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Attentional Deployment within Unpleasant Pictures: Neural Correlates & Functional Connectivity

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Jamie Ferri

We, the dissertation committee for the above candidate for the

Doctor of Philosophy degree, hereby recommend

acceptance of this dissertation.

Turhan Canli, Ph.D., Dissertation Advisor
Associate Professor, Department of Psychology, Stony Brook University

Hoi-Chung Leung, Ph.D., Chairperson of Defense
Associate Professor, Department of Psychology, Stony Brook University

Greg Hajcak Proudfit, Ph.D.
Associate Professor, Department of Psychology, Stony Brook University

Heather Urry, Ph.D.
Associate Professor, Department of Psychology, Tufts University

This dissertation is accepted by the Graduate School

Charles Taber
Dean of the Graduate School

Abstract of the Dissertation

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Attentional deployment is an emotion regulation strategy that involves shifting attentional focus towards or away from particular aspects of emotional stimuli. Previous studies have highlighted the prevalence of attentional deployment and demonstrated that it can have a significant impact on affect and psychophysiology. However, relatively little is known about the neural basis of attentional deployment, or how individual differences impact the use and success of this strategy. In two separate fMRI studies, visual attention was directed to more or less arousing portions of unpleasant images. For five subjects from Study 1, and all subjects from Study 2, fMRI and eye-tracking data were collected simultaneously. Together these studies examined three aims: (1) the impact of attentional deployment on negative affect and neural activation, (2) the functional connectivity patterns associated with attentional deployment and their relation to individual differences in eye gaze behavior, and (3) gender differences in neural activation during

emotional processing and attentional deployment. Results suggested that focusing on non-arousing, compared to arousing, portions of unpleasant images was associated with reduced negative affect, and with increased activation in fronto-parietal networks associated with inhibitory and attentional control, and reduced amygdala activation. Further, focusing on non-arousing regions, compared to freely viewing unpleasant images, resulted in increased functional connectivity between the precuneus and the amygdala; the degree of connectivity was positively related to visual compliance and trait reappraisal. Finally, gender differences were observed when comparing the free viewing of unpleasant to neutral images; compared to men, women demonstrated greater activation in regions associated with enhanced emotional processing including prefrontal regions and the amygdala, despite no gender differences in visual attention to emotional information. However, these differences appeared to be at least partially due to greater activation in emotion-related regions, including the amygdala, for males during the neutral (baseline) condition. There were no gender differences in brain activation during the unpleasant arousing focus, unpleasant non-arousing focus, or neutral focus conditions. Together, these studies suggest that visual attentional deployment is an effective emotion regulation strategy for both males and females that may critically depend on functional relationships between parietal regions and the amygdala.

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Introduction

In any given moment we experience an abundance of sensory input, yet our attentional resources only allow us to attend to and process a limited number of these inputs. Among these inputs, certain types of stimuli are more likely than others to capture our attention, and thereby shape our perception. Bottom-up theories of emotion suggest that emotional stimuli, because they relate to biological drives to survive and reproduce, have intrinsic properties that facilitate attention (Bradley, Codispoti, Cuthbert, & Lang, 2001). In support of this view, ample research has demonstrated that the processing of pleasant or unpleasant emotional stimuli is prioritized over neutral stimuli. For example, individuals generally make more fixations to and dwell longer on emotional compared to neutral information (Calvo & Lang, 2004; Carniglia, Caputi, Manfredi, Zambarbieri, & Pessa, 2012; Nummenmaa, Hyönä, & Calvo, 2006). In addition, emotional stimuli are detected faster (Öhman, Flykt, & Esteves, 2001; Vuilleumier & Schwartz, 2001), they hold attention more effectively (Lang, Bradley, & Cuthbert, 1997), and they are better remembered (Bradley, Greenwald, Petry, & Lang, 1992; Kensinger, Krendl, & Corkin, 2006). While the facilitated processing of emotional information is adaptive in many situations, it is not always beneficial. Among psychologically healthy individuals, involuntary attention to task-irrelevant emotional stimuli can slow reaction times, decrease accuracy (MacNamara & Hajcak, 2009; Vuilleumier, Armony, Driver, & Dolan, 2001), and negatively impact mood (Isaacowitz, 2006). At the extreme, being too attentive to unpleasant information represents a cognitive vulnerability for psychopathologies such as anxiety and depression (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007; Joormann, 2009).

Attention to emotional information is not driven solely by stimulus properties (i.e.

bottom-up processes), however. Top-down influences, including an individual's appraisal, intentions and goals (Scherer, Schorr, & Johnstone, 2001), interact with bottom-up influences to ultimately determine attention towards and response to emotional information. Accordingly, an emotion can be defined as a coordinated multisystem (subjective, behavioral, physiological) response to a particular stimulus that compels attention *and has particular meaning to an individual* (Barrett, Ochsner, & Gross, 2007). Importantly, responses to emotional stimuli are flexible and can be altered (or regulated) by an individual in accordance with their preferences and goals (Gross, 1998; Xing, 2006). While most individuals typically prefer to experience positive over negative emotions, when a negative emotion has a perceived utility, such as fostering emotional growth, or achieving a particular goal (i.e. confronting an adversary), an individual may wish to experience that emotion (Tamir, 2009). Therefore, emotion regulation may be best defined as maximizing desirable emotional states while minimizing undesirable states in the service of goals.

In the process model of emotion regulation, Gross (1998) delineates five overarching categories of emotion regulation in order of their temporal occurrence in the emotion generative process: situation selection, situation modification, attentional deployment, cognitive change/reappraisal, and response modulation (for a review see: Gross, 1998). The process model is an interactive model, allowing for the use of more than one strategy at multiple time points during the experience of emotion. Gross (1998) further divides these strategies into antecedent-focused strategies that are used before a full emotional response has unfolded, and response-focused strategies that are used after. In general, because antecedent-focused strategies occur earlier in the emotion generation process, they are thought to require fewer resources and less

effort to employ. Attentional deployment – a strategy that involves shifting attention towards or away from affective stimuli in the interest of an emotional goal, and cognitive reappraisal – a strategy that involves changing the meaning of emotional situations or stimuli in order to change emotional significance, are the two main antecedent-focused strategies that are employed after a person in immersed in an emotion generating situation (Gross, 1998; Gross & Thompson, 2007). Of the two, cognitive reappraisal is the more widely studied strategy. Therefore, much of what is known about emotion regulation, particularly with regard to neural mechanisms, stems from studies of cognitive reappraisal or other forms of cognitive change. However, furthering our understanding of the neural mechanisms associated with attentional deployment may be critical, as it a ubiquitous strategy used to effectively regulate affect throughout development.

Gross (1998) divided attentional deployment into three major strategies: distraction, concentration and rumination. Distraction refers to shifting attentional focus from one aspect of a situation to another, or away from the situation entirely. Concentration involves dedicating all attentional resources to a single aspect of a situation. Rumination refers to directing attention inwardly to feelings and consequences of feelings. While rumination is primarily cognitive in nature, both distraction and concentration can be accomplished either through cognitive efforts (e.g. thinking about a happy moment to feel better) or through physical changes in attention (e.g. looking away from a traffic accident).

The use of attentional deployment emerges early in life and persists throughout the lifespan. It is one of the earliest emotion regulation strategies evident in development: 6 month old infants use gaze-aversion in response to strangers (Mangelsdorf, Shapiro, & Marzolf, 1995), very young children use distraction to delay gratification (Mischel & Ayduk, 2011), and even

grade school children are aware that changes in attention can change the way they feel (Harris & Lipian, 1989). The use of attentional deployment continues beyond childhood; adults shift attention away from unpleasant parts of images to reduce negative affect even without instruction to do so (van Reekum et al., 2007; Xing, 2006). Older adults in particular seem to divert gaze away from negative information and towards positive information in the interest of regulating mood (Isaacowitz, Toner, & Neupert, 2009a, 2009b; Isaacowitz, Wadlinger, Goren, & Wilson, 2006; Mather & Carstensen, 2005), and these shifts in gaze are positively related to improvements in mood (Isaacowitz et al., 2009a).

Across the lifespan, individuals who are able to successfully deploy attention away from negative or towards positive information report both improved emotional state and decreased frustration with difficult tasks (Johnson, 2009; Urry, 2010; Webb, Miles, & Sheeran, 2012). Conversely, deficits in attentional deployment have been observed in disorders such as anxiety and depression, with those individuals showing attentional biases towards threat-related or disorder-congruent stimuli (Sears, Newman, Ference, & Thomas, 2011; Sears, Thomas, LeHuquet, & Johnson, 2010; Wieser, Pauli, Weyers, Alpers, & Mühlberger, 2009).

Studies have shown that attentional skills can be learned through training in pediatric, geriatric and clinical populations across a variety of domains. For example, older adults demonstrating a decline in attentional control skills were trained in attention regulation to the point at which performance was equivalent to that of younger adults (Bherer et al., 2005). Further, those attentional skills then generalized to new tasks involving attentional control. A number of training programs have been developed specifically to improve attention to emotion. These programs include training gaze patterns using methodologies such as the dot-probe,

flanker and stroop tasks to bias attention towards particular types of affective stimuli (Amir, Beard, Burns, & Bomyea, 2009; Amir, Beard, Taylor, et al., 2009; Dandeneau & Baldwin, 2009; Schmidt, Richey, Buckner, & Timpano, 2009; Wadlinger & Isaacowitz, 2008), clinical training methods using auditory paradigms that reorient attention to increasingly remote sound with increasing noise interference (Siegle, Ghinassi, & Thase, 2007; Wells, 1997), and various types of meditation training (Carmody, 2008; Shapiro, Oman, Thoresen, Plante, & Flinders, 2008; Shapiro, Schwartz, & Bonner, 1998). The effects of emotion-focused training tasks have been largely successful and have also been shown to generalize to other, similar, types of tasks (Wadlinger & Isaacowitz, 2011).

Together, these studies demonstrate that attentional deployment is an emotion regulation strategy that is prevalent across the lifespan, is effect when employed, and can be improved with training. As persistent attention to unpleasant emotions and experiences represents a cognitive vulnerability to depression and anxiety, furthering understanding of the basic mechanisms involved in attentional deployment will be critical for informing a comprehensive understanding of emotion regulation, as well as understanding risk factors in the development of psychopathology.

Aim 1: Neural Basis of Attentional Deployment

In addition to influencing emotional outcomes, previous studies have demonstrated that attentional deployment can have a dramatic impact on brain activity. A number of studies have used the late positive potential (LPP), a centro-parietal event-related potential that is larger for emotional compared to neutral stimuli (Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000;

Schupp et al., 2000), to measure attention to emotion and emotion regulation. To examine the impact of attentional deployment on the LPP, Dunning and Hajcak (2009) asked participants to passively view unpleasant and neutral images for three seconds, after which a circle was presented to direct participants to either an arousing or a non-arousing portion of an unpleasant image, or to a non-arousing portion of a neutral image. The LPP was larger in response to emotional images both during the passive viewing period and when attention was directed towards an arousing portion of the image, but not when attention was directed to a non-arousing portion of the same unpleasant image. In another study, Hajcak, Dunning and Foti (2009) found that using a tone, rather than a visual cue, to direct participants to an arousing or non-arousing portion of an unpleasant image produced an analogous effect – the LPP was reliably reduced when participants were instructed to attend to a non-arousing portion of unpleasant images. These findings are in concert with those reporting reduced LPP magnitude during cognitive reappraisal (Foti & Hajcak, 2008; Hajcak & Nieuwenhuis, 2006; MacNamara, Foti, & Hajcak, 2009), and suggest that attentional deployment, even in the absence of a goal to intentionally modify emotional experience, can function to reduce neural indices of attention to emotion.

Nevertheless, relatively little is known about the specific brain structures and networks involved in attentional deployment. The LPP is thought to reflect concurrent activation of multiple neural systems involved in attention to and processing of salient stimuli; however, the contibutions of specific brain regions is not well understood. Evidence from source localization studies and correlations between fMRI and ERP measures during the passive viewing of emotional images suggest that the LPP may reflect activity in visual and parietal attention networks (Keil et al., 2002; Sabatinelli, Keil, Frank, & Lang, 2013; Sabatinelli, Lang, Keil, &

Bradley, 2007) as well as the amygdala (Liu, Huang, McGinnis-Deweese, Keil, & Ding, 2012; Sabatinelli et al., 2013). However, the specific regions contributing to LPP magnitude appear to change depending whether the images are pleasant or unpleasant (Liu et al., 2012), underscoring the dynamic nature of the LPP. These findings also suggest that different regions may influence the magnitude of the LPP during passive viewing compared to when attention is being manipulated.

While it is clear that the LPP is reduced following attentional deployment, it is not clear what changes in brain activity support this reduction. Although fMRI would be an ideal methodology to explore the neural correlates of attentional deployment, thus far, the majority of fMRI studies of emotion regulation have focused on cognitive strategies such as reappraisal or creating psychological distance, while a limited number of studies have investigated cognitive distraction. The neural systems associated with cognitive strategies have been extensively studied over the last decade. Activity in the amygdala, a region involved in the detection and encoding of salient stimuli (Liberzon, Phan, Decker, & Taylor, 2003; Pessoa, 2011), is typically reduced during the use of cognitive strategies (McRae et al., 2010; Ochsner & Gross, 2008). This reduction in amygdala activity is typically accompanied by corresponding increases in regions related to top-down control, such as the prefrontal cortex, which are thought to down-regulate the amygdala (Ochsner & Gross, 2008). Together, studies on cognitive emotion regulation strategies have culminated in a model suggesting that successful emotion regulation relies on interactions between prefrontal regions associated with cognitive control, and limbic regions such as the amygdala (Ochsner & Gross, 2008).

In addition to prefrontal and limbic regions, many emotion regulation studies also report

increased activations in regions related to visual attention and inhibitory control, such as the superior parietal lobule and the precuneus (Hopfinger, Buonocore, & Mangun, 2000; Kanske, Heissler, Schönfelder, Bonger, & Wessa, 2011; McRae et al., 2010; Pessoa, Kastner, & Ungerleider, 2003). As fronto-parietal regions are critical for visuospatial attention and visual control, van Reekum and colleagues (2007) reasoned that activation in these regions might reflect shifts in gaze to achieve emotion regulation goals even though participants were instructed to use cognitive strategies such as reappraisal. Using eye-tracking, van Reekum and colleagues found that when participants were instructed to use cognitive reappraisal to increase or decrease their emotional response to unpleasant pictures, they spent more or less time, respectively, looking at the most arousing portions of these images. Further, when participants were instructed to decrease negative emotion using cognitive reappraisal, the amount of time spent looking at arousing portions of the images predicted a significant amount of variation in neural activity, including up to 35% in the amygdala, and as much as 75% in other regions often reported in emotion regulation studies such as the middle frontal gyrus, the precentral gyrus, and the cuneus (van Reekum et al., 2007). Thus, attentional deployment may account for some, but not all, of the variance in neural activity associated with cognitive reappraisal. Indeed, subsequent studies have shown that cognitive reappraisal results in reduced autonomic arousal and subjective affect even when gaze is held constant (Bebko, Franconeri, Ochsner, & Chiao, 2014; Urry, 2010). However, these findings highlight the importance of attentional deployment as an emotion regulation strategy and inspire questions regarding the underlying neural mechanisms.

As we know that individuals use shifts in gaze to achieve regulatory goals, it is likely

that, to some degree, the brain regions that have been reported to correspond to cognitive reappraisal overlap with regions that would be associated with attentional deployment. However, these strategies are rarely disentangled completely in fMRI studies. Paradigms that hold attention in a fixed location while instructing participants to use cognitive strategies are one means to isolate changes associated with cognitive strategies (Urry, 2010), but this does not elucidate the neural mechanisms associated with visual attentional deployment. A limited number of neuroimaging studies that have aimed to investigate attentional deployment have primarily focused on cognitive distraction and have relied on paradigms that require individuals to concurrently engage in difficult working memory or cognitive tasks while viewing unpleasant images. Studies directly comparing cognitive reappraisal and distraction have demonstrated that both strategies involve a similar network of regions, including reduced activation in the amygdala and increased activation in prefrontal and parietal regions (Kanske et al., 2011; McRae et al., 2010). However, these studies have reported that while both reappraisal and distraction result in similar reductions in self-reported negative affect, distraction yields greater reduction in amygdala activation, and greater corresponding increases in parietal regions, than reappraisal (Kanske et al., 2011). Task related activation stemming from cognitive distraction reflects both orienting and maintaining attention away from unpleasant information, as well as the engagement in cognitively challenging tasks. Therefore activation in prefrontal and parietal control regions may reflect shifts in attention, or engagement in cognitive challenges. Basic research aimed at understanding the impact of changes in visual attention to emotional information on brain activation has yet to be conducted.

Understanding how simple changes in visual attention to emotional information

influences brain activation, even in the absence of an explicit regulatory goal, will be an important step in understanding how this basic action functions as an emotion regulation strategy. To what extent do regions of the brain associated with shifts in visual attention to emotional information correspond with those associated with effortful cognitive strategies? Will attentional deployment in this context produce the same profound effects on amygdala activation? If attentional deployment does reduce amygdala activation in a similar fashion, will amygdala activation in this context also be associated with increases in prefrontal and parietal activation? As attentional deployment is a commonly used strategy, understanding these questions will be an important part of understanding the neural mechanisms associated with emotion regulation at large.

Considering that unpleasant information automatically captures attention (Bradley, Codispoti, Cuthbert, & Lang, 2001) and that individuals use gaze in the interest of achieving emotion regulation goals (van Reekum et al., 2007) it will be critical to incorporate eye-tracking into future studies of emotion regulation. While it is possible for an individual to covertly attend to information outside of their gaze, generally eye movements correspond with attention (Findlay & Gilchrist, 2003). Furthermore, there is substantial overlap among the brain regions associated with eye movements and shifts in attention (Corbetta et al., 1998). Therefore monitoring and recording eye movements may be the best objective means to track shifts in visual attention and neural networks associated with those shifts. As changes in brain activation are often used as markers of the "success" of a particular strategy, using eye-tracking could help to isolate changes in brain activation to a given strategy. Despite this, the majority of neuroimaging studies of emotion and emotion regulation do not account for gaze. As a result, we have a limited

understanding of the extent to which individual difference in gaze, particularly during the viewing of complex images such as the IAPS, impact brain activation during basic emotion processing. While, individuals generally make more fixations and dwell longer on emotional compared to neutral information (Calvo & Lang, 2004; Carniglia et al., 2012), it has also been demonstrated that a number of individual differences impact visual attention to emotional information including depression (Kellough, Beevers, Ellis, & Wells, 2008; Sears et al., 2011; Sears et al., 2010), anxiety (Wieser et al., 2009), gender (J. K. Hall, Hutton, & Morgan, 2010), motivational state (Xing, 2006), and even genotype (Beevers, Ellis, Wells, & McGeary, 2010). Controlling gaze, then, may be an important means of reducing the impact of individual differences while simultaneously ensuring that observed brain activations reflect appraisals of the same information across subjects.

When specifically examining visual attentional deployment, it will also be critical to quantify compliance using eye-tracking. As attention can be automatically captured by emotional content (Lang et al., 1997; Öhman et al., 2001), individuals who are instructed to fixate within relatively neutral portions of unpleasant images may be drawn to the arousing information in the periphery. As a result, even when attempting to be compliant, participants may make brief saccades to arousing information. Even very brief or unconscious exposure to highly arousing unpleasant information can have a large impact on brain activity in regions like the amygdala (Morris, Öhman, & Dolan, 1998; Whalen et al., 1998), making it particularly important to account for gaze. Together these results suggest that a greater understanding of the impact of group and individual differences in gaze on emotion processing and regulation is necessary. During attentional deployment, especially, eye-tracking will be an important means of assessing

compliance and then interpreting the significance of brain activation patterns.

