were investigated in areas specifically showing sensitivity to emotional distraction, and in some cases, also showing differences in activation between women and men. The pattern of negative covariation with WM performance in women was generally observed in brain regions of the ventral affective system, which also showed increased activity to angry-face distracters in women. Hence, these negative covariations are consistent with the idea that increased sensitivity in VAS areas is linked to impaired WM performance in women. Note that women also showed positive covariation in the left ventral PFC (BA 47), consistent with the engagement of this brain region in coping with emotional distraction (Denkova et al., 2010). On the other hand, the pattern of positive covariations in dorsal areas in men is consistent with less of an overall impact of negative distraction, as compared to women, possibly due to increased engagement of these

regions to maintain WM performance in the presence of emotional distraction. Overall, these findings suggest that the increased impact of emotional distraction in women is linked to "bottom-up" effects in VAS, whereas increased resilience to emotional distraction in men is linked to "top-down" effects in DES.

Finally, an important issue to consider is the generalizability of the present brain imaging results. Meta-analytical evidence (Sabatinelli et al., 2011) suggests that the particular class of visual stimuli (i.e., faces vs. scenes) has a substantial impact on the fMRI effects of emotion, and hence the type of emotional stimuli used influences the generalizability of the results. In addition, facial expressions have a stronger social-communicative function, whereas scene processing is inherently more observational, and this may also influence the interpretation of the observed results (Sabatinelli et al., 2011). Although the dependency of the fMRI results on the stimulus type might potentially limit the generalizability of the results, meta-analytical evidence also indicates overlaps between the brain mechanisms involved in processing emotional faces and scenes (Sabatinelli et al., 2011). Critically, in the present investigation, we used a functional mask which confined the identification of brain areas showing specific responses to angry-face distracters, investigated here, to the brain areas showing general sensitivity to negative distraction that had been investigated by Dolcos and McCarthy (2006) (see Methods section). Thus, based on our methodological approach and the available evidence, the generalizability of the observed effects from faces to scenes is highly plausible. Future research could further clarify this issue by directly comparing the distraction effects elicited by emotional faces vs. scenes.

Conclusions

In summary, the present study has provided evidence for sex differences in the context of similar behavioral and brain responses to negative distracters in women and men. Our results

suggest that enhanced emotional competence in women may have the side effect of increased emotional reactivity, which in turn may lead to enhanced emotional distractibility, although the present findings do not establish that direction for such a causal relationship. Behavioral results showed an increased impact of emotional distraction in women, which was reflected in decreased WM performance that was specific to trials associated with high-confidence responses, increased emotional ratings of the distracters, and increased posttask negative affect. Our fMRI findings identified sex differences in the patterns of activity in VAS and DES regions, in the context of overall similar responses to emotional distraction in women and men. The similarities in the engagement of the ventral-affective and dorsal-executive systems suggest that men and women deploy similar general mechanisms in response to transient emotional distraction. The sex-related dissociations are consistent with increased sensitivity in "bottom-up" responses in women, linked to impaired WM performance, and increased sensitivity in "top-down" responses in men, linked to increased performance, in the face of emotional distraction. Finally, the study also revealed a dorsal ventral hemispheric dissociation within the lateral PFC that was linked to the engagement of mechanisms to cope with emotional distraction, with the left ventral PFC being linked to individual differences in WM performance in women, and the right dorsal PFC being linked to individual differences in men. These results contribute to a better understanding of sex differences in responses to emotional distraction in healthy behavior, and have implications for understanding factors that may influence susceptibility to affective disorders.

References

Andrews-Hanna, J. R., Reidler, J. S., Sepulcre, J., Poulin, R., & Buckner, R. L. (2010). Functional-anatomic fractionation of the brain's default network. *Neuron, 65*(4), 550-562.

Anticevic, A., Repovs, G., & Barch, D. M. (2010). Resisting emotional interference: brain regions facilitating working memory performance during negative distraction. *Cognitive, Affective, & Behavioral Neuroscience, 10*(2), 159-173.

Anticevic, A., Repovs, G., & Barch, D. M. (2011). Working memory encoding and maintenance deficits in schizophrenia: Neural evidence for activation and deactivation abnormalities. *Schizophrenia Bulletin, 39*(1), 168-178.

Baeken, C., Van Schuerbeek, P., De Raedt, R., Ramsey, N. F., Bossuyt, A., De Mey, J., Vanderhasselt, M. A., Leyman, L., & Luypaert, R. (2010). Reduced left subgenual anterior cingulate cortical activity during withdrawal-related emotions in melancholic depressed female patients. *Journal of Affective Disorders, 127*(1–3), 326-331.

Ball, T. M., Sullivan, S., Flagan, T., Hitchcock, C. A., Simmons, A., Paulus, M. P., & Stein, M. B. (2012). Selective effects of social anxiety, anxiety sensitivity, and negative affectivity on the neural bases of emotional face processing. *Neuroimage 59*(2), 1879-1887.

Banich, M. T., Mackiewicz, K. L., Depue, B. E., Whitmer, A. J., Miller, G. A., & Heller, W. (2009). Cognitive control mechanisms, emotion and memory: a neural perspective with implications for psychopathology. *Neuroscience and Biobehavioral Reviews, 33*(5), 613-630.

Barrett, L. F., Lane, R., Sechrest, L., and Schwartz, G. (2000). Sex differences in emotional awareness *Personality and Social Psychology Bulletin, 26*(9), 1027-1035.

Bekker, M. H., & van Mens-Verhulst, J. (2007). Anxiety disorders: sex differences in prevalence, degree, and background, but gender-neutral treatment. *Gender Medicine, 4 Suppl B*, S178-193.

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network. *Annals of the New York Academy of Sciences, 1124*(1), 1-38.

Bush, G., Luu, P., & Posner, M. I. (2000). Cognitive and emotional influences in anterior cingulate cortex. *Trends in Cognitive Sciences, 4*(6), 215-222.

Butler, R., Pan, H., Epstein, J., Protopopescu, X., Tuescher, O., Goldstein, M., Cloitre, M., Yang, Y., Phelps, E. A., Gorman, J., Le Doux, J. E., Stern, E., & Silbersweig, D. (2005). Fear-related activity in subgenual anterior cingulate differs between men and women. *Neuroreport, 16*(11), 1233-1236.

Canli, T., Desmond, J. E., Zhao, Z., & Gabrieli, J. D. (2002). Sex differences in the neural basis of emotional memories. *Proceedings of the National Academy of Sciences of the USA, 99*(16), 10789-10794.

Chuah, L. Y. M., Dolcos, F., Chen, A. K., Zheng, H., Parimal, S., & Chee, M. W. L. (2010). Sleep deprivation and interference by emotional distracters. *SLEEP, 33*(10), 1305-1313.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science, 279*(5355), 1347-1351.

D'Argembeau, A., Stawarczyk, D., Majerus, S., Collette, F., Van der Linden, M., Feyers, D., Maquet, P., & Salmon, E. (2010). The neural basis of personal goal processing when envisioning future events. *Journal of Cognitive Neuroscience, 22*(8), 1701-1713.

D'Esposito, M. (2008). Working memory. *Handbook of Clinical Neurology, 88*, 237-247.

D'Esposito, M., Postle, B. R., & Rypma, B. (2000). Prefrontal cortical contributions to working memory: evidence from event-related fMRI studies. *Experimental Brain Research, 133*(1), 3-11.

Denkova, E., Dolcos, S., & Dolcos, F. (2012). Reliving emotional personal memories: affective biases linked to personality and sex-related differences. *Emotion, 12*(3), 515-528.

Denkova, E., Wong, G., Dolcos, S., Sung, K., Wang, L., Coupland, N., & Dolcos, F. (2010). The impact of anxiety-inducing distraction on cognitive performance: a combined brain imaging and personality investigation. *PLoS One, 5*(11), e14150. doi 14110.11371/journal.pone.0014150.

Diaz, M. T., He, G., Gadde, S., Bellion, C., Belger, A., Voyvodic, J. T., & McCarthy, G. (2011). The influence of emotional distraction on verbal working memory: an fMRI investigation comparing individuals with schizophrenia and healthy adults. *Journal of Psychiatric Research, 45*(9), 1184-1193.

Dimberg, U., & Lundquist, L. O. (1990). Gender differences in facial reactions to facial expressions. *Biological Psychology, 30*(2), 151-159.

Dolcos, F., & Denkova, E. (2008). Neural correlates of encoding emotional memories: a review of functional neuroimaging evidence. *Cell Science Reviews, 5*(2), 78-122.

Dolcos, F., Diaz-Granados, P., Wang, L., & McCarthy, G. (2008). Opposing influences of emotional and non-emotional distracters upon sustained prefrontal cortex activity during a delayed-response working memory task. *Neuropsychologia, 46*(1), 326-335.

Dolcos, F., Iordan, A. D., & Dolcos, S. (2011). Neural correlates of emotion-cognition interactions: A review of evidence from brain imaging investigations. *Journal of Cognitive Psychology, 23*(6), 669-694.

Dolcos, F., Kragel, P., Wang, L., & McCarthy, G. (2006). Role of the inferior frontal cortex in coping with distracting emotions. *Neuroreport, 17*(15), 1591-1594.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2005). Remembering one year later: role of the amygdala and the medial temporal lobe memory system in retrieving emotional memories. *Proceedings of the National Academy of Sciences U.S.A., 102*(7), 2626-2631.

Dolcos, F., & McCarthy, G. (2006). Brain systems mediating cognitive interference by emotional distraction. *The Journal of Neuroscience, 26*(7), 2072-2079.

Dolcos, F., Miller, B., Kragel, P., Jha, A., & McCarthy, G. (2007). Regional brain differences in the effect of distraction during the delay interval of a working memory task. *Brain Research, 1152*, 171-181.

Domes, G., Schulze, L., Bottger, M., Grossmann, A., Hauenstein, K., Wirtz, P. H., Heinrichs, M., & Herpertz, S. C. (2010). The neural correlates of sex differences in emotional reactivity and emotion regulation. *Human Brain Mapping, 31*(5), 758-769.

Drevets, W. C., & Raichle, M. E. (1998). Reciprocal suppression of regional cerebral blood flow during emotional versus higher cognitive processes: Implications for interactions between emotion and cognition. *Cognition and Emotion, 12*(3), 353-385.

Fisher, R. A. (1950). *Statistical methods for research workers*. London: Oliver and Boyd.

Goldstein, J. M., Seidman, L. J., Horton, N. J., Makris, N., Kennedy, D. N., Caviness, V. S., Jr., Faraone, S. V., & Tsuang, M. T. (2001). Normal sexual dimorphism of the adult human brain assessed by in vivo magnetic resonance imaging. *Cerebral Cortex, 11*(6), 490-497.

Gotlib, I. H., Sivers, H., Gabrieli, J. D., Whitfield-Gabrieli, S., Goldin, P., Minor, K. L., & Canli, T. (2005). Subgenual anterior cingulate activation to valenced emotional stimuli in major depression. *Neuroreport, 16*(16), 1731-1734.

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences of the USA, 100*(1), 253-258.

Grimshaw, G. M., Bulman-Fleming, M. B., & Ngo, C. (2004). A signal-detection analysis of sex differences in the perception of emotional faces. *Brain and Cognition, 54*(3), 248-250.

Gur, R. C., Gunning-Dixon, F., Bilker, W. B., & Gur, R. E. (2002). Sex differences in temporo-limbic and frontal brain volumes of healthy adults. *Cerebral Cortex, 12*(9), 998-1003.

Hall, J. A. (1978). Gender effects in decoding nonverbal cues. *Psychological Bulletin, 85*(4), 845-857.

Hamann, S., & Canli, T. (2004). Individual differences in emotion processing. *Current Opinion in Neurobiology, 14*(2), 233-238.

Harrison, B. J., Pujol, J., Ortiz, H., Fornito, A., Pantelis, C., & Yücel, M. (2008). Modulation of brain resting-state networks by sad mood induction. *PLoS ONE, 3*(3), e1794. doi 1710.1371/journal.pone.0001794.

Hopfinger, J. B., Buonocore, M. H., & Mangun, G. R. (2000). The neural mechanisms of top-down attentional control. *Nature Neuroscience, 3*(3), 284-291.

Iordan, A. D., Dolcos, S., & Dolcos, F. (2015). Brain activity and network interactions in regulating the impact of internal emotional distraction on working memory. *Manuscript in submission for publication*.

Kessler, R. C. (2003). Epidemiology of women and depression. *Journal of Affective Disorders, 74*(1), 5-13.

Koch, K., Pauly, K., Kellermann, T., Seiferth, N. Y., Reske, M., Backes, V., Stöcker, T., Shah, N. J., Amunts, K., Kircher, T., Schneider, F., & Habel, U. (2007). Gender differences in the cognitive control of emotion: An fMRI study. *Neuropsychologia, 45*(12), 2744-2754.

Kring, A. M., & Gordon, A. H. (1998). Sex differences in emotion: expression, experience, and physiology. *Journal of Personality and Social Psychology, 74*(3), 686-703.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2008). *International affective picture system (IAPS): Affective ratings of pictures and instruction manual. Technical Report A-8.*: University of Florida, Gainesville, FL.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: affective, facial, visceral, and behavioral reactions. *Psychophysiology, 30*(3), 261-273.

Levy, R., & Goldman-Rakic, P. S. (2000). Segregation of working memory functions within the dorsolateral prefrontal cortex. *Experimental Brain Research 133*(1), 23-32.

Lieberman, M. D., & Cunningham, W. A. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Social Cognitive and Affective Neuroscience, 4*(4), 423-428.

Macmillian, N. A., & Creelman, C. D. (1991). *Detection theory: a user's guide*. New York: Cambridge University Press.

Mak, A. K., Hu, Z. G., Zhang, J. X., Xiao, Z., & Lee, T. M. (2009). Sex-related differences in neural activity during emotion regulation. *Neuropsychologia, 47*(13), 2900-2908.

Matud, M. P. (2004). Gender differences in stress and coping styles. *Personality and Individual Differences, 37*(7), 1401-1415.

Mayberg, H. S. (1997). Limbic-cortical dysregulation: a proposed model of depression. *The Journal of Neuropsychiatry & Clinical Neurosciences 9*(3), 471-481.

McClure, E. B. (2000). A meta-analytic review of sex differences in facial expression processing and their development in infants, children, and adolescents. *Psychological Bulletin, 126*(3), 424-453.

McClure, E. B., Monk, C. S., Nelson, E. E., Zarahn, E., Leibenluft, E., Bilder, R. M., Charney, D. S., Ernst, M., & Pine, D. S. (2004). A developmental examination of gender differences in brain engagement during evaluation of threat. *Biological Psychiatry, 55*(11), 1047-1055.

McKiernan, K. A., Kaufman, J. N., Kucera-Thompson, J., & Binder, J. R. (2003). A parametric manipulation of factors affecting task-induced deactivation in functional neuroimaging. *Journal of Cognitive Neuroscience, 15*(3), 394-408.

McRae, K., Ochsner, K. N., Mauss, I. B., Gabrieli, J. J. D., & Gross, J. J. (2008). Gender differences in emotion regulation: An fMRI study of cognitive reappraisal. *Group Processes and Intergroup Relations, 11*(2), 143-163.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*(1), 167-202.

Mobbs, D., Marchant, J. L., Hassabis, D., Seymour, B., Tan, G., Gray, M., Petrovic, P., Dolan, R. J., & Frith, C. D. (2009). From threat to fear: The neural organization of defensive fear systems in humans. *The Journal of Neuroscience, 29*(39), 12236-12243.

Morey, R. A., Dolcos, F., Petty, C. M., Cooper, D. A., Hayes, J. P., LaBar, K. S., & McCarthy, G. (2009). The role of trauma-related distractors on neural systems for working memory and emotion processing in posttraumatic stress disorder. *Journal of Psychiatric Research, 43*(8), 809-817.

Nichols, T., Brett, M., Andersson, J., Wager, T., & Poline, J. B. (2005). Valid conjunction inference with the minimum statistic. *Neuroimage, 25*(3), 653-660.

Northoff, G., & Bermpohl, F. (2004). Cortical midline structures and the self. *Trends in Cognitive Sciences, 8*(3), 102-107.

Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., & Panksepp, J. (2006). Self-referential processing in our brain--a meta-analysis of imaging studies on the self. *Neuroimage, 31*(1), 440-457.

Ochsner, K. N. (2000). Are affective events richly recollected or simply familiar? The experience and process of recognizing feelings past. *Journal of Experimental Psychology: General, 129*(2), 242-261.

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage, 23*(2), 483-499.

Orozco, S., & Ehlers, C. L. (1998). Gender differences in electrophysiological responses to facial stimuli. *Biological Psychiatry, 44*(4), 281-289.

Phan, K. L., Taylor, S. F., Welsh, R. C., Ho, S. H., Britton, J. C., & Liberzon, I. (2004). Neural correlates of individual ratings of emotional salience: a trial-related fMRI study. *Neuroimage, 21*(2), 768-780.

Pitroda, S., Angstadt, M., McCloskey, M. S., Coccaro, E. F., & Phan, K. L. (2008). Emotional experience modulates brain activity during fixation periods between tasks. *Neuroscience Letters, 443*(2), 72-76.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences USA, 98*(2), 676-682.

Sabatinelli, D., Fortune, E. E., Li, Q., Siddiqui, A., Krafft, C., Oliver, W. T., Beck, S., & Jeffries, J. (2011). Emotional perception: meta-analyses of face and natural scene processing. *Neuroimage, 54*(3), 2524-2533.

Schacter, D., Addis, D., & Buckner, R. (2007). Remembering the past to imagine the future: the prospective brain. *Nature reviews. Neuroscience, 8*(9), 657-661.

Seidel, E.-M., Habel, U., Kirschner, M., Gur, R. C., & Derntl, B. (2010). The impact of facial emotional expressions on behavioral tendencies in females and males. *Journal of Experimental Psychology. Human Perception and Performance, 36*(2), 500-507.

Seidlitz, L., & Diener, E. (1998). Sex differences in the recall of affective experiences. *Journal of Personality and Social Psychology, 74*(1), 262-271.

Sharot, T., Delgado, M. R., & Phelps, E. A. (2004). How emotion enhances the feeling of remembering. *Nature Neuroscience, 7*(12), 1376-1380.

Shields, S. A. (1991). Gender in the psychology of emotion: A selective research review. In K. T. Strongman (Ed.), *International review of studies on emotion* (pp. 227-245). New York: Wiley.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, California: Consulting Psychologists Press.

Svoboda, E., McKinnon, M. C., & Levine, B. (2006). The functional neuroanatomy of autobiographical memory: a meta-analysis. *Neuropsychologia, 44*(12), 2189-2208.

Tanaka, S., Honda, M., & Sadato, N. (2005). Modality-specific cognitive function of medial and lateral human brodmann area 6. *The Journal of Neuroscience, 25*(2), 496-501.

Thayer, J. F., Rossy, L. A., Ruiz-Padial, E., & Johnsen, B. H. (2003). Gender differences in the relationship between emotional regulation and depressive symptoms. *Cognitive Therapy and Research, 27*(3), 349-364.

Tottenham, N., Borscheid, A., Ellertsen, K., Marcus, D. J., & Nelson, D. A. (2002). *Categorization of facial expressions in children and adults: Establishing a larger stimulus set*. Paper presented at the Annual Meeting of the Cognitive Neuroscience Society, San Francisco.

Wager, T. D., Phan, K. L., Liberzon, I., & Taylor, S. F. (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. *NeuroImage, 19*(3), 513-531.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS Scales. *Journal of Personality and Social Psychology, 54*(6), 1063-1070.

Weissman-Fogel, I., Moayedi, M., Taylor, K. S., Pope, G., & Davis, K. D. (2010). Cognitive and default-mode resting state networks: Do male and female brains "rest" differently? *Human Brain Mapping, 31*(11), 1713-1726.

Wiebking, C., de Greck, M., Duncan, N. W., Heinzel, A., Tempelmann, C., & Northoff, G. (2011). Are emotions associated with activity during rest or interoception? An exploratory fMRI study in healthy subjects. *Neuroscience Letters, 491*(1), 87-92.

Tables

Table 3.1. Common brain regions engaged in response to angry-face distraction by women and men.

Brain Regions		BA	Females			T values		Mask	Males			T values		Mask	Time (TR)
			Talairach Coordinates (x, y, z)						Talairach Coordinates (x, y, z)						
Increased Activity (Emo > Scr & Emo > Neu)						(Emo > Scr)	(Emo > Neu)	(Emo > Scr)				(Emo > Scr)	(Emo > Neu)	(Emo > Scr)	
vmPFC (1)	R Medial Frontal Gyrus	BA 10	4	50	-6	5.67	2.11	1.81	-	-	-	-	-	-	9
	L Medial Frontal Gyrus	BA 10	-	-	-	-	-	-	-8	46	-9	4.67	1.80	1.99	9
TOC	L Fusiform Gyrus	BA 37	-44	-59	-7	5.22	3.56	9.49	-44	-63	-7	7.09	5.74	7.63	9
	L Inferior Occipital Gyrus	BA 19	-40	-74	-3	7.72	4.02	8.89	-40	-70	0	9.38	3.92	9.42	9
	R Fusiform Gyrus	BA 37	40	-51	-8	8.49	6.63	5.91	40	-55	-7	12.16	6.58	6.23	9
	R Inferior Occipital Gyrus	BA 19	40	-70	-3	8.62	4.71	9.08	40	-82	-3	11.77	3.57	8.62	9
	R Middle Occipital Gyrus	BA 19	48	-77	11	6.83	6.21	7.80	44	-73	7	7.94	5.99	7.55	9
Amygdala	R Amygdala		20	-8	-13	4.13	2.95	7.93	20	-8	-13	7.67	3.43	7.93	9
Decreased Activity (Scr > Emo & Neu > Emo)						(Scr > Emo)	(Neu > Emo)	(Scr > Emo)				(Scr > Emo)	(Neu > Emo)	(Scr > Emo)	
dlPFC	R Middle Frontal Gyrus	BA 9	40	32	28	5.22	3.55	7.34	36	37	35	3.97	2.28	2.40	9
	L Middle Frontal Gyrus	BA 8	-40	25	43	6.62	2.39	1.59	-32	33	43	5.82	3.14	2.52	9
dmPFC	L Medial Frontal Gyrus	BA 6	-4	-9	59	7.52	4.08	2.57	0	-9	52	4.21	2.11	2.28	9
	L Precentral Gyrus	BA 6	-59	-3	11	5.33	2.87	2.43	-36	-20	64	3.48	2.35	2.40	8
LTC	R Superior Temporal Gyrus	BA 42	59	-26	16	4.84	4.23	3.27	59	-26	16	3.71	2.86	3.27	9
	L Superior Temporal Gyrus	BA 22	-51	-15	8	9.35	3.75	4.35	-63	-15	4	4.41	2.21	2.04	8
mPOC	L Precuneus/Superior Parietal Lobule	BA 7	-4	-71	48	5.70	2.41	4.40	-8	-63	55	4.59	4.33	2.12	9
	R Cuneus	BA 7	12	-68	33	5.89	3.39	2.92	8	-72	33	4.79	2.58	3.29	9
	L Cuneus (2)	BA 18	0	-73	15	3.89	1.87	3.34	-12	-76	41	4.24	2.32	2.06	9

Table 3.1. (continued). The displayed *t* values correspond to the peak voxels from the most dissimilar contrasts, as identified in brain areas showing activations and *de*activations (i.e., Emo > Scr and Scr > Emo, respectively). A joint threshold of *p* < 0.0005 was used for each of the contributing maps, calculated independently in women and men. The results were masked by regions showing general sensitivity to negative distraction [i.e., increased (Emo > Scr) or decreased (Scr > Emo) activity], on the basis of findings from a previous investigation (Dolcos & McCarthy, 2006); see the Methods section for details). BA, Brodmann area; TR, repetition time; Emo, emotional distracter; Scr, scrambled distracter; Neu, neutral distracter; vmPFC, ventro-medial prefrontal cortex; TOC, temporo-occipital cortex; dlPFC, dorso-lateral prefrontal cortex; dmPFC, dorso-medial prefrontal cortex; LFC, lateral frontal cortex; LTC, lateral temporal cortex; mPOC, medial parieto-occipital cortex. Although both women and men showed increased activity in adjacent vmPFC, the areas did not overlap. Left cuneus showed relative activation to negative distraction in the mask (Emo < Scr).

Table 3.2. Sex differences in activity linked to differences in working memory performance for level-of-confidence 3 trials.

