PREFRONTAL REGULATION OF BODY IMAGE IN AGING AND RECOVERY FROM ANOREXIA NERVOSA

By

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TABLE OF CONTENTS

TABLE OF CONTENTS (continued)

Abbreviations

AN Anorexia Nervosa
PFC Prefrontal cortex
fMRI functional Magnetic Resonance Imaging
FG Fusiform Gyrus
EBA Extrastriate Body Area

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Abstract

In addition to characterizing body image in these samples, the goals for this dissertation were to examine affective responses to bodies and to examine how affective regulation of body image affects prefrontal cortical function in the brain. Two models were used: 1) older versus younger women, and 2) women who had recovered from anorexia nervosa (AN) versus women who had never had an eating disorder.

The study in Chapter 1 compared body image in younger versus older women using standardized questionnaires and behavioral measures of women's responses to fatter and thinner images of their own bodies. Younger and older women reported similar body dissatisfaction, but younger women reported a higher drive for thinness and experienced more societal influence on their body image than older women. Images of one's own body versus line drawings of bodies resulted in similar ratings of body dissatisfaction in younger and older women. These data suggest that age affects particular facets of body image, but that ratings of body image do not differ in normal, healthy younger and older women when personalized measures are used.

For the study in Chapter 2, women assigned valence ratings to bodies of varying sizes, and then a subset of those bodies were used as distracters in a working memory task. Younger and older women both rated normal weight bodies as most positive, were slower to categorize bodies as positive than to categorize them as negative, and rated a smaller percentage of bodies as positive than as negative. Additionally, positive bodies were more disruptive to working memory performance than negative or neutral bodies in both younger and older women. Thus, despite older women experiencing less negative affect than younger women, these groups did not differ in their affective responses to

bodies or the disruption of working memory by bodies. This suggests that the positivity bias in aging does not extend to body stimuli in women nor influence the emotional disruption of working memory.

The study in Chapter 3 used fMRI to examine brain activity in women who had recovered from AN versus healthy controls when bodies of varying sizes were used as distracter stimuli in a working memory task. Bodies rated as negative were more disruptive to working memory than bodies rated as neutral or positive in women who had recovered from AN and in controls. Although working memory performance was similar in both groups, underlying brain activity differed. The amygdala activated during the working memory task in women who had recovered from AN but not in controls, and the fusiform responded more in response to bodies in women who had recovered from AN than in control women. There was more suppression of medial prefrontal cortex activity in women who had recovered from AN than in controls when the distracter stimulus was a negative body. These results suggested that higher amygdala and fusiform activity in response to body stimuli occurred despite recovery and that medial prefrontal suppression may have permitted recovery in the face of continued negativity towards bodies in women who had recovered from AN.

Overall, older women had similar behavioral outcomes regarding body stimuli as younger women, despite experiencing less negative affect and having overall better body image. Women who recovered from AN also had similar behavioral outcomes as control women; however, they had different underlying brain activation. This suggests that similar behavior relies on differential brain activity and that compensatory mechanisms involve suppression of the default network in order to produce normal cognitive performance.

Introduction

The cognitive and neural basis of body image issues are important to understand because the development of abnormal perceptions of body shape and size lead to life-threatening disorders of eating. Body image disturbance has been implicated in the development of anorexia nervosa (AN), which is associated with one of the highest standardized mortality ratios of any illness. In fact, women with AN have a higher mortality rate than the general population. Body image disturbance may also contribute to younger and older women's use of dieting, exercise, bingeing, surgery, smoking, and a variety of pills (e.g. laxatives, diuretics, herbal supplements) to change their bodies. Therefore, the long term goal of this research was to understand the cognitive and neural basis of body image in women. Two models were used: 1) older versus younger women, and 2) women who had recovered from AN versus women who had never had an eating disorder. In addition to characterizing body image in these samples, the goals for this dissertation were to examine affective responses to body stimuli and to examine how body stimuli affect prefrontal cortical function in the brain. Previous work in the fields of emotion, body image, body perception, eating disorders, and aging led to my questions about the neural control of body image. My hypotheses were that older women would have more positive responses to bodies than younger women and that women who had recovered from AN would have similar affective responses to bodies as control women. Furthermore, I proposed that a higher prefrontal response to body stimuli would yield less negative body image in both of my models.

The brain circuitry of body image

Many regions contribute to perception and analysis of body image. I chose to focus on brain regions involved in perceiving body stimuli (Peelen & Downing, 2005; Downing, Jiang, Shuman, & Kanwisher, 2001; Daprati, Sirigu, & Nico, 2010) and responding to emotional stimuli (Ochsner et al., 2004; Roalf, Pruis, Stevens, & Janowsky, 2009; Zald, 2003).

Brain regions that respond to body stimuli

The parietal cortex is involved in somatoperception and somatorepresentation, both of which may be disrupted in women with eating disorders (Longo, Azanon, & Haggard, 2010). Somatoperception includes the spatial representation and recognition of one's body and also the physical feelings inside of one's body (Longo et al., 2010). For example, in healthy, younger adults, the parietal cortex is involved in coding the location of body parts (McCrea, 2007), the spatial relationship among body parts (Corradi-Dell'Acqua, Hesse, Rumiati, & Fink, 2008), and the location of one's own body parts in space and time (Corradi-Dell'Acqua, Tomasino, & Fink, 2009). Somatorepresentation refers to the knowledge and attitude one has about one's body (Longo et al., 2010). For example, the names of body parts and how one feels about the appearance of their body (Longo et al., 2010). Lesions to the parietal cortex can lead to problems naming body parts, attending to and perceiving one's own body parts, and localizing one's body or body parts in space (Longo et al., 2010), which supports the idea that this region is involved in perception and representation of body stimuli. Although the parietal cortex is involved in the perception and representation of one's body, it is not necessarily body specific (Sack, 2009). This region is also involved in the spatial representation of many other types of stimuli and tasks (Culham & Kanwisher, 2001), including mental rotation (Cohen et al., 1996), angle orientation (Trojano et al., 2000; Sack et al., 2002), and color discrimination (Sack et al., 2002). In older adults, the parietal cortex responds to face stimuli (Gunning-Dixon et al., 2003), but little is known at present about the neural representation of body stimuli in older adults.

The extrastriate body area (EBA) contributes specifically to the perception of bodies (Peelen & Downing, 2007). In younger adults, the EBA responds more to human bodies and parts of bodies, either as pictures, silhouettes, or line drawings, than to other types of objects or parts of objects (Downing et al., 2001; Downing, Chan, Peelen, Dodds, & Kanwisher, 2006). Disruption of function in this area with repetitive transcranial magnetic stimulation slows reaction time for the perception of body parts but not the perception of face parts or objects (Urgesi, Berlucchi, & Aglioti, 2004), which supports the idea that this region's function is specific to bodies. To date, there are no studies explicitly localizing and testing the function of the EBA in older adults.

In younger adults, the fusiform region responds to faces and has been considered face-selective (Haxby, Petit, Ungerleider, & Courtney, 2000; O'Craven & Kanwisher, 2000), meaning that it responds more to faces than other types of stimuli. Lesions in this area impair face recognition (Meadows, 1974), perception of facial configuration (Barton, Press, Keenan, & O'Connor, 2002), and normal processing of upright and inverted faces and bodies (Righart & deGelder, 2007), which supports the idea that this region is involved in face perception. However, recent work in younger adults has shown that the fusiform also responds robustly to bodies (Peelen et al., 2005; Schwarzlose, Baker, & Kanwisher, 2005; Taylor, Wiggett, & Downing, 2007) and is functionally distinct from the EBA (Peelen et al., 2007). Furthermore, the fusiform is sensitive to emotion. Hadjikhani & de Gelder (2003) created body stimuli with blurred faces that were posed in fearful or neutral positions. They found that the fusiform region had higher activation in response to the fearful body expressions than the neutral body expressions (Hadjikhani & deGelder, 2003). Similar results have been found in studies involving face stimuli. Fearful faces activate the fusiform more than neutral (Ishai, Pessoa, Bikle, & Ungerleider, 2004; Pessoa, McKenna, Gutierrez, & Ungerleider, 2002; Vuilleumier, Armony, Driver, & Dolan, 2001) or happy faces (Pessoa et al., 2002), and happy (Morris et al., 1998) and pleasant (Lang et al., 1998) faces activate the fusiform more than neutral faces. In older adults, the fusiform activates in response to faces, including negative, positive, and neutral faces (Iidaka et al., 2002). In some cases, fusiform activation in older adults is equal to (Iidaka et al., 2002) or less than (Tessitore et al., 2005) younger adults. However, it is unknown whether or not the fusiform is sensitive to bodies or expression of emotion in bodies in older adults. The fusiform was chosen over part of the parietal cortex or EBA as a region-of-interest for this dissertation due to its activation in response to bodies and its sensitivity to emotion, which will be pertinent to the body stimuli used in Chapters 1 through 3.

Brain regions that respond to emotional stimuli

The amygdala processes emotional stimuli (Zald, 2003). In younger adults, it is activated by negative emotional stimuli, such as negative scenes (Lane et al., 1997; Liberzon et al., 2000) and fearful faces (Breiter et al., 1996; Morris et al., 1996), but it is also activated in response to positive stimuli (Breiter et al., 1996; Hamann, Ely, Grafton, & Kilts, 1999). The amygdala response decreases over time (i.e. habituates) to repeated emotional stimuli of the same valence category, regardless of whether the stimuli are negative or positive (Breiter et al., 1996; Fischer et al., 2003; Whalen et al., 1998). Furthermore, the amygdala is sensitive to emotion in body stimuli, since it activates more to fearful than to neutral body expressions (Hadjikhani et al., 2003). The amygdala also activates more to fatter than thinner images of one's own body, in comparison to one's actual size (Kurosaki, Shirao, Yamashita, Okamoto, & Yamawaki, 2006). In older adults, the amygdala is activated by emotional stimuli (Roalf et al., 2009; Mather et al., 2004) but less so than in younger adults (Roalf et al., 2009; Tessitore et al., 2005), and the amygdala does not habituate to emotional stimuli in older adults (Roalf et al., 2009). It is not known in older adults how the amygdala responds to emotion in body stimuli. The amygdala was chosen as a region-of-interest for this dissertation due to its role in responding to emotional stimuli, since I have hypotheses about affective responses to body stimuli.

In addition to the amygdala, several regions of the prefrontal cortex (PFC) are involved in processing emotion. In younger and older adults, lateral regions in the PFC activate in response to passively viewing (Levesque et al., 2003; Pruis, Roalf, & Janowsky, 2009) and making non-emotional judgments about emotional stimuli (Gunning-Dixon et al., 2003; Simpson et al., 2000; Tessitore et al., 2005). In younger adults, lateral prefrontal regions are also involved in reappraising (Ochsner, Bunge, Gross, & Gabrieli, 2002) and actively trying to increase or decrease one's affective response to emotional stimuli (Levesque et al., 2003; Ochsner et al., 2004). In younger and older adults, medial regions in the PFC are involved in self-reflection (Johnson et al., 2002; Mitchell et al., 2009; Gutchess, Kensinger, & Schacter, 2010) and fear responses

(Williams et al., 2006b; Williams et al., 2006a). In younger adults, medial PFC regions are additionally involved in self-referential emotions (Fossati et al., 2003). Specifically, medial prefrontal regions activate when younger adults are presented with a positive or negative personality trait and asked to think about how well it describes themself (Fossati et al., 2003). Additionally, patients with lateral and medial prefrontal lesions have impaired perception of social cues (Mah, Arnold, & Grafman, 2004) and lower cognitive and affective empathy (Shamay-Tsoory, Tomer, Goldsher, Berger, & Aharon-Peretz, 2004) than healthy controls and patients with lesions in other areas of the cortex. However, patients with medial lesions, but not patients with lateral lesions, have impaired recognition of emotion expressed in faces (Heberlein, Padon, Gillihan, Farah, & Fellows, 2008) and decreased accuracy on second-order emotional decisions, which involve making inferences about others emotions in order to make accurate task decisions (Shamay-Tsoory & Aharon-Peretz, 2007). Collectively, these studies suggest that the prefrontal cortex is integral to processing, making responses, and forming judgments about emotional or affective stimuli. Furthermore, lateral PFC regions activate more in response to fatter than to actual images of one’s own body in younger women, and women rate the fatter images as more unpleasant than the actual images (Kurosaki et al., 2006). This study suggests that prefrontal regions process affect and emotion in body stimuli in addition to other types of stimuli. Since I had hypotheses about affective responses to bodies and the effect of body stimuli on prefrontal function, I chose a lateral and a medial region of the prefrontal cortex as regions-of-interest for this dissertation.