Aim 2: Functional Connectivity during Attentional Deployment

There is substantial evidence that cognitive reappraisal, compared to maintaining or attending to emotional information, involves reduced activity in the amygdala and increased activity in prefrontal regions (Ochsner & Gross, 2008). Specifically, studies of cognitive reappraisal have noted that reductions in amygdala activation appear to be accompanied by increases in the orbitofrontal cortex, dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, and anterior cingulate cortex (Ochsner & Gross, 2008). Based on these patterns of activation and deactivation, it has been hypothesized that prefrontal regions exert a top-down inhibitory effect on amygdala activation.

Despite strong evidence for the top-down regulation of amygdala activation by the prefrontal cortex, few studies have directly examined functional relationships between these regions during emotion regulation. During reappraisal, inverse correlations have been observed between the amygdala and the lateral prefrontal cortex (Ochsner, Bunge, Gross, & Gabrieli, 2002) and between the amygdala and ventromedial prefrontal cortex (Urry et al., 2006; however see also: Wager, Davidson, Hughes, Lindquist, & Ochsner, 2008). In addition, increased functional connectivity between the amygdala and prefrontal regions has been reported during reappraisal, and greater coupling between the amygdala and the orbital frontal and dorsomedial prefrontal cortex has been associated with lower self-reported negative affect (Banks, Eddy, Angstadt, Nathan, & Phan, 2007; Wager et al., 2008). These functional relationships are supported by evidence for direct links between the amygdala and both medial and orbital regions

of the prefrontal cortex (Amaral & Price, 1984; Bozkurt, Kamper, Stephan, & Kötter, 2001). Together, these results provide support for the idea that prefrontal activation has a top-down inhibitory effect on the amygdala during cognitive reappraisal.

While these studies suggest the importance of interactions between prefrontal regions and the amygdala during cognitive reappraisal, the mechanisms by which amygdala activation is down-regulated during the use of other emotion regulation strategies is less well characterized. A direct comparison of cognitive reappraisal and cognitive distraction (remembering a six letter string while concurrently viewing unpleasant images), demonstrated that both reappraisal and distraction resulted in reductions in amygdala activation and increases in prefrontal and parietal activation; however, distraction resulted in greater increases in the middle frontal gyrus and the superior parietal lobe and in greater reductions in amygdala activation (McRae et al., 2010). Further, cognitive distraction, compared to reappraisal, appears to involve greater coactivation of the amygdala with prefrontal regions as well as with the precuneus and parietal cortex (Kanske et al., 2011). There are anatomical connections between prefrontal and parietal regions (Petrides & Pandya, 1984), supporting the possibility that these control regions may work concurrently to down regulate amygdala reactivity to affective stimuli. In addition, there is some evidence of direct anatomical connections between the parietal cortex and the amygdala (Amaral & Price, 1984), allowing for the possibility of an inhibitory relationship between parietal regions and the amygdala during emotion regulation. These finding support the idea that functional relationships between parietal regions, in addition to prefrontal regions, may be important during the successful down-regulation of amygdala activation when engaging in cognitive emotion regulation strategies. However, studies of cognitive distraction typically involve concentrating

on a difficult cognitive task while concurrently viewing unpleasant stimuli (Kanske et al., 2011; McRae et al., 2010). Simply directing attention away from unpleasant stimuli, in the absence of a regulatory goal or a concurrent cognitively demanding task, may not initiate activation in the same areas associated with cognitive control.

When examining functional relationships between brain regions associated with attentional deployment, it will also be important to consider the spontaneous and simultaneous use of other emotion regulation strategies. For example, individual differences in trait reappraisal have been shown to impact activation in the amygdala as well as in prefrontal and parietal regions during the passive viewing of emotional images (Drabant, McRae, Manuck, Hariri, & Gross, 2009). These findings have been interpreted to reflect spontaneous use of reappraisal during affective picture viewing (Drabant et al., 2009). Use of reappraisal also appears to be related to use of attentional deployment: studies explicitly manipulating cognitive reappraisal have demonstrated that individuals use shifts in gaze to achieve emotion regulation goals, and that these shifts in gaze can influence neural activation attributed to cognitive reappraisal (van Reekum et al., 2007). Together these studies suggest that participants engage in multiple emotion regulation strategies simultaneously, and that the spontaneous use of these strategies impacts neural activation. However, the extent to which trait reappraisal influences the neural mechanisms associated with attentional deployment is unknown.

Functional connectivity analyses during visual attentional deployment would be useful in determining the ways in which critical brain regions involved in cognitive control and emotion generation – frontal and parietal networks and the amygdala – interact to influence sensory processing and the evaluation of negative information in the context of attentional deployment.

Because previous studies have demonstrated that attention is automatically captured by emotional information (Bradley, Codispoti, Cuthbert, et al., 2001), and that individuals attend to emotional information even when they are explicitly instructed to avoid it (Nummenmaa et al., 2006), collecting eye-tracking data could ensure overall compliance when participants are asked to direct attention to particular portions of images. In addition, the collection of eye-tracking data allows for the assessment of the relationship between functional connectivity when participants are asked to attend to a non-arousing region of an unpleasant image and visual compliance (the extent to which they stayed in the non-arousing region as instructed). Finally, as previous studies have suggested that participants use multiple emotion regulation strategies simultaneously (van Reekum et al., 2007), and that trait reappraisal can have an impact on brain activation during passive viewing (Drabant et al., 2009), assessing trait reappraisal will allow for the identification of relationships between the successful use of attentional deployment in this task and use of reappraisal in everyday life.

Aim 3: Gender Differences in Emotion and Emotion Regulation

Most existing neural models of emotion regulation are generalized to men and women, however a striking number of studies are based on only female participants (Eippert et al., 2007; Goldin, McRae, Ramel, & Gross, 2008; Harenski & Hamann, 2006; Kim & Hamann, 2007; Johanne Lévesque et al., 2003; J. Lévesque et al., 2004; McRae et al., 2010; Ochsner et al., 2002; Ochsner et al., 2004; Ohira et al., 2006; Schaefer et al., 2002). In addition, there have been relatively few reported explorations of potential gender differences (however, see: Domes et al., 2010; Koch et al., 2007; McRae, Ochsner, Mauss, Gabrieli, & Gross, 2008; Schienle, Schäfer,

Stark, Walter, & Vaitl, 2005). Studies that do justify the use of only female participants cite greater emotional response in women as the primary motivation (Hutcherson, Goldin, Ramel, McRae, & Gross, 2008; Ochsner et al., 2004). However, if there are indeed gender differences in emotional expression and experience between men and women, then a systematic exploration of if and how these differences translate into the domain of emotion regulation is justified.

In popular culture, women are typically regarded as more emotional than men, with greater emphasis placed on experiencing, processing, and expressing emotions (Barrett & Bliss-Moreau, 2009; Brody, 1993; Fabes & Martin, 1991). Empirically, some consistent findings have emerged that support these assumptions. For example, compared to men, women are generally more emotionally expressive (Kring & Gordon, 1998), and have greater subjective and physiological response to specific emotions (Kring & Gordon, 1998). Women also report using more emotion regulation strategies, including strategies that are thought to be more typical of men, such as avoidance and distraction (Tamres, Janicki, & Helgeson, 2002). Women also have greater or more wide-spread brain activation to, and better memory for, negative compared to neutral stimuli (Stevens & Hamann, 2012) and more prefrontal activation during emotion regulation (McRae et al., 2008). Gender differences in emotion regulation appear early in childhood with girls scoring higher on effortful control – a dimension of temperament related to the ability to willfully control emotional reactions and impulses – skills required for a range of emotion regulation techniques (Else-Quest, Hyde, Goldsmith, & Van Hulle, 2006).

While some gender differences in emotional processing have been consistently reported, the underlying nature of these differences remains largely unknown. Gender stereotypes and response biases have been postulated to be potential sources of reported gender differences in

emotional expression and self-reported experience (Grossman & Wood, 1993; Hess et al., 2000). As a result, studies using physiological and neurological responses to emotion are thought to be better suited to identify and investigate the nature of gender differences independent of response biases. Physiological studies have produced mixed findings, however, with some reports of greater increases in skin conductance and startle potentiation to threatening scenes in women (McManis, Bradley, Berg, Cuthbert, & Lang, 2001) and other reporting no differences (Wrase et al., 2003).

Neuroimaging studies investigating gender differences have also produced less consistent findings in relation to subjective report. However, in general, studies of unpleasant (relative to neutral) picture processing support the idea that women have increased activation, particularly in the amygdala, compared to men (Domes et al., 2010; Hall, Witelson, Szechtman, & Nahmias, 2004; Han, Gao, Humphreys, & Ge, 2008; Kempton et al., 2009), and this relative increase in amygdala activation has been connected to the increased rates of depression and anxiety disorders in women (Hamann, 2005). Findings regarding gender differences in emotional processing have been somewhat mixed; however, a recent large scale meta-analysis of neuroimaging studies of emotion concluded that, for unpleasant stimuli, women showed greater activity in a variety of regions associated with emotional response, including the left amygdala, the hippocampus, the anterior cingulate, the medial prefrontal cortex, and portions of the thalamus (Stevens & Hamann, 2012). For pleasant stimuli, there were fewer increases for women; women were more likely to exhibit activation in a few clusters of the temporal gyrus and medial superior frontal gyrus. For men, the posterior cingulate was the only region more likely to be active during the processing of unpleasant stimuli while the left amygdala was more likely to

be active in response to pleasant stimuli, particularly erotica. This meta-analysis emphasizes the importance of continuing to consider gender in the investigation of emotion and emotion regulation, and helps to clarify previously conflicting reports by interpedently examining gender differences in response to unpleasant versus pleasant stimuli. However, the question of why these differences exist, even at the neural level, remains largely unanswered.

Two potential testable sources of gender differences in studies of emotion are (1) differences in visual attention and (2) differences in appraisal and/or reappraisal. Recently, a study using eye-tracking to quantify differences in visual attention as a function of gender reported that women attended more to the eye-region of faces and that this increase in attention to the eyes was correlated with faster expression recognition and increased accuracy (Hall et al., 2010). While they did not go on to test if controlling for gaze (showing only eyes) equated performance between the genders, their findings do suggest that gender differences in visual attention influence gender differences in emotion-related behavior.

Gender differences in both basic processing and reappraisal of emotional stimuli has been contrasted in two studies measuring neural activation during the passive viewing of unpleasant pictures and during reappraisal of unpleasant images. McRae and colleagues (2008) did not find differences between the genders during passive viewing (unpleasant view – neutral), however, during reappraisal (unpleasant reappraisal – unpleasant view) they found that men had a greater decrease in amygdala activity, less of an increase in prefrontal regions, and less engagement of ventral striatal regions compared to women. Using a similar paradigm, however, Domes and colleagues (2010) reported contrasting results: greater amygdala activation in women during passive viewing of unpleasant images, and no gender differences in amygdala activation during

down-regulation of negative affect via reappraisal. However, they did replicate the finding of greater increases in prefrontal regions in males during reappraisal. While these studies report conflicting findings regarding gender differences in amygdala activation during emotional processing and reappraisal, they underscore the need for further research on gender differences in emotional processing and highlight emotion regulation as a potentially important difference between men and women.

However, as noted previously, when individuals are instructed to regulate emotions using cognitive strategies, they can also change the way that they view stimuli (van Reekum et al., 2007; Xing, 2006). This creates an important confound and leads to an unanswered question regarding gender differences in emotional picture viewing tasks – are differences in brain activation due to gender difference in attention to arousing emotional information, or in differences in appraisals of attended information? A study using eye-tracking to assess attention to arousing information during passive viewing in combination with blocks of directed attention could assess the extent to which differences during passive viewing are accounted for by gaze, and the extent to which these differences remain the same, increase, or decrease as a function of controlling attention, and thereby controlling what information is available for appraisal.

Overview of the present studies

While previous studies have independently demonstrated that attentional deployment can have a significant impact on brain activity and behavior, the neural correlates of attentional deployment are not well understood, and it remains unknown whether successful attentional deployment relies on the same well-defined circuits as cognitive reappraisal. The primarily goal

of the present set of studies was to gain a comprehensive understanding of the effect of attentional deployment on neural activation and subjective affect while participants view unpleasant and neutral images. In addition, these studies aimed to address the impact of individual differences in visual attention through the analysis of eye-tracking data, as well as the impact of gender. Together, three main aims were addressed:

Aim 1a. The first aim was to examine the pattern of neural activation during the viewing of unpleasant images with a non-arousing, compared to an arousing, focus. As previous studies have reported that attentional deployment during cognitive reappraisal accounts for at least some of the variance in activity in limbic as well as fronto-parietal regions (van Reekum et al., 2007), I hypothesized that these regions will also be involved in attentional deployment in the absence of other explicit regulatory goals (i.e. cognitive reappraisal). Specifically, I hypothesized that directing gaze to a non-arousing, compared to an arousing, portion of a unpleasant image would result in reduced activation in areas of the brain implicated in emotional processing, including the amygdala, and corresponding increases in fronto-parietal regions associated with top-down attentional control, such as the precuneus and the middle frontal gyrus.

Aim 1b. I also aimed to understand the impact of attentional deployment on subjective negative affect and the relationship of subjective affect to brain activation. I hypothesized that participants would report reduced negative affect during unpleasant non-arousing compared to arousing focus trials, and that unpleasant arousing focus trials would not differ from unpleasant trials without a focus. In addition, I hypothesized that lower affect ratings would be associated with increased prefrontal and reduced amygdala activation.

Aim 1c. I aimed to assess the extent to which participants complied with task instructions

to attend to particular portions of unpleasant images and the extent to which they attend to arousing information during the free viewing of unpleasant images. I hypothesized that participants would stay in the focus region as instructed and that participants would attend more to arousing information than non-arousing information during the free viewing of unpleasant images.

Aim 1d. I also aimed to examine the ways in which individual differences in visual compliance influence brain activity and subjective affect. I hypothesized that (1) individuals who are less compliant during the negative non-arousing focus condition would have higher self-reported negative affect and (2) time spend in the arousing focus region would be correlated with increased activation in the amygdala, as well as decreased activity in cognitive control regions.

Aim 2a. The second aim was to examine the functional connectivity pattern associated with attentional deployment to non-arousing portions of unpleasant images. Previous studies have reported that attentional deployment during cognitive reappraisal accounts for at least some of the variance in the amygdala, prefrontal and parietal regions (van Reekum et al., 2007). In addition previous studies have reported that cognitive reappraisal is associated with increased connectivity between prefrontal regions and the amygdala (Wager et al., 2008). Accordingly, I hypothesized that attentional deployment would be associated with increased connectivity between the amygdala and both frontal and parietal regions.

Aim 2b. In addition, I aimed to examine the extent to which functional relationships were associated with individual differences in visual compliance. I hypothesized that reduced connectivity would be observed between the amygdala and fronto-parietal regions when participants were less compliant.

Aim 2c. As previous studies have highlighted the simultaneous use of attentional deployment and reappraisal, I also aimed to examine relationships between functional connectivity during attentional deployment and trait reappraisal. I hypothesized that individuals who scored higher on trait reappraisal would also be more successful when deploying attention to non-arousing regions of unpleasant stimuli.

Aim 3a. The final aim was to examine the influence of gender of brain activation, both during free viewing and during attentional deployment. In support of the idea that women differ in appraisal of negative information but not attention to negative information, I hypothesized that during free viewing of unpleasant images, men and women would demonstrate similar levels of visual attention to arousing information, but that women will have significantly higher activation in emotion-related regions. However during the unpleasant non-arousing condition I hypothesized that there would be similar levels of compliance between men and women, and that gender differences in brain activation would be reduced.

Aim 3b. In addition, I aimed to explore gender difference in trait emotion regulation, attentional control and self-reported negative affect, which may impact both neural activation and attention to arousing unpleasant information.

Methods

The above hypotheses were addressed through analyses performed on data from two separate studies. Study 1 included fMRI data from 41 participants who completed an attentional deployment paradigm. Eye-tracking data was simultaneously collected on a sub-set of 5 participants in Study 1 to assess compliance. Individual differences in eye-tracking behavior in

that sub-set motivated the collection of data in a new cohort, using a slightly modified version of the paradigm from Study 1 that was better suited for the collection of eye-tracking data. Study 2 included fMRI and eye-tracking data from 47 additional participants using that modified paradigm. Therefore, Study 1 and Study 2 provide neural and behavioral data from nearly identical paradigms, with the addition of eye-tracking data for participants in Study 2.

Data from Study 1 was used to address aims regarding group differences in affect and neural activation as a function of attentional deployment (Aims 1a and 1b) and data from Study 2 was used to replicate these findings. For Aim 1c - Aim 3, analyses were restricted to data from Study 2, either because those analyses involve using eye-tracking data as a variable of interest (Aims 1c and 2b) or because eye-tracking variables may be used as a control variable in the exploration of group differences (Aim 2a and 3).

Study 1

Participants

Forty-one healthy adults (22 female) with a mean age of 22.29 and no history of neurological or psychological illness were recruited to participate in the study. Participants self-identified as 53.7% Caucasian, 31.7% Asian, 9.8% African American, and 4.8% "Other." The study was approved by The Committees on Research Involving Human Subjects at Stony Brook University. All participants provided informed consent and received payment for their participation. Participants were native English speakers over the age of 18 who had normal or corrected-to-normal vision.

Procedure

Participants were recruited from the Stony Brook area through campus and community flyers. Each person was prescreened over the phone to ensure study eligibility. At the start of the experimental session, participants underwent the consent process and completed an additional MRI eligibility form. Following consent, the task was verbally explained to participants with visual examples before the scan session. Following the scan session, participants completed all questionnaires, and then were debriefed and compensated.

Stimuli and Task Design

Sixty unpleasant and forty neutral images from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008) were selected for this task. Normative ratings indicated that unpleasant images were less pleasant (M = 2.28, SD = 1.47) than neutral images (M = 5.14, SD = 1.28), and that unpleasant images were more arousing (M = 6.05, SD = 2.25) than neutral images (M = 2.91, SD = 1.92); higher numbers indicate higher self-reported pleasantness and arousal.

Stimuli were presented in a counterbalanced block design. Twenty unpleasant and twenty neutral pictures were presented without modification. For the remaining images, attention was directed to a smaller portion of the image by placing a blue circle over that portion. These images were taken from a set of stimuli created by Dunning and Hajcak (2009), along with 20 additional neutral images. For the neutral pictures, the blue circle was always placed over a non-arousing, but visually complex portion of the picture. For the unpleasant pictures, the blue circle was either placed over an arousing or non-arousing portion of the image. The procedure for selecting areas of focus is outlined by Dunning and Hajcak (2009). Therefore there are 5 conditions: neutral

images with no focus, neutral images with a non-arousing focus, unpleasant images with no focus, unpleasant images with an arousing focus, and unpleasant images with a non-arousing focus. Each participant viewed the same set of IAPS images; however, to ensure that differences between conditions were not due to the specific images selected for a given condition, pictures were counterbalanced across subjects such that each unpleasant picture appeared in the no focus, non-arousing focus, and arousing focus condition an equal number of times across subjects. For example, the set of images used for the unpleasant arousing focus condition for the first subject would be used for the unpleasant non-arousing focus condition for the second subject by moving the location of the circle. Similarly, the neutral pictures were counterbalanced so that they appeared in the no focus or focus conditions an equal number of times across subjects. The order of blocks was counterbalanced for each subject so that one condition did not follow another more than once during an experimental session. Images within each block were presented in a random order and were never repeated. No picture was presented in more than one condition for a given subject. Stimuli were presented in 2 runs of 10 blocks each.

The task for the first 36 subjects was presented using E-Prime 2 (Psychology Software Tools, Inc., version 2). For the remaining five subjects, the experiment was re-programmed using Experiment Builder software package (SR Research Ltd, version 1.10.165) in order to collect eye-tracking data during image acquisition. The experimental design for the eye-tracking version of the experiment was identical to that of the original experiment. Stimuli for both versions of the task were presented using an MRI-compatible 60 Hz projector with a 1024x768 resolution which back-projected stimuli onto a mirror attached to the head coil.

Task Procedure

Participants were instructed to passively view sets of images and then rate their negative affect following each set of images. Participants were told that for some sets of images they would be instructed to freely view the images, while for other sets they would be asked to focus their eyes and attention only on the part of the picture within the blue circle.