Brain Regions		BA	Talairach Coordinates (x, y, z)			T values		Mask	Time (TR)
(EmoF > EmoM) & (EmoF > Baseline)						*(EmoF > EmoM)*	*(EmoF > Baseline)*	*(Emo > Scr)*	
dmPFC	Superior Frontal Gyrus	6	0	11	66	3.32	4.69	1.95	9
sgACC	L Anterior Cingulate	24/25	-4	23	-5	2.73	3.08	5.16	9
LTC	R Superior Temporal Gyrus	13	44	-45	24	2.59	4.47	2.64	9
TOC	L Fusiform Gyrus	37	-51	-48	-18	4.22	4.05	9.62	9
	R Middle Temporal Gyrus	37	55	-62	7	3.19	4.80	7.79	9
Cerebellum	L Tuber	-	-51	-48	-21	3.76	4.04	5.27	9
	R Declive	-	48	-52	-21	2.22	4.12	5.48	9
(EmoF > EmoM) & (EmoM < Baseline)						*(EmoF > EmoM)*	*(EmoM < Baseline)*	*(Scr > Emo)*	
dlPFC	L Superior Frontal Gyrus	10	-24	47	5	3.10	5.15	5.00	9
	R Superior Frontal Gyrus	9	32	48	27	2.92	2.76	1.78	9
	R Middle Frontal Gyrus	10	32	43	5	4.06	5.62	3.27	9
LFC	L Superior Frontal Gyrus	8	-28	41	38	3.41	3.35	2.14	9
	R Superior Frontal Gyrus	6/8	36	10	47	3.31	4.21	2.83	9
PrCG	L Precentral Gyrus	4/6	-32	-17	49	2.43	3.16	2.39	9
PoCG	L Postcentral Gyrus	3	-40	-21	49	3.48	4.50	1.96	9
dACC	L Cingulate Gyrus	32	-8	25	25	2.70	3.72	2.25	9
LPC	L Postcentral Gyrus	40	-51	-23	16	2.99	5.84	5.08	9
	L Postcentral Gyrus	7	-20	-47	65	4.49	6.07	1.78	9
	R Inferior Parietal Lobule	40	44	-48	43	4.90	5.11	6.46	9
	L Inferior Parietal Lobule	40	-48	-67	51	3.70	4.80	4.56	9
		7	-44	-71	51	3.33	4.99	3.77	9
		39	-48	-68	48	3.36	4.27	4.24	9
MPC	L Superior Parietal Lobule	7	-4	-67	55	4.16	5.98	1.88	9
LTC	R Superior Temporal Gyrus	22	55	-15	4	3.35	3.78	7.10	9
	L Superior Temporal Gyrus	22	-51	-15	4	3.90	5.19	4.88	9
		13	-48	-19	8	3.19	6.62	4.42	9
		42	-55	-23	16	2.98	6.77	3.73	9
	R Middle Temporal Gyrus	21	67	-35	-2	4.08	4.33	1.26	9
PCC	R Cingulate Gyrus	31	12	-21	38	3.59	3.34	2.04	9
	L Cingulate Gyrus	31	-4	-44	43	3.59	3.89	2.98	9
LPOC	R Precuneus	19	40	-72	40	4.49	6.31	5.14	9
mPOC	R Precuneus	7	4	-63	51	2.71	3.52	2.27	9
	L Superior Parietal Lobule / Precuneus	7	-4	-67	55	4.16	5.98	1.88	9
	L Cuneus	19	-8	-80	30	2.54	4.57	2.02	9
Cerebellum	R Dentate	-	20	-56	-24	3.07	3.35	2.51	9
(EmoM > EmoF) & (EmoM > Baseline)						*(EmoM > EmoF)*	*(EmoM > Baseline)*	*(Emo > Scr)*	
vlPFC (1)	L Middle Frontal Gyrus	47	-48	42	-5	3.39	2.71	3.38	9
TOC	R Fusiform/Lingual Gyrus	19	32	-74	-10	2.90	5.23	9.36	9
LOC	R Cuneus	19	16	-96	27	2.93	5.79	3.80	9

Table 3.2. (continued). The *t* values displayed correspond to the peak voxels from the between-groups comparisons (i.e., women vs. men). A joint threshold of $p < 0.0005$ was used for the conjunction maps identifying differences between women and men. The results were masked by regions showing general sensitivity to negative distraction [i.e., increased (Emo > Scr) or decreased (Scr > Emo) activity], on the basis of findings from a previous investigation (Dolcos & McCarthy, 2006; see the Methods section for details). BA, Brodmann area; TR, repetition time; Emo, emotional distracter; Scr, scrambled distracter; Neu, neutral distracter; dmPFC, dorso-medial prefrontal cortex; sgACC, subgenual anterior cingulate cortex; LTC, lateral temporal cortex; TOC, temporo-occipital cortex; dlPFC, dorso-lateral PFC; vmPFC, ventro-medial prefrontal cortex; TOC, temporo-occipital cortex; dlPFC, dorso-lateral PFC; LFC, lateral frontal cortex; PrCG, precentral gyrus; PoCG, postcentral gyrus; dACC, dorsal ACC; LPC, lateral parietal cortex; MPC, medial parietal cortex; PCC, posterior cingulate cortex; POC, parieto-occipital cortex; mPOC, medial POC; vlPFC, ventro-lateral PFC; MOC, medial occipital cortex. Activity in the left ventro-lateral PFC (five voxels), a typical VAS area, was identified using the (Scr > Emo) mask (Dolcos & McCarthy, 2006), due to a specific pattern of deactivation in this region in women.

Table 3.3. Covariation between brain activity and level-of-confidence 3 working memory performance in women and men.

Brain Regions		BA	Talairach Coordinates (x, y, z)			Correlations (r values)			T values	Mask	Time (TR)
						Emo	Neu	Scr			
Women: Negative co-variation & (EmoF > Baseline)									(EmoF > Baseline)	(Emo > Scr)	
vlPFC	R Inferior Frontal Gyrus	45/47	55	24	6	-0.73***	-0.31	-0.21	4.37	7.42	9
LTC	R Superior Temporal Gyrus	38	32	3	-17	-0.65***	-0.39	0.13	3.17	3.53	9
		22	51	-46	10	-0.59**	-0.23	-0.02	3.92	3.71	9
TOC	R Fusiform Gyrus	19/37	32	-66	-7	-0.68***	0.03	-0.26	3.71	9.27	9
	L Fusiform Gyrus	37	-48	-48	-18	-0.58**	-0.34	-0.49*	5.40	10.06	9
	R Middle Temporal Gyrus	37	48	-62	3	-0.67***	0.07	-0.36	3.99	5.89	9
	R Inferior Temporal Gyrus	37	48	-66	-3	-0.69***	-0.07	-0.23	4.23	7.25	9
LOC	R Middle Occipital Gyrus	18	28	-97	12	-0.52*	0.21	0.13	6.54	5.47	9
	L Middle Occipital Gyrus	19/18	-40	-92	16	-0.61**	-0.28	-0.33	5.01	9.41	9
	L Inferior Occipital Gyrus	18	-24	-90	-6	-0.68***	-0.23	-0.2	3.15	5.36	9
MOC	R Lingual Gyrus	17	8	-89	4	0.76***	0.09	0.41	4.27	5.05	9
	R Cuneus	17/18	8	-93	5	-0.86***	-0.003	-0.29	5.19	5.98	9
MTL	R Amygdala/Uncus		28	-1	-17	-0.62**	-0.11	0.03	3.96	5.79	9
	L Parahippocampal Gyrus	27	-20	-31	-2	-0.66***	-0.12	-0.23	3.34	6.17	9
Cerebellum	R Declive	-	32	-63	-7	-0.78***	-0.23	-0.33	3.21	7.82	9
Men: Positive co-variation & (EmoM < Baseline)									(EmoM < Baseline)	(Scr > Emo)	
LFC	R Superior Frontal Gyrus	6	16	-8	67	0.77***	0.32	0.38	5.15	2.12	9
	R Middle Frontal Gyrus	6/8	28	18	54	0.64***	0.31	-0.03	4.72	3.24	9
MFC	R Medial Frontal Gyrus	6	12	-17	49	0.78***	-0.18	0.02	3.41	3.89	9
PcL	L Paracentral Lobule	31	-4	-25	45	0.69***	0.17	-0.21	4.99	2.28	9
dACC	L Cingulate Gyrus	24	-4	-6	44	0.52*	0.17	0.15	3.70	1.93	9
	R Cingulate Gyrus	24	4	-6	44	0.56*	0.12	0.27	3.17	1.84	9
LTC	L Superior Temporal Gyrus	22	-51	-15	4	0.56*	0.23	0.05	5.19	4.88	9
	L Transverse Temporal Gyrus	42	-55	-15	12	0.83***	0.36	0.27	5.62	2.51	9
mPOC	L Precuneus	7	-4	-68	44	0.76***	0.37	-0.01	4.92	5.18	9
	R Precuneus	7	4	-64	44	0.65***	0.21	-0.22	3.18	2.28	9
Cerebellum	R Declive	-	8	-59	-14	0.76***	0.28	0.05	4.31	2.64	9
Women: Positive co-variation & (EmoF < Baseline)									(Emo F < Baseline)	(Scr > Emo)	
LTC	L Inferior Temporal Gyrus	20	-63	-28	-19	0.61**	-0.08	0.62**	3.20	4.15	9

Asterisks indicate the significance of correlations at *$p < 0.05$, **at $p < 0.01$, *** at $p < 0.005$

Table 3.3. (continued). The displayed *r* and *t* values correspond to the peak voxels identified by brain-behavior correlations for the emotional level-of-confidence 3 trials. A joint threshold of *p* < 0.0005 was used for each of the conjunction maps. The results were masked by regions showing general sensitivity to negative distraction [i.e., increased (Emo > Scr) or decreased (Scr > Emo) activity], on the basis of findings from a previous investigation (Dolcos & McCarthy, 2006); see the Methods section for details). BA, Brodmann area; TR, repetition time; Emo, emotional distracter; Scr, scrambled distracter; Neu, neutral distracter; vlPFC, ventro-lateral PFC; LTC, lateral temporal cortex; TOC, temporo-occipital cortex; LatOC, lateral occipital cortex; MOC, medial OC; MTL, medial temporal lobe; LFC, lateral frontal cortex; MFC, medial frontal cortex; PcL, paracentral lobule; dACC, dorsal anterior cingulate cortex; mPOC, medial parieto-occipital cortex.
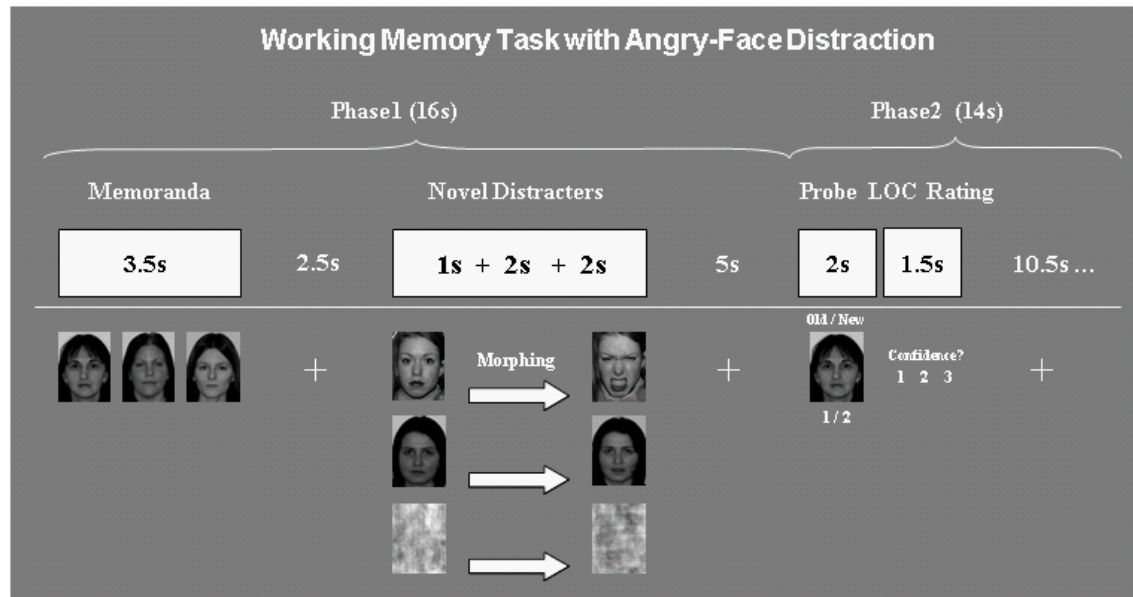
Figures

Figure 3.1. Diagram of the WM task with angry-face distraction. Functional magnetic resonance imaging (fMRI) data were recorded while subjects performed a working memory (WM) task with distraction. To increase the impact of distraction, the novel distracters were morphed. WM performance was measured using an old/new recognition memory task, followed by a level-of-confidence (LOC) task (1 = *low*, 2 = *medium*, 3 = *high*). Written informed consent was obtained for photograph publication of all faces illustrated in the figure that are not part of the standardized NimSitm Face Stimulus Set. From "The Impact of Anxiety-Inducing Distraction on Cognitive Performance: A Combined Brain Imaging and Personality Investigation," by E. Denkova, G. Wong, S. Dolcos, K. Sung, L. Wang, N. Coupland, and F. Dolcos, 2010, *PLoS ONE*, *5*, e14150, p. 3. Copyright 2010 by Denkova et al. Adapted with permission
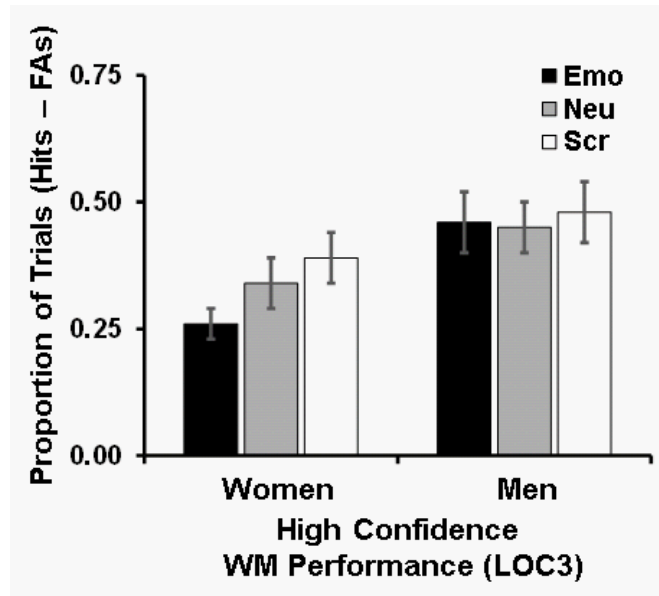
Figure 3.2. Angry-face distraction impairs high-confidence responses in women. Women showed impaired WM performance for the trials associated with the highest level of confidence (LOC 3 trials; 1 = *lowest*, 3 = *highest*), and this difference was driven by performance in the trials associated with emotional distraction. Error bars represent standard errors of the means. Emo, trials with emotional distraction; Neu, trials with neutral distraction; Scr, trials with scrambled distraction; FAs, false alarms; WM, working memory
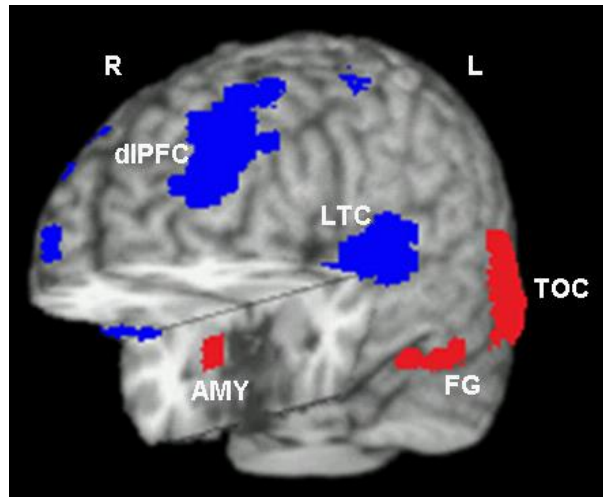
Figure 3.3. Brain regions sensitive to angry-face distraction in both women and men. Common responses to emotional distraction in both women and men were identified in brain regions associated with VAS (amygdala [AMY], fusiform gyrus [FG], and temporo-occipital cortex [TOC]), showing increased activity to emotional distraction (Emo > Neu ∩ Emo > Scr), and in brain regions associated with DES (dorsolateral prefrontal cortex [dlPFC] and lateral temporal cortex [LTC]), showing *de*creased activity to emotional distraction (Emo < Neu ∩ Emo < Scr). The cut-out of the brain reveals similar responses in women and men in the right AMY. The conjunction activation maps contributing to the overlapping activations were identified separately in male and female subjects and displayed at a joint threshold of $p < 0.0005$, superimposed on a high-resolution brain image displayed in a tridimensional view using MRI-cro (http://www.mccauslandcenter.sc.edu/mricro/mricro/). R, Right; L, Left
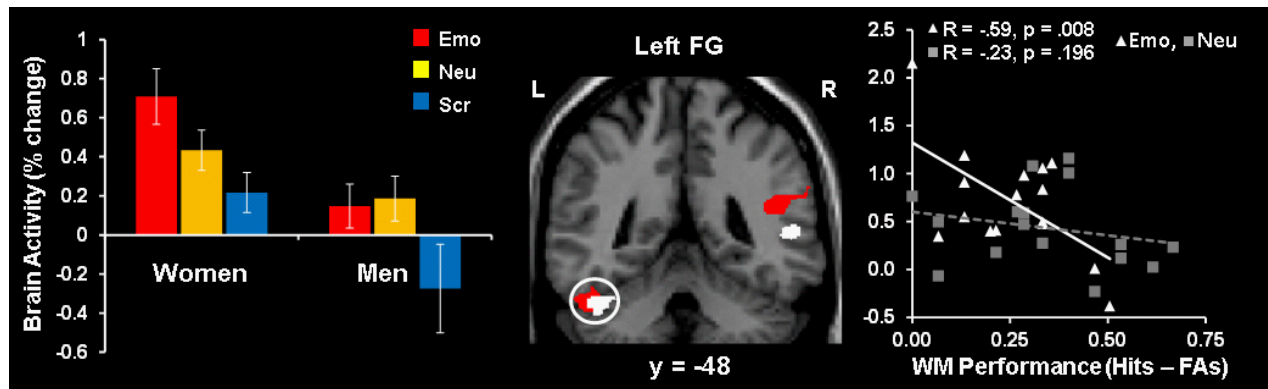
Figure 3.4. Increased sensitivity to emotional distraction in left fusiform gyrus (FG) in women. Women showed increased activity in response to angry faces and negative covariation with WM performance in the left FG (BA 37). In the middle panel, the white circle of the left side indicates the FG region showing the overlap between these two effects. Inside the circle, a darker (red) area illustrates the difference in activation in response to angry-face LOC 3 trials in women versus men, masked with the main effect of emotion relative to baseline in women. The overlapping white region inside the circle illustrates the negative covariation between brain activity and WM scores for angry-face LOC 3 trials in women, masked with the main effect of emotion relative to baseline in women. The bar graph illustrates the fMRI signal, as extracted from the region of interest (ROI) corresponding to the overlap between the two maps. The scatterplot illustrates the covariation between brain activity and LOC 3 WM scores in women, for the trials corresponding to the emotional (Emo) and neutral (Neu) distracters, as extracted from the same functional ROI. The activation maps are superimposed on a high-resolution brain image displayed in coronal view (with *y* indicating the Talairach coordinate on the anterior-posterior axis of the brain); the joint threshold of these conjunction maps is $p < 0.0005$. Error bars represent standard errors of means. Emo, emotional distracters; Neu, neutral distracters; Scr, scrambled distracters; L, left; R, right
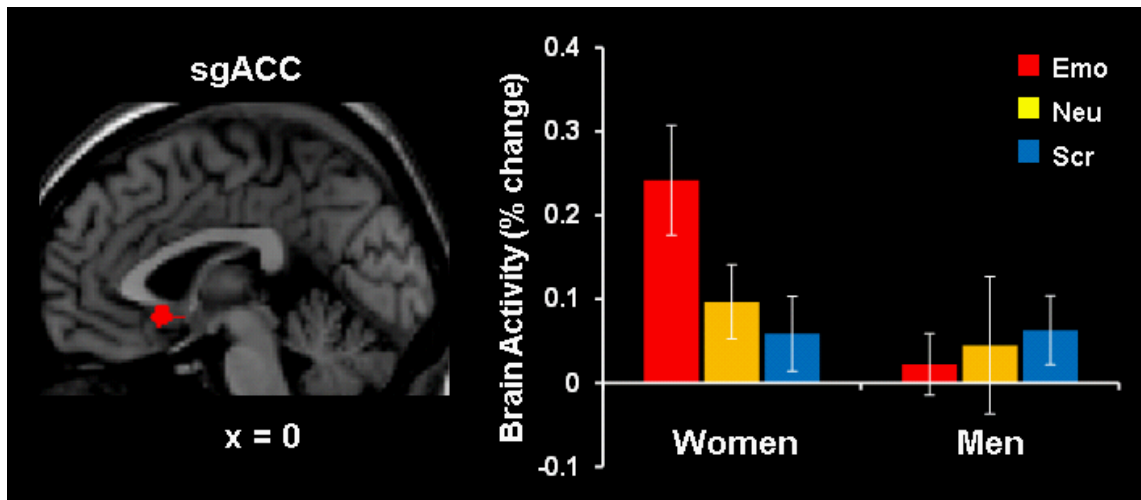
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Figure 3.5. Increased activity in the subgenual anterior cingulate cortex (sgACC) in women. Women showed an increased response to emotional distraction in the sgACC (BA 25). The area indicated by the white circle illustrates the difference in activation in response to angry faces in women versus men, masked with the main effect of emotion relative to baseline in women. The bar graph illustrates the fMRI signal, as extracted from the region of interest corresponding to the difference in activation between women and men. The activation map is superimposed on a high-resolution brain image displayed in sagittal view (with *x* indicating the Talairach coordinate on the left-right axis of the brain); the joint threshold of the conjunction maps is $p < 0.0005$. Error bars represent standard errors of means. Emo, emotional distracters; Neu, neutral distracters; Scr, scrambled distracters
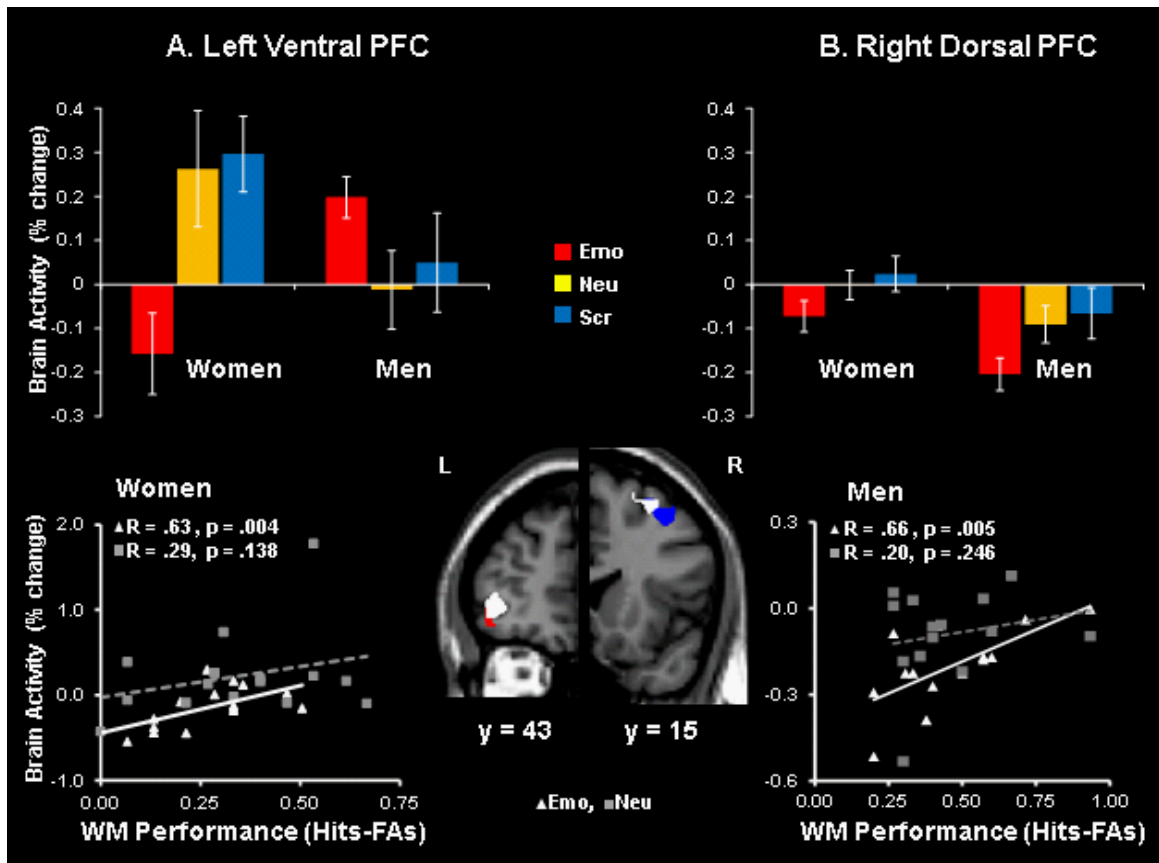
Figure 3.6. Sex-related dorso-ventral dissociation in the lateral prefrontal cortex (PFC) in response to emotional distraction, linked to WM performance. The left lateral PFC (BA 47) had overall reduced activity in women but showed increased activity in those women who coped successfully with emotional distraction (A); a similar pattern was observed in the right lateral PFC (BA 8/6) in men - although they overall showed reduced activity in this region as compared to women, those who had increased activity also coped successfully with emotional distraction (B). **(A)** The bar graph illustrates the fMRI signal, as extracted from the region of interest (ROI) corresponding to the difference in activation between women and men. The ROI is located inside the left circle, in the central panel, and illustrated with a darker color (red).