Structural and functional relationships among the regions of interest for this dissertation

Structures in the body image circuit are anatomically connected to one another. Studies in non-human primates suggest that there are reciprocal neural projections between the prefrontal cortex and the amygdala (Carmichael & Price, 1995; Price, 1999; Price, 2003) and that subregions of the prefrontal cortex are connected to each other (Carmichael & Price, 1994). In humans, the fusiform is anatomically connected to the amygdala via white matter tracts that extend from the occipital to the anterior temporal lobe (Catani, Jones, Donato, & Ffytche, 2003) and to the prefrontal cortex via white matter tracts that extend from the occipital lobe to frontal cortices (Thomas et al., 2008). The white matter tracts that connect the occipital lobe to the prefrontal cortex degrade with age, as evidenced by fewer white matter fibers and lower white matter integrity (Thomas et al., 2008). Collectively, these studies provide evidence for anatomical connections within and between regions likely involved in processing body stimuli, suggesting that the regions-of-interest for this dissertation are part of a broader circuit that responds to body stimuli.

Structures within the proposed body image circuit are functionally related to each other. Neuroimaging studies in younger adults (Kim, Somerville, Johnstone, Alexander, & Whalen, 2003) and electrophysiology studies in rodents and felines (Quirk, Likhtik, Pelletier, & Pare, 2003; Rosenkranz & Grace, 2002) suggest an inverse relationship between amygdala and PFC activity. Functional connectivity involves selecting a seed region in the brain and correlating activity from all other voxels in the brain with activity in that seed region. In younger adults, functional connectivity models find that increases in fusiform activity correlate with increases in inferior frontal gyrus, middle frontal gyrus, and amygdala activity during the maintenance phase of a working memory task when faces are being held in mind (Gazzaley, Rissman, & Desposito, 2004). In older adults, functional connectivity models find higher connectivity between amygdala and dorsolateral PFC activity, as well as between amygdala and fusiform activity, while viewing negative images that are subsequently remembered in comparison to viewing neutral images that are subsequently remembered (Jacques, Dolcos, & Cabeza, 2009). This difference in connectivity between subsequently remembered negative and neutral images is higher in older adults than in younger adults (Jacques et al., 2009). On the other hand, younger adults have higher connectivity between amygdala and hippocampal activity while viewing negative images that are subsequently remembered in comparison to neutral images (Jacques et al., 2009). Taken together, these data confirm that there is a functional relationship among regions involved in processing body stimuli, which is why the studies here explore relationships among brain activity in the regions-of-interest.

<u>Body image and AN in men</u>

This dissertation included women and not men. Body dissatisfaction is lower (Altabe & Thompson, 1993) and eating disorders are less common (Hudson, Hiripi, Pope, Jr., & Kessler, 2007) in men than in women. In comparison to men, a smaller percentage of women find their body size socially acceptable (Rand & Resnick, 2000). While both men and women recognize that they get heavier with age, women have a larger discrepancy than men between their perceptions of their current size and their ideal size (Altabe et al., 1993). Some evidence suggests that men do not process body image-related stimuli in the same way as women. Women, but not men, have a right lateralized response in the fusiform and EBA when viewing images of human bodies (Aleong &

Paus, 2010). Additionally, women, but not men, activated the amygdala in response to viewing negative words related to body image, while men activated the prefrontal cortex more than women in response to the same words (Shirao, Okamoto, Mantani, Okamoto, & Yamawaki, 2005). Furthermore, when viewing distorted images of their own bodies, women activated more of the limbic system, including the amygdala, than men, while men activated more of the occipital lobes and visual cortices than women (Kurosaki et al., 2006). Given the differences in prevalence and neural processing, women were selected as the primary population of interest for this study.

Body image in women

Quantifying body image

Body image is measured in a variety of ways. Body dissatisfaction is most commonly measured with some version of the Figure Rating Scale (Stunkard, Sorensen, & Schulsinger, 1983). In the traditional version, women choose what they think is their current body size and their ideal body size from a series of nine line drawings of female bodies that get progressively larger in body size (i.e. BMI) but remain the same height. The discrepancy between these two numbers is the measure of body dissatisfaction. Other variations on this include using a scale with a larger range of body sizes for obese populations (Johnstone et al., 2008), different shapes and skin colors for non-Caucasian populations (Stewart, Allen, Han, & Williamson, 2009), and morphed images of one's own body in healthy populations (Pruis & Janowsky, 2010). However, some argue that this is a very limited view of body dissatisfaction, because a woman could believe that her body was not ideal but still feel satisfied with it (Polivy & Herman, 2002). One proposed solution is to use measures that explicitly ask about satisfaction (or lack thereof) regarding one's body and specific body parts (Polivy et al., 2002). Other measures assess body image in terms of concern about body shape or weight (Cooper, Taylor, Cooper, & Fairburn, 1987), influence of media on body image (Thompson, van den Berg, Roehrig, Guarda, & Heinberg, 2004), or disordered eating symptomology (Garner, Olmsted, Bohr, & Garfinkel, 1982; Garner, Olmstead, & Polivy, 1983). Therefore, I chose to use the Body Shape Questionnaire, Societal Attitudes Towards Appearance Questionnaire, Eating Disorder Inventory, and Eating Attitudes Test, in addition to the Figure Rating Scale to assess self-perceptions of body image in my studies of younger and older women and women who recovered from AN. This will permit me to relate the women in the studies reported here to women in other studies of body image and also to have explicit information about their satisfaction (or not) with their bodies and body parts.

Body dissatisfaction in younger and older women

Body dissatisfaction refers to unhappiness with one's body shape or size and occurs in women of all ages. Healthy young women overestimate the actual size of their waist, hips, and thighs, when asked to make an estimate of their size based on their "rational" opinion of their body (Thompson & Dolce, 1989). This overestimation is even larger when they are asked to estimate their size based on how they "feel" about the size of each particular part (Thompson et al., 1989). In one study, 71% of women aged 30-74 want to be thinner, but 73% of those women are already in a normal weight range (Allaz, Bernstein, Rouget, Archinard, & Morabia, 1998). When broken down into age categories, younger, middle-aged, and older women are similarly dissatisfied with their bodies (Webster & Tiggemann, 2003). However, older women have less anxiety regarding their appearance (Tiggemann & Lynch, 2001) and lower drive for thinness (Lewis & Cachelin, 2001) than younger women. Body dissatisfaction correlates with self-esteem in younger, but not older women (Webster et al., 2003), suggesting that body image plays a larger role in self-evaluation in younger than in older women. There are a handful of theories proposed to explain these behavioral differences between younger and older women, including lower importance placed on body appearance in older women (Tiggemann et al., 2001), stronger societal pressure to be thin in younger than older women (Bedford & Johnson, 2006), and more perceived control over one's body leading to higher self-esteem in older women (Webster et al., 2003). The last theory is similar to the hypothesis of prefrontal regulation affecting responses to bodies and body image that is proposed here. Although I did not examine brain activation in older women, I hypothesized that higher prefrontal activity underlies the higher perceived control of appearance in older women, which would lead to a less negative assessment of their bodies in comparison to younger women.

Onset of, and factors affecting, body dissatisfaction

Current evidence shows that body dissatisfaction is present in adolescence (Neumark-Sztainer, Paxton, Hannan, Haines, & Story, 2006) but begins as early as grade school (Robinson, Chang, Haydel, & Killen, 2001). There are several theories as to why body dissatisfaction occurs, including peer influence (Lunner et al., 2000; Stice & Whitenton, 2002b); perceived pressure to be thin from friends, family, and media (Stice et al., 2002b); exposure to media sources that promote the stereotypical ideal female appearance (Tiggemann & Pickering, 1996), which has become increasingly thin (Byrd-Bredbenner, Murray, & Schlussel, 2005); and subsequent internalization of that thin ideal

(Stice & Bearman, 2001). Some studies suggest that pubertal development plays a large role in how girls feel about their bodies, since elevations in body mass index (Stice et al., 2002b) and bodily changes associated with puberty (Richards, Casper, & Larson, 1990) are predictive of body and weight dissatisfaction, respectively. In fact, body dissatisfaction is higher in girls that are later in puberty than those that are earlier in development (Hermes & Keel, 2003). Overall, a complex combination of factors likely determines the onset of body dissatisfaction in adolescent girls.

Anorexia nervosa in women

Characterization of AN

AN differs from general body dissatisfaction and poor body image. This disorder is characterized by refusal to maintain a healthy body weight for one's age and height, intense fear of gaining weight or becoming fat, denial of the seriousness of one's low body weight, and undue influence of body weight and shape on self-evaluation (American Psychiatric Association, 2000). In women who are post-menarcheal but pre-menopausal, there is typically a cessation of menstrual cycles due to low body weight (Swenne, 2004), lowered metabolism (Sterling, Golden, Jacobson, Ornstein, & Hertz, 2009), and altered hormones (Mitan, 2004). Women with AN suffer many physical consequences due to their extremely low weight and malnutrition, such as abnormal mitral valve function (Simone G. et al., 1994), lower cardiac output (Romano et al., 2003), lower blood pressure and heart rate (Cong et al., 2004; Misra et al., 2004; Romano et al., 2003), muscle wasting (McLoughlin et al., 1998; Melchior, 1998), dermatological problems (Strumia, 2010), and gastrointestinal problems, such as slowed digestion and constipation (Stacher, 2003). Mortality estimates indicate that 5.9% of women diagnosed with AN will die (Sullivan, 1995); however, estimates range from 0-26% depending on the study population and diagnostic criteria (Birmingham, Su, Hlynsky, Goldner, & Gao, 2005).

Onset, prevalence, and potential causes of AN

Onset of AN typically occurs in teenagers or women in their early twenties (Hudson et al., 2007; Woodside & Garfinkel, 1992); however, AN can also occur in middle-aged (Kally & Cumella, 2008; Midlarsky & Nitzburg, 2008) and older women (Hsu & Zimmer, 1988; Mangweth-Matzek et al., 2006). The lifetime prevalence for AN in women aged 18 and older is 0.9% (Hudson et al., 2007) with the highest incidence (~40% of cases) occurring in 15-19 age range (Hoek & vanHoeken, 2003). However, a recent internet survey of middle-aged women found that 14.8% of the sample met criteria for disordered eating, as defined by the Eating Attitudes Test (Midlarsky et al., 2008).

Several factors have been proposed as potential causes of eating disorders. External factors include the influence of peers and family. In middle school children, peer influence on eating and body concerns was a better predictor of disordered eating behaviors than age or gender (Meyer & Gast, 2008). Some disordered eating behaviors (e.g. severe restricting, use of diet pills) are geographically clustered, suggesting that there may be a social transmission of these types of behaviors (Forman-Hoffman & Cunningham, 2008). There is also some support for familial transmission of disordered eating behaviors. Jacobs et al (2008) found that patients with high symptomology had either moderate or high symptom mothers, while patients with moderate symptomology had healthy mothers (Jacobs et al., 2009). Additionally, patients with AN have a higher percentage of first-degree relatives with an eating disorder than women who have never had AN (Lilenfeld et al., 1998; Strober, Freeman, Lampert, Diamond, & Kaye, 2000). These studies suggest that external factors such as family and peers can influence disordered eating, although they do not distinguish the contribution of genetics in the family influence.

Internal factors that are potential causes of eating disorders include high body dissatisfaction (Stice & Shaw, 2002a), feeling lack of control over one's life (Williams et al., 1993), anxiety (Bulik, Sullivan, Fear, & Joyce, 1997), low self-esteem (Silverstone, 1992; Walters & Kendler, 1995), and high perfectionism (Bastiani, Rao, Weltzin, & Kaye, 1995). Most women who have AN that is co-morbid with an anxiety disorder report that their anxiety preceded AN (Bulik et al., 1997). Perfectionism is higher in women with AN than in controls and remains high after weight restoration (Bastiani et al., 1995). These studies suggest that anxiety and perfectionism are lasting personality traits that may contribute to the onset of AN. One hypothesis contends that high body dissatisfaction is the precursor to extreme dieting and negative affect that lead to eating pathology (Stice et al., 2002a). Others have suggested that low self-esteem is the final common pathway through which other potential causes come together to induce AN (Silverstone, 1992). Ultimately, there is not likely one single cause of AN, but instead a multitude of contributing factors that may vary from person to person. This dissertation explored several of these factors (e.g. body dissatisfaction, anxiety, brain function) in women who had recovered from AN.