Each trial began with a five second instruction to either "look freely at the following images" for no focus blocks, or to "look only at the part of the image within the blue circle" for focus blocks. Participants then viewed five pictures presented for four seconds each. Participants were then given five seconds to rate the intensity of their negative affect on a scale from one to four, with one being "not intense at all" and four being "very intense" using a four button custom built MRI-compatible response box. Fixation crosses were then presented in the center of the screen on a 10% to 50% saturated grey background, which alternated every 4 seconds for 20 seconds total. A schematic of the design can be seen in Figure 1.

Eye-Tracking Data Acquisition and Analysis

Eye position was sampled at 1000Hz, using a long-range mounted EyeLink 1000 eye-tracker with default saccade detection settings. Each run of trials began with a thirteen-point calibration routine used to map eye position to screen coordinates. Calibrations were not considered acceptable until the average error was less than 0.49° and the maximum error was less than 0.99°.

Data analysis was conducted off-line using the DataViewer software package (SR Research Ltd, version 1.11.1). The regions within the focus circles were defined as interest areas (IAs) and cumulative fixation duration (dwell time) within these regions was computed. During

focus trials, the time spent within the instructed focus circle (e.g. time spent in the non-arousing focus region during non-arousing focus trials) as well as the time spent in the alternate focus region (e.g. time spent in the arousing focus region during non-arousing focus trials) was calculated. During free viewing trials, time spent in both non-arousing and arousing interest areas was calculated. Similarly, during neutral trials, time spent in the focus region was calculated as well as the time spent in another, equally complex, region of the image to which they were not instructed to attend. Means for the eye data were obtained by first averaging fixation data across images within each block, then across blocks and finally across participants.

fMRI Data Acquisition and Analysis

A 3 Tesla Siemens TrioTim whole body scanner (Siemens Medical, Erlangen, Germany) with a 12 channel head coil was used to acquire 400 T2 star-weighted whole-brain volumes with an EPI sequence for analysis of BOLD signal. The following parameters were used: TR = 2500 ms, TE = 30 ms, flip angle = 90°, matrix dimensions = 64 x 64, FOV = 256, 256 mm, slices = 34, aligned to the AC-PC, slice thickness = 4mm, slice acquisition = interleaved, gap = 0.

Standard preprocessing procedures were performed in SPM8 starting with slice time correction, followed by realignment to the first volume in the image for motion correction. Realigned images were then normalized to standard Montreal Neurological Institute space, and spatial smoothing using a Gaussian kernel with 8mm FWHM.

First level single subject SPMs were then created for each subject from a model that specified the onset of each condition, the rating period and the instruction period. For each participant across both runs the following contrasts (and the reverse contrasts) were created: unpleasant no focus – neutral no focus, unpleasant arousing focus – unpleasant non-arousing

focus, focus (unpleasant arousing focus + unpleasant non-arousing focus + neutral focus) – no focus (unpleasant no focus + neutral no focus).

At the second level, random effects analyses were conducted to test for statistical differences between conditions of interest using a one-sample t-test with contrasts created for each individual at the first level. A height threshold set to FDR .05 was used to correct for multiple comparisons. A cluster threshold of 10 voxels with a FDR value of .025 was used to present peak activations following whole brain analysis. FDR correction at the whole brain level was chosen as the best method to correct for false positives as it provides more sensitivity than FWE correction with minimal false positives (Chumbley, Worsley, Flandin, & Friston, 2010).

Individual differences associated with behavioral or eye-tracking measures were entered into SPM. Regressions were conducted at the second level to test for relationships between individual difference measures and regions of the brain differentially activated between conditions of interest.

Behavioral Analyses

Data analysis began with an assessment of the integrity of the data to screen for outliers, unexpected data points, or skewed distributions. All self-report and behavioral data (including affect rating and eye-tracking data) were screened for violations of the assumptions of planned statistical tests. Relationships among or differences between behavioral measures were analyzed using Pearson's product correlations, independent samples t-tests, or ANOVAs using IBM SPSS Statistics 19 (SPSS Inc., Chicago IL).

Study 2

Participants

Fifty-one healthy adults with no history of neurological or psychological illness were recruited to participate in Study 2. No participants from Study 1 participated in Study 2. Four subjects were excluded from analysis as a result of spending less than 50% of dwell time in the interest area on neutral trials with a non-arousing focus. One of these subjects reported intentionally looking off screen to avoid unpleasant stimuli, while the remaining subjects closed their eyes for large portions of blocks of all types due to self-reported sleepiness. The final data set included 47 participants (25 female) with a mean age of 21.57. Participants self-identified as 57.4% Caucasian, 19.1% Latino/a, 17% Asian, 4.3% African American, and 1% "Other." The study was approved by The Committees on Research Involving Human Subjects at Stony Brook University. All participants provided informed consent and received payment for their participation. Participants were native English speakers who had normal or corrected to normal vision.

Stimuli and Procedure

The stimuli and procedure for Study 2 were identical to Study 1 with the following exceptions. In Study 2, the images within each block were no longer presented in a random order. Instead, images were carefully balanced such that the average distance between the centers of interest areas across condition types did not differ. This was to ensure that a difference in the distance that participants moved their eyes to reach the focus areas between unpleasant arousing focus and unpleasant non-arousing focus would not impact observed differences in brain activity for this contrast. In addition, the fixation crosses were no longer presented on alternating grey

backgrounds. Instead, the instruction screens and the fixation background were set to be the same value as the mean luminance of all affective pictures. This was done to minimize changes in pupil diameter as a function of changes in luminance, which can impact eye-tracking accuracy. Finally, subjects were asked to fixate on the center of the blue circle so that small errors in eye-tracking would not result in fixations being recorded as outside of the interest area.

Eye-Tracking Data Acquisition and Analysis

Eye position was sampled at 1000Hz, using a long-range mounted EyeLink 1000 eye-tracker with default saccade detection settings. Each run of trials began with a thirteen-point calibration routine used to map eye position to screen coordinates. Calibrations were not considered acceptable until the average error was less than 0.49° and the maximum error was less than 0.99°.

Data analysis was conducted off-line using the DataViewer software package (SR Research Ltd, version 1.11.1). The regions within the focus circles were defined as interest areas (IAs) and cumulative fixation duration (dwell time) within these regions was computed. During focus trials, time spent within the instructed focus circle (e.g. time spent in the non-arousing focus region during non-arousing focus trials) as well as the time spent in the alternate focus region (e.g. time spent in the arousing focus region during non-arousing focus trials) was calculated. During free viewing trials, time spent in both non-arousing and arousing interest areas was calculated. Similarly, during neutral trials, time spent in the focus region was calculated as well as the time spent in another, equally complex, region of the image to which they were not instructed to attend. Means for the eye data were obtained by first averaging fixation data across images within each block, then across blocks and finally across participants.

These data acquisition and analysis procedures for Study 2 were identical to those listed for the eye-tracking portion of Study 1 with one exception. In order to correct for drift during the course of the experiment due to changes in pupil size in response to changing luminance levels and emotional content, a drift correction procedure was enabled that allowed for the re-calibration the eye-tracker to the center of the screen during the presentation of fixation crosses.

fMRI Data Acquisition and Analysis

Imaging data acquisition for Study 2 was identical to that of Study 1. A 3 Tesla Siemens TrioTim whole body scanner (Siemens Medical, Erlangen, Germany) with a 12 channel head coil was used to acquire 400 T2 star-weighted whole-brain volumes with an EPI sequence for analysis of BOLD signal. The following parameters were used: TR = 2500 ms, TE = 30 ms, flip angle = 90°, matrix dimensions = 64 x 64, FOV = 256, 256 mm, slices = 34, aligned to the AC-PC, slice thickness = 4mm, slice acquisition = interleaved, gap = 0.

Image preprocessing steps were identical to Study 1. Standard preprocessing procedures will be performed in SPM8 starting with slice time correction, followed by realignment to the first volume in the image for motion correction. Realigned images were then normalized to standard Montreal Neurological Institute space, and spatial smoothing using a Gaussian kernel with 8mm FWHM. For PPI analysis, spatial smoothing was done using a Gaussian kernel with 6 mm FWHM.

First level single subject SPMs were then created for each subject from a model that specified the onset of each condition, the rating period and the instruction period. For each participant across both runs the following contrasts (and the reverse contrasts) were created: unpleasant no focus – neutral no focus, unpleasant arousing focus – unpleasant non-arousing

focus, focus (unpleasant arousing focus + unpleasant non-arousing focus + neutral focus) – no focus (unpleasant no focus + neutral no focus).

Imaging analyses for Study 2 were identical to those of Study 1. At the second level, random effects analyses were conducted to test for statistical differences between conditions of interest using a one-sample t-test with contrasts created for each individual at the first level. A height threshold set to FDR .05 was used to correct for multiple comparisons. A cluster threshold of 10 voxels with a FDR value of .05 was used to present peak activations following whole brain analysis. FDR correction at the whole brain level was chosen as the best method to correct for false positives as it provides more sensitivity than FWE correction with minimal false positives (Chumbley et al., 2010).

Region of interest analyses were conducted using the AAL atlas (Tzourio-Mazoyer et al., 2002) in WFU Pickatlas (Maldjian, Laurienti, Kraft, & Burdette, 2003). To examine gender difference during unpleasant no focus compared to neutral no focus conditions, ROI analyses were conducted using the following regions that were reported to reflect gender differences in a recent meta-analysis (Stevens & Hamann, 2012): the amygdala, hippocampus, thalamus, anterior cingulate cortex (ACC), middle frontal gyrus (BA 46), middle frontal gyrus (BA 9), medial frontal gyrus (BA 10), visual cortex (BA 17/18/19), middle temporal gyrus (BA 37), and cerebellum.

Individual differences associated with behavioral or eye-tracking measures were entered into SPM. Regressions were conducted at the second level to test for relationships between individual difference measures and regions of the brain differentially activated between conditions of interest.

PPI Analysis

Task related functional connectivity was assessed using psychophysiological interaction analysis (PPI; Friston et al., 1997). PPI analysis identifies activity in a given brain region that is explained by an interaction between the influence of activity in another area (physiological) and the experimental design (psychological). PPI analysis compares the functional relationship between regions across different conditions or tasks. A significant PPI interaction indicates that the contribution from one area to another changes significantly as a function of task. PPI analysis requires a design matrix which contains (1) a psychological variable which represents the experimental design, (2) the time series of a given seed/source region, (3) and the interaction term. The interaction term represents the covariance in activity between the source region and the region that is significantly different between task conditions. To determine the coordinates of the amygdala seed region, a conjunction analysis was conducted to identify the location of peak amygdala activity that is common across all unpleasant conditions (unpleasant no focus > neutral no focus, unpleasant arousing focus > neutral non-arousing focus, and unpleasant non-arousing focus > neutral non-arousing focus). The conjunction analysis was used to identify a region generally responsive to affective stimuli in order to avoid biasing the results towards task-related connectivity pattern. A 6mm spherical ROI (equivalent to the smoothing kernel) surrounding those coordinates was then used to generate the time series for the physiological term. Connectivity was examined across different task comparisons on a single subject level: unpleasant arousing focus vs. unpleasant non-arousing focus, unpleasant no focus vs. unpleasant non-arousing focus, unpleasant arousing focus vs. unpleasant no focus, and unpleasant no focus vs. neutral no focus. Each contrast was analyzed separately using the contrast [1 0 0] in which

the first column represents the interaction term. The single subject contrast images was then entered into the second level random effects analysis using a one-sample *t*-test in order to indentify different patterns of interaction as a function of task-dependent effects (e.g. unpleasant no focus > unpleasant non-arousing focus). A significant PPI effect indicates that the covariance between the source region (amygdala) and another region is significantly higher during, for example, unpleasant arousing focus compared to unpleasant non-arousing focus. A height threshold of .001 uncorrected was used with a cluster threshold of 10 voxels.

Questionnaires

Following the scan session, questionnaires aimed at capturing individual differences associated with emotion and attention were administered. Demographics were assessed with a self-report measure that asked participants to report their age, sex, ethnicity, education, handedness, and income. Attentional control was measured using the Attention Control Scale (ATTC) which contains the subscales of focusing and shifting (Derryberry & Reed, 2002). Emotion regulation skills were assessed using the Emotion Regulation Questionnaire (ERQ) which primarily assesses the use of reappraisal and suppression to regulate emotion (Gross & John, 2003).

Behavioral Analyses

Data analysis began with an assessment of the integrity of the data to screen for outliers, unexpected data points, or skewed distributions. All self-report and behavioral data (including affect rating and eye-tracking data) were screened for violations of the assumptions of planned statistical tests. Relationships among or differences between behavioral measures were analyzed using Pearson's product correlations, independent samples t-tests, and one-way ANOVAs using

IBM SPSS Statistics 19 (SPSS Inc., Chicago IL).

Results

Aim 1a: Neural Activation During Attentional Deployment (Study 1 & 2)

Neural activation associated with focusing on an arousing, compared to a non-arousing, region of an unpleasant image. In Study 1, there was no difference in amygdala activation between the unpleasant arousing focus condition and the unpleasant non-arousing focus condition. No regions of the brain were more active for the unpleasant arousing focus compared to the unpleasant non-arousing focus condition at $p > .05$, FDR corrected.

Contrary to Study 1, in Study 2, focusing on an arousing portion of an unpleasant image compared to a non-arousing portion of an unpleasant image resulted in significantly greater activations in the inferior occipital gyrus (BA 17), the insula (BA 13) and the amygdala. These activations are presented in Table 1 and Figure 2.

Neural Activation associated with focusing on a non-arousing, compared to an arousing, region of an unpleasant image. In Study 1, focusing on an unpleasant non-arousing region, compared to an arousing region produced significantly greater activations in parietal regions including the supramarginal gyrus (BA 40), the cuneus, the precuneus (BA 7), as well as greater activation in frontal regions including the inferior frontal gyrus (BA 47), the middle frontal gyrus (BA 10), the superior frontal gyrus (BA 9), the precentral gyrus (BA 6) and the cingulate gyrus (BA 32). These activations are presented in Table 2 and Figure 3.

Consistent with Study 1, in Study 2 focusing on a non-arousing portion of an unpleasant image also resulted in significantly greater activations in parietal regions including the

supramarginal gyrus (BA 40), as well as widespread activation in frontal regions including the middle frontal gyrus (BA 10) and the superior frontal gyrus (BA 9). These activations are presented in Table 3 and Figure 4.

Aim 1b: Attentional Deployment and Subjective Negative Affect (Study 1 & 2)

In Study 1, participants reported feeling less negative affect following the unpleasant non-arousing focus condition compared to both the unpleasant arousing focus ($t(40) = 8.96$, $p < .001$) and the unpleasant no focus conditions ($t(40) = 9.44$, $p < .001$). Participants also reported feeling more negative affect following the unpleasant non-arousing focus condition compared to both the neutral non-arousing focus ($t(40) = 8.90$, $p < .001$) and the neutral no focus conditions ($t(40) = 9.06$, $p < .001$). There were no significant differences between the unpleasant no focus and unpleasant arousing focus conditions ($t(40) = -.47$, $p = .64$) or between the neutral no focus and neutral non-arousing focus conditions ($t(40) = -.91$, $p = .37$). Means and standard deviations for affect ratings are presented in Table 4 (top).

Replicating Study 1, participants in Study 2 rated their negative affect during the unpleasant non-arousing focus condition as significantly less than both the unpleasant arousing focus ($t(46) = 8.21$, $p < .001$) and the unpleasant no focus conditions ($t(46) = 6.79$, $p < .001$). Participants also rated affect following the unpleasant non-arousing focus condition as significantly more negative than both the neutral non-arousing focus ($t(46) = 11.69$, $p < .001$) and the neutral no focus conditions ($t(46) = 23.02$, $p < .001$). There were no significant differences between the unpleasant no focus and unpleasant arousing focus conditions ($t(46) = .97$, $p = .34$) or the neutral no focus and neutral non-arousing focus conditions ($t(46) = .26$, $p =$

.80). Means and standard deviations for affect ratings are presented in Table 4 (bottom).

Self-reported negative affect (unpleasant non-arousing negative affect, unpleasant arousing negative affect, or unpleasant arousing negative affect minus unpleasant non-arousing negative affect) was not significantly associated with neural activation when entered as a covariate for the unpleasant arousing compared to unpleasant non-arousing focus contrast.

Aim 1c. Assessment of Compliance During Focus Trials and Gaze During Free Viewing (Study 1 & 2)

In Study 1, participants complied with task instructions to focus on the contents of the blue circle during focus trials, spending between 82 and 90 percent of total dwell time within the blue circle. During free viewing of unpleasant images, even though there were no circles directing attention to any portion of the image, participants spent significantly more time looking in the areas where the arousing focus region would be compared to where the non-arousing focus region would be ($t(4) = 4.63$, $p = .01$). Means and standard deviations for dwell time and percent dwell time are presented in Table 5 (top) for the 5 subjects who underwent eye-tracking during the fMRI experiment.

As in Study 1, during focus trials in Study 2, participants complied with task instructions to focus on the contents of the blue circle, spending between 96 and 99 percent of total dwell time within the blue circle. During free viewing of unpleasant images participants again spent significantly more time looking in the areas where the arousing focus region would be compared to where the non-arousing region would be ($t(46) = 23.67$, $p = .001$). Means and standard deviations for dwell time and percent dwell time are presented in Table 5 (bottom) for the 47

subjects in Study 2 who underwent eye-tracking.

Aim 1d: Impact of Individual Differences in Visual Compliance and Subjective Affect (Study 2)

Compliance and negative affect. During unpleasant non-arousing focus blocks, on average, participants fixated in the unpleasant region of the image on 7.85 out of 20 trials (minimum = 3, maximum = 17). Participants spent, on average, 126 ms in the arousing region, with a minimum duration of 41 ms and a maximum duration of 520 ms. The number of fixations participants made to arousing regions during unpleasant non-arousing focus trials was positively correlated with self-reported negative affect following unpleasant non-arousing focus blocks (r = .35, p = .02; Figure 5, left). Similarly, there was a positive correlation between average dwell time in the arousing region and negative affect following non-arousing focus blocks (r = .35, p = .02; Figure 5, right). There was a marginally significant negative correlation between time spend in the non-arousing region as instructed and negative affect (r = -.26, p = .08).

Negative affect following unpleasant no focus trials was not related to time spent in the arousing focus region (r = -.10, p = .51) or time spend in the non-arousing region (r = -.005, p = .96).

Compliance and neural activation. No regions of the brain were significantly correlated with time spent in either the arousing region or the non-arousing region during the unpleasant no focus condition using whole-brain analyses. Similarly, during the unpleasant non-arousing focus condition, no region of the brain was correlated with time spent in the non-arousing region as instructed, or in the arousing region.

Relationships between subjective affect and neural activation. Affect ratings were not significantly related to brain activation during attentional deployment: subjective affect following the unpleasant non-arousing or the unpleasant arousing focus conditions was not related to activation in any brain region during the unpleasant non-arousing compared to the unpleasant arousing focus conditions. Similarly, affect ratings were not related to brain activation during free viewing: subjective affect following the unpleasant no focus trials was not correlated with activation in any brain region during the unpleasant no focus compared to the neutral no focus conditions.

Aim 2a: Functional Connectivity During Attentional Deployment (Study 2)

Results related to this aim are all from Study 2 and involve comparisons between free viewing and directing attention to either an arousing or a non-arousing portion of an unpleasant image in a subset of 42 individuals with motion under 1mm. Whole brain fMRI results for these contrasts (unpleasant no focus versus unpleasant non-arousing focus and unpleasant no focus versus unpleasant arousing focus) are presented first, followed by the functional connectivity results for each of these contrasts.

Whole brain analysis: Unpleasant no focus vs. unpleasant arousing focus. Freely viewing unpleasant images, compared to focusing on an arousing portion of the image, resulted in enhanced activation in the middle occipital gyrus (BA 17/18), the cerebellum, and the middle temporal gyrus. Peak activations are presented for this contrast in Table 6 and Figure 6.