Figure 3.6. (continued). This area showed greater activation to angry faces in men than in women, masked with the effect of emotion relative to baseline activity in men. The overlapping white area inside the same circle illustrates the positive covariation between brain activity and LOC 3 WM performance in women, in an area sensitive to emotional distraction (see Figure 5 in Denkova et al., 2010). The scatterplot illustrates the covariation between brain activity and LOC 3 WM scores in women for the trials corresponding to the emotional (Emo) and neutral (Neu) distracters, as extracted from the ROI meeting the conjunction criteria (Denkova et al., 2010). **(B)** The bar graph illustrates the fMRI signal, as extracted from the ROI corresponding to the overlap between the two maps located inside the white circle on the right side, in the central panel. This circle surrounds a darker area (blue), illustrating greater *de*activation to angry faces in men than in women, masked with the effect of emotion relative to baseline activity in men. The overlapping white area inside the same circle illustrates the positive covariation between brain activity and LOC 3 WM scores in men, for the trials corresponding to the emotional distracters, masked with the effect of emotion relative to baseline. The scatterplot illustrates the covariation between brain activity and LOC 3 WM scores in men for the trials corresponding to the emotional (Emo) and neutral (Neu) distracters, as extracted from the ROI corresponding to the overlap of the two maps. The conjunction activation maps are displayed at a joint threshold of $p < 0.0005$, superimposed on a high-resolution brain image displayed in coronal view (with y indicating the Talairach coordinate on the anterior-posterior axis of the brain). Error bars represent standard errors of means. Emo, emotional distracters; Neu, neutral distracters; Scr, scrambled distracters; L, left; R, right.

CHAPTER 4:

THE IMPACT AND REGULATION OF

INTERNAL EMOTIONAL DISTRACTION

Brain Activity and Network Interactions in Regulating the Impact of Internal

Emotional Distraction on Working Memory

Introduction

Emotional distractions can be elicited not only by external stimuli, but they can also originate from the internal environment, and interfere with our goal-oriented performance. For instance, we might find it difficult to focus at work after witnessing a traffic accident during our commute, because images of the crash scene and thoughts about the victims keep intruding in our mind. Such "internal distractions" are typically generated by spontaneous cognitions (i.e., memories, thoughts, and images that rise into our awareness involuntarily), and they are often related to negative events. Although previous investigations have identified the mechanisms associated with the impact of and coping with external emotional distractions (e.g., seeing a car crash while driving) (reviewed in Dolcos, Iordan, & Dolcos, 2011; Iordan, Dolcos, & Dolcos, 2013b), the mechanisms associated with the response to and regulation of distractions originating from "within" the individual (e.g., subsequent thoughts about the car crash) are unclear. The present study investigated the impact of internal emotional distractions elicited by recollection of personal events (i.e., negative autobiographical memories) irrelevant for the task at hand, and the effects of instructed attempts at regulating them, on both the *subjective* emotional experience and the *objective* cognitive performance. Clarification of these issues is important because distracting phenomena such as intrusive memories, rumination, and mind-wandering have been linked to symptoms of affective dysfunctions (Gotlib & Joormann, 2010; McNally, 2006), and the ability to successfully regulate them has been associated with increased resilience against such disturbances (Southwick & Charney, 2012).

Involuntary recollections of negative autobiographical memories (AMs) have mainly been investigated in clinical conditions, such as post-traumatic stress disorder (PTSD) and depression, where they are more intrusive and distressing (Ono, Devilly, & Shum, 2015). PTSD is a clinical

condition characterized by recurrent re-experiencing of trauma due to the spontaneous recollection of an extreme, life-threatening event. Results of a previous investigation in war-veterans diagnosed with PTSD (Morey et al., 2009) suggest the possibility of a link between spontaneous recollection of such negative AMs with enhanced personal significance and increased cognitive distraction. More specifically, processing of cues related to traumatic events (e.g., combat-related pictures) may trigger automatic retrieval of traumatic memories and have an impairing effect on ongoing goal-oriented processing (Dolcos, 2013). Similar to PTSD, depression is also characterized by recurrent recollection of negative AMs (Kuyken & Brewin, 1994). Its key symptom, rumination (i.e., recurrent thoughts about the depressive symptoms and their implications) (Nolen-Hoeksema, 1991), has been linked to increased recollection of over-general AMs (Sumner, 2012; Williams, 2006), which may, in turn, contribute to increased distractibility in depression.

Although available evidence suggests that uncontrolled recollection of and rumination on distressing memories observed in PTSD and depression may lead to impaired cognition due to enhanced emotional distraction, the identity of the mechanisms underlying such effects is not clear. This may partly be due to the challenging nature of such investigations in clinical patients and the generally unpredictable nature of spontaneous AMs. Thus, investigation of such issues in healthy and/or subclinical samples, under controlled experimental conditions, is important for understanding the basic mechanisms whose (transient) perturbations may lead to similar impairing effects. This is supported also by evidence showing that negative AMs are the most common form of spontaneous cognitions reported by healthy individuals, and that they share many phenomenological characteristics with other types of intrusive cognitions (e.g., ruminations) (Krans, de Bree, & Moulds, 2015).

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A critical aspect regarding the way emotional distraction ultimately influences our cognition and behavior is the ability to engage control mechanisms in order to cope with it. Although much progress has recently been made in understanding the mechanisms of emotion regulation (ER) (Ochsner, Silvers, & Buhle, 2012) and of coping with external emotional distraction (Iordan et al., 2013b), the effects of engaging instructed ER to cope with internal emotional distraction are unclear. A recent investigation from our group (Denkova, Dolcos, & Dolcos, 2015) validated the use of "focused attention" (FA) as an ER strategy during emotional AMs recollection. This ER strategy involves shifting attention away from the emotional aspects of stimuli and events, by changing the focus of memories or thoughts, in order to alter the emotional responses (Gross, 2008). More specifically, the results of our previous investigation showed that instructing subjects to focus away from emotion and onto the non-emotional contextual aspects (e.g., "when did the event happened", "who else was involved" etc.) during AMs recollection was linked to reduced *subjective* emotional experience (Denkova et al., 2015). However, it is not known whether similar beneficial effects would be observed on *objective* cognitive performance. Because focused attention can be more promptly engaged than other ER strategies, such as reappraisal (Hajcak, Dunning, & Foti, 2009; Thiruchselvam, Blechert, Sheppes, Rydstrom, & Gross, 2011), it is well suited to investigate ER effects in the context of emotional distraction. Hence, the first main goal of the present investigation was to determine whether internal emotional distraction impacts cognitive performance and whether the instructed use of focused attention as an ER strategy diminishes this impact.

Turning to the neural level, previous investigations have identified the neural mechanisms mediating the response to and coping with external emotional distraction, but the neural correlates of the response to and regulation of internal emotional distraction are unknown. Brain

imaging studies in which emotional scenes were presented as task-irrelevant stimuli during WM tasks (Anticevic, Repovs, & Barch, 2010; Denkova et al., 2010; Diaz et al., 2011; Dolcos, Diaz-Granados, Wang, & McCarthy, 2008; Dolcos et al., 2013; Dolcos, Kragel, Wang, & McCarthy, 2006; Dolcos & McCarthy, 2006; Iordan & Dolcos, 2015; Iordan, Dolcos, Denkova, & Dolcos, 2013a; Oei et al., 2012) showed that the impairing effect of negative distraction originating from the external environment was linked to opposing patterns of activity in two large neural systems: a dorsal executive system (DES) involved in cognitive/executive processing, showing decreased/disrupted activity, and a ventral affective system (VAS) involved in emotion processing, showing increased activity (reviewed in Dolcos et al., 2011; Iordan et al., 2013b). As mentioned earlier, DES includes brain regions typically associated with cognitive control and maintenance of goal-relevant information (dorsolateral prefrontal cortex [dlPFC] and lateral parietal cortex [LPC]), which are also part of the fronto-parietal network (FPN) (D'Esposito, Cooney, Gazzaley, Gibbs, & Postle, 2006; Fuster, 1997; Koenigs, Barbey, Postle, & Grafman, 2009; Nee et al., 2012; Niendam et al., 2012; Smith & Jonides, 1999), whereas VAS includes regions involved in both basic emotion processing (amygdala [AMY]) and emotion integration and regulation (ventrolateral prefrontal cortex [vlPFC]), as well as regions involved in self-referential processing (medial prefrontal cortex [mPFC]), which are also part of the salience (SN) (Bressler & Menon, 2010; Corbetta, Patel, & Shulman, 2008; Seeley et al., 2007) and default-mode (DMN) networks (Buckner, Andrews-Hanna, & Schacter, 2008; Fox et al., 2005; Greicius, Krasnow, Reiss, & Menon, 2003; Raichle et al., 2001), respectively.

Regarding the neural correlates of manipulating attention as an ER strategy, current evidence generally points to down-regulation of emotion-sensitive brain regions (AMY) by the recruitment of cognitive/executive control regions (prefrontal and parietal cortices) during

attentional deployment, similar to other ER strategies, such as reappraisal (Kanske, Heissler, Schonfelder, Bongers, & Wessa, 2011; McRae et al., 2010; Ochsner et al., 2004; Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). In addition, focusing on context during AMs recollection has previously been linked to increased activity in medial temporal lobe (parahippocampal cortex, PHC) and parietal (inferior parietal lobule, IPL) regions (Denkova et al., 2015), which are memory-related brain regions implicated in retrieval of visuospatial/situational contexts (Hassabis & Maguire, 2007; Ranganath & Ritchey, 2012) and potentially also in attending to such information during retrieval (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Vilberg & Rugg, 2008), respectively. On the other hand, previous investigations of the neural correlates of coping with external emotional distraction suggest a potential role of vlPFC in *spontaneous* ER, because increased activity in this region has previous been associated with *in*creased (not *de*creased) WM performance under external emotional distraction (Dolcos et al., 2011; Iordan et al., 2013b).

Given that previous evidence has been exclusively based on investigations of external distraction, it is not known what the mechanisms involved in the control of internal distraction are. This is highly relevant because studies of emotional distraction have not included *instructed* manipulations of specific ER strategies, and ER studies (Goldin, McRae, Ramel, & Gross, 2008; Gross, 1998; Ochsner & Gross, 2005; Ochsner & Gross, 2008; Ochsner et al., 2012) have not been performed in the context of dual cognitive/emotional tasks, which more closely resemble real-life situations. Thus, the second main goal of the present study was to determine the neural correlates of the response to and regulation of internal emotional distraction and to clarify whether potential benefits of a specific ER strategy (FA) on WM performance are linked to changed dynamics between regions of the FPN.

These issues were addressed here by investigating the initial responses to and instructed regulation of the impact of internal emotional distraction on cognitive performance and the associated neural correlates. Behavioral assessments involved measures of WM performance in the presence of instructions to regulate emotion by focusing attention on either the emotional or non-emotional contextual aspects of recollected AMs. Brain activity was recorded using event-related fMRI, while healthy subjects performed the WM task with internal distraction. In order to clarify potential interactions between regions associated with the major brain networks, analyses of basic differences in brain activity were supplemented by functional connectivity analyses investigating task-induced dissociations in functional coupling between these regions.

Based on the extant evidence, we made the following predictions. First, regarding the behavioral results, we expected that focusing attention away from the emotional content will be reflected in both reduced emotional responses and reduced detrimental impact of recollecting goal-irrelevant negative AMs on WM performance. Second, at the neural level, we expected that internal emotional distraction will involve DES and VAS mechanisms overall similar to external emotional distraction, but also mechanisms specific to internal emotional distraction, linked to increased engagement of AM recollection and self-referential processing regions. Third, regarding the ER manipulation, we expected that focusing away from the emotional content will be reflected in reduced activity in VAS regions and superior engagement of executive regions, along with areas typically involved in the retrieval of contextual information. Finally, we expected increased functional coupling between executive regions under ER. The main study was preceded by a behavioral pilot study examining the role of valence in the impact of internal emotional distraction (see sub-section "Justification for inclusion of only negative AMs" below), and followed by exploratory analyses of sex differences in the response to internal emotional

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distraction (see sub-section "Additional exploratory analysis of sex differences in the response to internal emotional distraction" below).

Methods

Subjects

A total of 30 healthy, young adults (18-35 years of age, 11 males) participated in the behavioral study, out of which 18 young right-handed adults (5 males) also had fMRI data collected. All subjects were screened for neurological and/or psychiatric disorders using a questionnaire developed in consultation with trained clinicians. Additionally, the fMRI subjects were also screened for baseline WM performance using the Delayed Matching to Sample test, part of the Cambridge Automated Neuropsychological Testing Battery (CANTAB) (Cambridge-Cognition). Based on this assessment, data from one female participant were excluded from analyses because of chance-level WM performance, and hence behavioral and fMRI data are reported on 29 and 17 subjects, respectively. The experimental protocol was approved by the Internal Review Board of the University of Illinois at Urbana-Champaign, and all subjects provided written informed consent.

Collection and Selection of Emotional AMs

Personal memories were elicited from each participant during an interview performed about 10 days prior to the fMRI session, using a procedure similar to the one employed in our previous investigations (Denkova, Dolcos, & Dolcos, 2012; Denkova et al., 2015). In brief, we used an autobiographical memory questionnaire (AMQ) (Denkova et al., 2012) comprising 115 written cues for distinct life events (e.g. 'the birth of a family member' and 'being hospitalized'). For each cue, participants were asked to remember an unique episode from their life, that occurred in a specific place and time (e.g. one instance when s/he played in a specific basketball

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game), rather than remembering general or repeated events (e.g. playing high school basketball). Upon recollection, participants were asked to provide a brief description of the memory, which was then used as a personalized memory cue during the fMRI task; notably, at the time of collecting the AMs, participants were naïve to the specific purpose of the pre-scanning interview. To assess phenomenological characteristics of each event, participants dated their memories and rated them on several Likert scales, as follows: emotional valence (on a 7-point scale: -3 = very negative, 0 = neutral and +3 = very positive), emotional intensity, personal significance, the amount of contextual details, vividness (i.e. the amount of visuo-perceptual details) and frequency of retrieval (all of latter used a 7-point scale: 1 = not at all, 7 = extremely). Then, for each participant, the 20 most negative memories were selected, based on the ratings provided in the AMQ (i.e. rated -2 or -3) (For subjects who later performed the WM task outside the fMRI environment, between 18 and 20 negative memories were selected, based on availability). Half of the memories were assigned to the Emotion AM condition and the other half of the memories were assigned to the Context AM condition. The memories in the two conditions were matched as closely as possible in order to avoid differences in terms of age and phenomenological properties, and to ensure that any differences between the two retrieval foci during the fMRI session would not be due to initial differences in the properties of the memories assigned to the two conditions.

The inclusion of only negative memories in the fMRI session was justified by the findings of a behavioral pilot study showing that the recollection of negative but not positive emotional AMs interfered with WM performance. The results of this pilot study are presented in the sub-section "Justification of inclusion of only negative AMs" below.

fMRI tasks

The fMRI session comprised a dual WM-AM recollection task, comprising a *main* WM task and a *secondary* AM recollection task. Immediately before performing the fMRI task, participants were given detailed instructions and performed practice trials in order to familiarize themselves with the tasks and ensure that they understood the instructions.

The Main WM Task

The subjects performed a delayed match-to-sample WM task for shapes, adapted after Dolcos & McCarthy (2006), with cues for AMs presented as distracters during the delay interval between the memoranda and the probes (Figure 4.1). The memoranda consisted of pairs of polygons (Arnoult & Attneave, 1956) randomly generated using a MATLAB script (Collin & McMullen, 2002) to have a range of complexity. A total number of 80 trials were involved. All stimuli were presented using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA).

The pool of 80 trials was divided into 8 sets of 10 trials (counterbalanced across load and distracter-type categories), which were randomly assigned to 8 experimental blocks/runs. To avoid induction of longer-lasting effects, the trials within each block were pseudo-randomized, so that no more than two consecutive trials of the same type were presented. To prevent possible biases resulted from using the same run order, participants were assigned different run orders; a total of 8 different run orders were involved.

As illustrated in Figure 4.1, each trial started with the presentation of shape memoranda (3.5 s), which subjects were instructed to encode and maintain in WM during the delay interval between the offset of the memoranda and the onset of the memory probe (12.5 s). Participants were instructed to maintain focus on the main WM task, while performing the secondary task as instructed (see below), and then when the single-shape probes appeared they had to indicate by a

button press whether they were part of the current memorandum (*Old*) or not (*New*); 50% of the probes were *Old* and 50% were *New*. Subjects were instructed to make quick and accurate responses while the probes were on the screen, and then they also rated the level of confidence (LOC) of their responses, using a 3-point Likert scale (1 = *lowest*, 3 = *highest*). The LOC rating was followed by a 10.5 s inter-trial interval, to allow the hemodynamic response to return to baseline. During this time, participants were instructed to relax and refrain from doing anything systemically that could potentially affect the inter-trial baseline signal (e.g., counting).

The Secondary AM Task: Emotion vs. Context Focus

During the delay interval between the memoranda and the probes, participants were asked to retrieve the memories associated with each personalized memory cue by either focusing on emotional (Emotion condition) or non-emotional contextual (Context condition) aspects of their memories (Figure 4.1). Presentation of AM cues started 3 s after the offset of the memoranda, and occurred for 2.5 s. For the Emotion condition, participants were instructed to focus on the emotional aspects of their memories, including sensations and feelings that they may have triggered (e.g. 'burn in the stomach'). For the Context condition, participants were instructed to focus on the contextual aspects of their memories, by retrieving as many details as possible (e.g. about where and when the event occurred and who/what was present in the event). Each memory cue was preceded by an instruction cue ('Emotion Focus' or 'Context Focus', for the Emotion and Context conditions, respectively). After each memory cue appeared on the screen, participants continued remembering details of the event until cued again to rate their emotion. The emotion elicited by each recollection was rated for negativity on a 5-point Likert scale (1 = *not at all negative* and 5 = *very negative*). Participants were instructed to make quick and accurate responses and to use the whole scale.

We also employed a minimal-distraction control condition involving watching random strings of letters 'X', mimicking the structure of a sentence. For the control stimuli, subjects were instructed to look at the screen and maintain focus on the WM task. The control stimuli were preceded by the instruction 'Look'. For consistency with the AM conditions, each control trial was also rated for negativity.

Justification for Inclusion of Only Negative AMs – Behavioral Pilot Study of the Role of Valence in the Impact of Internal Emotional Distraction

A behavioral pilot study preceded the fMRI investigation and examined the role of valence in the impact of internal emotional distraction on WM performance. Consistent with previous findings regarding valence-related differences in the impact of external emotional distraction (Iordan & Dolcos, 2015), we expected greater cognitive interference under negative compared to positive internal distraction. A total of 27 healthy, young adults (18-37 years of age, 15 females) participated in the pilot study. Data from one participant were excluded from analyses because of chance-level WM performance, and hence the reported results are based on 26 subjects (14 females). The pilot study used a procedure for the collection and selection of emotional AMs similar to the main study. In order to test for valence-related effects, highly positive and negative emotional memories were selected, based on the ratings provided in the AMQ (i.e. rated 2 or 3 and -2 or -3, respectively). The memories in the two conditions were matched as closely as possible in order to avoid differences in terms of age and phenomenological properties. The behavioral task was similar to the one employed in the fMRI investigation. During the delay interval between the memoranda and the probes, participants were asked to retrieve memories associated with each personalized memory cue. There was no manipulation of attentional focus and the subjects did not provide trial-by-trial ratings of their

emotional experience. A sematic memory (SM) task (Denkova et al., 2015) was employed as a control condition for memory-related operations because it involved searches in memory and extended retrieval time, similar to the AM retrieval task. The SM task involved generation of exemplars from different semantic categories (e.g., musical instruments and sports) (Battig & Montague, 1969). The participants were presented with a semantic category name (e.g., fruits and vegetables) and instructed to recall as many exemplars as possible for each category.

Analyses of the pilot data showed increased WM interference for negative compared to positive AMs. The results of a one-way repeated measures ANOVA (Task: positive AM, negative AM, SM) on WM performance yielded a marginal effect [$F_{(2,50)} = 2.92$ $p < 0.063$], and planned comparisons showed significantly lower WM performance when subjects were recollecting negative ($M = 74.70\%$; $SD = 9.43\%$) compared to positive AMs ($M = 79.94\%$; $SD = 10.93\%$) [$t_{(25)} = 2.29$, $p = 0.031$]. Recollection of positive AMs did not impair WM performance, compared to the SM control [$t_{(25)} = 0.53$, $p > 0.1$]. These results suggest that negative but not positive internal distraction interferes with concurrent cognitive performance, and justify the inclusion of only negatively-valenced AM cues in the fMRI study. Furthermore, the present results are similar to our previous findings regarding the impact of negative versus positive external distraction (Iordan & Dolcos, 2015), and suggest both a specific impact of negatively valenced distraction and better coping with positively valenced distraction, irrespective of its originating source (external or internal). These findings are consistent with evidence suggesting a link between intrusive thoughts and ruminations that detract from goal-oriented processing with deleterious influences of negative emotions on cognitive performance (Eysenck, Derakshan, Santos, & Calvo, 2007; Mitchell & Phillips, 2007). On the other hand, these results are also in line with the theories of positive affect, which suggest a link between positive affect and

cognitive enhancement such as "broadening" the scope of attention and flexible integration of information (Fredrickson, 2001, 2004; Fredrickson & Branigan, 2005), and consistent with recent evidence suggesting facilitation of controlled processing by positive affect (Carpenter, Peters, Västfjäll, & Isen, 2013; Nadler, Rabi, & Minda, 2010; Yang, Yang, & Isen, 2013).

Imaging Protocol

Scanning was conducted on a 3T Siemens Trio scanner. After the sagittal localizer and the 3D MPRAGE anatomical images (TR = 1800 ms; TE = 2.26 ms; flip angle = 9°; FOV = 256 × 256 mm^2; matrix size = 256 × 256 mm^2; slice thickness = 1 mm; volume size = 192 slices; voxel size = 1 × 1 × 1 mm^3), 8 blocks of full-brain EPI functional images were acquired axially, co-planar with the AC-PC (TR = 2000 ms; TE = 40 ms; flip angle = 90°; FOV = 256 × 256 mm^2; matrix size = 64 × 64 mm^2; slice thickness = 4 mm, no gap; volume size = 28 slices; voxel size = 4 × 4 × 4 mm^3).

Behavioral Data Analyses

Responses in the WM task were classified in one of the four categories derived from signal detection theory (Macmillian & Creelman, 1991): (1) *Hits*, corresponding to memorandum faces correctly classified as Old, (2) *Misses*, corresponding to memorandum faces incorrectly classified as New, (3) *Correct Rejections* (CRs), corresponding to new faces correctly classified as New, and (4) *False Alarms* (FAs), corresponding to new faces incorrectly classified as Old. Percentages of probes correctly identified as being *Old* or *New* were also calculated for each participant [% Correct = (% Hits + % CR) / 2]. WM performance scores provided assessments of the *objective* impact of internal emotional distraction and of the effects of engaging ER on on-line cognitive performance. Complementarily, the ratings of negative experience associated with AM recollection provided *subjective* indices of the effectiveness of the ER manipulation on re-

experiencing the associated emotions (Denkova et al., 2015). Differences in WM performance and negativity ratings among the trial types were assessed using repeated-measures ANOVAs and follow-up *t* tests, using SPSS.

fMRI Data Analyses

Statistical analyses were preceded by the following pre-processing steps (performed with SPM12 – Statistical Parametric Mapping): slice timing, realignment, motion correction, co-registration, normalization, and smoothing (8 mm kernel). For the data analysis, we used in-house custom MATLAB scripts involving whole-brain voxel-wise analyses (Dolcos & McCarthy, 2006; Iordan & Dolcos, 2015; Iordan et al., 2013a), to compare the brain activity associated with the conditions of interest (e.g., trials with context vs. emotion focus). For subject-level analyses, the fMRI signal was selectively averaged in each subject's data as a function of trial type (e.g., context focus, emotion focus, and control) and time point (one pre-stimulus and 14 post-stimulus onset time points). Pair-wise *t* statistics for the contrasts of interest were calculated for each subject. No assumption was made about the shape of the hemodynamic response function because this method allows finer comparisons of the MR signal on a TR-by-TR basis and has been proven effective in dissociating responses produced by the WM task with emotional distraction (Denkova et al., 2010; Dolcos et al., 2008; Dolcos & McCarthy, 2006; Iordan & Dolcos, 2015; Iordan et al., 2013a; Morey et al., 2009). The individual analysis produced whole-brain average and activation *t* maps for each condition, contrast of interest, and TR/time point.