Another potential internal cause of AN is altered neurobiology (Kaye, Fudge, & Paulus, 2009). It has been suggested that the right combination of enduring personality traits, environmental stressors, stage of development, and altered serotonin neurobiology can lead to affective and neurobiological states that induce and maintain AN behaviors (Kaye et al., 2009). Women with AN show increases in their level of 5-H1AA, a metabolite of serotonin, in the cerebrospinal fluid (CSF) after they restore their weight to a healthy level (Kaye, Ebert, Raleigh, & Lake, 1984; Kaye, Gwirtsman, George, Jimerson, & Ebert, 1988). Women in long-term weight recovery have similar CSF 5-H1AA levels as women who have never had an eating disorder (Kaye et al., 1984). These studies suggest that serotonin levels are lowered during AN but restored during recovery. When women are depleted of the amino acid tryptophan, which is a precursor to serotonin, they experience reductions in their anxiety level (Kaye et al., 2003). In women with AN, larger levels of depletion correlate with larger reductions in anxiety; however, this relationship does not hold true in women who have recovered from AN or healthy controls (Kaye et al., 2003). This study suggests that anxiety reduction is a motivation for starvation in AN women, because starvation would result in tryptophan depletion. Other neurotransmitters in the brain are affected during AN. Women with AN show increases in their levels of CSF homovanillic acid (HVA), a metabolite of dopamine, after they restore their weight to a healthy level, and women in long-term weight recovery have CSF HVA levels similar to healthy controls (Kaye et al., 1984). Additionally, CSF norepinephrine is lower in women who are in long-term recovery from AN than in underweight AN patients, recently weight-recovered AN patients, and healthy controls (Kaye et al., 1984). Collectively, these studies suggest that multiple neurotransmitter systems are affected by, and contribute to, the pathology in AN. This type of work highlights the importance of studying the neural underpinnings of AN and body dissatisfaction, which is one goal of the fMRI study in Chapter 3.

Recovery from AN

Relapse and recovery are significant issues for women with AN. A 7.5 year longitudinal study found that relapse occurs in 40% of women who have been diagnosed with AN and only 33% ever reach full recovery (complete absence of symptoms), although 83% reach partial recovery (reduction of symptoms to less than full criteria) at some point (Herzog et al., 1999). Recovery is usually defined by biological criteria, such as restoration of weight and initiation of menstrual cycles, and behavioral criteria, such as absence of restricting or purging symptoms (Uher et al., 2003; Klump et al., 2004; Casper, 1990). Most women reach some form of this biological/behavioral recovery (Herzog et al., 1999); however, cognitive recovery is less common and not well-defined. Cognitive recovery generally requires that women no longer have a distorted body image or a fear of becoming fat (Bachner-Melman, Zohar, & Ebstein, 2006), but the criteria used to define these cognitive aspects vary from study to study (Bachner-Melman et al., 2006; Bardone-Cone et al., 2010). The assessment of predictive factors and treatment outcomes depends on how you define recovery (Couturier & Lock, 2006). Typically, when a personality trait or characteristic is predictive of developing AN or remains after the patient has recovered, it is interpreted to be a potential cause of AN. This is the case for traits like perfectionism (Bastiani et al., 1995) and harm avoidance (Klump et al., 2004). Women who both behaviorally and cognitively recover look similar to controls for traits like body dissatisfaction, perfectionism, and presence of mood disorders, while women who are only behaviorally recovered maintain elevated levels of these traits in comparison to controls (Bachner-Melman et al., 2006; Bardone-Cone, Sturm, Lawson, Robinson, & Smith, 2010; Bardone-Cone et al., 2010). This distinction of behavioral versus cognitive recovery is of interest, as higher body image distortion (e.g. a cognitive factor) is a predictor of relapse (Keel, Dorer, Franko, Jackson, & Herzog, 2005).

Affective responses to bodies in AN and recovery from AN

AN is associated with an intense aversion to the perception of being overweight, but recovery may ameliorate some of the negative emotions associated with bodies and body image. Women with AN have higher aversion to under, over, and normal weight line drawings of bodies than healthy women and find drawings of fatter bodies particularly negative in comparison to healthy women (Uher et al., 2005). This aversion is solely in response to bodies. Neither women with AN nor healthy women have aversion for non-emotional, non-body stimuli such as images of larger or smaller houses (Uher et al., 2005). Stimuli associated with weight are also negative stimuli to women with AN. They rate food stimuli as more negative and disgusting than healthy women, but women with AN do not differ from healthy women on ratings of non-food neutral stimuli (Uher et al., 2004). Interestingly, women who have recovered from AN do not differ from healthy women in their ratings of food, non-food, negative, or neutral stimuli, and also have lower ratings of fear and disgust for food stimuli than women with chronic AN (Uher et al., 2003). These data suggest that body image-related stimuli elicit strong negative emotional responses in women with AN and that with recovery from AN the intensity of that emotional response is lessened.

Conclusion

If we can understand what leads to biological and psychological recovery, perhaps better treatments can be developed for women who still suffer from this disorder. Women who have recovered from AN offer a unique opportunity to study persistent behavioral, psychological and neurobiological traits associated with AN without the physical effects that current starvation has on the body and brain. Overall, we need a better understanding of the underlying neurobiology that permits and maintains traits of AN, so that more effective treatments can be developed. Therefore, this dissertation examined body image and brain function in women who had recovered from AN.

Relationship between Emotion and Body Image

Aging & emotion

Emotional changes are a part of normal aging. Cross-sectional (Mroczek & Kolarz, 1998) and longitudinal (Charles, Reynolds, & Gatz, 2001) studies based on scales of health, well-being, and affect find that adults experience less negative emotion as they age. In fact, older adults have a bias towards positive emotional information (Mather & Carstensen, 2005a). They rate negative scenes as less arousing (Mather et al., 2004) and remember proportionately more positive than negative material, as compared to younger adults (Charles, Mather, & Carstensen, 2003; Mather & Carstensen, 2003). Reaction time and eye tracking experiments suggest that older adults attend more to positive and less to negative stimuli, while younger adults do not have this attentional bias (Isaacowitz, Wadlinger, Goren, & Wilson, 2006; Mather et al., 2003). Physiological data support this positivity bias. Older adults show a diminished cardiovascular response as compared to younger adults when discussing emotional conflicts (Levenson, Carstensen, & Gottman, 1994) or when viewing sad or amusing films (Tsai, Levenson, & Carstensen, 2000). Additionally, their physiological arousal does not correlate with their subjective arousal in response to emotional scenes, where as it is correlated in younger adults (Neiss, Leigland, Carlson, & Janowsky, 2007). However, the positivity bias in memory is reversed in older adults that score low on measures of cognitive control, as compared to older adults that score highly, or when older adults are distracted by other cognitive tasks (Mather & Knight, 2005b). Taken together, these data demonstrate a bias towards positive emotional information in older adults that is driven by their regulation of emotion. The hypothesis in this dissertation is that higher cognitive regulation of emotion in aging will affect responses to bodies in older women, such that they will find bodies less negative than younger women.

Brain basis of emotion in aging

Neuroimaging studies suggest that the brain basis of the positivity bias seen in older adults (not just women) is due to higher prefrontal activity and/or diminished amygdala response to emotion. Structural brain changes of aging include cortical thinning (Salat et al., 2004); loss of cortical volume (Resnick, Pham, Kraut, Zonderman, & Davatzikos, 2003; Walhovd et al., 2005), including the prefrontal cortex (Raz et al., 1997; Raz et al., 2004) and amygdala (Allen, Bruss, Brown, & Damasio, 2005); and loss of white matter in the cortex (Resnick et al., 2003; Walhovd et al., 2005; Salat et al., 2005). Based on these anatomical changes that occur with aging, it is reasonable to suggest that the function of these brain regions may change as well. In younger adults, the amygdala (Breiter et al., 1996; Hamann et al., 1999; Mather et al., 2004) and prefrontal cortex (Gunning-Dixon et al., 2003; Iidaka et al., 2002; Tessitore et al., 2005; Wright et al., 2001) are both activated by emotional stimuli. However, a number of studies indicate that emotion processing differs between older and younger adults (Gunning-Dixon et al., 2003; Iidaka et al., 2002; Mather et al., 2004; Tessitore et al., 2005). Our data suggest that prefrontal activation in older adults is higher to negative than to neutral or positive stimuli; however, prefrontal activation in younger adults is similar for negative, neutral, and positive stimuli (Roalf et al., 2009). Older adults have less amygdala activation to negative and positive emotional stimuli than younger adults (Tessitore et al., 2005; Roalf et al., 2009) and do not always activate the amygdala when discriminating or processing faces expressing negative emotion (Iidaka et al., 2002; Gunning-Dixon et al., 2003). Instead, older adults activate prefrontal regions in response to emotion (Gunning-Dixon et al., 2003; Iidaka et al., 2002; Urry et al., 2006), in some cases more so than young adults (Tessitore et al., 2005; Roalf et al., 2009). The diminished amygdala response to emotion in older adults may be due to a general decline in amygdala activity or inhibition of the amygdala by the prefrontal cortex (Urry et al., 2006) or both. Either way, in older adults, emotional stimuli induce more activity in prefrontal regions than in younger adults. Therefore, higher prefrontal activity could underlie a higher regulation of emotion in aging. My hypothesis is that this is what allows older women to regulate their emotional responses to body image-related stimuli, which leads to less negative body image and less negative assessment of bodies in older as compared to younger women.

Brain basis of body image & emotion in AN and recovery from AN

Neuroimaging studies in women who currently suffer from AN and women who have recovered from AN suggest that lower amygdala and higher prefrontal activity lead to healthier body image. Women with current AN activate the amygdala in response to viewing fatter images of their own bodies versus images of their actual size, while women who have never had an eating disorder activate the amygdala in addition to the medial, dorsolateral, and ventrolateral PFC for the same comparison (Miyake et al., 2010). Region of interest analyses show that amygdala activation is the same between women who currently have AN and healthy controls, but PFC activation is greater in controls than women with AN (Miyake et al., 2010). Women with AN also activate the amygdala in response to other women's bodies, more so than controls (Vocks et al., 2010). These studies suggest that women with AN and healthy controls both have emotional responses to bodies, but that prefrontal activity in healthy controls regulates those responses. Interestingly, women who have recovered from AN have higher prefrontal activation in response to food versus non-food stimuli than both women who currently have AN and healthy controls (Uher et al., 2003). Although food stimuli are not the same as body stimuli, this study suggested that recovery may occur due to higher prefrontal regulation of responses to body image-related stimuli. Of note, women who recovered from AN did not differ from women who currently had AN or healthy controls in their brain activation to negative versus neutral non-body image-related scenes, suggesting that there is something specific about body image-related stimuli that differentiate them from other emotional stimuli (Uher et al., 2003). Taken together, these results suggest that a neural network with a higher prefrontal response to body image-related stimuli leads to higher regulation of the emotional responses and healthier body image. This theory is similar to that proposed in younger versus older women, where older women have higher prefrontal activation and better body image than younger women (see Table 1 for hypothesized PFC and amygdala activity in each group).

There is some evidence to suggest that the lower prefrontal activation seen in women with AN could be due to the physical side effects of AN. Women with AN have lower cardiac output (Romano et al., 2003) and lower blood pressure and heart rate

(Cong et al., 2004; Misra et al., 2004; Romano et al., 2003) than healthy controls, which could potentially decrease blood flow in the brain. A longitudinal study of baseline cerebral blood flow (meaning not in response to any stimuli) found that women with AN had lower baseline prefrontal blood flow before behavioral therapy (which includes refeeding and weight gain) as compared to after (Matsumoto et al., 2006). Another study of cerebral blood flow shows that women in long-term recovery from AN have similar baseline prefrontal blood flow as women who never had an eating disorder (Frank et al., 2007), suggesting that baseline prefrontal blood flow is restored after recovery from AN. Thus, the lower prefrontal activation to body stimuli seen in women who currently suffer from AN could be due to physical side effects of the disorder; however, the studies here suggest that these side effects are mitigated with recovery. Therefore, this should not be an issue for the population used in Chapter 3. My hypothesis is that, although baseline prefrontal blood flow is similar between women who have recovered from AN and healthy control women, women who have recovered need prefrontal activation above and beyond that of control women to successfully regulate their emotional responses to body stimuli.