Focusing on an arousing region, compared to freely viewing an unpleasant image, resulted in enhanced activation in the inferior and superior parietal lobes (BA 40), the precuneus (BA 7),

the middle frontal gyrus (BA6/8), the inferior temporal gyrus (BA 20) and a region of the middle occipital gyrus (BA 19). Results from this contrast are presented in Table 7 and Figure 7.

Whole brain analysis: Unpleasant no focus vs. unpleasant non-arousing focus. Freely viewing unpleasant images, compared to directing attention to a non-arousing portion of the image, resulted in activation in cuneus (BA 17/18) the anterior cingulate cortex (BA 32), the precentral gyrus (3/4), and the amygdala. Peak results for this contrast are presented in Table 8 and Figure 8.

Focusing on a non-arousing region of an unpleasant image, compared to free viewing, resulted in activation in the inferior and superior parietal lobe (BA 7/40) the precuneus (BA 7) the middle frontal gyrus (BA6, 9, 10) and the middle temporal gyrus (BA 21). These results are presented in Table 9 and Figure 9.

Functional connectivity: Unpleasant no focus vs. unpleasant arousing focus. There were no differences in functional connectivity when comparing unpleasant images without a focus to unpleasant images with an arousing focus using the right or the left amygdala as the seed region.

Functional connectivity: Unpleasant no focus vs. unpleasant non-arousing focus. Freely viewing unpleasant images, compared to focusing on a non-arousing region, resulted in enhanced connectivity between the right amygdala and the visual cortex (BA 19) and fusiform gyrus (BA 20). Similarly freely viewing unpleasant images, compared to focusing on a non-arousing region, resulted in enhanced connectivity between the left amygdala and the visual cortex (BA 18/19), fusiform gyrus (BA 37), and orbital frontal cortex (BA 47). These results are presented in Table 10 and Figure 10. Conversely, focusing on a non-arousing region, compared

to freely viewing unpleasant images, resulted in enhanced connectivity between the precuneus (BA 7) and both the left and the right amygdala. These results are presented in Table 11 and Figure 11.

Aim 2b: Functional Connectivity and Visual Compliance (Study 2)

During the unpleasant non-arousing focus condition, compared to unpleasant no focus, the degree of connectivity between the right amygdala and the precuneus was positively correlated with time spent in the non-arousing region as instructed (r = .32, p = .04), and negatively correlated with time spent outside of the non-arousing region (r = -.32, p = .04). Connectivity between the left amygdala and the precuneus was not significantly related to time spend in the non-arousing region (r = .16, p = .32) or to time spent outside the non-arousing region (r = -.18, p = .23).

Aim 2c: Functional Connectivity and Trait Reappraisal (Study 2)

Trait reappraisal was positively related to connectivity between the precuneus and the right (r = .36, p =.02) and left (r = .395, p = .01) amygdala. Trait suppression was not significantly related to connectivity between the precuneus and the right (r = -.19, p = .24) or the left (r = -.17, p = .29) amygdala.

Trait reappraisal was not significantly related to time spent in the non-arousing region as instructed (r = .15, p = .37).

Aim 3: Gender Differences in Brain Activation During Free Viewing and During Attentional Deployment (Study 2)

Areas associated with viewing unpleasant images across both genders. In Study 2, the whole brain analysis for the simple effect of emotion (unpleasant no focus greater than neutral no focus) on the BOLD response revealed clusters of activation in occipital, frontal and parietal regions. Peak activations included the fusiform gyrus (BA 37), the medial frontal gyrus (BA 8), the anterior cingulate cortex (BA 32), and the postcentral gyrus (BA 2). An ROI analysis using a mask for bilateral amygdala revealed significant peaks in both the right and left amygdala. These results are reported in Table 12 and Figure 12**.**

Gender differences in negative affect. Women reported significantly more negative affect following the unpleasant no focus condition ($t(45) = 2.82$, $p = .007$), and the neutral no focus condition ($t(45) = 3.15$, $p = .003$), and marginally more negative affect following the unpleasant arousing focus condition ($t(45) = 1.82$, $p = .07$), and the neutral focus condition ($t(45) = 1.85$, $p = .07$) than men. There were no significant gender differences in negative affect following the unpleasant non-arousing focus condition ($t(45) = 1.10$, $p = .28$). Means and standard deviations for affect ratings for each gender are reported in Table 13.

Gender differences in emotion regulation and attentional control skills. There were no gender differences in self-reported use of reappraisal ($t(45) = .54$, $p = .59$) or suppression ($t(45) = -.69$, $p = .49$). Men report significantly higher scores on the attentional control scale ($t(45) = -2.16$, $p = .04$) and the attention focusing subscale ($t(45) = -2.26$, $p = .03$). There was a marginally significant gender difference for the attention shifting subscale ($t(45) = -1.70$, $p = .10$). Means and standard deviations for emotion regulation and attentional control are reported

in Table 14.

Gender differences in visual attention to arousing information. Men (M = 1447.83, SD = 260.11) and women (M = 1377.45, SD = 302.30) did not significantly differ in the amount of time spent in the arousing region during unpleasant no focus trials ($t(45) = .85$, $p = .40$). Men (M = 3225.86, SD = 321.17) and women (M = 3117.64, SD = 338.59) did not significantly differ in the amount of time the spent in the non-arousing region during unpleasant non-arousing focus trials ($t(45) = 1.12$, $p = .27$). Similarly, men (M = 108.04, SD = 70.08) and women (M = 141.63, SD = 110.20) did not differ in the amount of time they spent in the arousing region during unpleasant non-arousing focus trials ($t(45) = -1.23$, $p = .23$). Men (M = 3365.78, SD = 265.11) and women (M = 3264.84, SD = 296.45) also did not differ in the amount of time the spent in the arousing region during unpleasant arousing focus trials ($t(45) = 1.22$, $p = .23$). Finally, men (M = 3369.13, SD = 288.21) and women (M = 3271.58, SD = 316.96) did not differ in the amount of time the spent in the non-arousing region during neutral trials ($t(45) = 1.09$, $p = .28$). These results indicate men and women have comparable attention to unpleasant arousing information during free viewing, and comparable compliance during focus trials.

Gender differences in neural activation during viewing of unpleasant compared to neutral images without a focus. During the free viewing of unpleasant compared to neutral images, women had greater activation than men in a widespread network of regions with peak activations in the temporal gyrus, the cerebellum, the superior frontal gyrus (BA 8) and the superior temporal gyrus (BA 38). ROI analysis of regions previously associated with gender differences in the neural activation to unpleasant images revealed greater activation for women in all regions: the amygdala, hippocampus, thalamus, anterior cingulate cortex, middle frontal

gyrus (BA 9 and BA 46), medial frontal gyrus (BA 10), visual cortex (BA 17/18/19), middle temporal gyrus (BA 37), and cerebellum. Peak activations are presented in Table 15 and displayed in Figure 13.

Gender differences in neural activation during the viewing of unpleasant and neutral images without a focus compared to fixation. Unpleasant and neutral images without a focus were then each compared to the fixation period to determine if gender differences during unpleasant compared to neutral images were due to increased activation during the unpleasant no focus condition for women, or due to higher activation in these regions for men during the neutral no condition. There were no significant gender differences when comparing unpleasant no focus to fixation. However, men had significantly higher activation than women during the neutral no focus condition compared to fixation including peak activations in the insula, visual cortex (BA 19/18), postcentral gyrus (BA 5), precentral gyrus (BA 6), precuneus, cerebellum, and the amygdala. ROI analysis of regions previously associated with gender differences in the neural activation to unpleasant images revealed that during neutral no focus compared to fixation, men had higher activation than women in small clusters of the amygdala, middle frontal gyrus (BA 9), visual cortex (BA 17/18/19) and cerebellum. However, men did not have greater activation than women in the hippocampus, thalamus, middle frontal gyrus (BA 46), medial frontal gyrus (BA 10), anterior cingulate cortex, or middle temporal gyrus (BA 37). Peak activations are presented in Table 16 and displayed in Figure 14.

Gender differences in neural activation during attentional deployment. There were no significant gender differences in brain activation when comparing the fixation period to the unpleasant arousing focus, unpleasant non-arousing focus, or neutral focus conditions. There

were no significant gender differences when comparing unpleasant no focus to either unpleasant arousing focus or unpleasant non-arousing focus. There were also no significant gender differences when comparing then unpleasant arousing focus condition to the unpleasant non-arousing focus condition.

Discussion

Aim 1: Affect, Compliance and Neural Correlates

The intent of Aim 1 was to examine the impact of visual attentional deployment in the absence of an explicit regulatory goal on subjective negative affect and neural response. In Study 1 and Study 2 reductions in negative affect and increases in frontal and parietal regions were observed when subjects directed their attention to non-arousing, compared to arousing, portions of unpleasant images. Moreover, in Study 2, deploying attention to non-arousing, compared to arousing, regions was associated with reduced amygdala activation. Eye-tracking results in a sub-sample of participants in Study 1 and in all participants in Study 2 confirmed that subjects who underwent eye-tracking generally stayed within the focus region as instructed.

Studies on emotion regulation, particularly cognitive reappraisal, have postulated that the use of cognitive control to execute emotion regulation strategies may engage the prefrontal cortex. The prefrontal cortex, then, may exert top-down control over the amygdala, which modulates sensory processing of emotional information and causes corresponding reductions in subjective affect. Given that unpleasant stimuli have the capacity to automatically capture attention, deploying attention away from such stimuli may also require effortful action. Exercising visual and inhibitory control to deploy attention away from unpleasant information

may then rely on similar prefrontal regions and may promote similar decreases in amygdala activity and subjective negative affect as cognitive reappraisal.

In both Study 1 and Study 2 widespread increases in both frontal and parietal regions was observed for the unpleasant non-arousing focus compared to the unpleasant arousing focus condition, despite focus being a common demand across both conditions. That is, these regions were more active when participants had to maintain focus in a relatively non-arousing compared to an arousing region of the same picture. Prefrontal and parietal regions are considered essential for cognitive control during effortful tasks (Matsumoto & Tanaka, 2004), and fronto-parietal networks are known to underlie visuospatial attention and visual control (Corbetta & Shulman, 2002). As even task-irrelevant negative information is capable of capturing attention (Vuilleumier et al., 2001), increased activation in these regions may reflect additional effort required to direct and maintain attention within a non-arousing focus region in the presence of unpleasant arousing information. Some of the brain regions recruited as participants divert attention away from unpleasant arousing information substantially overlap with regions activated during effortful cognitive emotion regulation strategies. Specifically prefrontal regions including BA 6, 8, and 9, which are postulated to relate to the down-regulation of the amygdala, are common to both cognitive reappraisal and attentional deployment.

Reduced amygdala activation for the unpleasant non-arousing focus compared to the unpleasant arousing focus condition was observed in Study 2, but not Study 1. The design and analysis of Studies 1 and 2 were identical with one major exception: eye-tracking data was collected on all participants in Study 2, but only on a subset of five participants in Study 1. The divergent findings between these two studies highlight important challenges in imaging research,

as well as the advantages of utilizing eye-tracking in conjunction with fMRI. First, researchers rely on participants to stay awake and attend to presented stimuli. However, collecting eye-tracking data allowed the exclusion of four participants from Study 2 who were intentionally avoiding the stimuli or who were otherwise closing their eyes for a large portion of the study. Despite closing eyes for extended periods of time, these participants still pressed the button to rate their affect following each block of images. Without eye-tracking, there would be no objective means to remove these subjects from analyses. Because eye-tracking was only collected on 5 out of 41 subjects in Study 1, it is possible that non-compliance from a number of subjects in Study 1 attenuated more subtle effects. Second, it is possible that simply knowing that their eye movements were being tracked changed the degree to which subjects complied with task instructions. While differences in task compliance as a function of eye-tracking have not been explicitly examined, there is some evidence that eye-tracking alone can modify behavior to increase adherence to perceived social norms (Risko & Kingstone, 2010). It is possible that participants in Study 2 were more likely to consistently stay within the circle as instructed, particularly the unpleasant non-arousing circle, when they knew their eye movements were being monitored. Consequently, the observed amygdala and visual activation for the unpleasant arousing focus compared to unpleasant non-arousing focus condition in Study 2 is likely to reflect activations when subjects are complying with task instructions. Study 2, therefore, provides support for the idea that attentional deployment relies upon a similar network of brain regions as cognitive reappraisal; successful regulation via either strategy appears to involve increases in prefrontal and parietal regions associated with effortful control, as well as corresponding attenuations in amygdala activity. However, the specific relationships between

prefrontal and parietal regions and the amygdala, as well as their relationship to subjective affect, may differ between emotion regulation strategies. Finally, it cannot be ruled out that participants may have been engaging in some form of automatic emotion regulation using methods other than attentional deployment during the viewing of images, which may have contributed to the resulting activation patterns in either study.

In conclusion, these studies suggest that deploying attention to a non-arousing portion of an unpleasant image is associated with reduced subjective negative affect, reduced amygdala activity, and increased activity in fronto-parietal networks. This suggests that the neural circuitry associated with attentional deployment may significantly overlap with cognitive reappraisal and cognitive distraction – all three strategies seem to involve recruitment of common control regions and corresponding reductions in limbic activation. Understanding the shared and unique neural mechanisms associated with this commonly used strategy may be critical to understanding the processes underlying emotion regulation as well as for understanding deficits in the ability to deploy attention away from negative information when necessary.

Aim 2: Functional Connectivity

Aim 2 examined the neural correlates and functional connectivity patterns associated with visual attentional deployment compared to passive viewing. Consistent with previous findings in non-emotional attention paradigms, directing attention to either arousing or non-arousing portions of unpleasant images resulted in enhanced activation in frontal and parietal regions compared to free viewing (Hopfinger et al., 2000). However, only directing attention to non-arousing regions of unpleasant images resulted in reduced amygdala activation. Directing

attention to non-arousing regions of unpleasant images, compared to free viewing unpleasant images, was associated with reduced connectivity between the amygdala and visual cortex, and increased connectivity between the amygdala and the precuneus. Further, the extent of amygdala-precuneus connectivity was correlated with time spent in the non-arousing region during unpleasant trials and with trait reappraisal. There were no significant differences in functional connectivity between freely viewing unpleasant images and directing attention to arousing regions.

Compared to freely viewing unpleasant images, focusing on either an arousing or a non-arousing region of an unpleasant resulted in increased activation in prefrontal and parietal regions; however corresponding reductions in amygdala activation were only observed when focusing on non-arousing regions. These results are in line with previous studies that ask participants to increase or decrease their affect using cognitive reappraisal: both increasing and decreasing negative affect through reappraisal involve increased activation in prefrontal and/or parietal regions compared to free viewing (Eippert et al., 2007; Kim & Hamann, 2007; Ochsner et al., 2004; van Reekum et al., 2007). Previous studies of cognitive attentional deployment have typically asked participants to concurrently engage in difficult working memory or computational tasks during the viewing of unpleasant pictures and have also reported increases in parietal and prefrontal regions compared to passively viewing unpleasant images (Kanske et al., 2011; McRae et al., 2010). Changes in these regions during cognitive reappraisal are presumably due to changes in appraisals of stimuli while participants remain focused on the emotional content. Changes in these regions during cognitive distraction, however, are presumably due to orienting away from the emotional stimuli and engaging in cognitively

demanding tasks. In the current study, changes in brain activation should primarily reflect orienting away from emotional stimuli. Findings from the current study, then, suggest that simply directing visual attention to non-arousing information in an unpleasant context recruits similar control regions as does engaging in cognitive challenges, or constructing goal congruent reappraisals of emotional content.

Compared to freely viewing unpleasant images, focusing on a non-arousing region resulted in enhanced connectivity between the precuneus and both the left and right amygdala. Further, the degree of connectivity between these regions was positively related to compliance: the more participants stayed in the non-arousing region as instructed the greater the connectivity between the precuneus and the right amygdala. Both cognitive reappraisal (Banks et al., 2007) and cognitive distraction (Kanske et al., 2011) have been associated with enhanced connectivity between the left amygdala and prefrontal and parietal regions. Theories of emotion regulation, however, have primarily cited the importance of amygdala-frontal interactions as the critical neural mechanism underlying successful emotion regulation (Ochsner & Gross, 2008), which is supported by direct reciprocal anatomical connections between the medial prefrontal cortex and the amygdala (Amaral & Price, 1984; Bozkurt et al., 2001), and interconnections amongst prefrontal regions (Petrides & Pandya, 1984). However, there is also evidence for functional and anatomical connections between the precuneus and the amygdala. For example, negative functional connectivity between the precuneus and the amygdala has been consistently reported during rest (Roy et al., 2009; Zhang & Li, 2012). In addition, reduced functional connectivity between the precuneus and the amygdala has been observed during social and emotional processing in some psychiatric disorders, including children with bipolar disorder (Rich et al.,

2008) and individuals with schizophrenia (Mukherjee et al., 2012). Finally, there is some evidence for direct anatomical relationships between these regions (Leichnetz, 2001; Parvizi, Van Hoesen, Buckwalter, & Damasio, 2006), suggesting the possibility that the precuneus may independently play a direct role in regulating amygdala activation. Together these findings highlight a critical role of the precuneus during emotion regulation, particularly for orienting and maintaining attention away from unpleasant information, and suggest that the precuneus may play a direct role in the regulation of amygdala reactivity to emotional stimuli.

The degree of connectivity between the amygdala and the precuneus was also positively related to trait reappraisal. Previous studies have shown that individual differences in trait reappraisal can impact the neural response to emotional images even in the absence of instructions to regulate emotions: women who scored higher on trait reappraisal showed reduced amygdala activation and increased activation in prefrontal and parietal regions during the free viewing of unpleasant images (Drabant et al., 2009). Further, among depressed women, those who reported higher trait reappraisal displayed lower amygdala activation when anticipating negative images (Abler, Erk, Herwig, & Walter, 2007). Reduced amygdala and increased frontal and parietal activation as a function of trait reappraisal have been interpreted to reflect spontaneous use of reappraisal during affective picture viewing (Drabant et al., 2009). In the current study, individuals who scored higher on a measure of trait reappraisal had higher amygdala to precuneus connectivity during unpleasant non-arousing focus trials, despite trait reappraisal not being significantly related to compliance. These results suggest that the relationship between neural activation in this study and trait reappraisal is not simply due to increased compliance on the part of reappraisers, but instead may suggest that individuals who

score higher on reappraisal are more likely to employ this strategy automatically. These results underscore the difficultly in both dissociating emotional reactivity from regulation and in investigating the impact of a single emotion regulation strategy in isolation, and suggest that future work is needed to simultaneously assess the use of multiple strategies during emotion regulation.

The current study used PPI to explore temporal correlations between the left and the right amygdala and spatially remote locations. While this methodology was useful in this context to indentify regions of the brain that may regulate amygdala activation during visual attentional deployment, it is not able to assess functional relationships between regions independent of the amygdala. For example, there are direct anatomical connections between prefrontal and parietal regions, which may play an important role in coordinating attention to and processing emotional information. Other hypotheses driven approaches, such as dynamic causal modeling, may be better suited to infer causality in future studies examining the relationships between currently known emotion generative regions and control regions.

In conclusion, these findings extend previous work on connectivity during cognitive reappraisal (Banks et al., 2007) and cognitive distraction (Kanske et al., 2011) by demonstrating that coupling between the amygdala and precuneus is uniquely increased during visual attentional deployment. Further, the strength of coupling between these regions is positively related to both task compliance and trait reappraisal. These results demonstrate the importance of functional relationships between the precuneus and the amygdala when orienting and maintaining attention away from arousing unpleasant stimuli.

Aim 3: Gender Differences

Aim 3 explored gender differences in neural activation during emotional processing and attentional deployment. Consistent with a recent meta-analysis (Stevens & Hamann, 2012), when contrasting unpleasant images without a focus with neutral images without a focus, women had greater activation in a variety of emotion-related regions, including the prefrontal cortex and the amygdala, despite equivalent visual attention to arousing information. However, there were no significant gender differences when comparing the unpleasant no focus condition to fixation. In contrast, when comparing the neutral no focus condition to fixation, men had greater activation than women in several key regions, including the amygdala, the middle and inferior frontal gyrus, and the visual cortex. Further, there were no significant gender differences in neural activation when comparing attentional deployment conditions to either unpleasant images without a focus or to the fixation period.