The outputs of subject-level analyses were used as inputs for second-level random-effects within-group analyses. The analyses focused on effects observed in a 3 time points window (i.e., covering the 12-18 seconds period after the memoranda onset – TRs 8-10), when the differential

effects of the distracters are most evident (Denkova et al., 2010; Dolcos & McCarthy, 2006; Iordan & Dolcos, 2015; Iordan et al., 2013a). The inclusion of multiple time points was also justified by previous evidence indicating timing differences between components of AM recollection (Daselaar et al., 2008). Each random-effects t statistic map was thresholded at $p < 0.05$, corrected for multiple comparisons using Monte Carlo simulations (Slotnick, Moo, Segal, & Hart, 2003).

Identification of Brain Regions Involved in the Response to and Regulation of Internal Emotional Distraction

The goal of this investigation was to identify the neural correlates of the response to and regulation of internal emotional distraction. First, to identify brain regions involved in the initial response to internal emotional distraction, both Emotion and Context focus trials were collapsed into a single AM condition. Because the focus of this analysis was on identifying mechanisms shared by internal distracters regardless on their impact on WM performance, all trials were included. Specifically, to identify brain regions whose activity was sensitive to internal emotional distraction, we directly compared brain activity related to AM recollection and control. Reponses to internal emotional distraction were identified by *de*activations in DES regions (AM < Ctrl) and *in*creased activity in VAS and DMN regions (AM > Ctrl) for the AM recollection condition versus control. An intensity threshold of $p < 0.001$ was considered for this analysis, in conjunction with an empirically determined extent threshold of 18 voxels, equivalent to $p < 0.05$ corrected for multiple comparisons (Slotnick et al., 2003). Second, to identify brain regions involved in the regulation of internal emotional distraction, we directly compared brain activity related to Emotion and Context focus (i.e., Emotion > Context and Context > Emotion, respectively). Because these analyses were linked to differences in WM performance as a result

of the ER manipulation (see Results section), they were performed on correct trials (Hits and CR collapsed). This more stringent approach ensured that only instances where the subjects were performing the task were included in the analysis. A more lenient but widely accepted (Lieberman & Cunningham, 2009) intensity threshold of $p < 0.005$ was used for this more subtle dissociation, in conjunction with empirically determined extend thresholds of 19 and 17 voxels for the (Emotion > Context) and (Context > Emotion) contrasts, respectively, equivalent to $p < 0.05$ corrected for multiple comparisons (Slotnick et al., 2003).

Functional Connectivity Analyses

To investigate modulation of functional relationships between targeted fronto-parietal brain regions identified by the above analyses as showing sensitivity to regulation of emotional distraction (see Results section), functional connectivity analyses of delay activity among these regions were performed, using a procedure previously employed and validated by us (Dolcos et al., 2006; Iordan & Dolcos, 2015). This approach is similar to the "beta-series correlations" procedure described by Rissman, Gazzaley, and D'Esposito (2004), but uses the baseline-subtracted MR signal instead of beta values. For these analyses, at the first level, within-subject voxel-wise correlations were performed on a trial-by-trial basis, using as seeds activity extracted from the lateral PFC area (i.e., peak and neighboring voxels), which was independently identified by the analyses above as showing increased response to Context compared to Emotion focus (see Results section), and targeting activity in parietal regions. These trial-based analyses were performed for the time point of interest (TP 10), in each participant, for the two targeted trial types: i.e., trials associated with Emotion and Context focus. The resulting correlation maps were normalized using Fisher's z transformation. At the second level, across subject random-effects t comparisons of the individual correlation maps were performed, to identify regions

systematically showing greater functional connectivity with the seed regions, for one condition relative to the other (e.g., Context > Emotion). Because we targeted within-subjects differences in correlation strengths (e.g., increased correlations under Context compared to Emotion focus), no other pre-processing steps were involved, aside from those performed for the analyses targeting differences in activation. Of note, the selection criterion for the seeds (i.e., differences in activation) does not bias the functional connectivity results because the seeds were selected based on the "average" response to Emotion and Context focus conditions, whereas the functional connectivity analysis used trial-by-trial estimates, which are independent of the average responses (Iordan & Dolcos, 2015; Kinnison, Padmala, Choi, & Pessoa, 2012). Given our a priori hypotheses, an intensity threshold of $p < 0.005$ was considered for analysis (Lieberman & Cunningham, 2009), in conjunction with an empirically determined extend thresholds of 13 voxels, equivalent to $p < 0.05$ corrected for multiple comparisons (Slotnick et al., 2003).

Results

Behavioral Results

Diminished Negative Experience and Working Memory Interference for Context Focus

Analyses of the behavioral data showed both diminished experienced emotion and diminished working memory interference for context compared to emotion focus (Figure 4.2). First, the results of a one-way repeated measures ANOVA (Attention Focus: emotion, context, control) on negativity ratings yielded a significant effect [$F_{(2,56)} = 221.37$, $p < 0.001$], and planned comparisons showed significantly lower experienced negativity when subjects were focusing on context compared to emotion [$t_{(28)} = 6.61$, $p < 0.001$]. These results replicate and extend our previous findings (Denkova et al., 2015) to dual-task performance, thus suggesting

that focusing away from emotion leads to reduced emotional experience also when performing a combined WM-emotional AM recollection task. Second, the results of a one-way repeated measures ANOVA (Attention Focus: emotion, context, control) on WM performance yielded a significant effect [$F_{(2, 56)} = 5.61$, $p = 0.006$], and planned comparisons showed significantly better WM performance when subjects were focusing on context ($M = 76.8\%$; $SD = 8.81\%$) compared to emotion ($M = 71.34\%$; $SD = 9.49\%$) [$t_{(28)} = 3.05$, $p = 0.005$]. These results suggest that focusing away from emotion during internal distraction is also associated with lower cognitive interference. Together, the present behavioral results suggest that the instructed use of focused attention as an ER strategy to cope with internal emotional distraction is associated not only with reduced *subjective* emotional experience but also with reduced *objective* interference on WM performance.

fMRI Results

Analyses of fMRI data investigated both the response to internal emotional distraction, irrespective of WM performance, and brain activity linked to the instructed ER, associated with improvements in WM performance. Overall, these analyses yielded evidence consistent with both similar responses to internal emotional distraction, independent of the ER manipulation, and ER-related dissociations in DES, VAS, and DMN regions. These results are presented below.

Opposing Responses in DES vs. VAS & DMN Regions to Internal Emotional Distraction

To identify brain regions involved in the response to internal emotional distraction, analyses performed on all trials compared brain activity linked to AM recollection (irrespective of focus) and control. The results showed that internal emotional distraction was associated with both increased activity in VAS and DMN regions, and greater deactivation in DES regions, relative to control (Table 4.1 and Figure 4.3). Specifically, internal emotional distraction was

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associated with increased activity in basic emotion processing (AMY) and emotion integration (vlPFC, BA 45) regions, part of VAS. In addition, internal distraction was also associated with increased activity in brain regions involved in AM recollection and self-referential processing (mPFC, posterior cingulate cortex [PCC]), part of DMN. By contrast, internal emotional distraction evoked strong deactivation in LPC (IPL, BA 40), a brain region involved in WM and attentional processing. These findings regarding internal distraction extend previous results focusing on external distraction, and suggest that similar DES and VAS mechanisms are engaged independent of the originating source of distraction, whereas internal distraction is linked to specific DMN mechanisms. However, linked to the ER manipulation and the differences in behavioral performance, there were dissociations in brain activity in VAS and DES regions for emotion versus context focus. These results are presented below.

Reduced VAS Activity and Increased Recruitment of Executive and Context Retrieval Regions under Context Focus

To identify brain regions involved in the instructed ER of internal emotional distraction, analyses performed on correct trials compared brain activity linked to emotion and context focus (Table 4.2 and Figure 4.4). Consistent with the behavioral results showing reduced impact of internal distraction for context compared to emotion focus, the brain imaging results showed that focusing on context was associated with both reduced activity in VAS regions that overlap with SN, and increased activity in dlPFC and in regions associated with retrieval of contextual information. Specifically, focusing on context was associated with reduced activity in basic emotion processing regions (AMY) and in regions associated with integration and filtering of emotional information (ACC, aINS), which are also considered part of SN. By contrast, focusing on context was associated with sustained increased activity in an executive region (left dlPFC)

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and in memory-related regions involved in the retrieval of contextual information (PHG, angular gyrus [AG]). Interestingly, the responses in VAS regions occurred in a slightly earlier time frame (TRs 8-9) than responses in regions associated with the retrieval of contextual information (TR 10), suggesting early involvement of emotion processing regions during recollection of personal events. Overall, the brain imaging findings are consistent with the behavioral results and suggest that focusing away from emotion was associated with a shift in processing bias from emotion/salience regions to executive and context retrieval regions.

Increased Fronto-Parietal Functional Connectivity under Context Focus

To further clarify the interactions between brain regions recruited by focused attention, we performed functional connectivity analyses targeting the dlPFC region identified above, to determine whether focusing on context was associated with increased coupling between DES regions part of FPN, compared to focusing on emotion. These analyses were performed at the time point when the maximal effect of context focus was identified (TR 10). Results showed increased functional connectivity between left dlPFC and regions associated with FPN (right dlPFC and bilateral LPC) (Figure 4.5). Of note, the parietal region showing increased coupling with dlPFC also showed greater overall deactivation to AMs (see Table 4.1). Thus, although only a select dorsal prefrontal region (i.e., dlPFC) dissociated between context and emotion focus in terms of the mean level of activity, FPN regions showed stronger trial-by-trial functional coupling among themselves for context compared to emotion focus.

Additional Exploratory Analysis of Sex Differences in the Response to Internal Emotional Distraction

This exploratory analysis tested for sex differences in the impact of internal emotional distraction. Based on our previous study investigating sex differences in the impact of external

emotional distraction (Iordan et al., 2013a), we expected that women would be more susceptible to the detrimental impact of internal emotional distraction, and that this would affect high-confidence responses but not overall WM performance. Regarding the neural correlates, we expected increased sensitivity in women in regions involved in stimulus-driven processing of salient information, similar to the effects of external emotional distraction.

Exploratory analyses of sex differences in WM performance showed that focusing on emotion had greater impact in women than in men in the trials associated with the highest level of confidence (LOC 3), but not in the overall WM performance [$t_{(27)} = 0.55$, $p > 0.1$]. Planned t tests showed that women had marginally lower LOC 3 WM performance than men for trials associated with emotion focus [$t_{(27)} = 2.01$, $p = 0.055$], but no sex differences were apparent in the trials associated with context focus [$t_{(27)} = 0.33$, $p > 0.1$] or control [$t_{(27)} = 0.95$, $p > 0.1$]. These preliminary results suggest that differences between women and men in LOC 3 ratings were linked to a differential impact of internal emotional distraction on women's ability to make high-confidence ratings in the WM task, similar to the previously observed effects of external emotional distraction (Iordan et al., 2013a). Similar to the impact of external emotional distraction, no differences were observed in the overall WM performance between men and women, which suggests that sex differences in the response to emotional challenge, either external or internal, are more subtle and affect only some aspects of behavior.

Paralleling the behavioral results, exploratory analyses of fMRI data showed increased sensitivity to emotional distraction in women, in a medial region associated with the processing of salient information. Specifically, a region of the dorsomedial PFC bordering the ACC (BA 8/32) showed both increased response to emotion focus in women compared to men and negative correlation with WM performance in women (Figure 4.6). These preliminary results suggest

increased response in women to emotionally arousing stimuli, linked to their motivational significance (Dolcos, LaBar, & Cabeza, 2004; Phan, Wager, Taylor, & Liberzon, 2002), and potentially also increased conflict related to emotional processing concurrent with a goal-oriented cognitive task (Mohanty et al., 2007; Whalen et al., 1998). Although the medial PFC/ACC is a functionally heterogeneous area, recent evidence suggests a role of its dorsal-caudal aspect in evaluative operations, in contrast with the ventral-rostral aspect involved mainly in regulatory functions (Etkin, Egner, & Kalisch, 2011). This is also consistent with the affiliation of dorsomedial PFC/dorsal ACC with the salience or ventral attention network (Corbetta et al., 2008; Seeley et al., 2007), and hence the present results suggest increased interference in women by enhanced recruitment of this stimulus-driven, "bottom-up" system. This interpretation is further supported by the results of our brain-behavior covariation analysis, showing that women who engaged this region more in response to internal emotional distraction also had greater WM interference. However, given the low number of subjects (10 women[1] and 5 men), these results should be interpreted with caution.

It is important to note, though, the possibility that the observed effects could have been influenced by sex differences in the spontaneous engagement of ER strategies. Given that subjects are instructed to try and maximize cognitive performance in the context of the WM task with distraction, it is possible that they might have spontaneously engaged different ER when focusing on emotion. While investigation of sex differences in the habitual use of ER could provide potential clues into what ER strategies women and men might have been spontaneously engaged, it is impossible to know for sure. One possibility is that women have spontaneously engaged more complex and/or demanding ER strategies that have led to cognitive depletion, thus

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[1] Calculation of brain activity for emotional LOC3 was not possible for two female participants due to low number of trials; hence, the results are reported for 10 women.

hindering cognitive performance (Bardeen, Stevens, Murdock, & Christine Lovejoy, 2013; Nolen-Hoeksema, 2012; Tamres, Janicki, & Helgeson, 2002). However, it remains an open possibility that some of the differences might be related to differences in spontaneous engagement of ER strategies between women and men.

Discussion

The goal of the present study was to clarify the mechanisms associated with the response to and regulation of internal emotional distraction and its impact on WM performance. Cued recollection of task-irrelevant negative AMs was used as internal emotional distraction, and focused attention was used as an instructed ER strategy. There were four main findings. First, focusing away from emotion (i.e., context focus) diminished both the *subjective* negative experience and the *objective* WM interference, compared to focusing on emotion. Second, regarding the overall response to internal emotional distraction, brain imaging results identified both overall deactivation in DES regions (LPC) and increased activity in VAS regions (AMY, vlPFC) to internal distraction, similar to the responses to external distraction, as well as specific increased activity in medial regions part of DMN (mPFC, PCC). Third, regarding the neural mechanisms of internal distraction regulation, compared to emotion focus, context focus was associated with both diminished activity in VAS regions part of SN (AMY, aINS), and increased activity in executive (dlPFC) and memory-related regions involved in context retrieval (PHG, AG). Finally, context focus was also associated with increased functional connectivity between fronto-parietal regions. These findings are discussed in turn below.

Diminished Negative Experience and Working Memory Interference for Context Focus

The present findings showing both diminished negative experience and diminished WM interference when focusing away compared to focusing on emotion suggest that the engagement

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of focused attention as an ER strategy under internal distraction has beneficial effects not only on the *subjective* emotional experience but also on the *objective* cognitive performance. The results showing diminished negative experience for context focus replicate and considerably extend previous findings (Denkova et al., 2015) by showing that focused attention is an efficient ER strategy when AM recollection occurs in the context of a dual-task with distraction. Furthermore, the results showing reduced WM interference under context focus demonstrate that instructed ER allows coping with emotion while also facilitating cognitive performance compared to emotion focus. Thus, the present results show that prompt deployment of a minimally taxing ER strategy (i.e., focused attention) is an effective way of dealing with emotional distraction originating from the internal environment.

These results are consistent with the idea that focusing on context during AM recollection allows better deployment of attention to representations active within working memory (Gotlib & Joormann, 2010; Joormann & Gotlib, 2008). In other words, down-regulating the emotional experience while minimally taxing the cognitive system allows for more WM resources available to maintain the memoranda. This effect may be in contrast with effects of engaging more demanding manipulations of attentional deployment (e.g., distraction *from* emotion by engagement in a cognitively demanding task), which could lead to reduced emotional experience potentially via resource depletion (Van Dillen, Heslenfeld, & Koole, 2009). While the clarification of such an issue was beyond the scope of the present investigation, future studies could compare the effects of engaging different ER strategies on on-line cognitive performance.

To our knowledge, the present study is the first to provide insights into the effects of manipulating attentional focus during internal distraction on concurrent cognitive performance. The finding that simply focusing away from emotional aspects of AMs can reduce both the

subjective re-experiencing of emotion and WM interference demonstrates that this is an efficient and easy to use ER strategy when confronted with unwanted distractions. Although all irrelevant cognitions may be distracting to some degree, the deployment of an efficient ER strategy allows better coping with distraction, even in the context of dual tasks. This interpretation is consistent with our model of dynamic interactions between executive and affective systems (Dolcos et al., 2011; Iordan et al., 2013b), and is further supported by the brain imaging results discussed below.

Opposing Responses in DES vs. VAS & DMN Regions to Internal Emotional Distraction

The findings showing deactivation in DES (LPC) and increased activity in VAS (AMY, vlPFC) regions to internal emotional distraction suggest overall similar responses to the ones previously reported for external emotional distraction (Iordan et al., 2013b), consistent with the idea of a more general involvement of these two systems, independent of the originating source of distraction. On the other hand, the findings showing increased activation in midline cortical regions (mPFC, PCC) suggest specific engagement of AM retrieval/DMN regions by internal emotional distraction. The present DES results are consistent with previous findings linking deactivation in fronto-parietal areas to the effects of emotional distraction on WM processing regions (Anticevic et al., 2010; Denkova et al., 2010; Diaz et al., 2011; Dolcos et al., 2008; Dolcos et al., 2013; Dolcos et al., 2006; Dolcos & McCarthy, 2006; Iordan & Dolcos, 2015; Iordan et al., 2013a; Oei et al., 2012). The LPC is the posterior "hub" in the fronto-parietal executive network, which also includes the dlPFC (Dosenbach et al., 2006; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Dosenbach et al., 2007; Power et al., 2011; Power & Petersen, 2013; Seeley et al., 2007; Yeo et al., 2011), and increased activity in DES regions has been implicated in active maintenance of task-relevant information (Corbetta & Shulman, 2002;

D'Esposito et al., 2006; Fuster, 1997; Hopfinger, Buonocore, & Mangun, 2000; Koenigs et al., 2009; Nee et al., 2012; Niendam et al., 2012; Smith & Jonides, 1999). Interestingly, the deactivation in LPC was similar under both emotion and context focus, despite the differences in WM performance between the two conditions. This suggests that although recollection of task-irrelevant AMs may in fact be distracting irrespective focus, the advantage of focusing away from emotion for maintaining WM performance may be linked to a more complex neural dynamics than just differential impact on LPC activity. This interpretation is supported by our findings showing both differences in activity of VAS regions and functional connectivity within DES regions, for context compared to emotion focus. These findings as discussed below.

Reduced VAS Activity and Increased Recruitment of Executive and Context Retrieval Regions under Context Focus

The findings showing decreased activity in VAS regions associated with the salience/ventral attentional network (AMY, anterior insula [aINS], dorsal anterior cingulate cortex [dACC]) and increased activity in executive (dlPFC) and context retrieval regions (PHC, AG) suggest that the beneficial effects of the ER manipulation on both emotional experience and cognitive performance were linked to a shift in bias from emotion processing to recollection of contextual details. First, the present results suggest that context focus was associated with down-regulating of activity in regions of the salience network, compared to emotion focus. The salience network is a large system anchored in dACC and fronto-insular cortex, which has been implicated in detection, integration, and filtering of salient external and internal events (Bressler & Menon, 2010; Corbetta et al., 2008; Seeley et al., 2007). The salience network also includes subcortical structures, such as the amygdala, and has been implicated in emotion processing (Barrett & Satpute, 2013; Seeley et al., 2007) and stimulus driven ("bottom-up") reorienting of

attention (Corbetta et al., 2008). Hence, decreased activity in salience network regions under context focus may be linked to reduced processing of distracting emotions, leading to less cognitive interference.

Second, the results also suggest that context focus was associated with increased activity in executive (dlPFC) and memory-related regions associated with the retrieval of contextual information (PHC, AG). The left PFC has been implicated not only in executive operations associated with working memory and attention, but also in episodic memory (Kahn, Davachi, & Wagner, 2004), and in particular in subsequent elaboration and maintenance of AMs (Daselaar et al., 2008). The PHC is a key node in the posterior medial memory system (Ranganath & Ritchey, 2012), and has been implicated in episodic reconstructions that involve familiar visuospatial/situational contexts (Hassabis & Maguire, 2007), which are similar to AMs recollection (Buckner & Carroll, 2007). Some neuropsychological evidence also points to the role of AG in integrating or attending to contextual information (Cabeza et al., 2008; Vilberg & Rugg, 2008). In particular, lesions in the ventral parietal cortex (which includes AG) have been associated with less vivid and impoverished spontaneous recollections (Davidson et al., 2008) in the absence of clear deficits when patients are probed about specific episodic details (Berryhill, Phuong, Picasso, Cabeza, & Olson, 2007), suggesting a potential role of AG in spontaneous availability of contextual details.

Interestingly, the vlPFC, a brain region previously associated with spontaneous regulation of, and coping with, external emotional distraction (Dolcos et al., 2011; Iordan et al., 2013b), did not show increased response under context compared to emotion focus. Although this might seem at odds with previous evidence linking activity in this brain region with affect regulation (Kober et al., 2008; Ochsner et al., 2012; Vytal & Hamann, 2010), it should be noted that

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previous ER investigations have typically used pictorial stimuli for emotion elicitation and that our previous study investigating focused attention as an ER strategy during AMs recollection did not identify dissociations in vlPFC activity for context compared to emotion focus (Denkova et al., 2015). Hence, this null result might reflect differences in the mechanisms involved in regulating emotion elicited by "external" versus "internal" stimuli, or an implication of vlPFC in spontaneous rather than instructed ER, in the context of dual-tasks, similar to the one employed here.

The difference in timing between the responses in salience versus executive and context retrieval regions, with the former occurring slightly earlier (TRs 8-9) than the latter (TR 10), is consistent with previous AM evidence showing early involvement of emotion processing regions during recollection of personal events (Daselaar et al., 2008). In addition, the examination of the time-course of activity in the left dlPFC reveals a pattern of more sustained *in*creased activity for context relative to emotion focus, suggesting a role in "top-down" control operations necessary to bias processing towards further elaboration of the contextual aspects. These results support the interpretation that the change in processing bias from emotion to context during AM recollection is linked to both diminished early engagement of emotion/salience processing regions and more sustained engagement of executive and context retrieval regions, and emphasize the importance of giving the downregulation instructions before the engagement in the retrieval process (Denkova et al., 2015).

Increased Fronto-Parietal Functional Connectivity under Context Focus

The findings showing increased functional connectivity between left dlPFC and fronto-parietal regions for context compared to emotion focus suggest better integration within FPN when subjects were focusing away from emotion. These result are consistent with previous

evidence showing increased prefrontal-parietal coupling during WM tasks (Cohen, Gallen, Jacobs, Lee, & D'Esposito, 2014; Honey et al., 2002; Ma et al., 2012), and suggest a potential mechanism by which goal-relevant representations of the memoranda were better maintained in WM under context focus, which was also the condition associated with better WM performance. Importantly, the right parietal region showing increased functional connectivity with the dlPFC seed was also more impacted by internal distraction, as reflected in the pattern of deactivation to negative AMs in the LPC (BA 40), irrespective of the ER manipulation. Thus, although the parietal cortex did not dissociate between emotion and context focus in terms of the mean amplitude of activity, it showed increased trial-by-trial functional coupling with the dlPFC under context focus, consistent with the idea of better integration among FPN regions under ER. Furthermore, although the correlation-based FC does not allow for determining directionality, our results are also consistent with the idea that dlPFC modulates LPC, suggesting a critical role of the dlPFC in controlling activity in other task-related brain regions (D'Esposito, 2007).

Important Clarifications

The decision to use a manipulation of focused attention in the present investigation was justified by the careful consideration of important factors related to the specific properties of this ER strategy. These factors refer to the timing of ER engagement and the way the cueing was performed, the effectiveness of this manipulation in altering the emotional content while not inhibiting emotional memory retrieval, and its expected efficiency compared to other ER strategies. These clarifications are presented, in turn, below.

Related to the timing of ER engagement in the present task, the use of instruction cues presented prior to the memory cues was justified by evidence regarding the temporal dynamics of focused attention and of AM recollection, and by the constraints of the dual WM-AM

recollection task. First, focused attention as an ER strategy is thought to operate "early" in the emotion generation sequence, by limiting the processing of incoming emotional information in the subsequent stages of the emotional response (Denkova et al., 2015; Ochsner & Gross, 2005). Thus, the presentation of the instruction cues prior to the emotional stimuli (i.e., "early cues") likely facilitated the timely setup of the regulation goals and the deployment of ER promptly after the emotional stimuli were displayed (Denkova et al., 2015; Ochsner et al., 2012).

Although the presentation of the instruction cues at other moments (i.e., simultaneous with or after the AM cues) remains an empirical possibility, this would have been more susceptible to confounding effects, in the present context. Specifically, although the presentation of the instruction cues after the emotional stimuli (i.e. "late cues") would have arguably allowed for a more naturalistic initial response, it could have also been confounded by "default" engagements of ER strategies or by habituation of the emotion processing mechanisms (e.g., amygdala) during the initial presentation of the emotional stimuli [see (Ochsner et al., 2012) for a recent discussion]. Also, the use of early cues instead of simultaneous or late cues was supported by recent fMRI evidence regarding the temporal dynamics of AM recollection (Daselaar et al., 2008), showing an earlier engagement of brain regions involved in the emotional response (amygdala) compared to brain regions involved in AM elaboration (precuneus), thus suggesting that the retrieval cue elicits an early emotional response whereas the memory itself is assembled more slowly. Of note, the present fMRI data also support this view, showing faster engagement of emotional/salience processing regions compared to executive and context retrieval regions for emotion vs. context focus.