Working memory

Thus far, I have proposed the hypothesis that higher prefrontal activity underlies the ability to regulate emotional responses to images of bodies. One way to test this would be to determine the effect of emotional body stimuli on a task that engages regions of the PFC that process emotion. Working memory refers to the brain system used to maintain and manipulate information during a cognitive task (Baddeley, 2010). Working memory is divided into four components: a central executive that controls attention and supervises three subsystems (Baddeley, 2010). The phonological loop stores and rehearses verbal information, the visuospatial sketchpad manipulates visual images, and the episodic buffer integrates and acts as a temporary store for information from the other two subsystems (Baddeley, 2010; Baddeley, 1992). Working memory tasks tap prefrontal resources, as evidenced by lesion studies (Boisgueheneuc et al., 2006; Muller & Knight, 2006), functional neuroimaging studies (D'Esposito et al., 1998; D'Esposito, Postle, Ballard, & Lease, 1999), and studies that combine lesion and functional imaging techniques (Volle et al., 2008). Specifically, these tasks activate lateral prefrontal (Bunge, Ochsner, Desmond, Glover, & Gabrieli, 2001; Gazzaley et al., 2004; Ungerleider, Courtney, & Haxby, 1998) and suppress medial prefrontal brain regions (Drobyshevsky, Baumann, & Schneider, 2006), which are similar to regions of the brain that are involved during the processing and regulation of emotion (Goldin, McRae, Ramel, & Gross, 2008; Levesque et al., 2003; Ochsner et al., 2002; Williams et al., 2006b). This overlap in function was another reason for the selection of lateral and medial PFC regions-of-interest for this dissertation. Older adults activate similar prefrontal regions as younger adults during the maintenance phase of working memory tasks (Rypma, Prabhakaran, Desmond, & Gabrieli, 2001), but some studies suggest that this activation may be more robust and bilateral (instead of unilateral) in older adults (Cabeza et al., 2004). Furthermore, this may be a compensatory mechanism to maintain performance in older adults (Cabeza, 2002; Cabeza, Anderson, Locantore, & McIntosh, 2002). Additionally, emotional stimuli viewed during the retention interval of a working memory task disrupt performance and change brain activity, such that ventral prefrontal activity is higher than dorsal prefrontal activity (Dolcos & McCarthy, 2006). Therefore, in Chapters 2 and 3, I examined the disruption of prefrontal regulation using body stimuli as distracters during a working memory task.

Why use Magnetic Resonance Imaging?

Magnetic resonance imaging (MRI) is a high-quality, non-invasive method for assessing brain structure and function. Blood oxygenation level dependent (BOLD) imaging is one of the most common functional imaging methods used in MRI research and was used to collect the functional data in Chapter 3. BOLD imaging is an indirect measure of brain activity and exploits the magnetic properties of blood (Huettel, Song, & McCarthy, 2004). BOLD measures changes in deoxyhemoglobin (Huettel et al., 2004). Oxyhemoglobin is diamagnetic and does not largely disrupt the homogeneity of the magnetic field, so it does not produce a large signal (Huettel et al., 2004). However, deoxyhemoglobin is paramagnetic and does disrupt the homogeneity of a magnetic field, which produces a measurable MRI signal (Huettel et al., 2004). The theory behind this measure is that activation in the brain causes increased blood flow to a particular area (Detre & Wang, 2002). This leads to a local increase in oxyhemoglobin, which causes a local decrease in the proportion of deoxyhemoglobin because the influx of oxygenated blood is greater than local oxygen consumption (Detre et al., 2002). BOLD imaging detects that loss of signal from deoxyhemoglobin which translates into an increase in MRI signal. This is interpreted as an increase in brain activity (Detre et al., 2002). In Chapter 3 of this document, functional MRI data were registered to the anatomical images, in order to attribute activation to specific brain regions.

Conclusion

The goals for this dissertation were to examine affective responses to bodies and to examine how body stimuli affect prefrontal cortical regulation in the brain. The models used were older versus younger women and women who had recovered from AN versus women who had never had an eating disorder as models. Current literature suggests that older adults will have overall more positive body image that younger adults, while women who have recovered from AN will be similar to controls for some body image measures but more negative for others. This is why I chose standardized questionnaires to characterize body image in younger and older adults in Chapter 1 and women who had recovered from AN and controls in Chapter 3. Current neuroimaging work suggests that brain regions involved in perceiving bodies and processing emotion, which is why I selected ROIs that reflect those processes for the neuroimaging study in Chapter 3.

Table 1. Hypothesized amygdala and lateral PFC activity in response to body stimuli in younger/control women, older women, and women who have recovered from AN.

Brain region	Affective rating of body stimulus	Younger/Control	Older	RecAN
Amygdala	Negative	↑**	↑*	↑ ↑**
	Positive	↑**	↑*	↑**
	Neutral	↑	↑*	↑
Lateral PFC	Negative	↑***	↑↑***	↑↑***
	Positive	↑	↑	↑
	Neutral	↑	↑	↑

↑ or ↓ = increased or decreased from baseline

* = less than Younger women

↑↑ = increased more than the other groups in that row that only have with one arrow

** = increased more than neutral within that group

*** = increased more than neutral and positive within that group

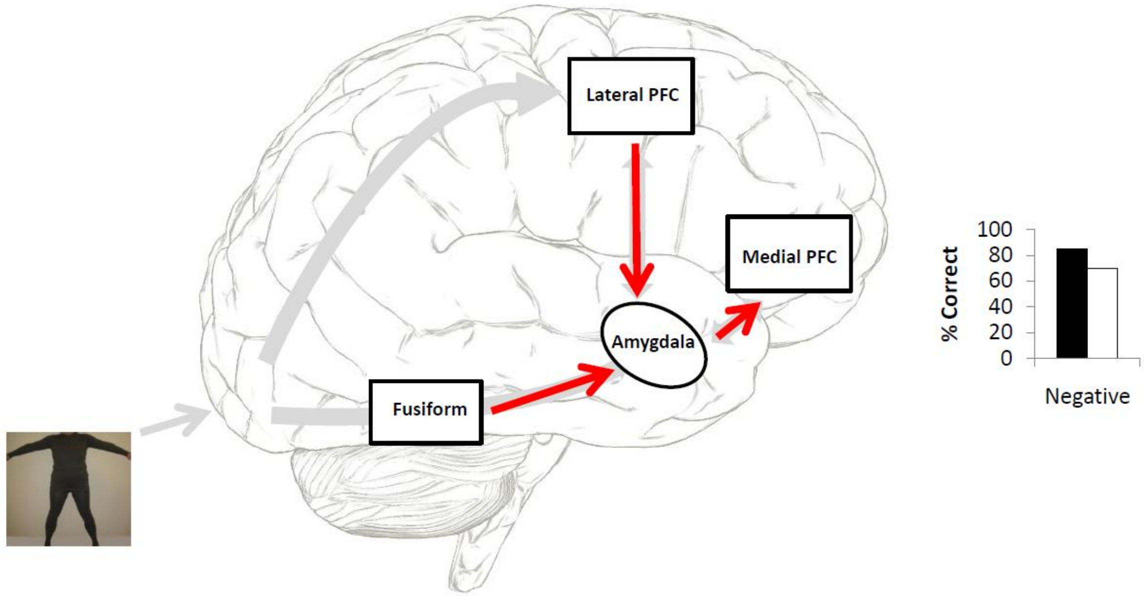

Figure 1. Hypothesized regulation of emotional responses to bodies in women. The amygdala, fusiform gyrus, lateral prefrontal cortex (PFC), and medial PFC were chosen as regions-of-interest for the functional neuroimaging portion of this dissertation. If women were only viewing body stimuli, I hypothesized that the amygdala would have higher activation in younger women and controls than women who had recovered from AN and older women, respectively. This would be due to regulation of the emotional responses by the lateral PFC, which would decrease the intensity of the negative response to bodies in women who have recovered AN and in older women. Thus, amygdala activation would be lower than the controls and younger women but the lateral PFC activation would be higher. However, since women are also performing a WM task at the same time, I predicted that women who had recovered from AN and older women would have a harder time regulating their negative responses to bodies in comparison to controls and younger women. Therefore, lateral PFC activation would still be higher in women who had recovered from AN than in controls and in older than in younger women, but amygdala activation in women who had recovered from AN and older

women would increase too. The combination of these things would disrupt performance on the working memory, such that women who had recovered from AN and older women would have worse performance than controls and younger women, respectively, when viewing body stimuli that they rated as negative. However, the women who recovered from AN versus controls and the older versus younger women will have similar performance for bodies they think are neutral or positive, because those bodies will not require as much regulation. Finally, I predicted that fusiform activation would be similar among groups, although it would be more sensitive to negative than positive emotion. Background brain image from: http://www.cs.princeton.edu/gfx/proj/sugcon/models.

Chapter 1: Assessment of body image in younger and older women

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Abstract

This study compared body image in younger versus older women using questionnaires and women's responses to fatter and thinner images of their own bodies versus responses to line drawings of bodies in the Figure Ratings Scale. We found that younger and older women have similar body dissatisfaction, but that younger women have a higher drive for thinness and experience more societal influence on their body image. Using images of one's own body did not result in different ratings than the Figure Rating Scale line drawings or different body dissatisfaction scores in younger versus older women. These data suggest that age affects some facets of body image, but not others, and that ratings of body image do not differ in normal, healthy younger and older women when personalized measures are used.

Key words: body image, aging, Figure Rating Scale

There are multiple reasons for poor body image to continue into the latter decades of life. Women's bodies change with age. They experience a shift in weight and fat distribution from the legs to the trunk (Genazzani & Gambacciani, 2006). They also experience an increase in fat mass (Hughes et al., 2004) and a decrease in muscle mass (Frontera, Hughes, Lutz, & Evans, 1991). Additionally, chronic health conditions impact how women view their bodies. Older women are bothered by the weight gain caused by some medications and lament that they cannot hide some physical changes or deformities (Clarke & Griffin, 2008). Furthermore, older women are still susceptible to eating disorders (Mangweth-Matzek et al., 2006), including a continuation of those they have battled their entire lives, as well as late onset eating disorders triggered by late life stressors (Hsu et al., 1988). Perhaps most important, older women still care about their appearance (Gosselink, Cox, McClure, & De Jong, 2008), even though they may not feel the same societal pressure as younger women to be thin and beautiful (Bedford et al., 2006). They report using dieting, exercise, laxatives, diuretics, smoking, and dietary supplements to control their weight (Bedford et al., 2006), and some feel that they need to make themselves look as young as possible (Gosselink et al., 2008). Collectively, these factors suggest that aging primes older women for negative body image.

Although there are multiple reasons for poor body image in older women, there is conflicting evidence regarding whether older women actually have a negative body image. Body dissatisfaction is comparable in younger and older women (Webster et al., 2003); however, older women have less anxiety regarding their appearance (Tiggemann et al., 2001) and have a lower drive for thinness and less restricted eating (Lewis et al., 2001). Additionally, body dissatisfaction correlates with self-esteem in younger, but not older women (Webster et al., 2003). Taken together, these data suggest that body dissatisfaction persists throughout the lifespan, but the negative impact of such feelings may lessen with age (Peat, Peyerl, & Muehlenkamp, 2008).

There are a handful of theories proposed to explain these behavioral differences between younger and older women. One postulates that while older women still care about their body appearance (Gosselink et al., 2008), they place less importance on it, leading to less self-objectification in comparison to younger women (Tiggemann et al., 2001). Another theory suggests that there is stronger societal influence on body image in younger than older women, particularly pressure to conform to the media ideal of women’s bodies (Bedford et al., 2006). However, television viewing is high in elderly populations and more advertising is being targeted at older adults (Wadsworth & Johnson, 2008), suggesting that societal influence in the elderly may be increasing. Thus, assessing societal influence may be pertinent to understanding body image in older women.

Women’s shapes vary widely (Simmons, Istook, & Devarajan, 2009), and women often dislike specific parts of their bodies (Monteath & McCabe, 1997). These aspects of body image are not represented in the standardized outlines of bodies used in common measures of body dissatisfaction, such as the Figure Rating Scale, suggesting that a personalized approach may be useful for studies of body image in women (Tovee, Benson, Emery, Mason, & Cohen-Tovee, 2003). In fact, younger women are differentially sensitive to their own bodies versus “others”. Women have a wider range of bodies that they consider fat or obese for themselves, in comparison to the range they consider fat or obese for other women (Smeets, 1999). Additionally, women who are exposed to images of other thin or attractive women have lower self-evaluations of their appearance than women exposed to averaged-sized or unattractive women, respectively, especially if those women are dissatisfied with their own bodies (Trampe, Stapel, & Siero, 2007; Stice & Shaw, 1994). Thus, in this study, we examined a personalized version of the Figure Rating Scale based on each woman's actual body size and shape, and compared the responses between younger and older women.