The majority of neuroimaging studies exploring emotional processing have compared emotional to neutral images or faces. In a recent meta-analysis of gender differences in emotion, 74 of the 80 included studies used a neutral condition as a baseline, while 6 used fixation (Stevens & Hamann, 2012). Based on analysis of these paradigms, Stevens and Hamann (2012) concluded that women, compared to men, have an increased neural response to unpleasant emotional stimuli including increased activation in the medial prefrontal cortex, the inferior frontal gyrus, the insula, the visual cortex and the left amygdala, compared to neutral stimuli. In line with findings from this meta-analysis, in the current study there were significant gender differences when comparing unpleasant images to a baseline of neutral images: women displayed greater activation than men in widespread network of expected regions, including prefrontal

regions and the amygdala. However, when comparing unpleasant images to fixation, there were no longer any significant gender differences. In addition, there were no differences in visual attention to the arousing unpleasant information: men and women spent comparable amounts of time in the arousing region during the viewing of unpleasant image. During the viewing of neutral images compared to fixation, men displayed increased activation in a subset of emotion-related regions that were more active for women during the unpleasant compared to neutral contrast, including the amygdala. These findings suggest that previous reports of gender differences in emotional processing may not be entirely due to hyperactivation of emotion related regions in women during the processing of emotional images, but rather, may at least partially reflect gender differences in the baseline comparison condition. While other behavioral and psychophysiological gender differences have been reported elsewhere (Bradley, Codispoti, Sabatinelli, & Lang, 2001), these findings have potentially important implications for work relating higher activation in emotion-related region in women to greater rates of psychopathology in women (Hamann, 2005).

Increased amygdala activation for men during the processing of neutral stimuli has been reported in previous studies. For example McClure and colleagues (2004) reported that women had greater activation in the orbital frontal cortex (OFC) and the amygdala than men when comparing angry to neutral faces. However, men, but not women, displayed increased activation in the amygdala and OFC when comparing neutral faces to fixation. Further, men also displayed increased OFC activation and ACC activation in response to angry and fearful faces when compared to fixation, whereas women only demonstrated greater amygdala and OFC activation to angry faces compared to fixation. These findings are consistent with those of the current

study, and suggest that women are not necessarily more reactive to threatening stimuli, but rather might more selectively engage frontal and limbic structures than men. Importantly, these gender differences were not apparent during adolescence: both male and female adolescents showed similar patterns of activation to adult men. Previous work has suggested that adult-like patterns of discrimination between emotional and neutral faces may not be apparent in young children (Pagliaccio et al., 2013), and may emerge and fully develop over the course of puberty, suggesting that the selective engagement of limbic structure in the processing of affective information may be a developmental process occurring primarily in women.

Greater activations during neutral trials compared to fixation in men could potentially be driven by affective information within neutral images. There is evidence that neutral faces can elicit neural responses comparable to emotional stimuli. For example, neutral images containing people elicit larger LPPs than neutral images without people (Ferri, Weinberg, & Hajcak, 2012). Further, increased amygdala activation in response to neutral faces has been linked to autism (Hamann, 2005; Tottenham et al., 2014) as well as individual differences in anxiety (Cooney, Atlas, Joormann, Eugène, & Gotlib, 2006; Ferri, Bress, Eaton, & Proudfit, under review; Sommerville, Kim, Johnstone, Alexander, & Whalen, 2004). These results suggest that neutral baselines, at least when they contain faces, elicit affective engagement that varies as a function of individual differences, and may therefore not function as a reliable baseline. The current study utilized IAPS images, rather than emotional faces; therefore blocks of neutral images in the current study depict neutral objects and scenes as well as neutral faces. While the current study demonstrated increased amygdala and prefrontal activation for neutral images compared to fixation, the extent to which these differences are driven by increased activation to neutral faces,

or simply increased activation to neutral stimuli in general is unclear. Future studies separating neutral blocks with and without faces might better disentangle these effects. Further, while eye-tracking data was collected during neutral trials in the current study, the interest area was not consistently placed on faces during neutral trials. Studies that index visual attention to face stimuli during the processing of neutral IAPS images may be able to determine if there is a relationship between attention to ambiguous neutral faces and amygdala activation. Finally, neuroimaging methodologies that have an absolute measurement of blood flow, such as arterial spin labeling, may be a viable method to overcome issues concerning subtractive effects in BOLD fMRI when exploring gender difference in the processing of emotional stimuli.

The current study did not provide evidence for gender differences during attentional deployment. In the behavioral literature, there is a relative lack of evidence for gender differences in the use of emotion regulation strategies. For example, men and women report using emotion regulation strategies in everyday life with similar frequency (Gross & John, 2003). There is some evidence that women tend to use strategies such as rumination or catastrophizing more often than men (Garnefski, Teerds, Kraaij, Legerstee, & van den Kommer, 2004; Tamres et al., 2002). However, for both men and women, greater use of these strategies was related to greater depression scores (Garnefski et al., 2004), suggesting that comparable cognitive mechanisms relate emotion regulation use to depression in men and women. Little is known about gender differences in the neural response to emotion regulation, as the majority of published neuroimaging studies of emotion regulation have focused primarily on women, and have not explicitly explored or reported gender differences when they included both genders. Two studies examining gender differences in reappraisal report that women display greater

activation in the anterior cingulate cortex and portions of the prefrontal cortex (Domes et al., 2010; McRae et al., 2008), suggesting potential differences in engagement with emotional stimuli during reappraisal, or gender differences in the effort required to engage in reappraisal. In the current study, however, there were no significant gender differences in neural activation when comparing unpleasant images without a focus to unpleasant images with an arousing or a non-arousing focus. Similarly, there were no significant gender differences when comparing unpleasant images with an arousing focus or unpleasant images with a non-arousing focus to the fixation period. Women and men did not significantly differ in the amount of time they spent in the arousing or non-arousing region as instructed and women and men did not differ in self-reported negative affect when focusing on a non-arousing region of an unpleasant image. Together these findings suggest that despite potential gender differences during reappraisal, when actively engaging in attentional deployment, there are no significant gender differences in the ability to deploy attention, in the neural activation associated with attentional deployment, or in the subsequent experience of negative affect.

In conclusion these findings replicate previous reports of gender differences in neural activation when comparing unpleasant to neutral images, but suggest that these differences are due, at least in part, to increased neural activation to neutral images in men. There were no gender differences in the ability to deploy attention away from unpleasant arousing information, in the associated neural activation, or in the self-reported negative affect following the deployment of attention. These findings suggest the importance of selecting adequate baselines in examinations of gender differences in emotional processing and suggestion attentional deployment may involve similar neural networks and may be equally effective for men and

women.

Future Directions

Together, these studies suggest that visual attentional deployment is an effective emotion regulation strategy for both males and females that may critically depend on functional relationships between parietal regions and the amygdala. This basic work on attentional deployment has potential applications for examining the development and use of emotion regulation over the lifespan, and for examining the impact of clinical interventions. In addition, these findings highlight the need for additional work examining gender differences in emotional processing and emotion regulation.

The current studies were conducted in younger adults, but attentional deployment is widely used across the lifespan. It is one of the first strategies to emerge in children, but it is also particularly prevalent in older adults. Compared to younger adults, older adults report higher levels of positive affect (Stawski, Sliwinski, Almeida, & Smyth, 2008), and longitudinal studies suggest that overall well-being improves as individuals age, despite declines in physical health and cognitive performance (Cacioppo et al., 2008). While older adults seem to be less successful than their younger counterparts at using cognitive reappraisal to down-regulate negative affect (Opitz, Rauch, Terry, & Urry, 2012), older adults appear particularly adept at using attentional deployment. Compared to younger adults, older adults look away from negative information and towards positive information when experiencing negative mood (Isaacowitz, Toner, & Neupert, 2009a, 2009b; Isaacowitz, Wadlinger, Goren, & Wilson, 2006; Mather & Carstensen, 2005), and the degree to which they make these shifts in gaze are related to subsequent improvements in

mood (Isaacowitz et al., 2009a). These findings suggest that attentional deployment may be one important determinant of well being in older adulthood. Employing the current paradigm in a cross sectional manner would help to elucidate the neural mechanisms associated with the successful deployment of attention in older adults. Further, while deficits have been observed in the ability of older adults to recruit prefrontal regions in the interest of cognitive reappraisal (Opitz et al., 2012), the engagement of parietal regions such as the precuneus, and their functional relationships with the amygdala may remain intact, or even strengthen in older adulthood.

Examining changes in neural activation and functional connectivity between frontal and parietal control regions and the amygdala in clinical populations, and investigating how activation in these regions change as a function of treatment, may be another promising application of this paradigm. Visual attention to emotional information is altered in both depression and anxiety (Bar-Haim et al., 2007; Joormann, 2009; Kellough et al., 2008; Sears et al., 2011; Sears et al., 2010; Wieser et al., 2009) and abnormalities in the employment of both distraction and cognitive reappraisal have been reported (Kanske, Heissler, Schönfelder, & Wessa, 2012). Attentional training appears to have some impact on visual attention to affective stimuli, and on reductions in symptom severity in some forms of anxiety and depression (Baert, De Raedt, Schacht, & Koster, 2010; Schmidt et al., 2009; Wadlinger & Isaacowitz, 2008, 2011). Similarly, mindfulness training has been shown to improve anxiety and depression symptoms (Baert et al., 2010; Goldin & Gross, 2010) and to strengthen connectivity between parietal and prefrontal regions (Hasenkamp & Barsalou, 2012). These improvements in attentional control and associated connectivity may also influence functional relationships between parietal regions

and the amygdala during the processing of affective information in both healthy and clinical populations. These changes, in turn, may be related to improvements in negative affect and symptoms of anxiety and depression. This simple paradigm might serve as a means to first assess deficits in neural activation and functional connectivity patterns when engaging with affective stimuli, and then for tracking the impact of attentional training.

Finally, considering that gender differences were not significant in the current study when comparing unpleasant images to a fixation baseline, future work is needed to determine if and when gender differences exist in basic emotional processing. Using imaging methodologies that do not rely on relative activations, such as arterial spin labeling, would be ideal for investigating potential absolute differences in blood flow between males and females in response to emotional and neutral images. Collecting eye-tracking data, in combination with arterial spin labeling, and placing interest areas on both emotional information and social information (i.e. people and faces), may better explain potential gender differences in the context of visual attention. Further, as individual differences in response to neutral images have been widely reported, results from arterial spin labeling studies examining emotion may allow for the development of better baseline conditions in order to investigate individual differences in both emotional processing and emotion regulation.

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Table 1.
Peak activations for the unpleasant arousing focus greater than unpleasant non-arousing focus conditions in Study 2 (n = 47)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
L Inferior Occipital Gyrus	17	851	-18 -91 -6	10.55	7.48
R Inferior Occipital Gyrus	17		22 -91 1	8.88	6.74
L Cerebellum			-33 -78 -16	6.85	5.66
L Insula	13	26	-36 -3 16	5.52	4.01
L Amygdala		11	-21 -11 -9	4.22	3.86
L Inferior Parietal Lobe	40	29	-55 -24 34	3.73	3.47
L Postcentral Gyrus	2		-58 -27 39	4.74	4.26
L Postcentral Gyrus	2		-55 -24 50	3.53	3.30
L Inferior Parietal Lobe	40	15	-36 -39 49	3.60	3.36
L Fusiform Gyrus	37	14	-40 -48 -17	4.14	3.80

Peak activations from random effects analysis are listed with a threshold of $p < .025$, FDR corrected, and cluster filter of 10 contiguous voxels.
BA = Brodmann's area, R = right, L = left.

Table 2.
Peak activations for the unpleasant non-arousing focus compared to unpleasant arousing focus conditions in Study 1(n = 41)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
R Supramarginal Gyrus	40	1900	57 -41 37	6.43	5.30
L Superior Occipital Gyrus	19		-34 -72 28	5.78	4.90
L Precuneus	19		-18 -76 42	5.73	4.87
R Middle Frontal Gyrus	9	1712	34 33 30	6.19	5.16
R Middle Frontal Gyrus / R Cingulate Gyrus	32		14 14 42	5.33	4.60
R Middle Frontal Gyrus	6		18 7 57	5.29	4.58
L Insula	13	141	-30 23 1	4.42	3.97
L Insula	13		-42 12 5	4.07	3.70
R Middle Temporal Gyrus	21	41	65 -24 -11	4.34	3.91
R Middle Temporal Gyrus, Temporal Parietal Junction	21		65 -43 -3	2.72	2.59
L Middle Frontal Gyrus	9	255	-30 29 34	4.22	3.81

L Superior Frontal Gyrus	10		-34 47 14	3.88	3.55
L Middle Frontal Gyrus	11		-38 50 -11	3.71	3.42
L Cerebellum		293	-42 -56 -29	4.10	3.73
L Cerebellum			-34 -56 -26	3.77	3.47
L Cerebellum			-26 -58 -2	3.52	3.27
R Parahippocampal Gyrus	19	62	30 -47 -6	3.80	3.49
R Parahippocampal Gyrus	36		30 -39 -10	3.63	3.35
L Middle Temporal Gyrus	21	11	-65 -31 -7	3.31	3.09
L Middle Temporal Gyrus	21		-65 -43 -3	2.96	2.80
R Thalamus		55	14 -19 18	3.22	3.01
R Thalamus			10 -12 2	3.09	2.91
R Lentiform Nucleus, Putamen			26 -8 2	2.75	2.61
R Supramarginal Gyrus	40	1900	57 -41 37	6.43	5.30

Peak activations from random effects analysis are listed with a threshold of $p < .025$, FDR corrected, and cluster filter of 10 contiguous voxels.
BA = Brodmann's area, R = right, L = left.

Table 3.
Peak activations for unpleasant non-arousing focus compared to unpleasant arousing focus conditions in Study 2 (n = 47)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
R Supramarginal Gyrus	40	2214	56 -50 28	9.78	7.16
R Superior Temporal Gyrus	39		48 -53 30	9.21	6.90
L Superior Temporal Gyrus	39		-48 -53 29	6.42	5.40
R Middle Frontal Gyrus	8	1220	34 25 41	6.74	5.59
R Superior Frontal Gyrus	10		19 49 25	5.93	5.08
R Superior Frontal Gyrus	10		34 49 19	5.86	5.04
L Parahippocampal Gyrus	37	78	-25 -45 -9	4.74	4.26
L Inferior Temporal Gyrus	20	51	-55 -34 -12	4.57	4.12
R Middle Temporal Gyrus	21	13	42 1 -29	4.32	3.93
L Superior Frontal Gyrus	10	64	-33 49 25	4.14	3.80
L Superior Frontal Gyrus	10		-25 46 17	3.33	3.13
L Middle Frontal Gyrus	8	136	-33 17 43	4.10	3.76

L Middle Frontal Gyrus	9		-33 29 34	3.33	3.13
L Middle Frontal Gyrus	6		-44 13 46	3.05	2.89
L Cerebellum		56	-36 -54 -36	3.80	3.53
L Cerebellum			-40 -46 -36	3.18	3.01

Peak activations from random effects analysis are listed with a threshold of $p < .025$, FDR corrected, and cluster filter of 10 contiguous voxels.
BA= Brodmann's area, R = right, L = left.

Table 4.
Means (and standard deviations) for ratings of negative affect intensity (1 being "not intense at all" and 4 being "very intense") following each condition

	Unpleasant No Focus	Unpleasant Arousing Focus	Unpleasant Non-arousing Focus	Neutral No Focus	Neutral Non-arousing Focus
Affect Rating Study 1 (n = 41)	3.18 (.84)	3.22 (.77)	2.11 (.75)	1.05 (.28)	1.07 (.30)
Affect Rating Study 2 (n = 47)	3.09 (.65)	3.16 (.63)	2.43 (.74)	1.14 (.27)	1.15 (.29)

Table 5.
Means (and standard deviations) for average dwell time and percent dwell time (dwell time in IA/total dwell time – time to first fixation in IA) in the interest area (IA) per image (4000 ms presentation)

	Unpleasant No Focus (No visible IA)	Unpleasant Arousing Focus	Unpleasant Non-arousing Focus	Neutral No Focus (No visible IA)	Neutral Non-arousing Focus
Study 1 Dwell Time in ms (n = 5)	Arousing: 1136.74 (496.18) Non-arousing: 126.38 (24.00)	2800.43 (382.80)	2774.68 (281.67)	434.48 (170.46)	3085.68 (343.55)
Study 1 Percent Dwell Time (n = 5)	Arousing: 41% Non-arousing: 4%	82%	87%	17%	90%
Study 2 Dwell Time in ms (n = 47)	Arousing: 1410.39 (282.53) Non-arousing: 202.39 (115.04)	3312.09 (283.77)	3168.30 (331.49)	447.24 (132.65)	3317.24 (304.56)
Study 2 Percent Dwell Time (n = 47)	Arousing: 47% Non-arousing: 5%	96%	97%	18%	99%

Table 6.
Peak activations for unpleasant no focus compared to unpleasant arousing focus conditions in Study 2 (n = 42)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
L Cuneus	17	2463	-3 -85 9	17.56	>8
L Middle Occipital Gyrus	18		-14 -89 15	14.49	>8
R Middle Occipital Gyrus	18		11 -93 15	14.42	>8
L Caudate		44	-14 16 18	5.02	4.41
L Caudate			-18 16 11	4.8	4.25
L Lentiform Nucleus, Putamen			-21 9 10	4.29	3.88
L Cerebellum		111	-14 -50 -39	4.82	4.26
L Cerebellum			-3 -54 -39	4.78	4.23
L Cerebellum			-17 -58 -36	4.39	3.95
R Caudate		64	16 20 15	4.8	4.25
R Caudate			19 13 11	4.72	4.19
R Lentiform Nucleus, Putamen			19 14 0	4.3	3.88
R Middle Temporal Gyrus	21	15	53 -4 -19	3.99	3.65

Peak activations from random effects analysis are listed with a threshold of $p < .001$, uncorrected, and cluster filter of 10 contiguous voxels. BA= Brodmann's area, R = right, L = left.

Table 7.
Peak activations for unpleasant arousing focus compared to unpleasant no focus conditions in Study 2 (n = 42)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
L Inferior Parietal Lobe	40	662	-37 -43 41	8.91	6.61
L Precuneus	7		-29 -47 41	8.62	6.48
L Superior Parietal Lobe	7		-26 -63 54	7.72	6.03
L Precentral Gyrus	6	149	-48 -1 34	7.46	5.9
L Middle Frontal Gyrus	6		-26 -6 52	4.39	3.95
L Precentral Gyrus	6		-48 -2 48	4.36	3.93
R Inferior Parietal Lobe	40	667	33 -44 49	7.45	5.89
R Superior Parietal Lobe	7		14 -67 54	7.39	5.86
R Inferior Parietal Lobe	40		37 -39 39	6.63	5.43
R Middle Frontal Gyrus	6	107	26 -4 60	5.8	4.92
R Precentral Gyrus	6		41 -10 45	3.98	3.64
L Middle Frontal Gyrus	10	32	-32 43 6	4.22	3.82
L Inferior Temporal Gyrus	20	26	-55 -57 -11	4.08	3.72
L Middle Occipital Gyrus	19		-47 -61 -8	4.03	3.68
L Inferior Temporal Gyrus	20		-55 -49 -14	3.82	3.51
R Middle Frontal Gyrus	8	10	41 29 38	3.61	3.35

Peak activations from random effects analysis are listed with a threshold of $p < .001$, uncorrected, and cluster filter of 10 contiguous voxels. BA= Brodmann's area, R = right, L = left.