Thus, the presentation of the regulation instructions prior to the presentation of the emotional stimuli likely facilitated establishing the regulation goals while the emotional intensity

was low, impacting the initial processing of the emotional stimuli (Hajcak Proudfit, Dunning, Foti, & Weinberg, 2014). The "early cue" approach was also better suited for the faster pace of the dual WM-ER task compared with typical single-task paradigms, given the temporal constraints imposed by the delay interval of the WM task (i.e., a too long delay would have rendered the task too difficult).

In addition, the presentation of the instruction cues in text format, compared to color-coding of the conditions, for instance, served to eliminate from WM potential associations related to the previous trial and as an additional reminder to ensure that the subjects were performing the task as instructed for the current trial. This approach was also validated by a previous investigation in our group (Denkova et al., 2015).

Second, the engagement of focused attention as an ER strategy was supposed to alter only the emotional content while not inhibiting the retrieval of the emotional memories. The present behavioral and brain imaging results, as well as the results of a previous investigation from our group using a similar ER manipulation (see Denkova et al., 2015), suggest that this was indeed the case. Namely, they indicate that although focusing on non-emotional contextual details attenuated the effect of emotion, it did not completely eliminate the reactivation of emotional aspects. Although the negativity ratings were higher for emotion compared to context focus, the differences were subtle but significant [M emotion focus = 3.39; M context focus = 2.7; $t_{(28)} = 6.61$, $p < 0.001$]. Importantly, in *both* cases, they were largely different compared to control (M control = 1.07; ps < 0.001). Furthermore, the results of a previous investigation (Denkova et al., 2015) showed that using a similar attention manipulation altered the emotional experience while not affecting other experiential properties of recollection, such as reliving and vividness. Consistent with this behavioral evidence, the brain imaging results showed that

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although emotion focus elicited increased responses in emotion/salience processing regions compared to context focus, both foci engaged brain regions part of VAN, including the amygdala and the vlPFC, relative to control. These findings were also consistent with previous evidence (Denkova et al., 2015). Thus, the present difference between the emotion and context foci is more a matter of degree rather than a binary (i.e., "all-or-nothing") response, and emotional memories are retrieved even when using a context focus. This points to a clear advantage of using this ER strategy instead of suppression (see also discussion below), which would have likely interfered with AM retrieval. These results are also consistent with previous AM literature (Conway & Pleydell-Pearce, 2000; Daselaar et al., 2008; Neumann, Blairy, Lecompte, & Philippot, 2007; Philippot, Schaefer, & Herbette, 2003), as well as with ERP evidence suggesting that attentional resources might be initially allocated to the emotional stimuli *before* the regulatory effects of attentional deployment actually start operating (Schönfelder, Kanske, Heissler, & Wessa, 2014).

Finally, the reasons for using a manipulation of focused attention are also related to the expected efficiency of this ER strategy compared to others, such as distraction, reappraisal and suppression. A useful framework for discussing the differences between these different ER strategies is provided by the "process model" of ER (Gross, 1998, 2014). This influential model recognizes five types of ER strategies, distinguishable by their features and time points at which they intervene in the emotion generation sequence: situation selection, situation modification, attentional deployment, cognitive change, and response modulation. Although both focused attention and distraction are forms of "attentional deployment" that intervene early in the ER process and limit the degree to which affective information is subsequently processed (Gross, 2014; Hajcak Proudfit et al., 2014), they are conceptualized to operate in relatively different

ways. Specifically, whereas distraction mainly involves engaging in a competing, cognitively demanding task to divert attention altogether from processing the emotional stimuli (e.g., solving math problems to distract from remembering negative events), focused attention involves simply switching the focus while the task remains in essence the same [e.g., remembering negative events while focusing on either emotional or contextual aspects (Denkova et al., 2015)]. Compared to the use of focused attention, the use of distraction as an ER strategy comes at the cost of potentially depleting WM capacity due to the processing of additional, extraneous information (Sheppes & Meiran, 2008). Thus, focused attention is a more efficient ER strategy under restricted processing resources, such as in the case of dual-task performance, due to its minimal processing requirements (Mauss, Bunge, & Gross, 2007). Its efficiency is also supported by the present results showing both reduced subjective negative experience and maintained WM performance when subjects were focusing away from emotion (context focus).

Compared to reappraisal, which is a form of "cognitive change", focused attention operates at an earlier stage and is a simpler ER strategy. By contrast, reappraisal is a more complex and cognitively demanding ER strategy because it involves higher-level processes, such as language and memory, required to reinterpret the meaning of the stimuli and the subject's relation to them (Ochsner & Gross, 2005). Consistent with this view, ERP evidence (Schönfelder et al., 2014) suggests that attentional deployment strategies are implemented prior to emotional stimulus elaboration, thus limiting the degree to which the affective significance is subsequently appraised. By contrast, reappraisal operates at a later stage and takes longer to implement (Schönfelder et al., 2014; Thiruchselvam et al., 2011). Thus, reappraisal is more than attentional (re)deployment, because it involves attending to and constructing an initial evaluation of the emotional stimulus, before a re-interpretation can be implemented. Differences between the two

types of ER strategies are also reflected in fMRI evidence showing enhanced immediate down-regulation of amygdala activity under distraction compared to reappraisal (Kanske et al., 2011; McRae et al., 2010).

Thus, although reappraisal is an effective ER strategy, it would have been more difficult to apply under temporal and processing constraints, such as in the context of dual-task performance, due to its increased complexity and cognitive demands. By contrast, focused attention as a form of attentional deployment is a less demanding ER strategy which can be rapidly deployed with minimal effort [i.e., more automatically (Mauss et al., 2007; Schönfelder et al., 2014; Thiruchselvam et al., 2011)].

By contrast with the antecedent-focused strategies emphasized above, *suppression* is a form of "response modulation" that occurs "late" in the emotion generation sequence, and involves refraining from expressing the emotional response such that an outside observer would not know the emotion one's experiencing (Gross, 2014). Compared with antecedent-focused strategies such as focused attention and reappraisal, expressive suppression is both costly in terms of resource demands and overall less effective (Gross, 2008; Ochsner et al., 2012), leading to exacerbations of the autonomic component of the emotional response (Gross, 1998). Also, as alluded above, focused attention was a more appropriate ER strategy in the present context because it does not inhibit emotional memory retrieval, something likely to happen when using suppression. In addition, evidence points to a disadvantage of using suppression on the long-run, as individuals who habitually engage suppression experience more negative affect and more emotional dysregulation compared to subjects who habitually use reappraisal (Denkova et al., 2012; Gross & John, 2003; Llewellyn, Dolcos, Iordan, Rudolph, & Dolcos, 2013).

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Regarding similarities and dissociations between the neural mechanisms engaged by different ER strategies, the present results suggests increased efficiency of focused attention relative to reappraisal and suppression, which extensively recruit executive and even emotion processing mechanisms (for expressive suppression) [see (Ochsner et al., 2012), for a recent meta-analysis]. Interestingly, our results also suggest greater efficiency of focused attention relative to distraction, which appears to heavily involve fronto-parietal mechanisms, at least in some task implementations (e.g., Dorfel et al., 2014). In summary, current evidence suggests that focused attention is an effective and versatile ER strategy, that can be rapidly deployed and engages minimal cognitive resources.

Conclusions

In summary, the present findings clarified the effects of internal emotional distraction by identifying mechanisms mediating both the response to and regulation of task-irrelevant AMs recollected concurrently with an on-going cognitive task. Consistent with the idea of beneficial effects of focused attention as an ER strategy on maintaining cognitive performance, our results show that focusing away from emotion and onto the non-emotional contextual aspects while recollecting task-irrelevant negative AMs is associated with both diminished emotional experience and diminished cognitive interference. The present fMRI findings identified specific responses to internal emotional distraction in midline regions (mPFC, PCC), in the context of overall responses in dorsal (LPC) and ventral (AMY, vPFC) regions, similar to the ones previously observed for external distraction. Linked to the engagement of focused attention as an ER strategy to cope with internal distraction, our results identified both down-regulated responses in regions associated with emotion detection, integration, and filtering (AMY, aINS, dACC), part of the salience network, and superior engagement of executive (dlPFC) and

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contextual memory-related (PHC, AG) regions, under context compared to emotion focus. Moreover, there were different patterns of connectivity between the fronto-parietal regions, for context versus emotion focus. Overall, these findings show that focused attention is an effective ER strategy that can be promptly deployed to cope with internal emotional distraction and that its engagement is linked to a shift in processing bias from emotion/salience regions to executive and context retrieval regions. Collectively, the present study provides initial fMRI evidence regarding the neural mechanisms of focused attention as an ER strategy deployed to resist the impact of internal emotional distraction on concurrent cognitive performance, and has implications for understanding affective disorders, such as PTSD and depression, which are characterized by increased emotional distractibility (Gotlib & Joormann, 2010; McNally, 2006).

References

Anticevic, A., Repovs, G., & Barch, D. M. (2010). Resisting emotional interference: brain regions facilitating working memory performance during negative distraction. *Cognitive, Affective, & Behavioral Neuroscience, 10*(2), 159-173.

Arnoult, M. D., & Attneave, F. (1956). The quantitative study of shape and pattern perception. *Psychological Bulletin, 53*(6), 452-471.

Bardeen, J. R., Stevens, E. N., Murdock, K. W., & Christine Lovejoy, M. (2013). A preliminary investigation of sex differences in associations between emotion regulation difficulties and higher-order cognitive abilities. *Personality and Individual Differences, 55*(1), 70-75.

Barrett, L., & Satpute, A. (2013). Large-scale brain networks in affective and social neuroscience: towards an integrative functional architecture of the brain. *Current Opinion in Neurobiology, 23*(3), 361-372.

Battig, W. F., & Montague, W. E. (1969). Category norms of verbal items in 56 categories A replication and extension of the Connecticut category norms. *Journal of Experimental Psychology, 80*(3 PART 2), 1-46.

Berryhill, M. E., Phuong, L., Picasso, L., Cabeza, R., & Olson, I. R. (2007). Parietal lobe and episodic memory: bilateral damage causes impaired free recall of autobiographical memory. *The Journal of Neuroscience, 27*(52), 14415-14423.

Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: emerging methods and principles. *Trends in Cognitive Sciences, 14*(6), 277-290.

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network. *Annals of the New York Academy of Sciences, 1124*(1), 1-38.

Buckner, R. L., & Carroll, D. C. (2007). Self-projection and the brain. *Trends in Cognitive Sciences, 11*(2), 49-57.

Cabeza, R., Ciaramelli, E., Olson, I. R., & Moscovitch, M. (2008). The parietal cortex and episodic memory: an attentional account. *Nature Reviews Neuroscience, 9*(8), 613-625.

Cambridge-Cognition. Cambridge Neuropsychological Test Automated Battery (CANTAB). http://www.camcog.com/cantab-tests.asp.

Carpenter, S. M., Peters, E., Västfjäll, D., & Isen, A. M. (2013). Positive feelings facilitate working memory and complex decision making among older adults. *Cognition and Emotion, 27*(1), 184-192.

Cohen, J. R., Gallen, C. L., Jacobs, E. G., Lee, T. G., & D'Esposito, M. (2014). Quantifying the reconfiguration of intrinsic networks during working memory. *PLoS ONE, 9*(9), e106636.

Collin, C. A., & McMullen, P. A. (2002). Using Matlab to generate families of similar Attneave shapes. *Behavior Research Methods, Instruments, & Computers, 34*(1), 55-68.

Conway, M. A., & Pleydell-Pearce, C. W. (2000). The construction of autobiographical memories in the self-memory system. *Psychological Review, 107*(2), 261-288.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. *Neuron, 58*(3), 306-324.

Corbetta, M., & Shulman, G. L. (2002). Control of goal-directed and stimulus-driven attention in the brain. *Nature Reviews. Neuroscience, 3*(3), 201-215.

D'Esposito, M. (2007). From cognitive to neural models of working memory. *Philosophical Transactions of the Royal Society B: Biological Sciences, 362*(1481), 761-772.

D'Esposito, M., Cooney, J. W., Gazzaley, A., Gibbs, S. E., & Postle, B. R. (2006). Is the prefrontal cortex necessary for delay task performance? Evidence from lesion and FMRI data. *Journal of the International Neuropsychological Society, 12*(2), 248-260.

Daselaar, S. M., Rice, H. J., Greenberg, D. L., Cabeza, R., LaBar, K. S., & Rubin, D. C. (2008). The spatiotemporal dynamics of autobiographical memory: neural correlates of recall, emotional intensity, and reliving. *Cerebral Cortex, 18*(1), 217-229.

Davidson, P. S., Anaki, D., Ciaramelli, E., Cohn, M., Kim, A. S., Murphy, K. J., Troyer, A. K., Moscovitch, M., & Levine, B. (2008). Does lateral parietal cortex support episodic memory? Evidence from focal lesion patients. *Neuropsychologia, 46*(7), 1743-1755.

Denkova, E., Dolcos, S., & Dolcos, F. (2012). Reliving emotional personal memories: affective biases linked to personality and sex-related differences. *Emotion, 12*(3), 515-528.

Denkova, E., Dolcos, S., & Dolcos, F. (2015). Neural correlates of 'distracting' from emotion during autobiographical recollection. *Social Cognitive and Affective Neuroscience, 10*(2), 219-230.

Denkova, E., Wong, G., Dolcos, S., Sung, K., Wang, L., Coupland, N., & Dolcos, F. (2010). The impact of anxiety-inducing distraction on cognitive performance: a combined brain imaging and personality investigation. *PLoS One, 5*(11), e14150. doi 14110.11371/journal.pone.0014150.

Diaz, M. T., He, G., Gadde, S., Bellion, C., Belger, A., Voyvodic, J. T., & McCarthy, G. (2011). The influence of emotional distraction on verbal working memory: an fMRI investigation comparing individuals with schizophrenia and healthy adults. *Journal of Psychiatric Research, 45*(9), 1184-1193.

Dolcos, F. (2013). Linking enhancing and impairing effects of emotion-the case of PTSD. *Frontiers in Integrative Neuroscience, 7*, 26. doi 10.3389/fnint.2013.00026.

Dolcos, F., Diaz-Granados, P., Wang, L., & McCarthy, G. (2008). Opposing influences of emotional and non-emotional distracters upon sustained prefrontal cortex activity during a delayed-response working memory task. *Neuropsychologia, 46*(1), 326-335.

Dolcos, F., Iordan, A. D., & Dolcos, S. (2011). Neural correlates of emotion-cognition interactions: A review of evidence from brain imaging investigations. *Journal of Cognitive Psychology, 23*(6), 669-694.

Dolcos, F., Iordan, A. D., Kragel, J., Stokes, J., Campbell, R., McCarthy, G., & Cabeza, R. (2013). Neural correlates of opposing effects of emotional distraction on working memory and episodic memory: An event related fMRI investigation. *Frontiers in Psychology, 4*, 293. doi 210.3389/fpsyg.2013.00293.

Dolcos, F., Kragel, P., Wang, L., & McCarthy, G. (2006). Role of the inferior frontal cortex in coping with distracting emotions. *Neuroreport, 17*(15), 1591-1594.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004). Dissociable effects of arousal and valence on prefrontal activity indexing emotional evaluation and subsequent memory: an event-related fMRI study. *Neuroimage, 23*(1), 64-74.

Dolcos, F., & McCarthy, G. (2006). Brain systems mediating cognitive interference by emotional distraction. *The Journal of Neuroscience, 26*(7), 2072-2079.

Dorfel, D., Lamke, J. P., Hummel, F., Wagner, U., Erk, S., & Walter, H. (2014). Common and differential neural networks of emotion regulation by Detachment, Reinterpretation, Distraction, and Expressive Suppression: a comparative fMRI investigation. *Neuroimage, 101*, 298-309.

Dosenbach, N., Visscher, K., Palmer, E., Miezin, F., Wenger, K., Kang, H., Burgund, E., Grimes, A., Schlaggar, B., & Petersen, S. (2006). A core system for the implementation of task sets. *Neuron, 50*(5), 799-812.

Dosenbach, N. U., Fair, D. A., Cohen, A. L., Schlaggar, B. L., & Petersen, S. E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences, 12*(3), 99-105.

Dosenbach, N. U., Fair, D. A., Miezin, F. M., Cohen, A. L., Wenger, K. K., Dosenbach, R. A., Fox, M. D., Snyder, A. Z., Vincent, J. L., Raichle, M. E., Schlaggar, B. L., & Petersen, S. E. (2007). Distinct brain networks for adaptive and stable task control in humans. *Proceedings of the National Academy of Sciences USA, 104*(26), 11073-11078.

Etkin, A., Egner, T., & Kalisch, R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences, 15*(2), 85-93.

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: attentional control theory. *Emotion, 7*(2), 336-353.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences USA, 102*(27), 9673-9678.

Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *American Psychologist, 56*(3), 218-226.

Fredrickson, B. L. (2004). The broaden-and-build theory of positive emotions. *Philosophical Transactions of the Royal Society B: Biological Sciences, 359*(1449), 1367-1378.

Fredrickson, B. L., & Branigan, C. (2005). Positive emotions broaden the scope of attention and thought-action repertoires. *Cognition and Emotion, 19*(3), 313-332.

Fuster, J. M. (1997). Network memory. *Trends in Neurosciences, 20*(10), 451-459.

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Goldin, P. R., McRae, K., Ramel, W., & Gross, J. J. (2008). The neural bases of emotion regulation: reappraisal and suppression of negative emotion. *Biological Psychiatry, 63*(6), 577-586.

Gotlib, I. H., & Joormann, J. (2010). Cognition and depression: current status and future directions. *Annual Review Clinical Psychology, 6*, 285-312.

Greicius, M. D., Krasnow, B., Reiss, A. L., & Menon, V. (2003). Functional connectivity in the resting brain: a network analysis of the default mode hypothesis. *Proceedings of the National Academy of Sciences of the USA, 100*(1), 253-258.

Gross, J. J. (1998). Antecedent- and response-focused emotion regulation: divergent consequences for experience, expression, and physiology. *Journal of Personality and Social Psychology, 74*(1), 224-237.

Gross, J. J. (2008). Emotion regulation. In M. Lewis, J. M. Haviland-Jones, & L. F. Barrett (Eds.), *Handbook of Emotions* (pp. 497-512). New York, NY: Guilford.

Gross, J. J. (2014). Emotion regulation: conceptual and empirical foundations. In J. J. Gross (Ed.), *Handbook of Emotion Regulation* (2nd ed., pp. 3-20). New York: Guilford.

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology, 85*(2), 348-362.

Hajcak, G., Dunning, J. P., & Foti, D. (2009). Motivated and controlled attention to emotion: time-course of the late positive potential. *Clinical Neurophysiology, 120*(3), 505-510.

Hajcak Proudfit, G., Dunning, J. P., Foti, D., & Weinberg, A. (2014). Temporal dynamics of emotion regulation. In J. J. Gross (Ed.), *Handbook of Emotion Regulation* (2nd ed., pp. 43-57). New York: Guilford.

Hassabis, D., & Maguire, E. A. (2007). Deconstructing episodic memory with construction. *Trends in Cognitive Sciences, 11*(7), 299-306.

Honey, G. D., Fu, C. H., Kim, J., Brammer, M. J., Croudace, T. J., Suckling, J., Pich, E. M., Williams, S. C., & Bullmore, E. T. (2002). Effects of verbal working memory load on corticocortical connectivity modeled by path analysis of functional magnetic resonance imaging data. *Neuroimage, 17*(2), 573-582.

Hopfinger, J. B., Buonocore, M. H., & Mangun, G. R. (2000). The neural mechanisms of top-down attentional control. *Nature Neuroscience, 3*(3), 284-291.

Iordan, A. D., & Dolcos, F. (2015). Brain activity and network interactions linked to valence-related differences in the impact of emotional distraction. *Cerebral Cortex*, doi 10.1093/cercor/BHV1242.

Iordan, A. D., Dolcos, S., Denkova, E., & Dolcos, F. (2013a). Sex differences in the response to emotional distraction: an event-related fMRI investigation. *Cognitive, Affective & Behavioral Neuroscience, 13*(1), 116-134.

Iordan, A. D., Dolcos, S., & Dolcos, F. (2013b). Neural signatures of the response to emotional distraction: A review of evidence from brain imaging investigations. *Frontiers in Human Neuroscience, 7*, 200. doi 210.3389/fnhum.2013.00200.

Joormann, J., & Gotlib, I. H. (2008). Updating the contents of working memory in depression: Interference from irrelevant negative material. *Journal of Abnormal Psychology, 117*(1), 182-192.

Kahn, I., Davachi, L., & Wagner, A. D. (2004). Functional-neuroanatomic correlates of recollection: implications for models of recognition memory. *The Journal of Neuroscience, 24*(17), 4172-4180.

Kanske, P., Heissler, J., Schonfelder, S., Bongers, A., & Wessa, M. (2011). How to regulate emotion? Neural networks for reappraisal and distraction. *Cerebral Cortex, 21*(6), 1379-1388.

Kinnison, J., Padmala, S., Choi, J. M., & Pessoa, L. (2012). Network analysis reveals increased integration during emotional and motivational processing. *The Journal of Neuroscience, 32*(24), 8361-8372.

Kober, H., Barrett, L. F., Joseph, J., Bliss-Moreau, E., Lindquist, K., & Wager, T. D. (2008). Functional grouping and cortical-subcortical interactions in emotion: a meta-analysis of neuroimaging studies. *Neuroimage, 42*(2), 998-1031.

Koenigs, M., Barbey, A. K., Postle, B. R., & Grafman, J. (2009). Superior parietal cortex is critical for the manipulation of information in working memory. *The Journal of Neuroscience, 29*(47), 14980-14986.

Krans, J., de Bree, J., & Moulds, M. L. (2015). Involuntary cognitions in everyday life: exploration of type, quality, content, and function. *Frontiers in Psychiatry, 6*, 7. doi 10.3389/fpsyt.2015.00007.

Kuyken, W., & Brewin, C. R. (1994). Intrusive memories of childhood abuse during depressive episodes. *Behaviour Research and Therapy, 32*(5), 525-528.

Lieberman, M. D., & Cunningham, W. A. (2009). Type I and Type II error concerns in fMRI research: re-balancing the scale. *Social Cognitive and Affective Neuroscience, 4*(4), 423-428.

Llewellyn, N., Dolcos, S., Iordan, A. D., Rudolph, K. D., & Dolcos, F. (2013). Reappraisal and suppression mediate the contribution of regulatory focus to anxiety in healthy adults. *Emotion, 13*(4), 610-615.

Ma, L., Steinberg, J. L., Hasan, K. M., Narayana, P. A., Kramer, L. A., & Moeller, F. G. (2012). Working memory load modulation of parieto-frontal connections: evidence from dynamic causal modeling. *Human Brain Mapping, 33*(8), 1850-1867.

Macmillian, N. A., & Creelman, C. D. (1991). *Detection theory: a user's guide*. New York: Cambridge University Press.

Mauss, I. B., Bunge, S. A., & Gross, J. J. (2007). Automatic emotion regulation. *Social and Personality Psychology Compass, 1*(1).

McNally, R. J. (2006). Cognitive abnormalities in post-traumatic stress disorder. *Trends in Cognitive Sciences, 10*(6), 271-277.

McRae, K., Hughes, B., Chopra, S., Gabrieli, J. D., Gross, J. J., & Ochsner, K. N. (2010). The neural bases of distraction and reappraisal. *Journal of Cognitive Neuroscience, 22*(2), 248-262.

Mitchell, R. L., & Phillips, L. H. (2007). The psychological, neurochemical and functional neuroanatomical mediators of the effects of positive and negative mood on executive functions. *Neuropsychologia, 45*(4), 617-629.

Mohanty, A., Engels, A. S., Herrington, J. D., Heller, W., Ho, M. H., Banich, M. T., Webb, A. G., Warren, S. L., & Miller, G. A. (2007). Differential engagement of anterior cingulate cortex subdivisions for cognitive and emotional function. *Psychophysiology, 44*(3), 343-351.

Morey, R. A., Dolcos, F., Petty, C. M., Cooper, D. A., Hayes, J. P., LaBar, K. S., & McCarthy, G. (2009). The role of trauma-related distractors on neural systems for working memory and emotion processing in posttraumatic stress disorder. *Journal of Psychiatric Research, 43*(8), 809-817.

Nadler, R. T., Rabi, R., & Minda, J. P. (2010). Better mood and better performance. Learning rule-described categories is enhanced by positive mood. *Psychological Science, 21*(12), 1770-1776.

Nee, D. E., Brown, J. W., Askren, M. K., Berman, M. G., Demiralp, E., Krawitz, A., & Jonides, J. (2012). A meta-analysis of executive components of working memory. *Cerebral Cortex, 23*(2), 264-282.

Neumann, A., Blairy, S., Lecompte, D., & Philippot, P. (2007). Specificity deficit in the recollection of emotional memories in schizophrenia. *Consciousness and Cognition, 16*(2), 469-484.