The current study compares body dissatisfaction and other aspects of body image in younger versus older women using traditional questionnaires, and, in addition, we examine the Body Shape Questionnaire, which has not been examined in older women. Finally, we compare women's responses to morphed fatter and thinner images of their own bodies versus their responses to line drawings of bodies in the Figure Ratings Scale.

Methods

Participants

Healthy women aged 25-35 (n=22) and 65-80 (n=19) were recruited for this study. All women were recruited in the same manner, which included phone contact and through advertisements to the general public via fliers and newspaper ads. A subset of women was in prior lab studies that were unrelated to body image and thus was contacted from our database of previous study participants. Health histories were obtained via phone interview and confirmed in person. General inclusion and exclusion criteria for our lab have been previously described (Pruis et al., 2009). Exclusion criteria specific to this study included depression in younger women, as determined by a score > 16 on the Center for Epidemiologic Studies Depression Scale (Radloff, 1977); disordered eating behavior, as determined by a score > 20 on the Eating Attitudes Test-26 (Garner et al., 1982); previous or current diagnosis of an eating disorder; and body mass index (BMI) <18 and > 30. This BMI range includes "overweight" sizes, but is reflective of the average size of American women (McDowell, Fryar, Hirsch, & Ogden, 2005). One younger woman was excluded for depression and one for disordered eating behavior. Data from another younger woman was excluded because of a technical error in test administration. These three subjects are not included in the demographics or any study measures (final participants: N=19 younger and 19 older women). Our final groups of younger and older women were matched for years of education and raw scores on the Wechsler Adult Intelligence Scale Vocabulary Test-Revised (WAIS-R). Table 1 contains all demographic information. This study was approved by the Institutional Review Board of OHSU. All participants provided written informed consent and were paid for their time and involvement in the study.

Procedures

Study participants visited the lab on two occasions ~1 week apart. Screening (described under Participants) and body image-related questionnaires (described below) were completed at the first study visit. Participants were photographed in tights and a t-shirt and returned for a second study visit to complete two versions of the Figure Rating Scale.

Sociocultural Attitudes Towards Appearance Questionnaire-3 (SATAQ-3). The four subscales of the SATAQ-3 (Thompson et al., 2004)comprise: general media influence (General), influence of athletic and sports figures (Athletic), pressure to conform to the media ideal (Pressure), and using the media as a resource for appearance-related information (Information). Women used a 5-point Likert scale to indicate how much they agreed with each statement (1= Definitely Disagree, 5=Definitely Agree).

Eating Disorder inventory. Women used a 6-point scale (1= never, 6 = always) to indicate how much each statement regarding psychological and behavioral traits of disordered eating applied to them (Garner et al., 1983). Since this was a non-clinical population, responses were scored using the untransformed scale (Schoemaker, van Strien, & van der Staak, 1994).

Body Shape Questionnaire. Women used a 6-point scale (1 = never, 6 = always) to indicate how often each statement about body shape, weight, and composition was true for them in the past four weeks (Cooper et al., 1987).

Figure Rating Scales. The Figure Rating Scale (Stunkard et al., 1983)is composed of nine line drawings of bodies that progressively increase in size from very thin to overweight (1=very thin, 9 = overweight). Women selected the bodies that they thought represented their current and ideal body size as well as the bodies that represented their minimum and maximum acceptable sizes. Body dissatisfaction was calculated as the discrepancy between the perceived current and ideal bodies. The acceptable range of body sizes was calculated as the difference between the maximum and minimum acceptable sizes.

We also developed a version of the Figure Rating Scale using morphed images of each woman's own body (Figure 1). Women were photographed in grey tights and a grey t-shirt against a white wall. The t-shirt was pinned in back to fit snugly on each woman's torso. Each woman faced forward with their arms ~60 degrees out from their sides and their feet ~20 inches apart. Head, neck, feet, and hands were cropped out of the images. The cropped images were morphed to 35% thinner and 35% fatter than each woman's actual size using Abrosoft Fantamorph 4.0.5. The size increment between each image was ~8.75%. Size change was based on the two-dimensional width of the body in the original images. The software morphed images using the placement and movement of a series of dots. Approximately 130 dots were placed around each body. The coordinates of the dots were used to calculate the extension or contraction of each point on the body to create the +/-35% morphs. The coordinates in the chest and under arm region were often problematic (e.g. created "wrinkles" in the image) due to the varying proportions of each woman's body in that area, and, therefore, images were manually adjusted in that region.

Each woman saw eight images of her own body ranging from 35% thinner to 35% fatter than her actual size centered on an image of her actual size (Figure 1). Women selected their current, ideal, minimum acceptable, and maximum acceptable bodies. Body dissatisfaction and acceptable range were calculated in the same manner as the Figure Rating Scale with line drawings. Additionally, accuracy was calculated as the discrepancy between their perceived current body and their actual current body.

Results

Data analysis

Older women had marginally higher BMI ($t(36)=1.87$, $p=0.07$) than younger women. Thus, ANCOVA (SPSS version 15.0) was used to compare younger and older women on all study measures with BMI as a covariate. Younger and older women did not differ on any other demographic measures. Subscales were analyzed with separate ANOVAs. Post-hoc analyses included using paired t-tests on BMI-adjusted means to compare current vs. maximum acceptable bodies for the Figure Rating Scale within each age group and using Chi-square to compare the number of younger vs. older women with body dissatisfaction as measured by the Figure Rating Scale. As an additional exploratory post-hoc analysis, we put both BMI and SATAQ-3 total scores in one regression model and used them to predict all measures of body dissatisfaction (e.g. from the Eating Disorder Inventory and from both versions of the Figure Rating Scale); the acceptable range of sizes; drive for thinness; and body shape concern. Two-tailed significance level was set at 0.05. Some measures deviated from a normal distribution. Transforming the data did not improve normality, and the pattern of results remained the same when non-parametric statistics were used. Thus, parametric statistics are reported here. Additionally, there was one outlier (>3 standard deviations from mean) for the Figure Rating Scale measures. Removing her data did not change the results, so she has not been excluded from the analyses reported here.

SATAQ-3

Younger women had higher scores than older women on the General, Athletic, and Pressure subscales of the SATAQ-3, but had similar scores for the Information subscale. Table 2 shows means, F values, and p-values for this data. Since three of four subscales suggested larger societal influence on body image in younger than older women, the total SATAQ-3 score was used as a post-hoc predictor with BMI in regression analyses of other measures.

Eating Disorder Inventory

Drive for Thinness was higher in younger than older women, but Body Dissatisfaction and the other six subscales did not differ between the age groups. Refer to Table 3 for means, F values, and p-values. The exploratory regression analyses found that BMI was a significant predictor of Drive for Thinness and Body Dissatisfaction in younger, but not older adults. SATAQ-3 total scores predicted Drive for Thinness in both younger and older women, but only predicted Body Dissatisfaction in older, but not younger women. Table 5 contains standardized regression coefficients (beta) and p-values for all regression analyses.

Body Shape Questionnaire

Younger and older women did not differ on their BSQ scores. Table 3 contains means, F values, and p-values. The exploratory regression analyses found that BMI predicted BSQ scores in younger, but not older women. SATAQ-3 total scores predicted BSQ scores in both younger and older women.

Figure Rating Scale with line drawings

Younger and older women had similar body dissatisfaction and acceptable ranges of body size. Mean current, ideal, minimum acceptable, and maximum acceptable sizes also did not differ between age groups. Means, F values, and p-values are shown in Table 4. Post-hoc analyses showed that current size differed from maximum acceptable size in younger women, but not in older women. Additionally, 13 of 19 younger women and 16 of 19 older women had body dissatisfaction (i.e. a body dissatisfaction score not equal to zero, which would mean that their current and ideal bodies are not the same). The number of women who experienced body dissatisfaction did not differ between age groups ($\chi 2(1)=1.31$. $p=0.25$). Finally, the exploratory regression analyses found that BMI predicted body dissatisfaction in both younger and older women, but SATAQ-3 total scores did not. Neither BMI nor SATAQ-3 scores predicted the acceptable range of body sizes in either group.

Figure Rating Scale with own body

Younger and older women had similar body dissatisfaction and acceptable ranges of body size when viewing morphed images of their own bodies. Mean current, ideal, minimum acceptable, and maximum acceptable sizes did not differ between age groups. Table 4 contains means, F values, and p-values. Post-hoc analyses showed that current size differed from maximum acceptable size in younger women, but not in older women. Similar to the Figure Rating Scale with line drawings of bodies, 13 of 19 young women and 16 of 19 old women had body dissatisfaction. The number of women who experienced body dissatisfaction did not differ between age groups ($\chi2(1)=1.31$. $p=0.25$). Seven of the nine women who had no body dissatisfaction with the line drawings also had no body dissatisfaction with images of their own body. Additionally, the exploratory regression analyses found that BMI predicted body dissatisfaction in both younger and older women, but SATAQ-3 total scores did not. Neither BMI nor SATAQ-3 scores predicted the acceptable range of body sizes in either group. Finally, younger and older women were similarly accurate at selecting their own bodies. The bodies women selected as their current size did not differ from their actual current size (which was always body #5; see Figure 1) for either age group (one-sample t-test vs. 5: $t(18)$'s<1.17, $ps>0.25$), and accuracy scores did not differ between younger and older women.

Discussion

We found that younger and older women have similar body dissatisfaction, but that younger women have a higher drive for thinness and experience more societal influence on their body image, which replicates other studies of body image and aging (Lewis et al., 2001; Bedford et al., 2006). Using images of one's own body did not result in different ratings than the Figure Rating Scale line drawings or different body dissatisfaction scores in younger versus older women. We also found that younger and older women have similar acceptable ranges of body sizes and similar body shape concerns. Additionally, our exploratory regression analyses found that predictors of body image differed between younger and older women. BMI was a significant predictor for most of the body image variables in younger women (e.g. body dissatisfaction as measured by the Eating Disorder Inventory, drive for thinness, body shape concern); however, it was societal influence (not BMI) that was the significant predictor of those same variables in older women.

The lack of difference between younger and older women on multiple measures of body dissatisfaction lends support to the idea that women who experience body dissatisfaction may experience it throughout their lifetime. Many younger, middle-aged, and older women are dissatisfied with their bodies (Webster et al., 2003). In fact, body dissatisfaction in mid-life is related to BMI as early as age 7 (McLaren, Hardy, & Kuh, 2003), suggesting that body dissatisfaction starts at a young age. We also found that younger and older women do not differ in their concern about body shape or feeling fat. Additionally, younger and older women had similar ranges of acceptable sizes for their bodies. This is in contrast to other studies that used line drawings of bodies and found that the number of sizes selected as socially acceptable increases with age, at least up to middle-aged adults (Rand & Wright, 2000). However, we asked younger and older women to determine the acceptable range for their own bodies. Thus, age may affect what women consider acceptable for other people, but not for themselves. Although younger and older women had similar ranges of acceptable sizes, older women's maximum acceptable size was the same as their current size, suggesting that older, but not younger, women are at the "brink" of what they consider acceptable. Collectively, these data indicate that older women have similar concerns as younger women for several aspects of body image. This suggests that some facets of body image are maintained throughout one's life, although longitudinal data would be needed to confirm this.

As we and others have shown, body image in younger women is more susceptible to societal influence than in older women (Lewis et al., 2001). Older women felt less pressure than younger women to conform to the media's ideal. Additionally, TV, movies, magazines, and athletic figures had a larger influence on body image in younger women than older women. This may be due to generational differences in television exposure; however, older adults report heavy television viewing (Wadsworth et al., 2008). This may eventually close the gap in media exposure, and thus societal influence, between younger and older women. In fact, we show here that societal influence predicted body dissatisfaction, drive for thinness, and body shape concerns in older women, while BMI did not. This suggests that societal influence is an important factor in the body image of older women, sometimes more so than body size. Thus, younger women may experience more societal influence on their body image than older women, but older women's body image is not completely immune to society's effects.