Table 8.
Peak activations for unpleasant no focus compared to unpleasant non-arousing focus conditions in Study 2 (n = 42)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
L Occipital Lobe, Cuneus	17	3944	-7 -85 5	15.51	>8
L Occipital Lobe, Cuneus	18		-10 84 -6	15.47	>8
L Occipital Lobe, Cuneus	17		-14 -92 4	15.37	>8
L Anterior Cingulate	32	26	-3 44 -1	4.98	4.38
L Precentral Gyrus	4	15	-30 -27 68	4.69	4.17
L Postcentral Gyrus	3		-41 -26 61	3.7	3.41
R Subcallosal Gyrus	34	15	27 7 -11	4.12	3.75
R Amygdala			23 0 -19	3.88	3.56

Peak activations from random effects analysis are listed with a threshold of $p < .001$, uncorrected, and cluster filter of 10 contiguous voxels. BA= Brodmann's area, R = right, L = left.

Table 9.
Peak activations for unpleasant non-arousing focus compared to unpleasant no focus conditions in Study 2 (n = 42)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
R Inferior Parietal Lobe	40	880	45 -50 38	11.32	7.58
R Precuneus	7		11 -66 47	7.33	5.83
L Superior Parietal Lobe	7	705	-19 -67 57	7.93	6.14
L Inferior Parietal Lobe	40		-48 -54 36	7.93	6.14
R Middle Frontal Gyrus	10	644	34 46 15	7.31	5.81
R Middle Frontal Gyrus	6		30 0 61	6.88	5.58
R Middle Frontal Gyrus	9		38 29 35	6.72	5.49
L Middle Frontal Gyrus	10	77	-36 43 13	5.81	4.93
L Precentral Gyrus	6	47	-33 -13 44	5.34	4.63
R Middle Temporal Gyrus	21	37	56 -27 -10	4.87	4.3
R Middle Temporal Gyrus	21		56 -39 -4	4.32	3.9
R Insula	13	11	30 16 12	4.46	4
L Middle Temporal Gyrus	21	17	-58 -30 -12	4.22	3.82
L Precentral Gyrus	9	32	-40 21 40	4.21	3.82
L Middle Frontal Gyrus	8		-29 17 40	3.71	3.42
L Precentral Gyrus	6	10	-44 -1 34	4	3.66

Peak activations from random effects analysis are listed with a threshold of $p < .001$, uncorrected, and cluster filter of 10 contiguous voxels. BA= Brodmann's area, R = right, L = left.

Table 10.
PPI results using the right (top) and left (bottom) amygdala as a seed region for unpleasant no focus compared to unpleasant non-arousing focus conditions in Study 2 (n = 42)

	Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
R Amygdala	R Middle Temporal Gyrus	39	566	45 -74 14	5.31	4.61
	L Cerebellum			-36 -60 -15	4.90	4.32
	L Middle Occipital Gyrus	19		-44 -78 12	4.71	4.19
	R Fusiform Gyrus	20	57	38 -41 -15	4.88	4.31
	R Parahippocampal Gyrus	36		27 -42 -8	4.59	4.10
L Amygdala	L Cerebellum		252	-36 -64 -11	5.31	4.60
	L Lingual Gyrus	18		-18 -76 -9	4.66	4.15
	L Middle Occipital Gyrus	18		-29 -93 11	4.28	3.86
	R Fusiform Gyrus	37	176	30 -45 -12	4.57	4.08
	R Fusiform Gyrus	19		23 -68 -7	4.25	3.84
	R Fusiform Gyrus	37		45 -64 -10	4.03	3.67
	R Middle Temporal Gyrus	39	84	45 -74 14	4.38	3.94
	R Middle Occipital Gyrus	18		41 -81 3	3.97	3.63
	R Middle Occipital Gyrus	19		34 -82 20	3.95	3.62
	L Orbital Frontal Gyrus	47	10	-36 30 -10	4.17	3.78
	L Orbital Frontal Gyrus	47		-43 37 -6	3.87	3.55
	L Lingual Gyrus	17	11	-7 -88 1	3.90	3.57
	Left Lingual Gyrus	18		-11 -99 -3	3.33	3.12

Peak activations are listed with a threshold of $p < .001$, uncorrected, and cluster filter of 10 contiguous voxels. BA= Brodmann's area, R = right, L = left.

Table 11.
PPI results using the right (top) and left (bottom) amygdala as a seed region for unpleasant non-arousing focus compared to unpleasant no focus conditions in Study 2 (n = 42)

	Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
R Amygdala	R Cuneus	7	48	4 -68 32	3.95	3.62
	R Precuneus	7		11 -61 33	3.85	3.53
	R Precuneus	7		-11 -61 36	3.84	3.53
L Amygdala	R Precuneus	7	35	7 -57 33	4.27	3.86
	R Precuneus	31		15 -53 30	4.21	3.81
	R Precuneus	31		11 -45 27	3.62	3.35

Peak activations are listed with a threshold of $p < .001$, uncorrected, and cluster filter of 10 contiguous voxels. BA= Brodmann's area, R = right, L = left.

Table 12.
Peak activations for unpleasant no focus compared to neutral no focus in Study 2 (n = 47)

Region	BA	Cluster Size	Talairach Coordinates	T	Z
Whole Brain Analysis					
L Inferior Temporal Gyrus		8836	-44 -73 2	15.83	Inf.
R Inferior Occipital Gyrus	19		40 -75 -8	15.13	Inf.
R Fusiform Gyrus	37		45 -61 1	13.58	Inf.
L Medial Frontal Gyrus	8	876	1 40 42	8.57	6.59
L Anterior Cingulate Cortex	32		-3 44 -4	5.92	5.08
R Superior Frontal Gyrus	6		8 30 60	4.85	4.33
R Post Central Gyrus	2	61	56 -24 37	4.68	4.21
Amygdala ROI Analysis					
R Amygdala		27		6.92	5.70
L Amygdala		27		6.48	5.44
L Amygdala				5.72	4.95
L Amygdala				5.40	4.72

Peak activations from random effects analysis are listed with a threshold of $p < .025$, FDR corrected, and cluster filter of 10 contiguous voxels.
BA = Brodmann's area, R = right, L = left.

Table 13.
Means (and standard deviations) for ratings of negative affect intensity (1 being "not intense at all" and 4 being "very intense") following each condition for men and women in Study 2 (n = 47)

	Unpleasant No Focus	Unpleasant Arousing Focus	Unpleasant Non-arousing Focus	Neutral No Focus	Neutral Non-arousing Focus
Men	2.83 (.60)	2.98 (.59)	2.30 (.74)	1.02 (.07)	1.06 (.11)
Women	3.33 (.61)	3.31 (.64)	2.54 (.73)	1.25 (.33)	1.22 (.37)

Table 14.
Means (and standard deviations) for scores on the emotion regulation questionnaire and the attentional control scale for men and women in Study 2 (n = 47)

	Reappraisal	Suppression	Attentional Control Scale Total	Attentional Control Scale Shifting	Attentional Control Scale Focusing
Men	29.23 (8.29)	15.09 (5.38)	55.68 (9.03)	31.23 (5.67)	24.45 (4.12)
Women	30.40 (6.68)	14 (5.38)	50.24 (8.21)	28.84 (3.90)	21.40 (5.00)

Table 15.
Peak activations for regions with greater activation for women compared to men during the unpleasant no focus compared to neutral no focus conditions in Study 2 (n = 47)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
Whole Brain Analysis					
R Superior Temporal Gyrus	22	7402	58 -52 14	5.54	4.81
R Middle Temporal Gyrus	21		54 -48 2	5.34	4.67
L Cerebellum, Culmen			-46 -52 -18	4.91	4.37
L Superior Frontal Gyrus	8	39	-18 60 34	3.98	3.67
R Superior Temporal Gyrus	38	16	46 8 -34	2.93	2.79
ROI Analysis					
Amygdala		12	22 4 -18	2.83	2.70
			30 0 -14	2.74	2.62
Hippocampus		10	-34 -28 -6	3.58	3.34
		23	-26 -12 -18	3.06	2.90
		18	34 -12 -14	2.93	2.79
			42 -20 -14	2.57	2.47
Thalamus		238	-14 -24 6	4.10	3.76
			6 -12 14	3.88	3.58
			6 -24 10	3.63	3.38
ACC		23	-2 0 30	3.59	3.35
			-2 20 30	2.54	2.44
Middle Frontal Gyrus	46	19	54 28 14	3.89	3.59
		19	-42 36 14	3.82	3.54
Middle Frontal Gyrus	9	43	-54 8 38	4.13	3.78
			-42 16 38	3.26	3.07
			-46 24 42	3.03	2.87

		17	6 52 42	3.90	3.60
			14 60 34	3.87	3.58
			26 56 34	2.69	2.58
		61	54 16 30	3.64	3.39
			50 16 38	3.33	3.13
			62 12 30	3.19	3.02
Medial Frontal Gyrus	10	38	18 60 30	3.91	3.61
			10 64 26	3.60	3.36
			26 56 26	3.41	3.20
		13	-18 56 30	3.14	2.97
Visual Cortex	17/18/19	124	-18 -84 -18	3.72	3.45
			-10 -92 10	3.27	3.08
			-2 -80 -6	3.22	3.04
Middle Temporal Gyrus	37	31	-46 -52 -18	4.91	4.37
			-58 -60 -10	4.29	3.91
			-58 -52 -14	4.27	3.89
Cerebellum		10	46 -64 -22	4.04	3.71
			42 -72 -22	2.87	2.73
		267	-18 -80 -42	3.85	3.56
			-34 -76 -42	3.52	3.29
			-14 -84 -18	3.48	3.26
		118	22 -76 -46	3.25	3.07
			10 -72 -34	3.14	2.97
			34 -48 -30	2.80	2.67

Peak activations are listed with a threshold of $p < .025$, FDR corrected, and cluster filter of 5 contiguous voxels. BA= Brodmann's area, R = right, L = left.

Table 16.
Peak activations for regions with greater activation for men compared to women during the neutral no focus compared to fixation in Study 2 (n = 47)

Region	BA	Cluster Size	Talairach Coordinates	Peak T	Peak Z
Whole Brain Analysis					
R Insula	13	127	30 32 -2	5.43	4.74
R Inferior Frontal Gyrus	13		46 24 2	4.44	4.02
R Inferior Frontal Gyrus	45		54 28 6	4.06	3.73
L Cuneus,	19	239	-2 -76 42	4.89	4.36
L Postcentral Gyrus	5		-2 -36 74	4.61	4.15
R Cuneus	19		18 -80 42	4.32	3.94
L Cerebellum, Declive		119	-22 -76 -22	4.74	4.25
L Cerebellum, Culmen			-18 -36 -26	3.97	3.66
L Cerebellum			-26 -56 -30	3.79	3.51
L Lingual Gyrus	18	11	-6 -96 -6	4.28	3.89
L Cerebellum, Declive			2 -84 -6	3.25	3.06
L Superior Frontal Gyrus	6	7	-6 28 66	4.16	3.81
R Cuneus	17	19	14 -96 14	4.06	3.73
L Inferior Frontal Gyrus	13	19	-54 16 -2	4.00	3.68
L Precuneus	19	14	-26 -72 38	3.93	3.62
R Precentral Gyrus	6	18	50 4 34	3.86	3.57
R Precentral Gyrus	6	7	42 -4 62	3.69	3.43
R Cerebellum, Declive		22	6 -68 -14	3.59	3.35
R Cerebellum, Culmen			6 -56 2	3.40	3.19
R Amygdala		8	22 -4 -18	3.57	3.33
L Middle Frontal Gyrus	8	10	-34 28 38	3.48	3.28
L Cuneus	17	6	-6 -80 14	3.48	3.26
L Insula	13	7	-42 20 6	3.44	3.22

L Insula	13		-38 20 -2	3.33	3.13
L Superior Frontal Gyrus	6	5	-6 -8 70	3.40	3.19
ROI Analysis					
Amygdala		5	22 -4 -18	3.57	3.33
Hippocampus		0		n/a	n/a
Thalamus		0		n/a	n/a
ACC		0		n/a	n/a
Middle Frontal Gyrus	46	0		n/a	n/a
Middle Frontal Gyrus	9	8		3.86	3.57
Medial Frontal Gyrus	10	0		n/a	n/a
Visual Cortex	17/18/19	8	-6 -96 -6	4.28	3.89
			2 -84 -6	3.24	3.06
		6	14 -84 34	3.95	3.64
			6 -80 34	3.78	3.51
		12	14 -100 14	3.86	3.57
Middle Temporal Gyrus	37	0		n/a	n/a
Cerebellum		112	-22 -76 -22	4.74	4.25
			-18 -36 -26	3.97	3.66
			-26 -56 -30	3.79	3.51

Peak activations are listed with a threshold of $p < .025$, FDR corrected, and cluster filter of 5 contiguous voxels. BA= Brodmann's area, R = right, L = left

Figure 1. Depiction of a neutral non-arousing focus block followed by a neutral no focus block. Each block began with a 5000 ms instruction screen indicating if the subject was to focus on the contents of the blue circle or to freely view the following set of images. This was followed by the presentation of 5 images for 4000 ms each. Participants were then given 5000 ms to rate the intensity of their negative affect on a scale of 1 to 4. Finally, participants saw fixations presented on a grey background for 20000 ms (Font size is not to scale).

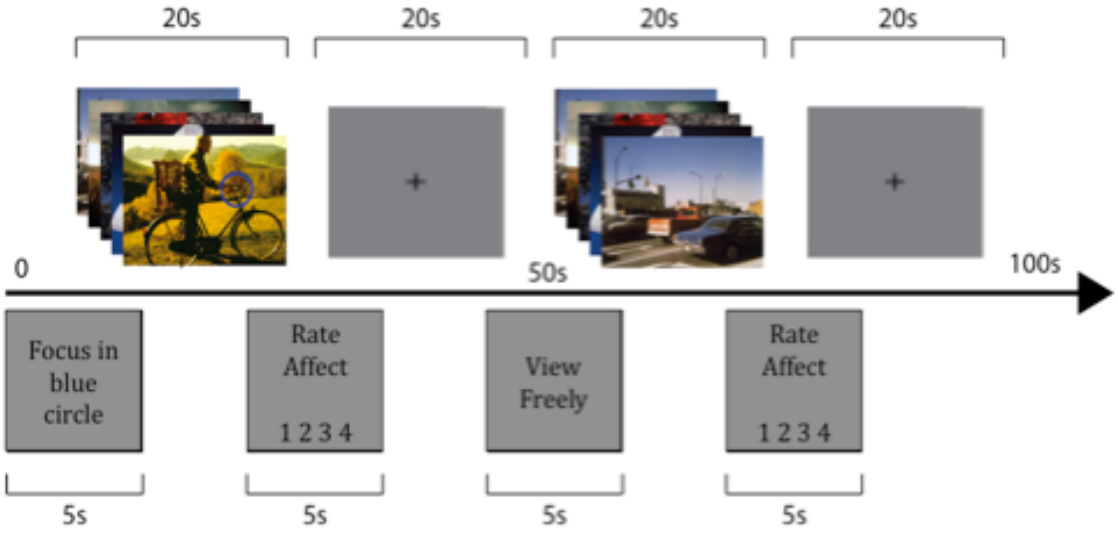

Figure 2. Regions of the brain more active in response to unpleasant arousing focus compared to unpleasant non-arousing focus trials in Study 2.

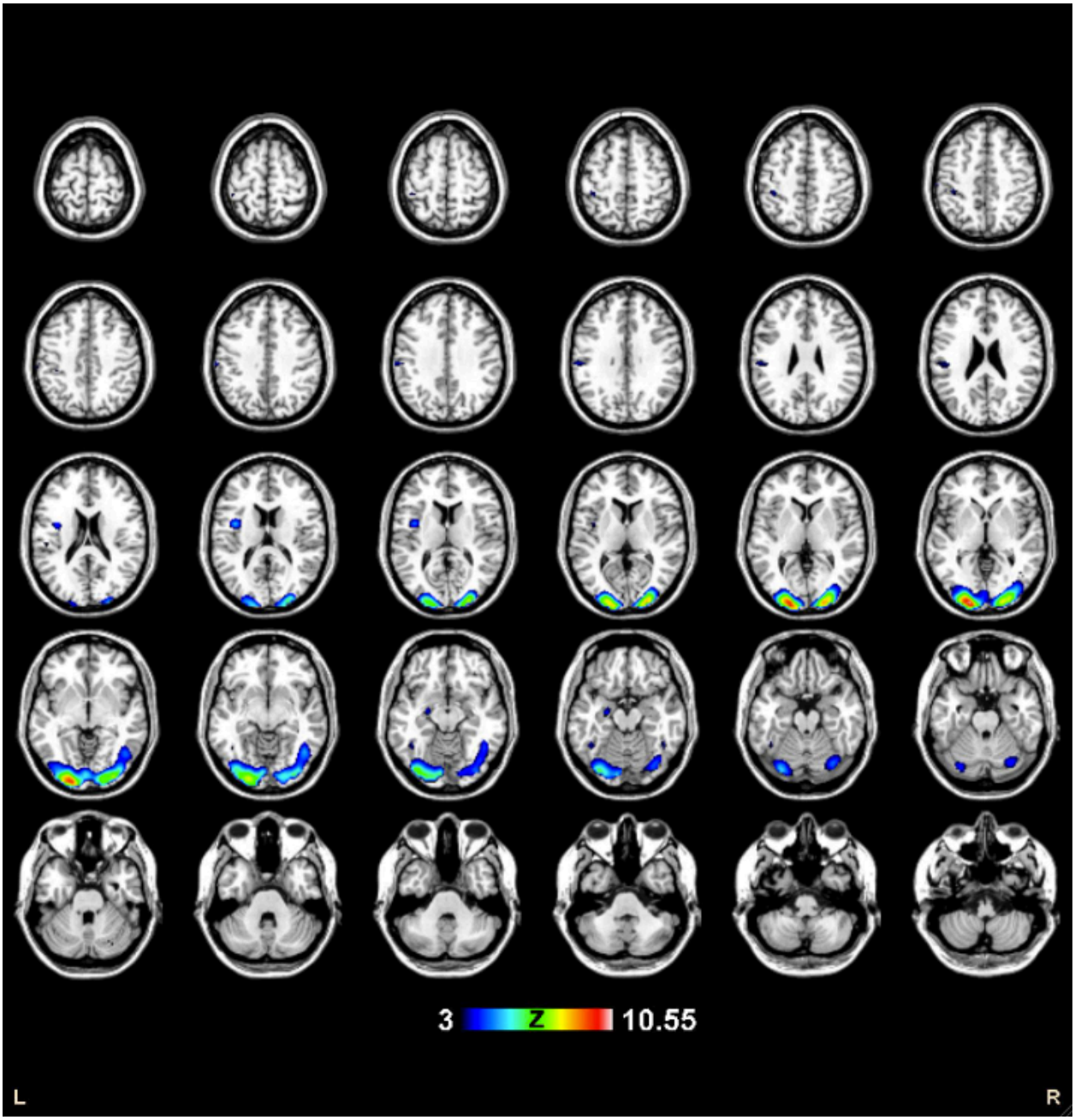

Figure 3. Regions of the brain more active for unpleasant non-arousing focus compared to unpleasant arousing focus in Study 1 (n = 41).