Niendam, T. A., Laird, A. R., Ray, K. L., Dean, Y. M., Glahn, D. C., & Carter, C. S. (2012). Meta-analytic evidence for a superordinate cognitive control network subserving diverse executive functions. *Cognitive, Affective & Behavioral Neurosience, 12*(2), 241-268.

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *Journal of Abnormal Psychology, 100*(4), 569-582.

Nolen-Hoeksema, S. (2012). Emotion regulation and psychopathology: The role of gender. *Annual Review of Clinical Psychology, 8*, 161-187.

Ochsner, K., & Gross, J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences, 9*(5), 242-249.

Ochsner, K. N., & Gross, J. J. (2008). Cognitive emotion regulation: Insights from social cognitive and affective neuroscience. *Current Directions in Psychological Science, 17*(2), 153-158.

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage, 23*(2), 483-499.

Ochsner, K. N., Silvers, J. A., & Buhle, J. T. (2012). Functional imaging studies of emotion regulation: a synthetic review and evolving model of the cognitive control of emotion. *Annals of the New York Academy of Sciences, 1251*, E1-24.

Oei, N. Y., Veer, I. M., Wolf, O. T., Spinhoven, P., Rombouts, S. A., & Elzinga, B. M. (2012). Stress shifts brain activation towards ventral 'affective' areas during emotional distraction. *Social Cognitive and Affective Neuroscience, 7*(4), 403-412.

Ono, M., Devilly, G. J., & Shum, D. H. (2015). A meta-analytic review of overgeneral memory: The role of trauma history, mood, and the presence of posttraumatic stress disorder. *Psychological Trauma : Theory, Research, Practice and Policy*, doi 10.1037/tra0000027.

Phan, K. L., Wager, T., Taylor, S. F., & Liberzon, I. (2002). Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. *Neuroimage, 16*(2), 331-348.

Philippot, P., Schaefer, A., & Herbette, G. (2003). Consequences of specific processing of emotional information: Impact of general versus specific autobiographical memory priming on emotion elicitation. *Emotion, 3*(3), 270-283.

Power, J. D., Cohen, A. L., Nelson, S. M., Wig, G. S., Barnes, K. A., Church, J. A., Vogel, A. C., Laumann, T. O., Miezin, F. M., Schlaggar, B. L., & Petersen, S. E. (2011). Functional network organization of the human brain. *Neuron, 72*(4), 665-678.

Power, J. D., & Petersen, S. E. (2013). Control-related systems in the human brain. *Current Opinion in Neurobiology, 23*(2), 223-228.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences USA, 98*(2), 676-682.

Ranganath, C., & Ritchey, M. (2012). Two cortical systems for memory-guided behaviour. *Nature Reviews. Neuroscience, 13*(10), 713-726.

Rissman, J., Gazzaley, A., & D'Esposito, M. (2004). Measuring functional connectivity during distinct stages of a cognitive task. *Neuroimage, 23*(2), 752-763.

Schönfelder, S., Kanske, P., Heissler, J., & Wessa, M. (2014). Time course of emotion-related responding during distraction and reappraisal. *Social Cognitive and Affective Neuroscience, 9*(9), 1310-1319.

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., Reiss, A. L., & Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *The Journal of Neuroscience, 27*(9), 2349-2356.

Sheppes, G., & Meiran, N. (2008). Divergent cognitive costs for online forms of reappraisal and distraction. *Emotion, 8*(6), 870-874.

Slotnick, S. D., Moo, L. R., Segal, J. B., & Hart, J., Jr. (2003). Distinct prefrontal cortex activity associated with item memory and source memory for visual shapes. *Brain Reseach. Cognitive Brain Research, 17*(1), 75-82.

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science, 283*(5408), 1657-1661.

Southwick, S. M., & Charney, D. S. (2012). The science of resilience: implications for the prevention and treatment of depression. *Science, 338*(6103), 79-82.

Sumner, J. A. (2012). The mechanisms underlying overgeneral autobiographical memory: an evaluative review of evidence for the CaR-FA-X model. *Clinical Psychology Review, 32*(1), 34-48.

Tamres, L. K., Janicki, D., & Helgeson, V. S. (2002). Sex differences in coping behavior: A meta-analytic review and an examination of relative coping. *Personality and Social Psychology Review, 6*(1), 2-30.

Thiruchselvam, R., Blechert, J., Sheppes, G., Rydstrom, A., & Gross, J. J. (2011). The temporal dynamics of emotion regulation: an EEG study of distraction and reappraisal. *Biological Psychology, 87*(1), 84-92.

Van Dillen, L. F., Heslenfeld, D. J., & Koole, S. L. (2009). Tuning down the emotional brain: An fMRI study of the effects of cognitive load on the processing of affective images. *NeuroImage, 45*(4), 1212-1219.

Vilberg, K. L., & Rugg, M. D. (2008). Memory retrieval and the parietal cortex: a review of evidence from a dual-process perspective. *Neuropsychologia, 46*(7), 1787-1799.

Vytal, K., & Hamann, S. (2010). Neuroimaging support for discrete neural correlates of basic emotions: a voxel-based meta-analysis. *Journal of Cognitive Neuroscience, 22*(12), 2864-2885.

Wager, T. D., Davidson, M. L., Hughes, B. L., Lindquist, M. A., & Ochsner, K. N. (2008). Prefrontal-subcortical pathways mediating successful emotion regulation. *Neuron, 59*(6), 1037-1050.

Whalen, P. J., Rauch, S. L., Etcoff, N. L., McInerney, S. C., Lee, M. B., & Jenike, M. A. (1998). Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. *Journal of Neuroscience, 18*(1), 411-418.

Williams, J. M. G. (2006). Capture and rumination, functional avoidance, and executive control (CaRFAX): Three processes that underlie overgeneral memory. *Cognition and Emotion, 20*(3-4), 548-568.

Yang, H., Yang, S., & Isen, A. M. (2013). Positive affect improves working memory: Implications for controlled cognitive processing. *Cognition and Emotion, 27*(3), 474-484.

Yeo, B. T., Krienen, F., Sepulcre, J., Sabuncu, M., Lashkari, D., Hollinshead, M., Roffman, J., Smoller, J., Zöllei, L., Polimeni, J., Fischl, B., Liu, H., & Buckner, R. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*(3), 1125-1165.

Tables

Table 4.1. Brain Regions Showing Overall Responses to Internal Emotional Distraction.

Brain Regions			BA	Talairach Coordiantes			*t* Values	Time point
				x	*y*	*z*		
AM > Ctrl								
vlPFC	L	Inferior Frontal Gyrus	45	-42	21	4	11.54	9
IFJ	L	Middle Frontal Gyrus	9	-46	15	28	9.65	9
TC	L	Superior Temporal Gyrus	22	-57	-59	18	10.37	9
TOC	L	Middle Temporal Gyrus	19	-35	-79	27	8.51	9
mPFC	L	Superior Frontal Gyrus	9	-9	49	29	10.62	9
		Superior Frontal Gyrus	6	-5	8	61	8.95	9
PCC	L	Posterior Cingulate	23	-9	-55	15	11.96	9
		Posterior Cingulate	30	-12	-51	8	9.95	9
mPC	L	Precuneus	31	-5	-68	25	11.84	9
MTL	L	Amygdala		-19	-4	-9	6.96	9
vlPFC	R	Inferior Frontal Gyrus	45	43	21	5	8.64	9
		Inferior Frontal Gyrus	47	44	14	-10	8.18	9
IFJ	R	Middle Frontal Gyrus	9	39	14	30	6.39	8
PrCG	R	Precentral Gyrus	6	46	-3	53	5.47	9
TP	R	Superior Temporal Gyrus	38	55	3	-7	5.22	9
TC	R	Middle Temporal Gyrus	21	51	0	-15	5.78	9
TPC	R	Superior Temporal Gyrus	39	54	-56	23	6.09	9
	R	Middle Temporal Gyrus	39	43	-61	26	5.99	9
TOC	R	Fusiform Gyrus	37	43	-35	-4	4.37	9
mPFC	R	Superior Frontal Gyrus	9	3	52	29	10.2	9
IC	R	Insula	13	43	-20	-2	4.55	9
MTL	R	Parahippocampal Gyrus	36	36	-34	-11	4.36	9
Cerebellum	R	Declive		36	-60	-21	8.65	9
		Declive		36	-68	-14	8.41	9
Ctrl > AM								
PoCG	L	Postcentral Gyrus	2	-61	-27	38	6.03	9
		Postcentral Gyrus	5	-39	-41	63	4.71	9
		Postcentral Gyrus	40	-53	-22	21	4.59	9
		Postcentral Gyrus	43	-60	-14	18	5.27	9
LPC	L	Inferior Parietal Lobule	40	-42	-35	42	5.77	9
IC	L	Insula	13	-42	-17	7	5.54	9
PoCG	R	Postcentral Gyrus	2	43	-33	58	4.89	9
LPC	R	Inferior Parietal Lobule	40	35	-40	50	5.14	9
SPC	R	Superior Parietal Lobule	7	35	-49	60	5.18	9
mPC	R	Precuneus	7	9	-67	50	5.58	9

Table 4.1 (continued). The table identifies brain regions showing overall responses to internal emotional distraction: i.e., increased or decreased responses to autobiographical memory (AM) recollection. Significance threshold is $p < 0.001$ and 18 contiguous voxels, equivalent to $p < 0.05$, corrected for multiple comparisons. AM, Autobiographical Memories (Emotion + Context Focus collapsed); Ctrl, Control; vlPFC, Ventro-Lateral Prefrontal Cortex; IFJ, Inferior Frontal Junction; TC, Temporal Cortex; TOC, Temporo-Occipital Cortex; mPFC, Medial Prefrontal Cortex; PCC, Posterior Cingulate Cortex; mPFC, Medial Parietal Cortex; MTL, Medial Temporal Lobe; PrCG, Precentral Gyrus; TP, Temporal Pole; TPC, Temporo-Parietal Cortex; IC, Insular Cortex; PoCG, Postcentral Gyrus; LPC, Lateral Parietal Cortex; SPC, Superior Parietal Cortex.

Table 4.2. Brain Regions Sensitive to the Focused Attention Manipulation.

Brain Regions			BA	Talairach Coordiantes			*t* Values	Time point
				x	*y*	*z*		
Emo > Cont								
aPFC	L	Superior Frontal Gyrus	9	-16	48	32	7.48	9
PrCG	L	Precentral Gyrus	6	-49	1	13	6.9	9
PoCG	L	Postcentral Gyrus	40	-57	-18	21	6.16	9
dACC	L	Cingulate Gyrus	32	-9	18	29	6.19	9
		Cingulate Gyrus	24	-2	-6	45	6.37	9
IC	L	Insula	13	-38	2	6	5.75	9
MTL	L	Amygdala		-30	0	-12	3.22[*]	8
Cerebellum	L	Declive		-19	-67	-19	6.11	9
IPC	R	Inferior Parietal Lobule	40	54	-23	26	6.14	9
mFC	R	Medial Frontal Gyrus	6	5	-16	70	6.53	9
dACC	R	Cingulate Gyrus	24	6	2	46	7.02	9
IC	R	Insula	13	47	9	4	7.62	9
mPC	R	Precuneus	7	17	-78	49	4.55	9
Subcortical	R	Putamen		32	-17	5	5.87	9
	R	Thalamus		25	-21	12	6.54	9
Cont > Emo								
dlPFC	L	Middle Frontal Gyrus	9	-42	14	36	4.23	10
PHC	L	Parahippocampal Gyrus	36	-31	-34	-12	4.69	10
TOC	L	Fusiform Gyrus	37	-27	-38	-12	5.99	10
IPC	L	Precuneus/Angular Gyrus	39	-42	-68	31	4.49	10
PC	L	Precuneus	19	-28	-77	42	4.39	10
MTL	R	Parahippocampal Gyrus	35	25	-26	-14	4.6	10
		Parahippocampal Gyrus	36	29	-31	-11	4.02	10

The table identifies brain regions showing sensitivity to the focused attention manipulation: i.e., increased activity to emotion vs. context focus. Significance threshold is $p < 0.005$ and 19 (Emo > Cont) or 18 (Cont > Emo) contiguous voxels, equivalent to $p < 0.05$, corrected for multiple comparisons. [*]$p < 0.01$. Emo, Emotion Focus; Cont, Context Focus; aPFC, Anterior Prefrontal Cortex; PrCG, Precentral Gyrus; PoCG, Postcentral Gyrus; dACC, Dorsal Anterior Cingulate; IC, Insular Cortex; MTL, Medial Temporal Lobe; IPC, Inferior Parietal Cortex; mFC, Medial Frontal Cortex; mPC, Medial Parietal Cortex; dlPFC, Dorso-Lateral Prefrontal Cortex; TOC, Temporo-Occipital Cortex; PC, Parietal Cortex.
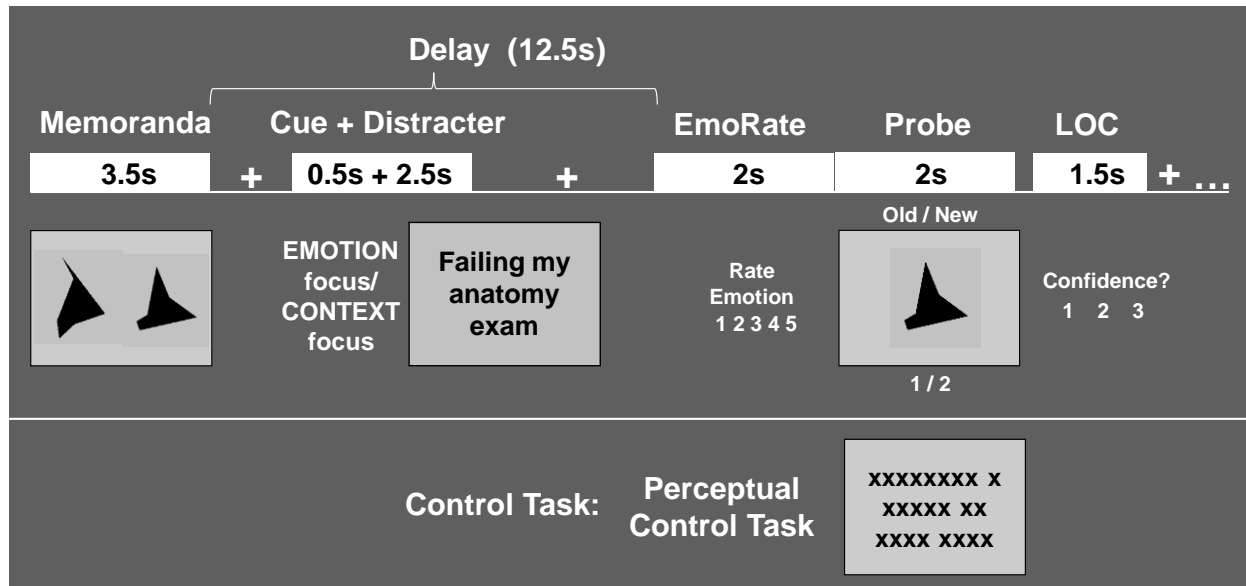
Figures

Figure 4.1. Diagram of the combined working memory-emotion regulation (WM-ER) task.
Functional magnetic resonance imaging (fMRI) data were recorded while subjects performed a WM task for shapes. Cues for recollection of negative autobiographical memories (AMs) were presented during the delay interval between the memoranda and the probes. Preceding the AM cue, an instruction cue prompted participants to focus either on emotional (Emotion focus) or non-emotional contextual (Context focus) details of their recollections The WM performance was measured using a recognition memory task, in which participants indicated by pushing a button whether single-shape probes were part of the memoranda (*Old* = 1) or not (*New* = 2), and then they indicated their level of confidence (LOC) in their responses by pushing one of three buttons (1 = *low*, 2 = *medium*, 3 = *high*).
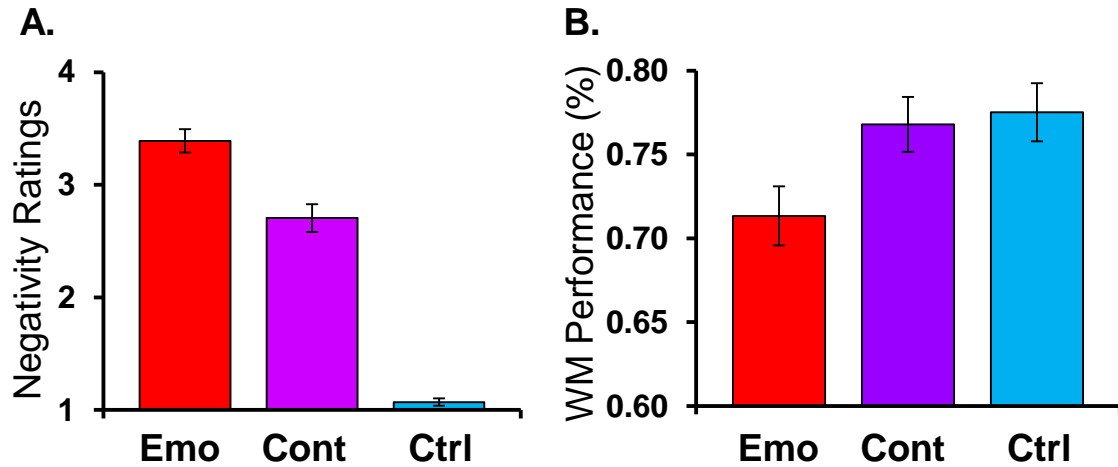
Figure 4.2. Diminished experienced emotion and working memory interference under emotion regulation. Focusing on context during recollection of task-irrelevant emotional AMs reduced both (A) *subjective* negativity ratings and (B) *objective* working memory interference. Emo, Emotion Focus; Cont, Context Focus; Ctrl, Control Condition. Working memory performance is % correct. Error bars represent standard errors of means.
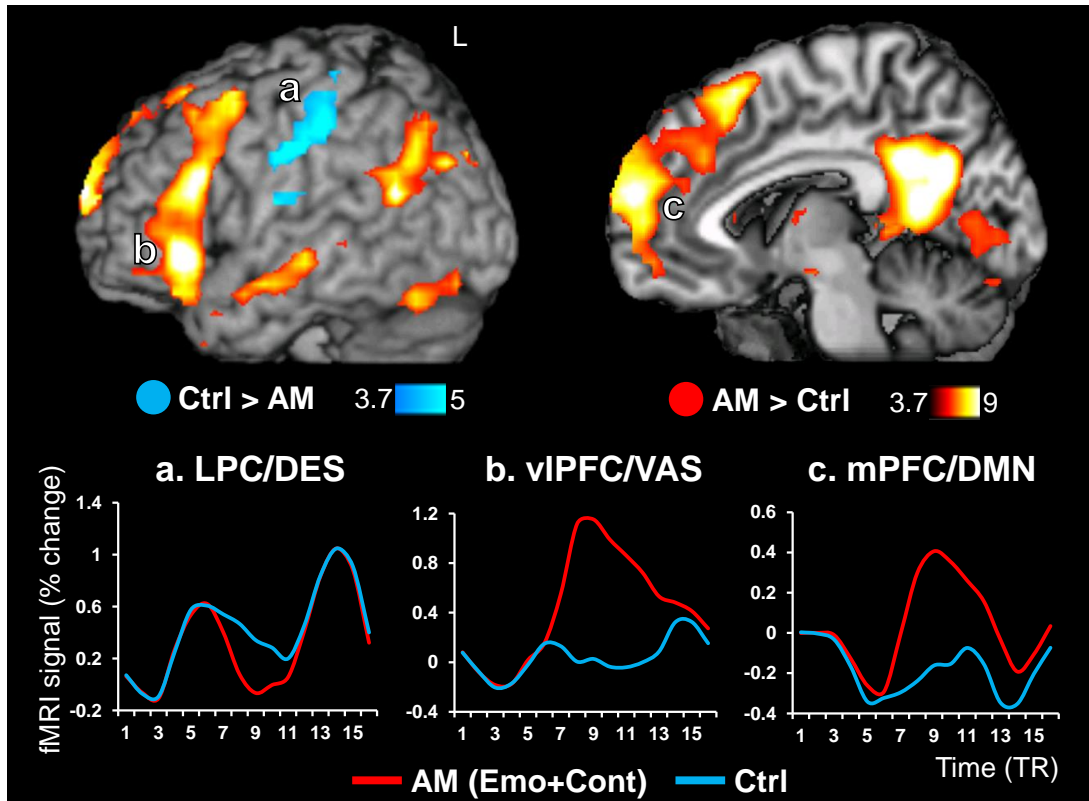
Figure 4.3. Opposing responses in DES versus VAS and DMN regions under internal emotional distraction. Brain responses to internal emotional distraction were characterized by (A) deactivation in DES regions (LPC) and increased activity in VAS regions (vlPFC), as well as (B) increased activity in midline regions part of DMN (mPFC). The line graphs display the time courses of brain activity extracted from the peak voxels of the AM vs. Ctrl comparison [Talairach coordinates (x, y, z): -42, -35, 42 (LPC); -42, 21, 4 (vlPFC); -9, 49, 29 (mPFC)]. The colored horizontal bars represent the gradient of the t values. The t maps are displayed at $p < 0.001$ and 18 contiguous voxels, equivalent to $p < 0.05$, corrected for multiple comparisons. DES, Dorsal Executive System; VAS, Ventral Affective System; DMN, Default Mode Network; LPC, Lateral Parietal Cortex; vlPFC, Ventro-Lateral Prefrontal Cortex; mPFC, Medial PFC; AM (Emo + Cont), Autobiographical Memories (Emotion and Context Focus collapsed); Ctrl, Control Condition; TR, Repetition Time (2 s); L, Left.
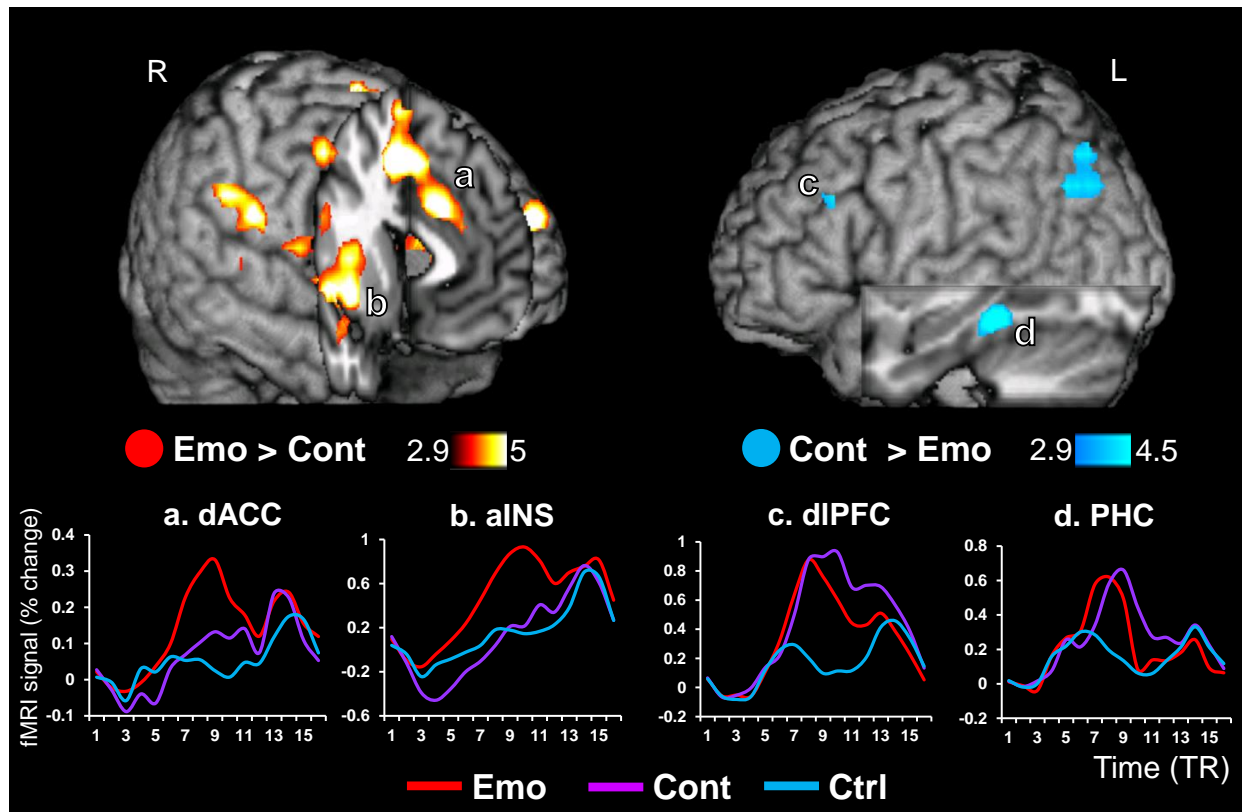
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Figure 4.4. Reduced VAS activity and increased recruitment of executive and context retrieval regions under context focus. Focusing on context was associated with both (A) reduced activity in VAS regions part of the salience network (dACC, aINS) and (B) increased activity in executive (dlPFC) and context retrieval regions (PHC). The line graphs display the time courses of brain activity extracted from the peak voxels of the Cont vs. Emo comparison [Talairach coordinates (x, y, z): -9, 18, 29 (dACC); 47, 9, 4 (aINS); -42, 14, 36 (dlPFC); -31, -34, -12 (PHC)]. The colored horizontal bars represent the gradient of the t values. The t maps are displayed at p < 0.005 and 19 (red) or 17 (blue) contiguous voxels, equivalent to $p < 0.05$, corrected for multiple comparisons. dACC, Dorsal Anterior Cingulate Cortex; aINS, Anterior Insula; dlPFC, Dorsolateral Prefrontal Cortex; PHC, Parahippocampal Cortex; Emo, Emotion Focus; Cont, Context Focus; Ctrl, Control Condition; TR, Repetition Time (2 s); L, Left; R, Right.
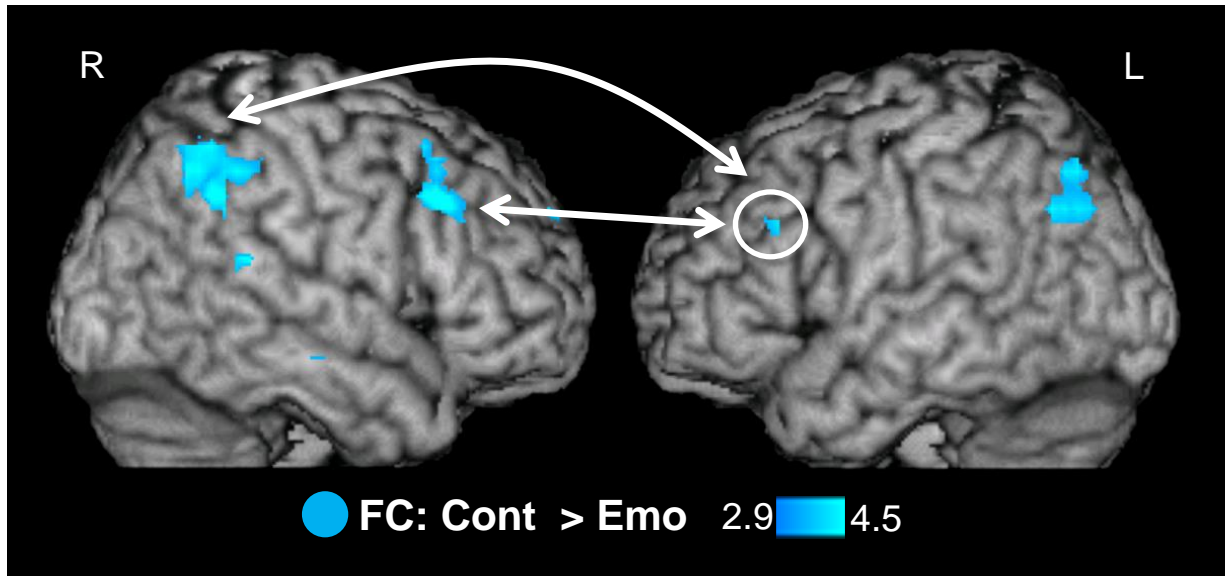
Figure 4.5. Increased fronto-parietal functional connectivity under context focus. The left dlPFC region showing more sustained increased activity to context focus (see Figure 4.4) also showed increased functional connectivity with the right dlPFC and the bilateral LPC, under context focus. The functional connectivity t map (left panel) is displayed at $p < 0.005$ and 13 contiguous voxels, equivalent to $p < 0.05$, corrected for multiple comparisons. Emo, Emotion Focus; Cont, Context Focus; TR, Repetition Time (2 s); L, Left; R, Right.
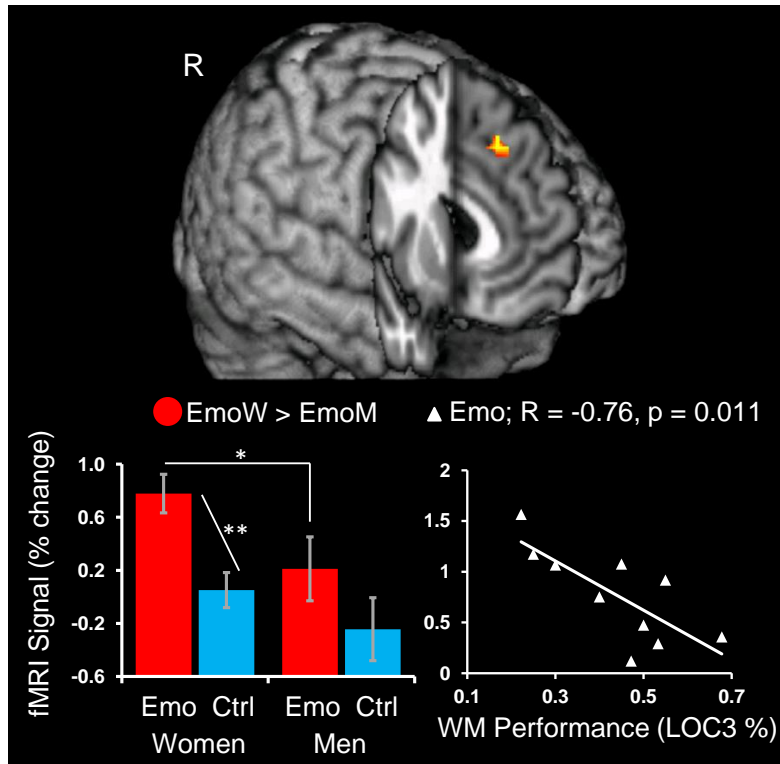
Figure 4.6. Increased activity in the dorsomedial PFC/dorsal ACC linked to greater WM interference in women. Women showed greater response to internal emotional distraction in the dorsomedial PFC/dorsal ACC (BA 8/32) (bottom left panel) and increased activity in this region was associated with lower WM performance for emotional LOC 3 trials (bottom right panel). The heat map displays the overlap between two individual maps showing increased activity in women compared to men and negative correlation with LOC 3 WM performance in women, respectively. An exploratory threshold of $p < 0.05$ and 20 contiguous voxels was used for each of the contributing maps. The bar graph illustrates the fMRI signal, as extracted from the peak voxel of the difference in activation between women and men (Talairach coordinates: $x = 2$, $y = 21$, $z = 44$), for LOC 3 trials associated with emotion versus context focus. The scatterplot displays the brain-behavior covariation for women, for emotion focus LOC 3 trials, extracted from the same voxel. $^{*}p = 0.017$; $^{**}p = 0.004$. Emo, Emotion; Ctrl, Control; W, Women; M, Men; LOC3, Level of confidence 3.