Using images of women's own bodies is emerging as a method to study body image. Other work has shown that similar body morphing techniques are useful in studying populations whose size and/or shape may not be accurately represented by standardized bodies, such as obese (Johnstone et al., 2008), eating-disordered (Tovee et al., 2003), and non-Caucasian populations (Stewart et al., 2009). Older women have different body composition and fat distribution than younger women (Genazzani et al., 2006; Hughes et al., 2004), suggesting that an individualized technique might be a useful tool for studying body image in an elderly population. However, we did not find any differences using women's own bodies versus using outlines of bodies in our sample. This may be due to the fact that our women were predominantly Caucasian, healthy, and in the normal BMI range for American women. Thus, the outlines of bodies may represent their sizes and shapes well enough for accurate results. Furthermore, we expect that these measures would be sensitive in Caucasian women given that they report body dissatisfaction at lower weights than black or Hispanic women (Fitzgibbon, Blackman, & Avellone, 2000). Another explanation for these results could be that healthy women with a normal BMI are good at identifying their own bodies, since both age groups were very accurate at selecting their current body. Some evidence suggests that anorexic and obese individuals are worse at identifying their actual size than normal weight individuals (Johnstone et al., 2008; Bell, Kirkpatrick, & Rinn, 1986). Therefore, personalized stimuli may be most useful in clinical populations, where the perception of body image can be skewed, or for specific assessments of body shape.

In summary, we have shown that age affects some facets of body image (e.g. drive for thinness), but not others (e.g. body dissatisfaction, body shape concern, acceptable body size). This is despite significant changes in women's weight and shape as they enter old age, and may be due to increasing societal influence on body image in older women. Studies assessing the effects of media use (e.g. internet, cell phone, TV) on body image in younger versus older women will elucidate the degree to which media in new technologies affects younger versus older women. Our data suggests that ratings of body image do not differ in normal, healthy younger and older women when personalized measures are used. Studies of “self” versus “other” in older women may elucidate some of the questions raised here.

Acknowledgments

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Disclosure statement

Authors have no actual or potential conflicts of interest. This study was approved by the Institutional Review Board of OHSU. All participants provided written informed consent and were paid for their time and involvement in the study.

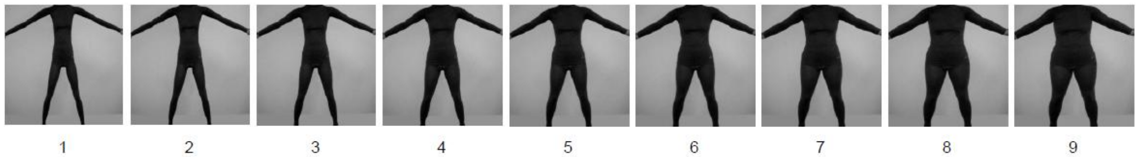

Figure 1. Example images of the Figure Rating Scale based on each woman's own body. Image 5 (the middle image) was the woman's current body. Images were morphed so that there was an ~8.75% change between increments, and images 1 and 9 were 35% thinner and fatter than the woman's current body size, respectively. Women chose their current, ideal, minimum acceptable, and maximum acceptable sizes.

Table 1. Participant demographics

	Younger (*n* = 19)	Younger SE	Younger Range	Older (*n* = 19)	Older SE	Older Range
Age (years)	27.5	0.58	25-33	72.9	1.19	65-80
Education (years)	15.8	0.25	25-33	16.6	0.49	13-21
WAIS-R Vocabulary raw scores	57.4	1.74	44-67	60.6	1.60	47-70
Geriatric Depression Scale	NA	NA	NA	3.3	0.46	0-7
CES-D[a]	6.53	0.83	1-14	NA	NA	NA
Mini-Mental Status Examination	NA	NA	NA	29.2	0.18	27-30
Eating Attitudes Test-26	4.63	1.13	0-17	4.95	0.77	0-10
Body Mass Index[b]	**23.2**	0.62	19-28	**25.0**	0.70	20-31

[a] Center for Epidemiologic Depression Scale.
[b] Older marginally greater than younger (p=0.07).

Table 2. Sociocultural Attitudes Towards Appearance Questionnaire-3

Subscale (Total possible)	**Young Mean (SD)[a]**	**Older mean (SD)[a]**	**F-values**	**p-values**
Total (150)	**82.1** (21.0)	**67.1** (17.8)	5.18	0.03
General (45)	**23.6** (7.70)	**18.3** (6.06)	4.92	0.03
Athletic (25)	**17.4** (3.67)	**12.2** (4.68)	14.6	0.001
Pressure (35)	**20.1** (7.98)	**15.3** (5.85)	4.00	0.05
Information (45)	21.0 (8.90)	21.3 (7.19)	0.01	0.94

[a] Means adjusted for BMI.

Table 3. Eating Disorder Inventory (EDI) & Body Shape Questionnaire (BSQ)

Subscale (Total score possible)	**Younger Mean (SD)[a]**	**Older Mean (SD)[a]**	**F-value**	**p-value**
EDI: Total (384)	142 (26.0)	133 (24.7)	1.17	0.29
EDI: Drive for Thinness (42)	**17.8** (7.35)	**13.1** (4.91)	6.57	0.02
EDI: Body Dissatisfaction (54)	27.1 (9.70)	25.4 (8.22)	0.37	0.55
EDI: Interoceptive Awareness (60)	17.8 (4.51)	17.1 (4.81)	0.17	0.68
EDI: Bulimia (42)	10.7 (2.24)	10.4 (2.88)	0.11	0.74
EDI: Ineffectiveness (60)	17.4 (4.17)	18.4 (4.74)	0.39	0.53
EDI: Maturity Fears (48)	16.9 (5.12)	15.9 (3.84)	0.43	0.52
EDI: Perfectionism (36)	21.0 (4.81)	18.3 (4.85)	2.88	0.10
EDI: Interpersonal Distrust (42)	13.4 (3.36)	14.6 (3.27)	1.15	0.29
BSQ Total (204)	66.4 (22.2)	63.0 (19.6)	0.24	0.63

[a] Means adjusted for BMI.

Table 4. Figure Rating Scale[a].

	Younger mean (SD)[a]	Older mean (SD)[a]	F-value	p-value
Line drawing				
Current	4.28 (1.18)	4.67 (1.10)	1.71	0.20
Ideal	3.26 (0.79)	3.53 (0.61)	1.33	0.26
Body Dissatisfaction	1.02 (0.90)	1.14 (0.89)	0.24	0.63
Maximum acceptable	4.97 (0.74)	4.93 0.67)	0.04	0.85
Minimum acceptable	2.71 (0.75)	3.03 (0.62)	1.82	0.19
Acceptable Range	2.26 (0.71)	1.90 (0.52)	2.99	0.09
Own Body				
Current	4.90 (0.99)	4.89 (1.03)	0.001	0.97
Ideal	3.57 (0.68)	3.53 (0.51)	0.05	0.83
Body Dissatisfaction	1.33 (0.99)	1.36 (1.07)	0.02	0.90
Maximum acceptable	5.70 (0.99)	5.25 (1.36)	1.21	0.28
Minimum acceptable	2.98 (0.78)	2.91 (0.76)	0.08	0.78
Acceptable Range	2.71 (1.00)	2.34 (0.96)	1.25	0.27
Accuracy	-0.10 (0.99)	0.11 (1.03)	0.001	0.97

[a] Means adjusted for BMI.
[b] Different from maximum acceptable size ($p<0.01$).

Table 5. Exploratory regression analyses.

	YOUNG				OLD			
Measure	**BMI b-value**[b]	**BMI p-value**	**SATAQ b-value**[b]	**SATAQ p-value**	**BMI b-value**[b]	**BMI p-value**	**SATAQ b-value**[b]	**SATAQ p-value**
FRS[a] Line Drawing								
Body dissatisfaction	0.700	**0.001**	0.172	0.318	0.582	**0.006**	0.302	0.122
Acceptable range	0.349	0.126	0.344	0.131	0.050	0.842	0.134	0.597
FRS[a] Own Body								
Body dissatisfaction	0.763	**0.001**	-0.053	0.760	0.652	**0.002**	0.254	0.166
Acceptable range	0.246	0.310	0.279	0.252	-.075	0.759	-.251	0.313
Eating Disorder Inventory								
Body dissatisfaction	0.684	**0.001**	0.285	0.081	0.104	0.627	0.530	**0.022**
Drive for thinness	0.655	**0.001**	0.434	**0.003**	0.243	0.213	0.601	**0.005**
Body Shape Questionnaire	0.393	**0.007**	0.682	**0.001**	-.025	0.888	0.718	**0.001**

[a] Figure Rating Scale.
[b] Standardized regression coefficient (beta).

Chapter 2: Effect of body stimuli on working memory performance in younger and older women

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Abstract

Older women have lower anxiety about their appearance and less drive for thinness than younger women. This may be due to better regulation of emotions in older women. We tested emotional regulation with regard to body image by examining whether bodies differentially disrupted working memory performance in younger and older women. Women assigned valence ratings to body stimuli of varying sizes, and then a subset of those body stimuli were used as distracters in a working memory task. Women also completed questionnaires about affect and cognitive control. Overall, younger and older women had similar responses to body stimuli. Both groups were faster to assign negative ratings than positive or neutral ratings, and both groups categorized fewer body stimuli as positive than as negative or neutral. Working memory performance in both groups was more disrupted by scrambled images than bodies, but, within body stimuli, bodies rated as positive were more disruptive than negative bodies. Finally, older women had less negative affect but similar use of cognitive control strategies as younger women on questionnaire measures. These questionnaire measures were not predictive of valence ratings or working memory performance. These results suggest that bodies are affective stimuli to women and, depending on their valence, differentially disrupt working memory. However, despite older women experiencing less negative affect than younger women, these groups did not differ in their affective responses to, or the disruption of working memory by, body stimuli. This suggests that the cognitive mechanisms that permit the positivity bias in aging are not differentially disrupted by body stimuli.

Key words: body image, aging, distraction, body valence

Bodies are affective stimuli to women. Women who are exposed to images of other attractive women have lower self-evaluations of their own appearance than women exposed to unattractive women, and women who are dissatisfied with their bodies are more prone to compare their bodies to other women's bodies (Trampe et al., 2007). Furthermore, viewing bodies elicits activation in the emotion system in the brain. In younger women, viewing bodies that are posed in expressions of fear elicits more activation in the amygdala than viewing bodies that are posed in neutral stances (Hadjikhani et al., 2003). Additionally, the amygdala activates when younger women view fatter, but not thinner, images of their own bodies in comparison to their actual size (Kurosaki et al., 2006). Taken together, these studies provide behavioral and brain-based evidence suggesting that bodies are affective stimuli in women. This study will examine differences in emotional responses to body stimuli between younger and older women.

As seen in Chapter 1, age affects some facets of body image, but not others. Younger and older women in Chapter 1 were similarly dissatisfied with their bodies and had similar ranges of body sizes that they considered acceptable (Pruis et al., 2010). Other studies have found similar results for body dissatisfaction in aging (Tiggemann et al., 2001; Allaz et al., 1998). However, older women have less anxiety regarding their appearance (Tiggemann et al., 2001), a lower drive for thinness (Pruis et al., 2010), and report less body monitoring and self-objectification (Tiggemann et al., 2001) than younger women. Additionally, younger women experience more societal influence on their body image than older women (Bedford et al., 2006), although societal influence is still a significant predictor of body dissatisfaction and drive for thinness in older women, as evidenced in the previous chapter (Pruis et al., 2010). Collectively, data from work presented here and by others suggests that older women experience fewer negative emotions in relation to body image.

As suggested in the overall Introduction to this document, age-related changes in the regulation of emotion may explain the behavioral body image differences between younger and older women. Older adults have a positive bias in their emotions that is thought to be due to improved regulation of emotion with aging (Mather et al., 2005a). They rate negative scenes as less arousing in comparison to younger adults (Mather et al., 2004). Older adults also attend more to positive and less to negative stimuli when each is paired with a neutral stimulus, but younger adults do not have this attentional bias (Isaacowitz et al., 2006; Mather et al., 2003). Furthermore, older adults remember proportionately more positive than negative material, as compared to younger adults (Mather et al., 2003; Charles et al., 2003). One study found that older adults recall proportionally more positive than negative material, while younger adults recall proportionally more negative than positive material (Mather et al., 2005b). However, the pattern is reversed in older adults that score low on measures of cognitive control (as compared to older adults that score highly) or when older adults are distracted by other cognitive tasks (Mather et al., 2005b). For example, when they have to attend to, and make decisions about, the content of sound patterns while viewing the negative and positive scenes, older adults subsequently recall proportionally more negative than positive scenes and recall proportionally more negative scenes than do younger adults (Mather et al., 2005b). Furthermore, the positivity bias is not likely due to a change in which stimuli "grab" the attention of older adults. An eye tracking study showed that older adults did not shift their gaze towards happy or away from angry faces that were paired with neutral faces until 500msec and 3500msec, respectively (Isaacowitz, Allard, Murphy, & Schlangel, 2009). Furthermore, the shift towards happy faces was not sustained and did not differ from younger adults until 4000msec had passed (Isaacowitz et al., 2009). These data suggest that the attentional bias in older adults is not "automatic" because their attention was not drawn to positive stimuli immediately upon presentation of the stimulus (Isaacowitz et al., 2009). One possibility to explain the more positive body image in older women is that the cognitive control strategies employed by older women help them protect their self-concept and self-esteem from the negative influence of body dissatisfaction (Webster et al., 2003). Thus, cognitive regulation of emotional responses to bodies and body image-related stimuli may explain the more positive body image that comes with aging.