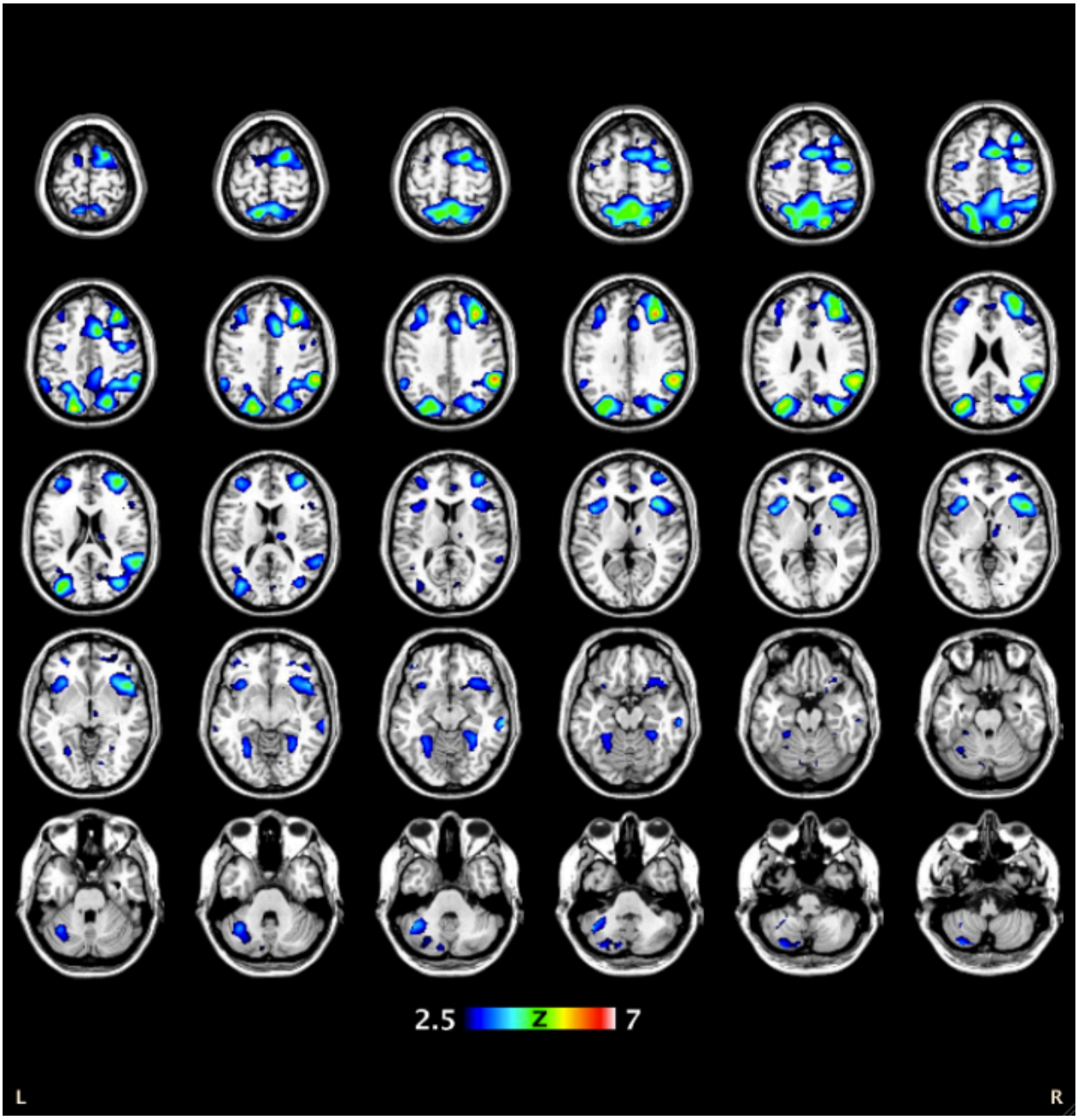

Figure 4. Regions of the brain more active for unpleasant non-arousing focus compared to unpleasant arousing focus in Study 2 (n = 47).

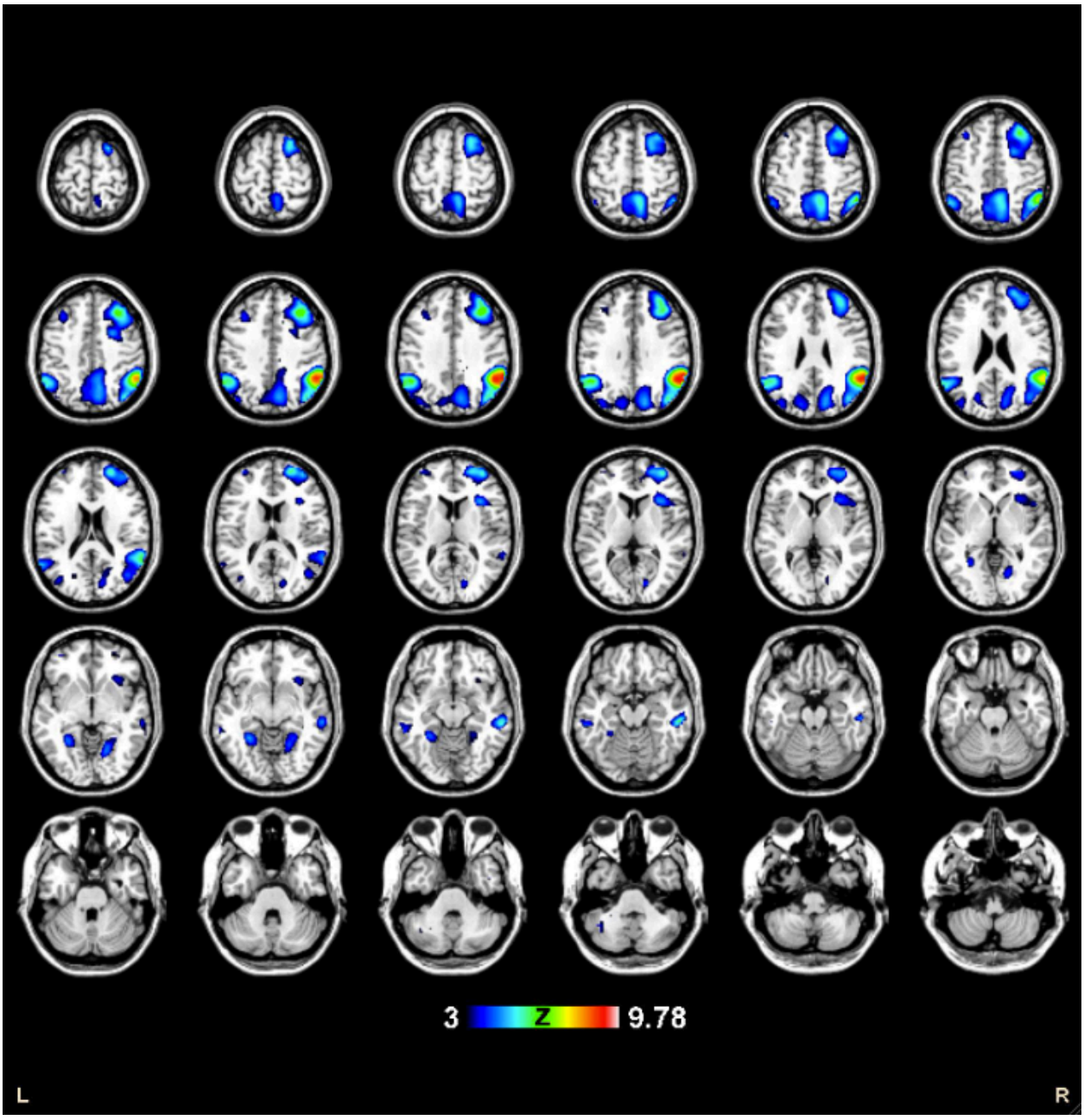

Figure 5. Positive correlation between negative affect following unpleasant non-arousing focus trials and number of fixations to the arousing region during unpleasant non-arousing focus trials (left) and between negative affect following unpleasant non-arousing focus trials and dwell time in the arousing region during unpleasant non-arousing focus trials (right) in Study 2 (n = 47).

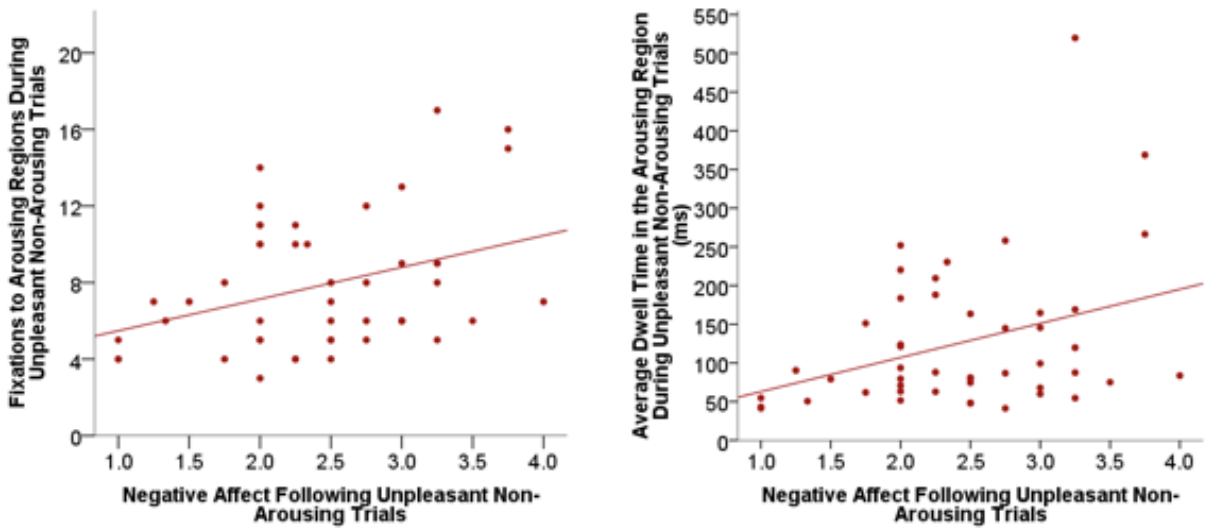

Figure 6. Regions of the brain more active in response to unpleasant no focus compared to unpleasant arousing focus trials in Study 2 (n = 42).

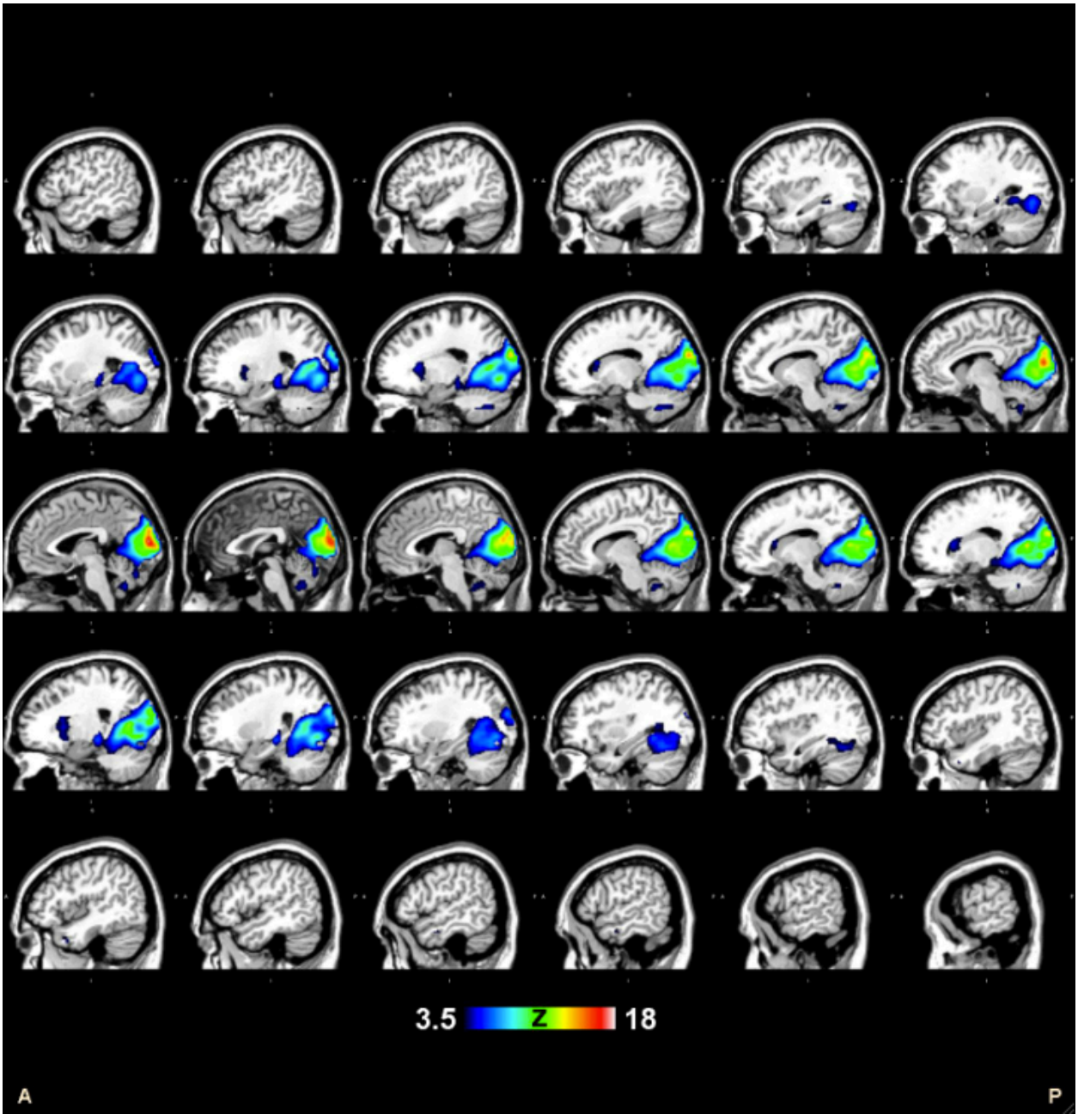

Figure 7. Regions of the brain more active in response to unpleasant arousing focus compared to unpleasant no focus trials in Study 2 (n = 42).

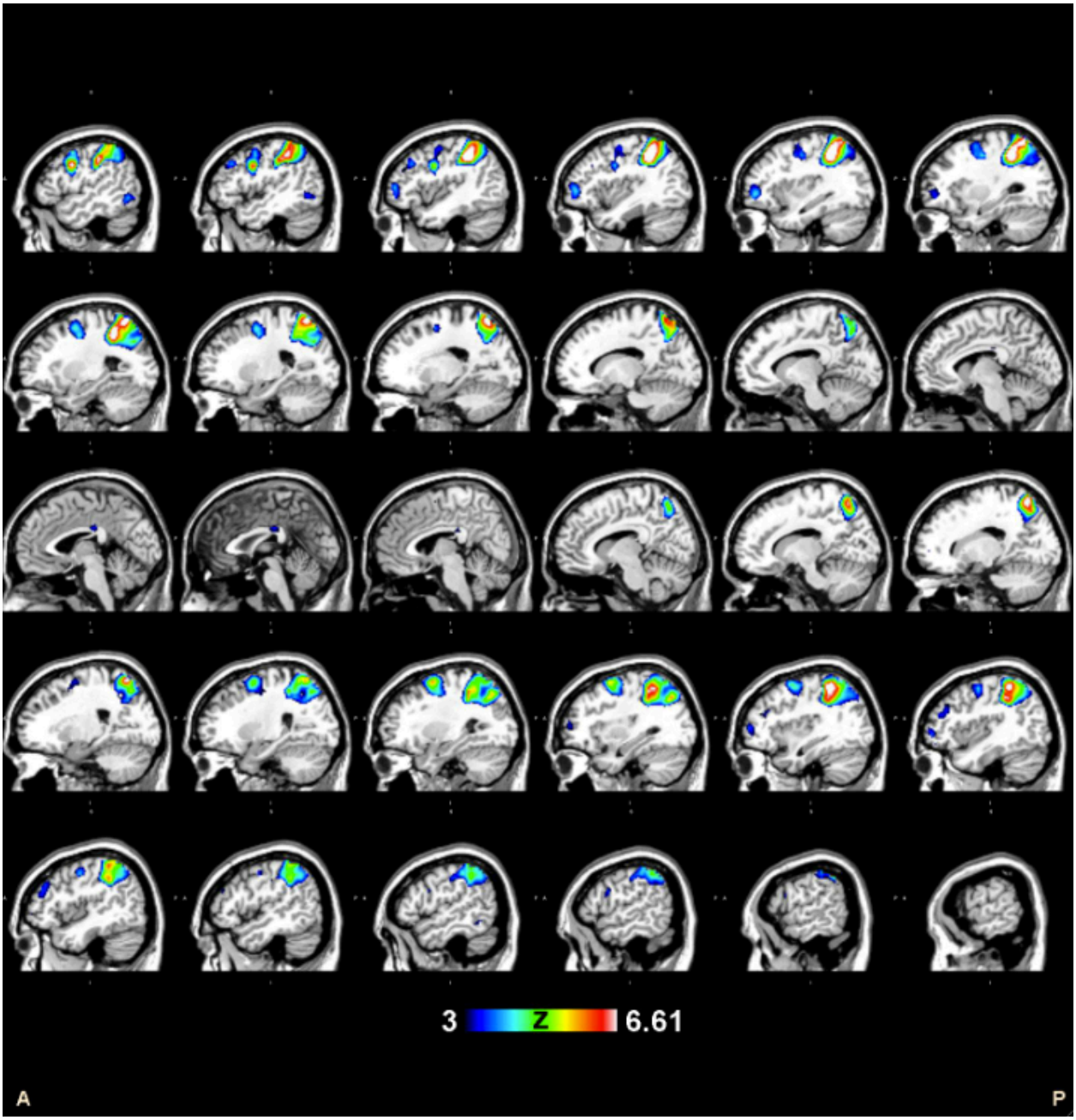

Figure 8. Regions of the brain more active in response to unpleasant no focus compared to unpleasant non-arousing focus trials in Study 2 (n = 42).

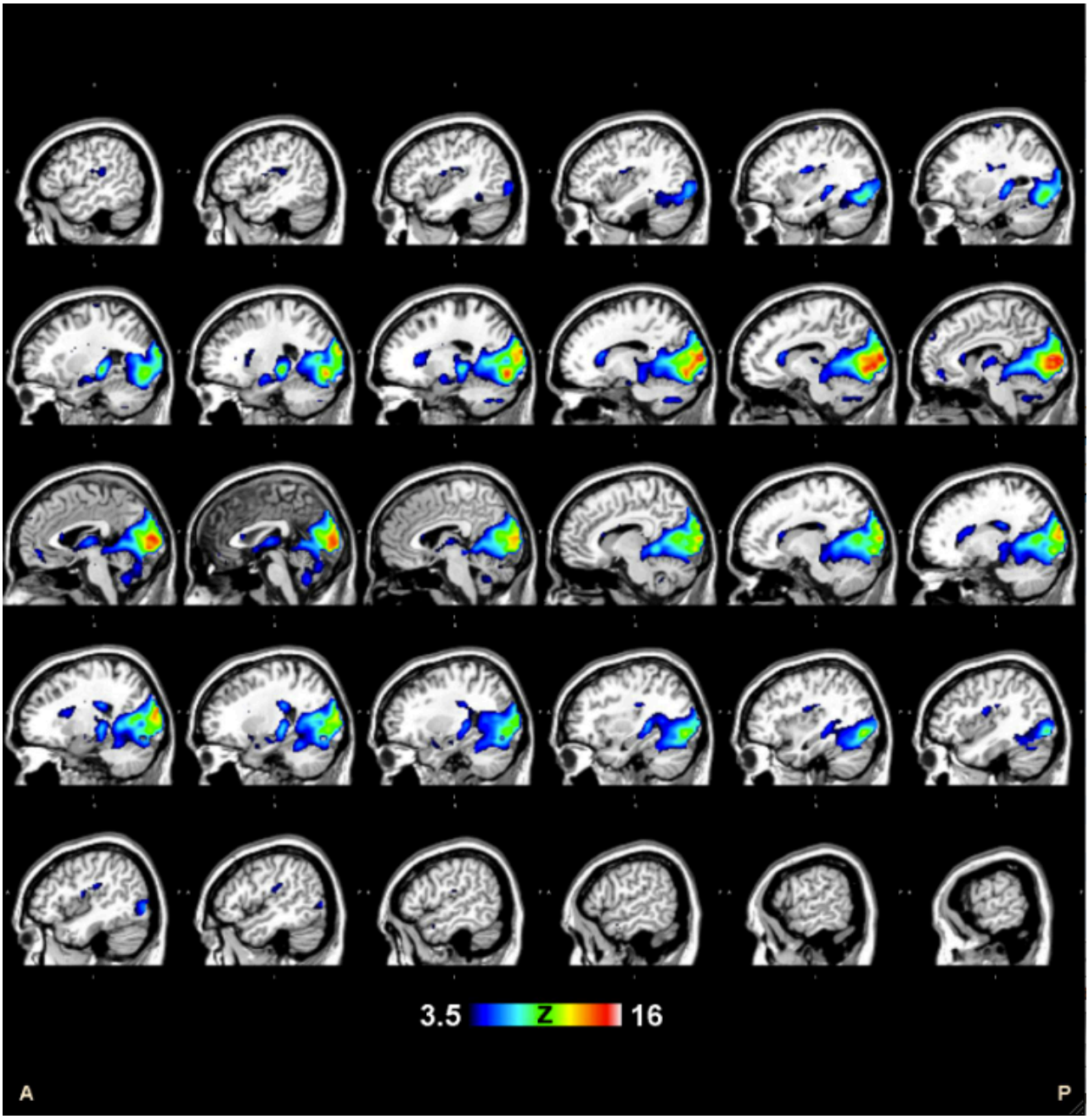

Figure 9. Regions of the brain more active in response to unpleasant non-arousing focus compared to unpleasant no focus trials in Study 2 (n = 42).