CHAPTER 5:

GENERAL DISCUSSION

Review of the Main Findings

       The overarching goal of the present dissertation was to clarify the neural mechanisms associated with the impact and control of external and internal emotional distraction, and the role of sex differences in these effects. Two complementary types of emotional distraction in the context of goal-oriented cognitive tasks have been investigated, namely distraction originating from the "external" environment (i.e., seeing task-irrelevant emotional scenes and faces) and distraction originating from the "internal" environment (i.e., recollecting task-irrelevant emotional autobiographical memories). The first two studies of the present dissertation, presented in Chapters 2 and 3, focused on the response to *external* emotional distraction. The third study, presented in Chapter 4, focused on the response to *internal* emotional distraction. Below I will briefly discuss the main findings for each of the aspects highlighted in the introductory section and addressed in the corpus of the present work.

<u>Study I.</u> The Role of Valence in the Impact of External Emotional Distraction

       As presented in Chapter 2, this study (Iordan & Dolcos, 2015) investigated the roles of arousal and valence in the impact of external emotional distraction on WM performance, and yielded four main findings. First, positive distraction had reduced impact on WM performance, compared with negative distraction. Second, fMRI results identified valence-specific effects in DES regions and overlapping arousal and valence effects in VAS regions, suggesting both increased impact of negative distraction and enhanced engagement of coping mechanisms for positive distraction. Third, a valence-related rostro-caudal dissociation was identified in medial frontal regions associated with the default-mode network (DMN). Finally, these DMN regions showed increased functional connectivity with DES regions for negative compared with positive distraction.

The study tested two competing accounts: the "arousal account", positing that the impairing effects of emotion may be mainly driven by the intensity of the stimuli, similar to the enhancing effects of emotion on episodic memory (e.g., Dolcos, Iordan, & Dolcos, 2011; Dolcos, LaBar, & Cabeza, 2004; Murty, Ritchey, Adcock, & LaBar, 2010), and the "valence account", assuming that the positive stimuli may be less distracting due to the engagement of different processing strategies, as suggested by the theories of motivational dispositions (Berntson, Boysen, & Cacioppo, 1993; Bradley & Lang, 2007; Cacioppo, Gardner, & Berntson, 1997) and of positive affect (Ashby, Isen, & Turken, 1999; Fredrickson, 2001; Isen, 2005).

The results of this study mainly supported the "valence account" by showing that positive distraction was associated with both reduced cognitive interference and better coping compared to negative distraction, consistent with the idea of a facilitating effect of positive emotion on controlled processing. Complementing previous investigations that examined arousal- and valence-related effects linked to the emotional content manipulated in WM (Kensinger & Corkin, 2003; Levens & Phelps, 2008; Lindstrom & Bohlin, 2011), this study demonstrated that task-irrelevant positive stimuli are better controlled compared with the negative ones, and thus negative distracters are more interfering with on-going cognitive performance, even at similar arousal levels. Thus, potential interference from positive distraction may be compensated by facilitatory effects that would allow maintaining the memoranda in WM while still processing the distracters, in line with recent evidence suggesting facilitation of controlled processing by positive affect (Carpenter, Peters, Västfjäll, & Isen, 2013; Nadler, Rabi, & Minda, 2010; Yang, Yang, & Isen, 2013). Our findings support both the idea of a "negativity bias" (i.e., negative reactions tend to be stronger than the positive ones even at similar levels of stimulus intensity), as predicted by the theories of motivational dispositions (Berntson et al., 1993; Bradley & Lang,

2007; Cacioppo et al., 1997) and an association between positive emotions and cognitive enhancements (e.g., "broadening" the scope of attention, flexible integration of information), as predicted by the theories of positive affect (Fredrickson, 2001, 2004; Fredrickson & Branigan, 2005). These dissociations may be due to different processing strategies engaged by positive and negative stimuli (Eysenck, Derakshan, Santos, & Calvo, 2007; Mitchell & Phillips, 2007), linked to their distinct evolutionary values.

The fMRI results are consistent with this interpretation, because they showed both reduced impact of positive compared to negative distraction on dorsal brain regions (lateral parietal cortex) and superior recruitment of ventral regions (ventrolateral prefrontal cortex – PFC). The lateral parietal cortex is the posterior "hub" in the fronto-parietal executive network (Dosenbach et al., 2006; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008; Dosenbach et al., 2007; Power et al., 2011; Power & Petersen, 2013; Seeley et al., 2007; Yeo et al., 2011), and its putative role in WM processing has been linked to top-down biasing in order to foreground in WM the representation that is the focus of attention (Nee & Jonides, 2008). Hence, negative stimuli may interfere more with this process compared to positive stimuli, probably due to their increased imperativeness (Berntson et al., 1993; Bradley & Lang, 2007; Cacioppo et al., 1997). At the same time, increased activity in the ventrolateral PFC has previously been linked to both increased WM performance and reduced distractibility (Dolcos, Kragel, Wang, & McCarthy, 2006; Dolcos & McCarthy, 2006; Iordan, Dolcos, & Dolcos, 2013b), consistent with a role of this region in cross-modal inhibition (Aron, 2007; Aron, Robbins, & Poldrack, 2004; Berkman, Burklund, & Lieberman, 2009) and inhibition of negative emotion (Ochsner et al., 2004; Petrovic, Kalso, Petersson, & Ingvar, 2002). In addition, the results of our brain-behavior covariation analysis support the idea that increased vlPFC activity for positive distraction reflects

better engagement of coping with distraction mechanisms, showing that subjects who engaged this region more in response to positive than negative distraction also performed better in the WM task. Of note, these valence-related dissociations were observed in the context of similar responses to both positive and negative distraction in dorsal (dorsolateral PFC) and ventral (amygdala, ventrolateral PFC) brain regions, suggesting similar engagement of certain brain mechanisms irrespective of valence, partially supporting the arousal account.

In addition, the results showing increased functional connectivity between regions of the default mode (medial PFC) and fronto-parietal (lateral parietal cortex) networks, under higher impact by negative distraction, suggest a potential mechanism by which goal-irrelevant negative emotions impact on-going cognitive performance. Activity in the default-mode network, also called the "task negative" network, is typically anti-correlated with activity in the fronto-parietal network (Fox et al., 2005) and in particular during the maintenance phase of WM processing (Piccoli et al., 2015). Hence, increased coupling between "task negative" (default-mode) and "task positive" (fronto-parietal) regions under negative compared to positive distraction suggest greater interference of affective information integrated by the medial PFC with goal-relevant representations maintained by the fronto-parietal network.

In sum, this study provided novel evidence regarding the roles of arousal and valence in the impact of external emotional distraction on WM, by identifying valence-related dissociations in the response and interactions between brain regions associated with executive and emotion processing. Overall, the findings of this study demonstrate that, although positive and negative distraction may engage partly similar arousal-dependent mechanisms, their differential impact on concurrent cognitive performance is linked to valence dissociations in the engagement of and coupling between regions associated with basic emotion processing and higher-level cognitive

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control. As discussed below, similar findings regarding the effect of positive valence were also found in the case of internal distraction, thus suggesting that negative but not positive distraction impairs concurrent cognitive performance irrespective of its originating source.

Study II. Sex Differences in the Impact of External Emotional Distraction

As presented in Chapter 3, this study (Iordan, Dolcos, Denkova, & Dolcos, 2013a) investigated sex differences in the response to external emotional distraction and yielded three main findings. First, we identified an increased impact of emotional distraction among women in trials associated with high-confidence responses, in the context of overall similar WM performance in women and men. Second, women showed increased sensitivity to emotional distraction in VAS regions, whereas men showed increased sensitivity in DES regions, in the context of overall similar patterns of response to emotional distraction in women and men. Third, a sex-related dorsal-ventral hemispheric dissociation emerged in the lateral PFC related to coping with emotional distraction, with women showing a positive correlation with WM performance in left ventral PFC, and men showing similar effects in the right dorsal PFC.

The results showing decreased WM performance for high-confidence responses, as well as increased emotional ratings of the distracters and increased post-task negative affect, for women relative to men, indicate greater impact of emotional distraction in women. These results support the idea that enhanced emotional competence in women may have the side effect of increased emotional reactivity, which in turn may lead to enhanced emotional distractibility. Of note, sex-related differences in WM performance were observed only for responses associated with the highest level of confidence, which suggests that sex differences in the response to emotional challenge are more subtle and affect only some aspects of behavior.

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Consistent with the behavioral findings, the fMRI results identified sex differences in the patterns of activity in VAS and DES regions, in the context of overall similar responses to emotional distraction in women and men. Whereas similarities in VAS and DES engagement suggest that men and women deploy overall similar mechanisms in response to transient emotional distraction (reviewed in Dolcos et al., 2011; Iordan et al., 2013b), the observed sex differences suggest increased sensitivity in "bottom-up" responses in women, linked to impaired WM performance, and increased sensitivity in "top-down" responses in men, linked to increased performance. Notably, the increased response to emotional distraction among women in the subgenual anterior cingulate cortex, a VAS region closely tied with the autonomic nervous system and associated with the experience of negative emotion in both healthy and clinical samples (Baeken et al., 2010; Ball et al., 2012; Gotlib et al., 2005; Mobbs et al., 2009), suggests a link between enhanced emotional reactivity in women and stronger autonomic reactions to emotional stimuli (Butler et al., 2005; Wager, Phan, Liberzon, & Taylor, 2003). In contrast, men showed reduced activity in polar and dorsal PFC, suggesting increased sensitivity in DES regions in men. In addition, the simultaneous deactivation in posterior midline, lateral parietal, and superior temporal regions that partially overlap with the default-mode network suggests that men were also more successful in disengaging the "task-negative" regions as a result of the demand to perform goal-directed processing, and consequently performed better in the WM task (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003; Raichle et al., 2001).

These sex differences in the response to external emotional distraction were also supported by a dissociation within the lateral PFC, linked to the engagement of mechanisms to cope with emotional distraction. Thus, although the left ventral PFC showed overall reduced activity in women relative to men, it also showed a positive correlation with WM performance in

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women, suggesting its superior recruitment by women who successfully coped with emotional distraction (Denkova et al., 2010). This result is consistent with previous evidence linking activity in this region to coping with emotional distraction (Banich et al., 2009; Dolcos, Diaz-Granados, Wang, & McCarthy, 2008; Dolcos et al., 2006). By contrast, although the right dorsal PFC showed reduced activity in men relative to women, it also showed a positive correlation with WM performance in men, suggesting its superior recruitment by men who also successfully coped with emotional distraction. This result is consistent with evidence linking activity in lateral PFC with WM processing, especially in the spatial domain (Courtney, Petit, Maisog, Ungerleider, & Haxby, 1998; D'Esposito, 2008; Tanaka, Honda, & Sadato, 2005).

In summary, the present study extended to men results that have previously been reported in women, by showing that both sexes engage mechanisms that are overall similar in response to external emotional distraction, and identified subtle sex differences in the neural mechanisms involved both in the response to and coping with emotional distraction. These results provide support for the idea that women may be more sensitive to external emotional distraction and suggest a link between increased emotional reactivity and increased emotional distractibility in women relative to men. As discussed below, similar findings consistent with the idea of greater impact of emotional distraction in women were also found in the case of internal distraction, thus suggesting that these sex differences, albeit being subtle, are consistently identified independent of the source of distraction.

Study III. The Response to and Regulation of Internal Emotional Distraction

III.1. The Role of Valence in the Impact of Internal Emotional Distraction: Behavioral Pilot Study. Consistent with the valence account, the results of the behavioral pilot investigating the role of valence in the impact of internal emotional distraction on WM performance showed that

the recollection of task-irrelevant negative but not positive AMs interfered with concurrent WM performance. Together with the findings of Study I, these results suggest a specific impact of negatively valenced distraction, irrespective of its originating source (external or internal), on concurrent cognitive performance. These findings are consistent with both evidence linking intrusive thoughts and ruminations with deleterious effects on cognitive performance (Eysenck et al., 2007; McNally, 2006; Mitchell & Phillips, 2007), and evidence linking positive affect with cognitive enhancements (Carpenter et al., 2013; Fredrickson, 2001, 2004; Fredrickson & Branigan, 2005; Nadler et al., 2010; Yang et al., 2013). This also justified the inclusion of only negative autobiographical memories in Study III.

III.2. The Effect of Emotional Control on Internal Negative Distraction. As presented in Chapter 4, this study (Iordan, Dolcos, & Dolcos, 2015) investigated the response to and regulation of internal emotional distraction, and yielded four main findings. First, focusing away from emotion and onto the non-emotional contextual aspects (i.e., context focus), while recollecting negative autobiographical memories, diminished both the *subjective* negative experience and the *objective* WM interference, compared to focusing on emotion. Second, regarding the overall response to internal distraction, the fMRI results identified both deactivation in DES regions and increased activity in VAS regions, similar to the response to external distraction, as well as specific increased activity in medial regions part of DMN. Third, regarding the neural mechanisms of internal distraction regulation, focusing on context was associated with both diminished activity in VAS regions part of the salience network, and increased activity in executive and memory-related regions involved in context retrieval, compared to emotion focus. Finally, context focus was also associated with increased functional connectivity between fronto-parietal regions.

The results showing that focusing away from emotion was associated with both diminished emotional experience and diminished cognitive interference demonstrate that instructed emotion regulation enables coping with emotion while maintaining concurrent cognitive performance. This suggests that down-regulating the emotional experience while minimally taxing the cognitive system allows for more WM resources available to maintain the memoranda, supporting the idea that focusing away from emotion allows better deployment of attention to representations active within working memory (Gotlib & Joormann, 2010; Joormann & Gotlib, 2008). To our knowledge, this is the first study to provide insights into the effects of manipulating attentional focus during internal distraction on concurrent cognitive performance.

Regarding the neural mechanisms of internal emotional distraction, the fMRI findings suggest specific engagement of autobiographical memory retrieval/default-mode network regions, in the context of overall responses to internal emotional distraction in DES (lateral parietal cortex) and VAS (amygdala, ventrolateral PFC) regions, similar to the ones previously reported for external emotional distraction (Anticevic, Repovs, & Barch, 2010; Denkova et al., 2010; Diaz et al., 2011; Dolcos et al., 2008; Dolcos et al., 2013; Dolcos et al., 2006; Dolcos & McCarthy, 2006; Iordan & Dolcos, 2015; Iordan et al., 2013a; Oei et al., 2012). Thus, these findings support the idea that DES and VAS are more generally involved in the response to emotional distraction, independent of the originating source of distraction.

Regarding the engagement of focused attention as an emotion regulation strategy to cope with internal distraction (i.e., context focus), the findings suggest that the observed beneficial effects of the emotion regulation manipulation are linked to a shift in bias from emotion processing (salience network regions) to recollection of contextual details (executive and memory-related regions). First, the results showing that context focus was associated with

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reduced activity in VAS regions part the salience network (amygdala, anterior insula, dorsal anterior cingulate cortex), suggest down-regulation of activity in regions associated with both emotion processing (Barrett & Satpute, 2013; Seeley et al., 2007) and stimulus-driven ("bottom-up") reorienting of attention (Corbetta, Patel, & Shulman, 2008), leading to decreased cognitive interference. Second, the results showing that context focus was also associated with increased activity in executive (dorsolateral PFC) and memory-related regions (parahippocampal and angular gyri) suggest better coordination of goal-oriented processing with the retrieval of contextual information (Cabeza, Ciaramelli, Olson, & Moscovitch, 2008; Daselaar et al., 2008; Hassabis & Maguire, 2007; Kahn, Davachi, & Wagner, 2004; Vilberg & Rugg, 2008). Of note, the ventrolateral PFC, a brain region previously associated with coping with external emotional distraction (Dolcos et al., 2011; Iordan et al., 2013b) did not show increased activity under context compared to emotion focus, supporting the idea of its involvement in spontaneous (i.e., coping), rather than instructed, regulation of emotional distraction in dual tasks.

Finally, the different patterns of connectivity between the fronto-parietal regions, for context versus emotion focus suggest better integration within the fronto-parietal network when subjects were focusing away from emotion. These findings are consistent with previous evidence showing increased prefrontal-parietal coupling during WM tasks (Cohen, Gallen, Jacobs, Lee, & D'Esposito, 2014; Honey et al., 2002; Ma et al., 2012), and suggest a potential mechanism by which goal-relevant representations of the memoranda were better maintained in WM under context focus.

In summary, the present findings provided novel evidence regarding neural mechanisms mediating the response to and regulation of internal emotional distraction. Regarding the response to internal distraction, the findings suggest that it involves both overall similar and

dissociable mechanisms relative to external distraction. Regarding the regulation of internal distraction, the findings suggest that focused attention is an effective strategy that can be deployed to cope with internal distraction and that its engagement is linked to a shift in processing bias from emotion/salience regions to executive and context retrieval regions.

III.3. Sex Differences in the Response to Internal Emotional Distraction: Exploratory Analysis. This exploratory analysis tested for sex differences in the impact of internal emotional distraction. Consistent with the idea of increased susceptibility to emotional distraction in women compared to men, the results showed increased impact of internal emotional distraction in women, linked to increased sensitivity in a brain region involved in processing of salient information (dorsomedial PFC/dorsal anterior cingulate cortex). Similar to the findings of Study II, which focused on external distraction, sex differences in the impact of internal emotional distraction on cognitive processing were observed in the responses with the highest level of confidence but not in the overall WM performance. Together with the results of Study II, these findings support the idea that sex differences in the response to emotional challenge, either external or internal, are more subtle and affect only certain behavioral aspects. Consistent with the behavioral results, the fMRI findings suggest that increased susceptibility to internal emotional distraction in women is linked to enhanced responses in regions involved in stimulus-driven processing of salient information, such as the dorsomedial PFC/dorsal anterior cingulate cortex (Bressler & Menon, 2010; Seeley et al., 2007).

Summary, Conclusions and Future Directions

The present research brings novel insights concerning the neural mechanisms associated with the impact and control of emotional distraction, and the role of sex differences in these effects. In brief, the main findings of these studies were: (1) positive distraction, either external

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or internal, is associated with reduced cognitive interference, compared to negative distraction; (2) internal emotional distraction involves both similar and dissociable neural mechanisms compared to external emotional distraction; (3) the instruction to engage a specific emotion regulation strategy (i.e., focused attention) to cope with internal distraction diminishes both the subjective emotional experience and the impact on cognitive performance; (4) both external and internal emotional distraction produce subtle but stronger impact in women than in men, which affects high-confidence responses but not the overall cognitive performance.

Concerning external emotional distraction, the present dissertation extended previous research focusing on negative valence and including mainly female participants by adding novel evidence regarding the influence of positive valence and the role of sex differences. Specifically, the present results (1) showed that positive external distraction had reduced impact on WM performance, compared to negative external distraction, linked to valence-related dissociations in the response of and interactions between brain regions associated with executive and emotion processing; and (2) identified subtle sex differences in the response to external emotional distraction consistent with greater impact in women, as well as sex-related dissociations in brain mechanisms, in the context of overall similar behavioral and brain responses to external emotional distraction across sexes.