A working memory task was used to directly test whether negative versus positive body stimuli differentially disrupt cognitive regulation in older versus younger women. The hypothesis was that older women would rate body stimuli more positively and would categorize a larger percentage of body stimuli as positive than would younger women. Furthermore, bodies rated as negative would be more disruptive to working memory performance in older than in younger women. Although older adults are better at regulating negative emotion and allocate more resources towards that goal (Mather et al., 2005a), they experience age-related cognitive decline (Hedden & Gabrieli, 2004). Thus, I hypothesized that the available cognitive resources in older women would be taken up by maintaining working memory, which would not permit them to regulate their emotional responses, thereby making negative stimuli more disruptive to their performance. In short, bodies rated as negative would be more disruptive to working memory performance than bodies rated as positive or neutral, and older women would me more disrupted by negative bodies than younger women.

Methods

Participants

Healthy women aged 25-35 (n=28) and 65-80 (n=27) were recruited for this study (Table1). All women were recruited through phone contact and advertisements to the general public. A subset of the women was in prior lab studies and thus was contacted from our database of previous study participants. Nine younger and 16 older women had additionally participated in a previous study of body image (Pruis et al., 2010). Health histories were obtained via phone interview and confirmed in person. Inclusion criteria included fluency in English and adequate vision (with correction if necessary) to view computer tasks. General exclusion criteria included: smoking or having quit less than one month from the study date; consuming >3 alcoholic beverages per day; score >10 on the Geriatric Depression Scale for older adults (Yesavage et al., 1983); score > 16 on the Center for Epidemiologic Studies Depression Scale for younger adults (Radloff, 1977); Mini-Mental Status Examination score < 26 for older adults (Folstein et al., 1975); psychiatric conditions that could influence emotion (e.g. schizophrenia or mood disorders); significant medical problems (e.g. uncontrolled hypertension); current use of medications likely to affect cognition (e.g. anti-depressants or anxiolytics); and history of neurological problems (e.g. stroke, seizure, or head trauma). Exclusion criteria specific to body image issues included: disordered eating behavior, as measured by a score > 20 on the Eating Attitudes Test-26 (Garner et al., 1982); previous or current diagnosis of an eating disorder, as determined by self-report;

and body mass index (BMI) less than18 or greater than 30, as determined by experimenter measurement of height and weight. This BMI range included “overweight” sizes, but was reflective of the average size of American women (McDowell et al., 2005). Two younger woman were excluded for depression, one for a score on the Wechsler Adult Intelligence Scale Vocabulary Test-Revised (WAIS-R) that was 3SD+ below the mean, one for a working memory task score that was 3SD+ below the mean, and one due to a technical error in test administration. Data from these five younger women were not included in the demographics or any study measures. No older women were excluded (final participants: N=23 younger and 27 older women). Our final groups of younger and older women were matched for years of education and raw scores on the Wechsler Adult Intelligence Scale-Revised (Wechsler, 1981). This measure provides a standardized approximation of functional intelligence. It was used as an additional measure of education, because years of schooling in the elderly may not reflect intellectual ability due to lifelong education and changes in education requirements over the last eight decades. This study was approved by the Institutional Review Board of OHSU. All participants provided written informed consent and were paid for their time and involvement in the study.

Procedures

Women completed screening measures, questionnaires, and all study tasks in one test session.

Stimuli

Detailed procedures for creating the body stimuli have been previously described (Pruis et al., 2010). In brief, these stimuli were made from photographs of real women that were incrementally morphed to be 35% fatter and 35% thinner than their actual size. The sizes of the body stimuli selected for this study ranged from underweight (BMI=16) to obese (BMI=33). Thus, women viewed morphed images of a broad size range of other women's bodies. Scrambled images of the bodies served as control stimuli. The scrambled images were created in Adobe Photoshop using a 5-pixel setting on the Scramble feature and then applying a 100% blur.

Valence ratings of bodies

Women viewed 180 morphed body stimuli and had 3 seconds to assign each one a valence rating using a 9 point scale (1=most negative, 5= neutral, 9=most positive). Every 45 trials the task paused for 30 seconds to provide the women with a brief break. Body stimuli that were assigned ratings 1- 3 were binned as negative, ratings 4- 6 neutral, and ratings 7-9 as positive. These body stimuli were then used in the Working memory Task (see below). In order to use each woman's most negative and most positive stimuli in the Working Memory Task, we selected the 36 lowest and highest scores from the negative and positive bins, respectively. Stimuli with ratings of 5 were used for the neutral body category. If more stimuli were needed to obtain 36 neutral bodies, then stimuli rated 4 or 6 were randomly selected until 36 stimuli were achieved. In cases where there were not 36 bodies assigned to the negative, positive, or neutral bins, bodies in that bin were used more than once. Bodies assigned 1's, 5's, and 9's were selected first for reuse in order to keep each bin as negative, neutral, and positive as possible. This occurred in 2 participants for negative bodies, 12 participants for neutral bodies, and 34 participants for positive bodies. Outcome measures were mean valence ratings of the body stimuli, median reaction time to assign valence ratings, and percent of body stimuli that fell into each valence bin.

Working Memory Task

During each trial, women viewed an arrow (750msec), a distracter stimulus (2000msec retention interval), and then another arrow (2000msec). Each was presented one at a time on the screen. Women were instructed to keep in mind the orientation of the first arrow while viewing the intervening distracter stimulus, and then decided whether the second arrow was in the same or a different orientation as the first arrow (Figure 1) and indicated their responses using a key pad. Therefore, the women had competition between the resources needed for the working memory task and the resources needed when viewing the distracter stimulus. There were four distracter types: bodies rated as negative, bodies rated as positive, bodies rated as neutral, and scrambled images. There were 36 trials for each stimulus type for a total of 144 trials. Outcome measures for this task included percent correct and median reaction time for the response to the second arrow. Mean valence rating of bodies rated negative, neutral, and positive that were used during the working memory task (n=108) were also assessed to ensure that valence levels were similar between groups.

Questionnaires

The Positive and Negative Affect Schedule (PANAS) was used to assess positive and negative affect on a general level using a 5-point Likert-type scale (Watson, Clark, & Tellegen, 1988). Primary and secondary control over age-related changes in appearance were measured with 22 standardized items rated on a 7-point Likert-type scale (Thompson et al., 1998). In this case, primary control refers to believing that one can control and change one's appearance, while secondary control refers to accepting your appearance the way it is (Thompson et al., 1998). The Drive for Thinness and Body Dissatisfaction subscales of the Eating Disorder Inventory (Garner et al., 1983) and the total score on the Societal Attitudes Towards Appearance Questionnaire-3 (Thompson et al., 2004) were used to assess general body image so that these women could be related to other studies of body image and aging in the literature.

Results

Data analysis

The Working Memory Task, Valence Rating Task, and questionnaire outcome measures were analyzed using mixed-model ANOVA or mixed-model repeated measures ANOVA where appropriate (SPSS version 17.0). Outcome measures for the Working Memory Task were first analyzed for the effect of viewing body stimuli versus viewing scrambled images and then analyzed for the effect of viewing bodies rated as negative, neutral, or positive. Only reaction times for correct trials were used to calculate the median reaction time in the Working Memory Task. Older women had higher BMI than younger women ($t(49)=4.51$, $p=0.04$), so BMI was used as a covariate in all analyses except the PANAS subscales. Exploratory regression analyses were conducted to examine relationships between behavioral measures and questionnaires. Some data did not fit a normal distribution. However, transforming the data did not improve normality, and non-parametric statistics yielded the same pattern of results. Thus, untransformed data and parametric statistics were reported. Two-tailed significance level was set at 0.05 for all analyses. Post-hoc p-values were Bonferroni corrected.

Valence Rating Task

The valence ratings of the 180 bodies rated in the Valence Rating Task did not differ by age group ($F(1,47)=1.01$, $p=0.32$), but they did differ by valence category ($F(2,96)=2555$, $p<0.001$), as expected by the study design. Bodies rated as negative had lower valence ratings than bodies rated as neutral, which were lower than bodies rated as positive ($Mean\%(SE)_{Negative}=2.15(0.05)$; $Mean\%(SE)_{Neutral}=4.90(0.03)$; $Mean\%(SE)_{Positive}=7.55(0.06)$; $t(49)$'s>40.9, $ps<0.003$). There were no significant interactions with age group.

In a separate analysis, body stimuli were divided into size bins based on BMI guidelines from the National Institutes of Health. There was a main effect of size bin on valence ratings ($F(3,144)=92.2$, $p<0.001$). Both younger and older women rated normal weight bodies as most positive followed by underweight and overweight bodies, which did not differ from each other, and then obese bodies, which were rated as most negative (Normal > Underweight = Overweight > Obese; Figure 2A; $t(49)$'s>3.43, $ps<0.003$). There was no interaction between age and BMI size bin.

Reaction time to assign valence ratings to body stimuli did not differ between younger and older women ($F(1,47)=0.11$, $p=0.74$) but did differ by valence category ($F(2,96)=43.6$, p<0.001). Women were faster to assign negative valence ratings to body stimuli than to assign neutral or positive valence ratings (Figure 2B; $t(49)$'s>7.11, $ps<0.003$). Reaction times to assign neutral and positive ratings did not differ from each other. There were no significant interactions.

The 180 bodies to which women assigned valence ratings did not fall equally into each valence category ($F(2,96)=29.3$, $p<0.001$). Women assigned positive ratings to a smaller percentage of the body stimuli than negative or neutral ratings (Figure 2C; $t(49)$'s>6.08, $ps<0.003$). The percentage of body stimuli that were assigned negative and neutral ratings did not differ from each other. There were no significant interactions.

Valence ratings of the body stimuli used in the Working Memory Task

The valence ratings of the 108 bodies (36 of each valence) used in the Working Memory Task did not differ by age group ($F(1,47)=0.19$, $p=0.67$), but they did differ by valence category ($F(2,96)=2211$, $p<0.001$), as expected per the study design. Bodies rated as negative had a lower valence ratings than bodies rated as neutral, which were lower than bodies rated as positive (Mean(SE)$_{Negative}$=1.64(0.08); Mean%(SE)$_{Neutral}$=4.99(0.01); Mean%(SE)$_{Positive}$=7.68(0.07); $t(49)$'s>44.0, $ps<0.003$). There were no interactions with age group.

Working Memory Task

Effect of viewing body stimuli versus viewing scrambled images during the retention interval

Younger and older women did not differ on percent correct for matching the arrow orientation in the working memory task when including trials that had body stimuli or scrambled images as distracters ($F(1,47)=1.51$, p=0.23). Viewing body stimuli was less disruptive to working memory performance than viewing scrambled images (Mean(SE)$_{Bodies}$=66.1(0.73); Mean(SE)$_{Scrambled}$=63.0(0.80); $F(1,48)=18.8$, $p<0.001$). There was no interaction between type of distracter and age group.

Younger women were faster at matching arrow orientation than older women ($F(1,47)=11.7$, $p=0.001$). Reaction times for matching arrow orientation did not differ when women viewed bodies or scrambled images during the retention interval

(Mean(SE)$_{Bodies}$=952(29.6); Mean(SE)$_{Scrambled}$=950(29.3); $F(1,48)=0.02$, $p=0.89$). There was no interaction between type of distracter and age group.

Effect of viewing bodies rated as negative versus neutral versus positive during the retention interval

Younger and older women did not differ for percent correct for matching the arrow orientation in the working memory task when only trials that had body stimuli as distracters were included ($F(1,47)=1.62$, p=0.21). However, there was a main effect of the affective rating of the body distracter ($F(2,96)=6.00$, $p=0.004$), such that viewing bodies rated as positive was more disruptive to working memory performance than viewing bodies rated as negative or neutral (Figure3A; $t(49)$'s>2.63, $ps<0.04$). Percent correct did not differ when distracters were bodies rated as negative versus bodies rated as neutral. There was no interaction between affective rating of the body distracter and age group.