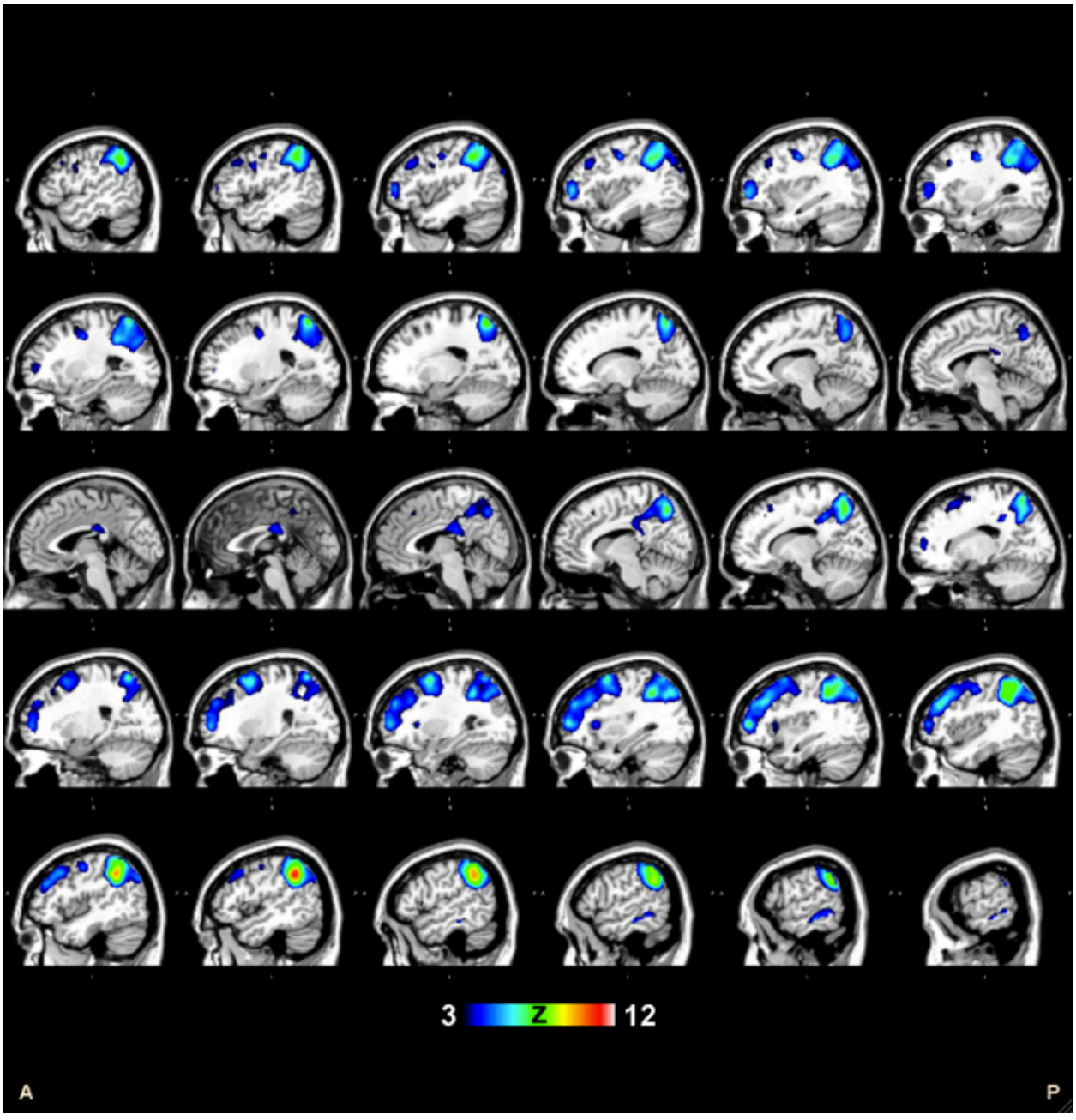

Figure 10. Regions of the brain depicting greater connectivity during the unpleasant no focus condition compared to the unpleasant non-arousing focus condition with the left amygdala (top) and right amygdala (bottom) in Study 2 (n = 42).

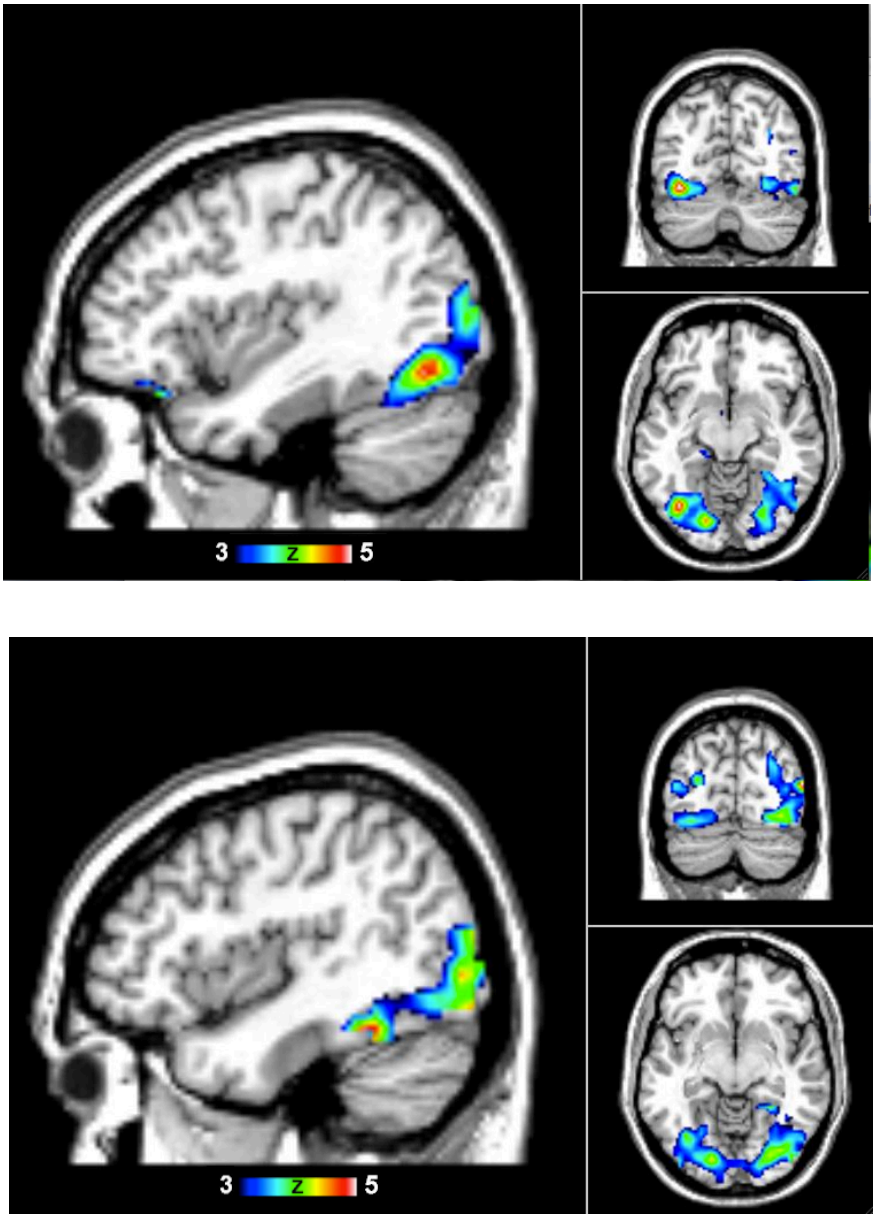

Figure 11. Regions of the brain depicting greater connectivity during the unpleasant non-arousing focus condition compared to the unpleasant no focus condition with the left amygdala (top) and right amygdala (bottom) in Study 2 (n = 42).

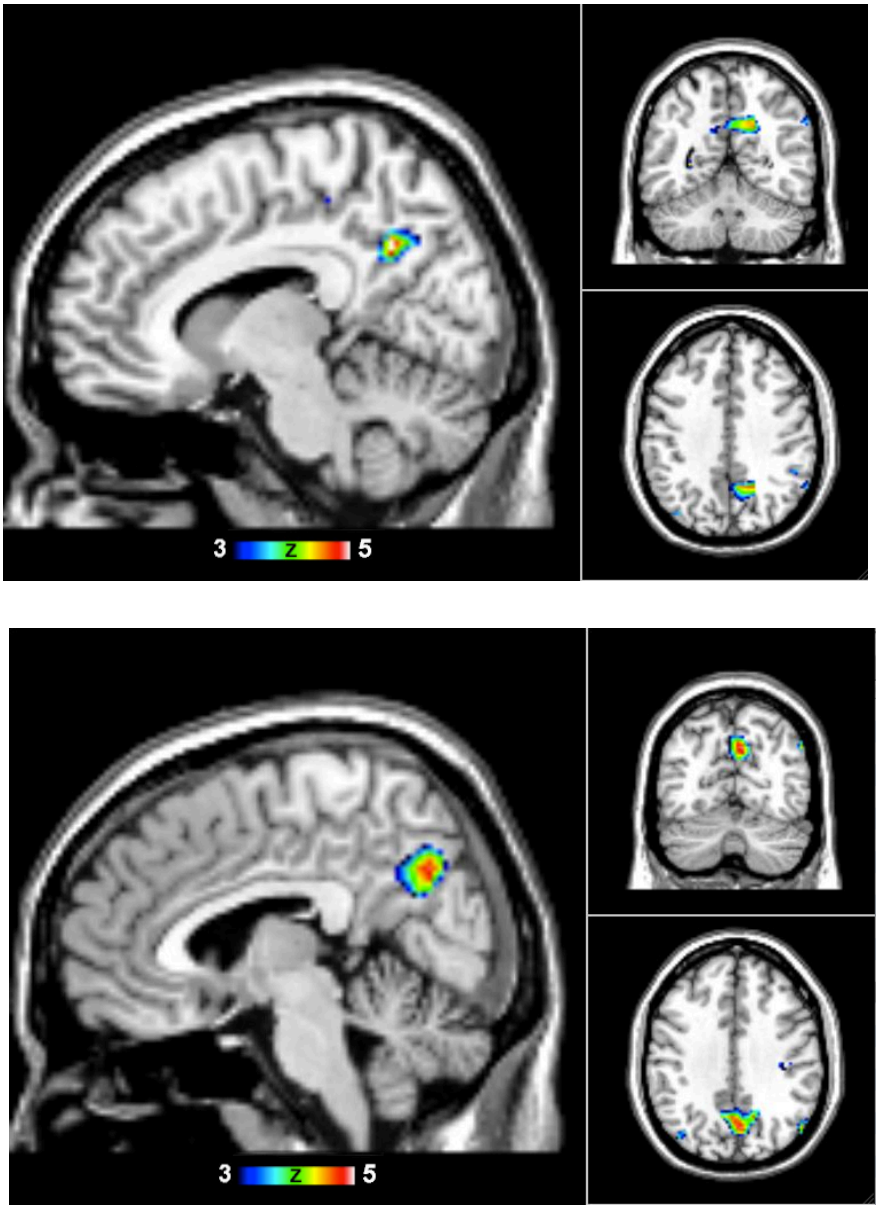

Figure 12. Regions of the brain more active in response to unpleasant no focus compared to neutral no focus trials in Study 2 (n = 47).

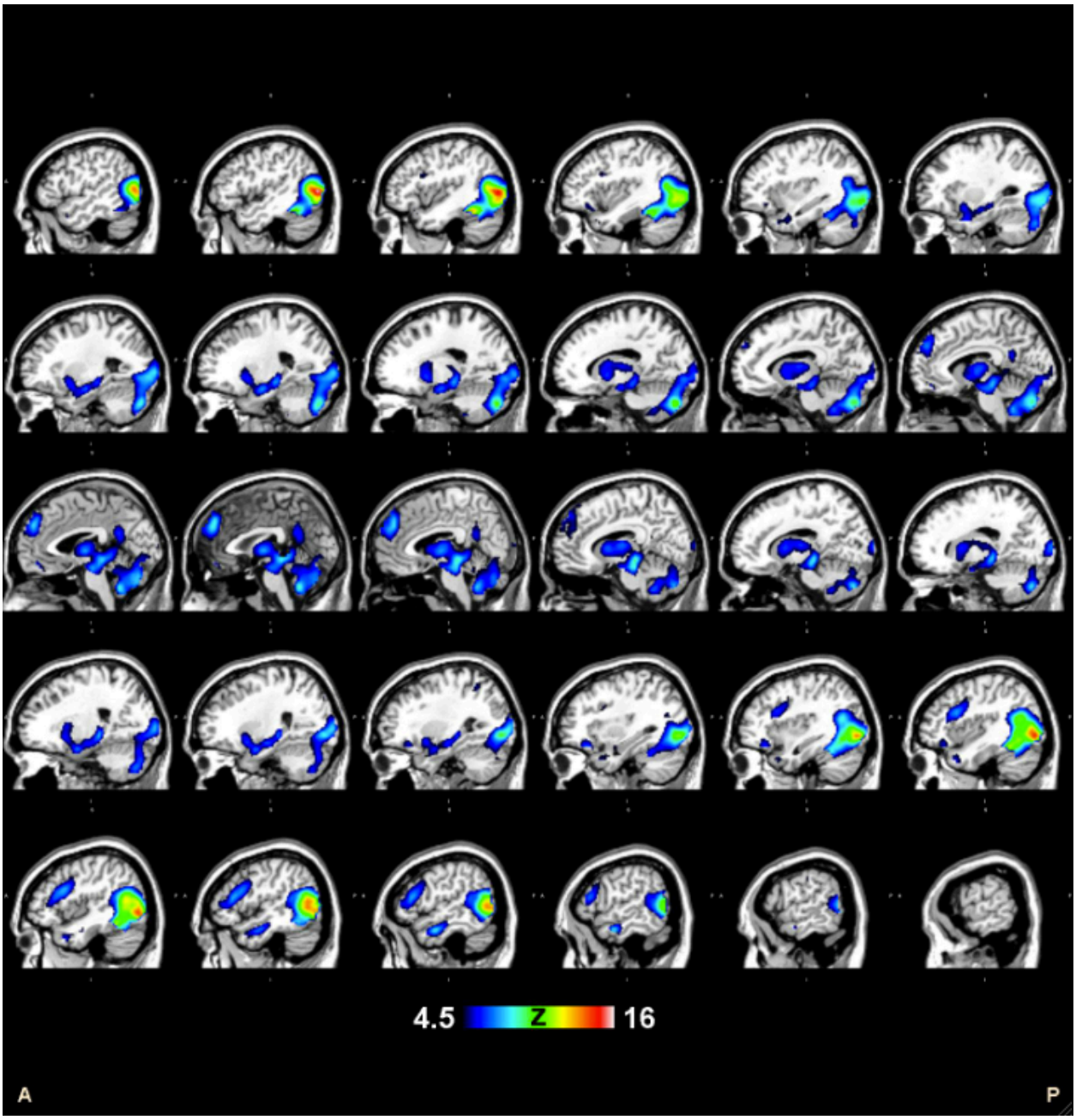

Figure 13. Regions of the brain depicting gender differences in response to unpleasant no focus compared to neutral no focus trials in Study 2 (n = 47).

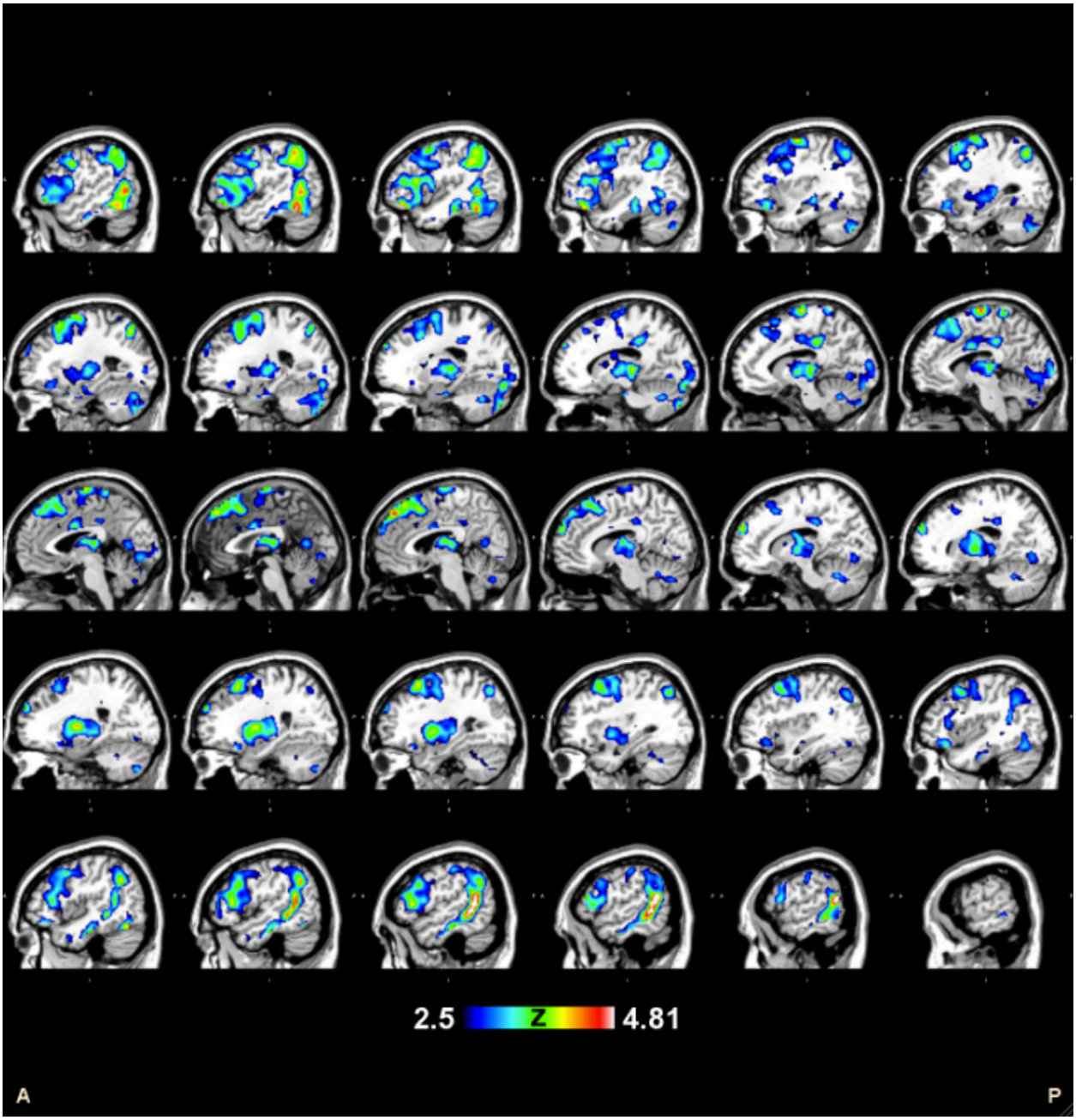

Figure 14. Regions of the brain depicting gender differences in response to neutral no focus trials compared to fixation in Study 2 (n = 47).