Concerning internal emotional distraction, the present dissertation added novel evidence regarding the role of valence in its impact on cognitive performance, the neural mechanisms of internal distraction, the consequences of engaging emotion regulation to cope with it, and the role of sex differences. Specifically, the present results showed that (1) positive internal distraction had reduced impact on WM performance, compared to negative internal distraction, similar to the effects observed in the case of external distraction; (2) internal distraction involved

both dorsal executive and ventral affective mechanisms, similar to external distraction, as well as specific mechanisms associated with the default-mode network; (3) the benefits of engaging emotion regulation strategies to cope with internal distraction are linked to down-regulating emotion processing regions and increased coupling between fronto-parietal executive regions; and also (4) identified similar sex differences in the response to internal emotional distraction, consistent with increased impact in women, and consistent sex-related dissociations in brain mechanisms, relative to external distraction.

These findings contribute to a better understanding of healthy functioning under transient emotional distraction. In addition, they have implications for understanding mood and anxiety disorders, which are characterized by increased susceptibility to negatively-valenced distraction and diminished processing of positive emotions (Forbes & Dahl, 2005; Gilbert, 2012; Izard, 2002; Watson & Naragon-Gainey, 2010; Waugh & Koster, 2014), as well as by increased emotional distractibility to external and internal emotional stimuli (Gotlib & Joormann, 2010; McNally, 2006), and are more prevalent in women compared to men (Bekker & van Mens-Verhulst, 2007; Kessler, 2003).

The present dissertation also opens new avenues for future investigations linking emotion-cognition interactions with the large-scale functional organization of the brain. Directly comparing the brain mechanisms engaged by external and internal emotional distraction would potentially allow a more fine-grained dissociation between the network-level components of the dorsal-executive and ventral-affective systems, in the context of active task performance. Although the study of large-scale neural networks (e.g., Dosenbach et al., 2007; Power & Petersen, 2013; Seeley et al., 2007; Yeo et al., 2011) has become possible as a result of assessing resting-state functional connectivity, this method has limited ability to capture dynamic

interactions among these networks, and thus it provides only a "static picture" of their connectivity. By contrast, specific task manipulations used by studies of emotion-cognition interactions (reviewed in Dolcos et al., 2011; Iordan et al., 2013b) have proven effective in eliciting active dissociations among the major brain networks. Hence, such dual tasks with cognitive/executive and emotional components may provide a useful way of studying active interactions between the large-scale brain networks. Among the major brain networks, the salience network appears to most reliably track the emotional response (Lindquist & Barrett, 2012), and hence investigating the conditions leading to its recruitment, in conjunction or in conflict with other brain networks, provides a promising avenue for determining links and dissociations between the opposing effects of emotion and their relevance for psychopathology (Menon, 2011; Sylvester et al., 2012; Uddin, 2015). For instance, recent evidence (Di & Biswal, 2013; Goulden et al., 2014) suggests that the salience network mediates the interactions between the fronto-parietal and default-mode networks. Biasing towards processing of internal or external information by manipulating the originating source of emotion in the context of a dual cognitive-emotional task performance could provide a direct way to test this hypothesis in the future.

Another promising avenue for future investigations concerns using instructed manipulations of specific emotion regulation strategies, such as focused attention, to compare the neural mechanisms involved in controlling the impact of external vs. internal distraction. Although the results of Study III provide initial fMRI evidence regarding the neural mechanisms of instructed regulation of internal emotional distraction, the neural underpinnings of the instructed regulation of external emotional distraction remain unclear. Linked to this aspect, of particular interest is further clarification of the role of the ventrolateral PFC in spontaneous vs. instructed regulation of external emotional distraction. The ventrolateral PFC, a brain region

characterized by high "functional heterogeneity" (Cai, Ryali, Chen, Li, & Menon, 2014; Levy & Wagner, 2011; Warren et al., 2014), has been linked to both affective and control systems (Aron et al., 2004; Aron, Robbins, & Poldrack, 2014; Dolcos et al., 2011; Iordan et al., 2013b) and is also a site of convergence between the ventral attention and cingulo-opercular networks (Gordon et al., 2014; Power et al., 2011). Investigation of functional dissociations in this area, by combining task manipulations and resting-state recordings, could clarify critical aspects related to sub-regional specificity and dissociations within ventrolateral PFC area.

Finally, investigation of the spatial distribution of network-level interactions linked to the impact and regulation of external and internal emotional distraction could be integrated with investigations of its temporal dynamics. This would be best achieved by using paradigms similar to the ones described here, in conjunction with multimodal functional imaging methodologies, such as simultaneous electroencephalographic and fMRI recordings (Ritter & Villringer, 2006), and by using imaging methodologies that combine high temporal resolution with high spatial resolution, such as even-related optical signal recordings (Gratton & Fabiani, 2010). Of particular interest in this context is clarification of the temporal dynamics of the interactions between the dorsolateral and the ventrolateral PFC, which are putative sites of distinct hubs associated with cognitive control and emotion integration, respectively. Identification of the links between spatial (*where*) and temporal (*when*) aspects of the neural correlates of external and internal emotional distraction could contribute to an updated model of emotion-cognition interactions, which will allow the articulation of new hypotheses and enable their testing by using a more integrative approach.

References

Anticevic, A., Repovs, G., & Barch, D. M. (2010). Resisting emotional interference: brain regions facilitating working memory performance during negative distraction. *Cognitive, Affective, & Behavioral Neuroscience, 10*(2), 159-173.

Aron, A. R. (2007). The neural basis of inhibition in cognitive control. *Neuroscientist, 13*(3), 214-228.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences, 8*(4), 170-177.

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2014). Inhibition and the right inferior frontal cortex: one decade on. *Trends in Cognitive Sciences, 18*(4), 177-185.

Ashby, F. G., Isen, A. M., & Turken, A. U. (1999). A neuropsychological theory of positive affect and its influence on cognition. *Psychological Review, 106*(3), 529-550.

Baeken, C., Van Schuerbeek, P., De Raedt, R., Ramsey, N. F., Bossuyt, A., De Mey, J., Vanderhasselt, M. A., Leyman, L., & Luypaert, R. (2010). Reduced left subgenual anterior cingulate cortical activity during withdrawal-related emotions in melancholic depressed female patients. *Journal of Affective Disorders, 127*(1–3), 326-331.

Ball, T. M., Sullivan, S., Flagan, T., Hitchcock, C. A., Simmons, A., Paulus, M. P., & Stein, M. B. (2012). Selective effects of social anxiety, anxiety sensitivity, and negative affectivity on the neural bases of emotional face processing. *Neuroimage 59*(2), 1879-1887.

Banich, M. T., Mackiewicz, K. L., Depue, B. E., Whitmer, A. J., Miller, G. A., & Heller, W. (2009). Cognitive control mechanisms, emotion and memory: a neural perspective with implications for psychopathology. *Neuroscience and Biobehavioral Reviews, 33*(5), 613-630.

Barrett, L., & Satpute, A. (2013). Large-scale brain networks in affective and social neuroscience: towards an integrative functional architecture of the brain. *Current Opinion in Neurobiology, 23*(3), 361-372.

Bekker, M. H., & van Mens-Verhulst, J. (2007). Anxiety disorders: sex differences in prevalence, degree, and background, but gender-neutral treatment. *Gender Medicine, 4 Suppl B*, S178-193.

Berkman, E. T., Burklund, L., & Lieberman, M. D. (2009). Inhibitory spillover: intentional motor inhibition produces incidental limbic inhibition via right inferior frontal cortex. *Neuroimage, 47*(2), 705-712.

Berntson, G. G., Boysen, S. T., & Cacioppo, J. T. (1993). Neurobehavioral organization and the cardinal principle of evaluative bivalence. In F. M. Crinella & J. Yu (Eds.), *Annals of the New York Academy of Sciences: Vol. 702. Brain mechanisms: Papers in memory of Robert Thompson* (pp. 75-102). New York: New York Academy of Sciences.

Bradley, M. M., & Lang, P. J. (2007). Motivation and emotion. In J. T. Cacioppo, L. G. Tassinary, & G. G. Berntson (Eds.), *Handbook of psychophysiology (2nd edition)*. New York: Cambridge University Press.

Bressler, S. L., & Menon, V. (2010). Large-scale brain networks in cognition: emerging methods and principles. *Trends in Cognitive Sciences, 14*(6), 277-290.

Butler, R., Pan, H., Epstein, J., Protopopescu, X., Tuescher, O., Goldstein, M., Cloitre, M., Yang, Y., Phelps, E. A., Gorman, J., Le Doux, J. E., Stern, E., & Silbersweig, D. (2005). Fear-related activity in subgenual anterior cingulate differs between men and women. *Neuroreport, 16*(11), 1233-1236.

Cabeza, R., Ciaramelli, E., Olson, I. R., & Moscovitch, M. (2008). The parietal cortex and episodic memory: an attentional account. *Nature Reviews Neuroscience, 9*(8), 613-625.

Cacioppo, J. T., Gardner, W. L., & Berntson, G. G. (1997). Beyond bipolar conceptualizations and measures: The case of attitudes and evaluative space. *Personality and Social Psychology Review, 1*(1), 3-25.

Cai, W., Ryali, S., Chen, T., Li, C. S., & Menon, V. (2014). Dissociable roles of right inferior frontal cortex and anterior insula in inhibitory control: evidence from intrinsic and task-related functional parcellation, connectivity, and response profile analyses across multiple datasets. *The Journal of Neuroscience, 34*(44), 14652-14667.

Carpenter, S. M., Peters, E., Västfjäll, D., & Isen, A. M. (2013). Positive feelings facilitate working memory and complex decision making among older adults. *Cognition and Emotion, 27*(1), 184-192.

Cohen, J. R., Gallen, C. L., Jacobs, E. G., Lee, T. G., & D'Esposito, M. (2014). Quantifying the reconfiguration of intrinsic networks during working memory. *PLoS ONE, 9*(9), e106636.

Corbetta, M., Patel, G., & Shulman, G. L. (2008). The reorienting system of the human brain: from environment to theory of mind. *Neuron, 58*(3), 306-324.

Courtney, S. M., Petit, L., Maisog, J. M., Ungerleider, L. G., & Haxby, J. V. (1998). An area specialized for spatial working memory in human frontal cortex. *Science, 279*(5355), 1347-1351.

D'Esposito, M. (2008). Working memory. *Handbook of Clinical Neurology, 88*, 237-247.

Daselaar, S. M., Rice, H. J., Greenberg, D. L., Cabeza, R., LaBar, K. S., & Rubin, D. C. (2008). The spatiotemporal dynamics of autobiographical memory: neural correlates of recall, emotional intensity, and reliving. *Cerebral Cortex, 18*(1), 217-229.

Denkova, E., Wong, G., Dolcos, S., Sung, K., Wang, L., Coupland, N., & Dolcos, F. (2010). The impact of anxiety-inducing distraction on cognitive performance: a combined brain imaging and personality investigation. *PLoS One, 5*(11), e14150. doi 14110.11371/journal.pone.0014150.

Di, X., & Biswal, B. B. (2013). Modulatory interactions of resting-state brain functional connectivity. *PLoS ONE, 8*(8), e71163.

Diaz, M. T., He, G., Gadde, S., Bellion, C., Belger, A., Voyvodic, J. T., & McCarthy, G. (2011). The influence of emotional distraction on verbal working memory: an fMRI investigation comparing individuals with schizophrenia and healthy adults. *Journal of Psychiatric Research, 45*(9), 1184-1193.

Dolcos, F., Diaz-Granados, P., Wang, L., & McCarthy, G. (2008). Opposing influences of emotional and non-emotional distracters upon sustained prefrontal cortex activity during a delayed-response working memory task. *Neuropsychologia, 46*(1), 326-335.

Dolcos, F., Iordan, A. D., & Dolcos, S. (2011). Neural correlates of emotion-cognition interactions: A review of evidence from brain imaging investigations. *Journal of Cognitive Psychology, 23*(6), 669-694.

Dolcos, F., Iordan, A. D., Kragel, J., Stokes, J., Campbell, R., McCarthy, G., & Cabeza, R. (2013). Neural correlates of opposing effects of emotional distraction on working memory and episodic memory: An event related fMRI investigation. *Frontiers in Psychology, 4*, 293. doi 210.3389/fpsyg.2013.00293.

Dolcos, F., Kragel, P., Wang, L., & McCarthy, G. (2006). Role of the inferior frontal cortex in coping with distracting emotions. *Neuroreport, 17*(15), 1591-1594.

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron, 42*(5), 855-863.

Dolcos, F., & McCarthy, G. (2006). Brain systems mediating cognitive interference by emotional distraction. *The Journal of Neuroscience, 26*(7), 2072-2079.

Dosenbach, N., Visscher, K., Palmer, E., Miezin, F., Wenger, K., Kang, H., Burgund, E., Grimes, A., Schlaggar, B., & Petersen, S. (2006). A core system for the implementation of task sets. *Neuron, 50*(5), 799-812.

Dosenbach, N. U., Fair, D. A., Cohen, A. L., Schlaggar, B. L., & Petersen, S. E. (2008). A dual-networks architecture of top-down control. *Trends in Cognitive Sciences, 12*(3), 99-105.

Dosenbach, N. U., Fair, D. A., Miezin, F. M., Cohen, A. L., Wenger, K. K., Dosenbach, R. A., Fox, M. D., Snyder, A. Z., Vincent, J. L., Raichle, M. E., Schlaggar, B. L., & Petersen, S. E. (2007). Distinct brain networks for adaptive and stable task control in humans. *Proceedings of the National Academy of Sciences USA, 104*(26), 11073-11078.

Eysenck, M. W., Derakshan, N., Santos, R., & Calvo, M. G. (2007). Anxiety and cognitive performance: attentional control theory. *Emotion, 7*(2), 336-353.

Forbes, E. E., & Dahl, R. E. (2005). Neural systems of positive affect: relevance to understanding child and adolescent depression? *Development and Psychopathology, 17*(3), 827-850.

Fox, M. D., Snyder, A. Z., Vincent, J. L., Corbetta, M., Van Essen, D. C., & Raichle, M. E. (2005). The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences USA, 102*(27), 9673-9678.

Fredrickson, B. L. (2001). The role of positive emotions in positive psychology: The broaden-and-build theory of positive emotions. *American Psychologist, 56*(3), 218-226.

Fredrickson, B. L. (2004). The broaden-and-build theory of positive emotions. *Philosophical Transactions of the Royal Society B: Biological Sciences, 359*(1449), 1367-1378.

Fredrickson, B. L., & Branigan, C. (2005). Positive emotions broaden the scope of attention and thought-action repertoires. *Cognition and Emotion, 19*(3), 313-332.

Gilbert, K. E. (2012). The neglected role of positive emotion in adolescent psychopathology. *Clinical Psychology Review, 32*(6), 467-481.

Gordon, E. M., Laumann, T. O., Adeyemo, B., Huckins, J. F., Kelley, W. M., & Petersen, S. E. (2014). Generation and evaluation of a cortical area parcellation from resting-state correlations. *Cerebral cortex*, doi 10.1093/cercor/bhu1239.

Gotlib, I. H., & Joormann, J. (2010). Cognition and depression: current status and future directions. *Annual Review Clinical Psychology, 6*, 285-312.

Gotlib, I. H., Sivers, H., Gabrieli, J. D., Whitfield-Gabrieli, S., Goldin, P., Minor, K. L., & Canli, T. (2005). Subgenual anterior cingulate activation to valenced emotional stimuli in major depression. *Neuroreport, 16*(16), 1731-1734.

Goulden, N., Khusnulina, A., Davis, N. J., Bracewell, R. M., Bokde, A. L., McNulty, J. P., & Mullins, P. G. (2014). The salience network is responsible for switching between the default mode network and the central executive network: replication from DCM. *Neuroimage, 99*, 180-190.

Gratton, G., & Fabiani, M. (2010). Fast optical imaging of human brain function. *Frontiers in Human Neuroscience, 4*, 52. doi 10.3389/fnhum.2010.00052.

Hassabis, D., & Maguire, E. A. (2007). Deconstructing episodic memory with construction. *Trends in Cognitive Sciences, 11*(7), 299-306.

Honey, G. D., Fu, C. H., Kim, J., Brammer, M. J., Croudace, T. J., Suckling, J., Pich, E. M., Williams, S. C., & Bullmore, E. T. (2002). Effects of verbal working memory load on corticocortical connectivity modeled by path analysis of functional magnetic resonance imaging data. *Neuroimage, 17*(2), 573-582.

Iordan, A. D., & Dolcos, F. (2015). Brain activity and network interactions linked to valence-related differences in the impact of emotional distraction. *Cerebral Cortex*, doi 10.1093/cercor/BHV1242.

Iordan, A. D., Dolcos, S., Denkova, E., & Dolcos, F. (2013a). Sex differences in the response to emotional distraction: an event-related fMRI investigation. *Cognitive, Affective & Behavioral Neuroscience, 13*(1), 116-134.

Iordan, A. D., Dolcos, S., & Dolcos, F. (2013b). Neural signatures of the response to emotional distraction: A review of evidence from brain imaging investigations. *Frontiers in Human Neuroscience, 7*, 200. doi 210.3389/fnhum.2013.00200.

Iordan, A. D., Dolcos, S., & Dolcos, F. (2015). Brain activity and network interactions in regulating the impact of internal emotional distraction on working memory. *Manuscript in submission for publication*.

Isen, A. M. (2005). Positive affect. In T. Dalgleish & M. J. Power (Eds.), *Handbook of Cognition and Emotion* (pp. 521-539): John Wiley & Sons, Ltd.

Izard, C. E. (2002). Translating emotion theory and research into preventive interventions. *Psychological Bulletin, 128*(5), 796-824.

Joormann, J., & Gotlib, I. H. (2008). Updating the contents of working memory in depression: Interference from irrelevant negative material. *Journal of Abnormal Psychology, 117*(1), 182-192.

Kahn, I., Davachi, L., & Wagner, A. D. (2004). Functional-neuroanatomic correlates of recollection: implications for models of recognition memory. *The Journal of Neuroscience, 24*(17), 4172-4180.

Kensinger, E. A., & Corkin, S. (2003). Effect of negative emotional content on working memory and long-term memory. *Emotion, 3*(4), 378-393.

Kessler, R. C. (2003). Epidemiology of women and depression. *Journal of Affective Disorders, 74*(1), 5-13.

Levens, S. M., & Phelps, E. A. (2008). Emotion processing effects on interference resolution in working memory. *Emotion, 8*(2), 267-280.

Levy, B. J., & Wagner, A. D. (2011). Cognitive control and right ventrolateral prefrontal cortex: reflexive reorienting, motor inhibition, and action updating. *Annals of the New York Academy of Sciences, 1224*, 40-62.

Lindquist, K., & Barrett, L. (2012). A functional architecture of the human brain: emerging insights from the science of emotion. *Trends in Cognitive Sciences, 16*(11), 533-540.

Lindstrom, B. R., & Bohlin, G. (2011). Emotion processing facilitates working memory performance. *Cognition & Emotion, 25*(7), 1196-1204.

Ma, L., Steinberg, J. L., Hasan, K. M., Narayana, P. A., Kramer, L. A., & Moeller, F. G. (2012). Working memory load modulation of parieto-frontal connections: evidence from dynamic causal modeling. *Human Brain Mapping, 33*(8), 1850-1867.

McKiernan, K. A., Kaufman, J. N., Kucera-Thompson, J., & Binder, J. R. (2003). A parametric manipulation of factors affecting task-induced deactivation in functional neuroimaging. *Journal of Cognitive Neuroscience, 15*(3), 394-408.

McNally, R. J. (2006). Cognitive abnormalities in post-traumatic stress disorder. *Trends in Cognitive Sciences, 10*(6), 271-277.

Menon, V. (2011). Large-scale brain networks and psychopathology: a unifying triple network model. *Trends in Cognitive Sciences, 15*(10), 483-506.

Mitchell, R. L., & Phillips, L. H. (2007). The psychological, neurochemical and functional neuroanatomical mediators of the effects of positive and negative mood on executive functions. *Neuropsychologia, 45*(4), 617-629.

Mobbs, D., Marchant, J. L., Hassabis, D., Seymour, B., Tan, G., Gray, M., Petrovic, P., Dolan, R. J., & Frith, C. D. (2009). From threat to fear: The neural organization of defensive fear systems in humans. *The Journal of Neuroscience, 29*(39), 12236-12243.

Murty, V. P., Ritchey, M., Adcock, R. A., & LaBar, K. S. (2010). fMRI studies of successful emotional memory encoding: A quantitative meta-analysis. *Neuropsychologia, 48*(12), 3459-3469.

Nadler, R. T., Rabi, R., & Minda, J. P. (2010). Better mood and better performance. Learning rule-described categories is enhanced by positive mood. *Psychological Science, 21*(12), 1770-1776.

Nee, D. E., & Jonides, J. (2008). Neural correlates of access to short-term memory. *Proceedings of the National Academy of Sciences of the USA, 105*(37), 14228-14233.

Ochsner, K. N., Ray, R. D., Cooper, J. C., Robertson, E. R., Chopra, S., Gabrieli, J. D., & Gross, J. J. (2004). For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage, 23*(2), 483-499.

Oei, N. Y., Veer, I. M., Wolf, O. T., Spinhoven, P., Rombouts, S. A., & Elzinga, B. M. (2012). Stress shifts brain activation towards ventral 'affective' areas during emotional distraction. *Social Cognitive and Affective Neuroscience, 7*(4), 403-412.

Petrovic, P., Kalso, E., Petersson, K. M., & Ingvar, M. (2002). Placebo and opioid analgesia-- imaging a shared neuronal network. *Science, 295*(5560), 1737-1740.

Piccoli, T., Valente, G., Linden, D. E., Re, M., Esposito, F., Sack, A. T., & Di Salle, F. (2015). The default mode network and the working memory network are not anti-correlated during all phases of a working memory task. *PLoS One, 10*(4), e0123354. doi 0123310.0121371/journal.pone.0123354.

Power, J. D., Cohen, A. L., Nelson, S. M., Wig, G. S., Barnes, K. A., Church, J. A., Vogel, A. C., Laumann, T. O., Miezin, F. M., Schlaggar, B. L., & Petersen, S. E. (2011). Functional network organization of the human brain. *Neuron, 72*(4), 665-678.

Power, J. D., & Petersen, S. E. (2013). Control-related systems in the human brain. *Current Opinion in Neurobiology, 23*(2), 223-228.

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences USA, 98*(2), 676-682.

Ritter, P., & Villringer, A. (2006). Simultaneous EEG-fMRI. *Neuroscience and Biobehavioral Reviews, 30*(6), 823-838.

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., Reiss, A. L., & Greicius, M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *The Journal of Neuroscience, 27*(9), 2349-2356.

Sylvester, C. M., Corbetta, M., Raichle, M. E., Rodebaugh, T. L., Schlaggar, B. L., Sheline, Y. I., Zorumski, C. F., & Lenze, E. J. (2012). Functional network dysfunction in anxiety and anxiety disorders. *Trends in Neurosciences, 35*(9), 527-535.

Tanaka, S., Honda, M., & Sadato, N. (2005). Modality-specific cognitive function of medial and lateral human brodmann area 6. *The Journal of Neuroscience, 25*(2), 496-501.

Uddin, L. Q. (2015). Salience processing and insular cortical function and dysfunction. *Nature Reviews Neuroscience, 16*(1), 55-61.

Vilberg, K. L., & Rugg, M. D. (2008). Memory retrieval and the parietal cortex: a review of evidence from a dual-process perspective. *Neuropsychologia, 46*(7), 1787-1799.

Wager, T. D., Phan, K. L., Liberzon, I., & Taylor, S. F. (2003). Valence, gender, and lateralization of functional brain anatomy in emotion: a meta-analysis of findings from neuroimaging. *NeuroImage, 19*(3), 513-531.

Warren, D. E., Power, J. D., Bruss, J., Denburg, N. L., Waldron, E. J., Sun, H., Petersen, S. E., & Tranel, D. (2014). Network measures predict neuropsychological outcome after brain injury. *Proceedings of the National Academy of Sciences of the USA, 111*(39), 14247-14252.

Watson, D., & Naragon-Gainey, K. (2010). On the specificity of positive emotional dysfunction in psychopathology: Evidence from the mood and anxiety disorders and schizophrenia/schizotypy. *Clinical Psychology Review, 30*(7), 839-848.

Waugh, C. E., & Koster, E. H. (2014). A resilience framework for promoting stable remission from depression. *Clinical Psychology Review, 41*(2015), 49-60.

Yang, H., Yang, S., & Isen, A. M. (2013). Positive affect improves working memory: Implications for controlled cognitive processing. *Cognition and Emotion, 27*(3), 474-484.

Yeo, B. T., Krienen, F., Sepulcre, J., Sabuncu, M., Lashkari, D., Hollinshead, M., Roffman, J., Smoller, J., Zöllei, L., Polimeni, J., Fischl, B., Liu, H., & Buckner, R. (2011). The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of Neurophysiology, 106*(3), 1125-1165.