Younger women were faster at matching arrow orientation than older women when only trials that had body stimuli as distracters were included ($F(1,47)=11.4$, $p=0.001$). There was no effect of the valence rating of the body distracter on reaction time for matching arrow orientation (Figure3B; $F(2,96)=0.99$, $p=0.38$), and there was no interaction between affective rating of the body distracter and age group.

Relationship between speed and accuracy

It was possible that older adults had similar accuracy on the working memory task as younger adults because they took longer to make their decisions. However, reaction time did not predict total percent correct in either age group (Young: $r=-0.16$, $p=0.23$; Old: $r=0.24$, $p=0.12$). Additionally, a between-groups ANOVA on percent correct for the working memory task with reaction time and BMI as covariates yielded no change in the pattern of results. Younger and older women still had similar performance on this task (without reaction time: $F(1,47)=1.78$, $p=0.19$; with reaction time: $F(1,46)=2.13$, $p=0.15$).

Questionnaires

Both groups of women experienced more positive than negative affect (ts>15.1, $ps<0.001$), as assessed by the PANAS. Younger and older women experienced similar levels of positive affect ($F(1,48)=0.30$, $p=0.59$) , but older women experienced less negative affect than younger women (Table 2; $F(1,48)=6.16$, $p=0.02$). Since negative affect differed between younger and older women, we used exploratory regression analyses to examine the relationship between negative affect and performance on the valence rating and working memory tasks. Negative affect did not predict valence ratings for the 180 bodies in the valence rating task in either age group (Younger: $b=-0.23$, $p=0.30$; Older: $b=-0.02$, $p=0.92$). It also did not predict total percent correct in the working memory task in younger women ($b=-0.15$, $p=0.49$) but was marginally predictive of working memory performance in older women ($b=-0.33$, $p=0.09$).

Younger and older women did not differ on cognitive control scores (Table 2; $F(1,47)=0.003$, $p=0.95$). Women used primary control strategies more than secondary control strategies ($F(1,48)=5.54$, $p=0.02$). There was no significant interaction with age. Others have found relationships between primary cognitive control and emotional distress in younger and older women (Thompson et al., 1998). We used exploratory regression analyses to examine the relationship between primary cognitive control and valence ratings. Primary cognitive control did not predict mean valence ratings of the 180 bodies used in the valence rating task in younger or older women ($bs<0.19$, $ps>0.35$).

Younger and older women had similar body dissatisfaction (Table 2; $F(1,47)=0.68$, $p=0.41$). However, younger women had higher drive for thinness ($F(1,47)=4.71$, $p=0.04$) and experienced more societal influence on their appearance than older women ($F(1,47)=9.51$, $p=0.003$).

Discussion

There were no effects of age on any study measure except overall reaction time on the working memory task and negative affect on the PANAS. Older women were slower on the working memory task and had less negative affect than younger women. Both younger and older women rated normal weight bodies as most positive, were slower to categorize bodies as positive than to categorize bodies as negative, and categorized a smaller percentage of bodies as positive than as negative or neutral. Furthermore, viewing bodies that were rated as positive was more disruptive to working memory performance than viewing bodies rated as negative or neutral in both younger and older women. However, viewing scrambled images was more disruptive to working memory performance than viewing body stimuli. Finally, younger and older women endorsed similar use of primary versus secondary control with respect to age-related changes in appearance, and older women experienced less negative affect than younger women.

The similarity in ratings of, and reaction time to, body stimuli during the Valence Rating Task between younger and older women was unexpected. We hypothesized that the positivity bias seen in older adults for other emotional stimuli (Charles et al., 2003; Mather et al., 2003) would translate to bodies. Meaning, for example, that older women would have higher (i.e. more positive) valence ratings of bodies, a higher percentage of bodies categorized as positive, and/or faster reaction times to categorize bodies as positive versus negative, as compared to younger women. Of note, these older women are similar to other groups of older women reported in the literature in terms of affect (Mroczek et al., 1998; Charles et al., 2001) and body image (Bedford et al., 2006; Lewis et al., 2001). These older women have lower negative affect, lower drive for thinness, and experience less societal influence on their body image, but have similar body dissatisfaction in comparison to the younger women. However, it appears that the affective and body image factors that differentiate younger and older women do not, in fact, translate to differential affective responses to bodies. Overall, these data suggest two things: 1) that affective responses to body stimuli do not change with age in women, although longitudinal studies would be needed to confirm this, and 2) the positivity bias seen in older adults for other types of affective stimuli does not apply to body stimuli, at least not in women.

We hypothesized that viewing bodies rated as negative would be more disruptive to working memory performance in older than in younger women, because older women would not have enough available cognitive resources to regulate their response to the negative bodies in addition to maintaining working memory. However, this was not the case. Instead, viewing bodies rated as positive was more disruptive to working memory performance than viewing bodies rated as negative, regardless of age. This begs the question: why? One possibility is that women, regardless of their age, have more difficulty deciding that a body is positive than deciding a body is negative, which is supported by their slower reaction time to assign positive valence ratings to body stimuli than to assign negative valence ratings. This longer processing time results in a larger disruption in the maintenance of working memory. Women may have a more visceral "gut" reaction to the bodies they perceive as negative, which is why they are faster to categorize them. However, the response to bodies rated as positive may not be as visceral, and thus a more deliberative process occurs, which takes longer and is more disruptive to working memory. This hypothesis would fit with what is known of neurobiological responses to other affective stimuli. The prefrontal cortex is involved in appraisal of stimuli (Ochsner et al., 2002), suggesting that higher prefrontal activation to positive over negative body stimuli may underlie this behavioral finding. However, neuroimaging studies would be needed to confirm this hypothesis. Overall, these data suggest that body stimuli do not induce the same emotion regulation mechanisms as other emotional stimuli.

Cognitive control over appearance did not have the effect on valence ratings or working memory disruption that we anticipated. Both groups of women used primary more than secondary control strategies, which was expected based on a study that saw a similar pattern using this questionnaire in middle-aged and younger adults (Thompson et al., 1998). However, higher primary control of appearance did not correspond to less negative ratings of bodies or better working memory performance in either group of women. The results from this questionnaire lend further support to the suggestion that the cognitive control that older adults use with other affective stimuli does not apply to bodies in older women.

Working memory performance was the same between younger and older women. This was surprising because older adults frequently perform worse on working memory tasks than younger adults, provided the working memory load is high enough (Van der Linden, Bredart, & Beerten, 1994). In the current study, older adults also took more time to make their responses than younger adults. This pattern has been seen in other tasks that examine age effects on working memory (Cabeza et al., 2004). The Processing-Speed Theory of aging contends that slower processing speed partially accounts for the worse cognitive performance seen in older adults (Salthouse, 1996). In some cases, giving older adults more time to make their responses can improve their performance (Salthouse, 1996). We examined the relationship between speed and accuracy in our data, but did not find a relationship between working memory performance and reaction time. Finally, neither group here performed at floor or ceiling, suggesting that task sensitivity was not an issue.

Contrary to our predictions, viewing body stimuli was not more disruptive to working memory performance than viewing scrambled images. Our results are in contrast to a working memory study with a similar design that used negative and neutral scenes and scrambled images as distracters (Dolcos et al., 2006). In that study, negative scenes were more disruptive to performance than scrambled images. However, their participants were seeing both the scenes and the scrambled images for the first time while they performed the working memory task. The women in our study had previously seen the body stimuli during the valence rating task but not the scrambled images. The previous exposure to the body stimuli may have made them less novel than the scrambled images, making the scrambled images more disruptive to performance. On the other hand, the scrambled images were more similar to each other than the body stimuli, which suggested that women would habituate faster to scrambled images, and, therefore, they should be less disruptive. However, there were 3 times the numbers of body distracters than scrambled image distracters during the working memory task, so their infrequent presentation could have made them more surprising, and thus more disruptive to performance.

In conclusion, bodies were affective stimuli that disrupted performance when viewed during the retention interval of a working memory task, and disruption was greater for viewing bodies rated as positive. However, the affective responses to body stimuli and their disruption of the working memory task did not differ between younger and older women. Our data suggest that age does not affect emotional responses to body stimuli in the same way it affects emotional responses to other types of stimuli. More specifically, the positivity bias seen in older adults likely does not apply to the body stimuli used here. Furthermore, our data suggest that there is something unique about bodies that are rated as positive, because a smaller percentage of body stimuli are classified as positive, it takes longer to assign a positive valence rating to a body than to assign a negative rating, and viewing them disrupts working memory performance more than viewing bodies rated as neutral or positive. This data raises questions about the neurobiological underpinnings of these results, which will be addressed in the MRI study in Chapter 3.

Acknowledgments

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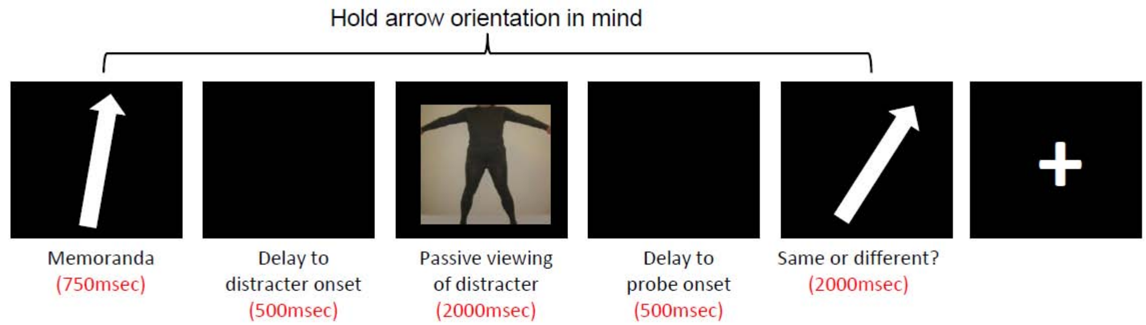

Figure 1. Task design. A crosshair signaled the beginning of each new trial. Women viewed the first arrow for 750msec, had 2000msec to view the body or scrambled image, and then had an additional 2000msec to decide if the second arrow was in the same or different orientation as the first arrow.

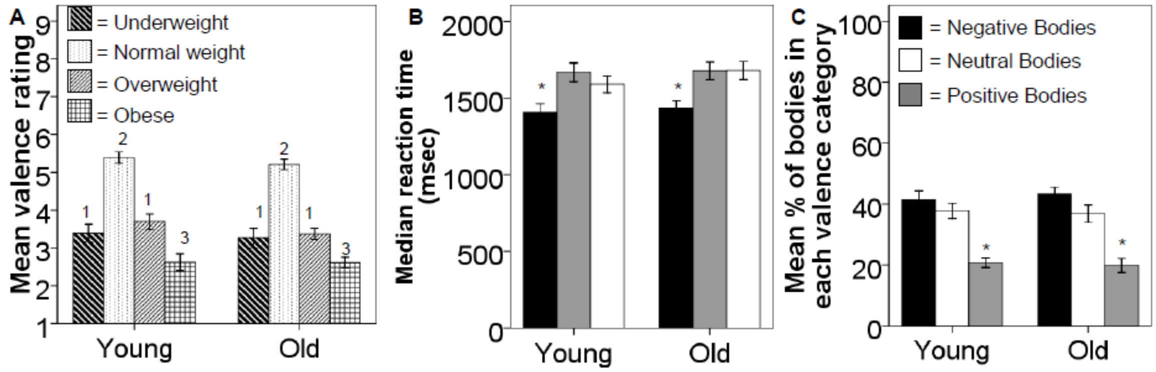

Figure 2. Valence rating task. (A) Younger and older women rated normal weight bodies as most positive followed by underweight and overweight bodies and then obese bodies, which were rated most negatively (i.e. Normal < Under, Over < Obese). NIH BMI Guidelines: Underweight < 18.5; Normal weight = 18.5 – 24.9; Overweight = 25.0 – 29.9; Obese = 30+. Different numbers above each bar meant that those sizes were significantly different from each other. (B) Younger and older women were slower to categorize body stimuli as negative than as positive or neutral. * = Negative < Positive, Neutral. (C) Younger and older women categorized fewer body stimuli as positive than as negative or neutral. * = Positive < Negative, Neutral.

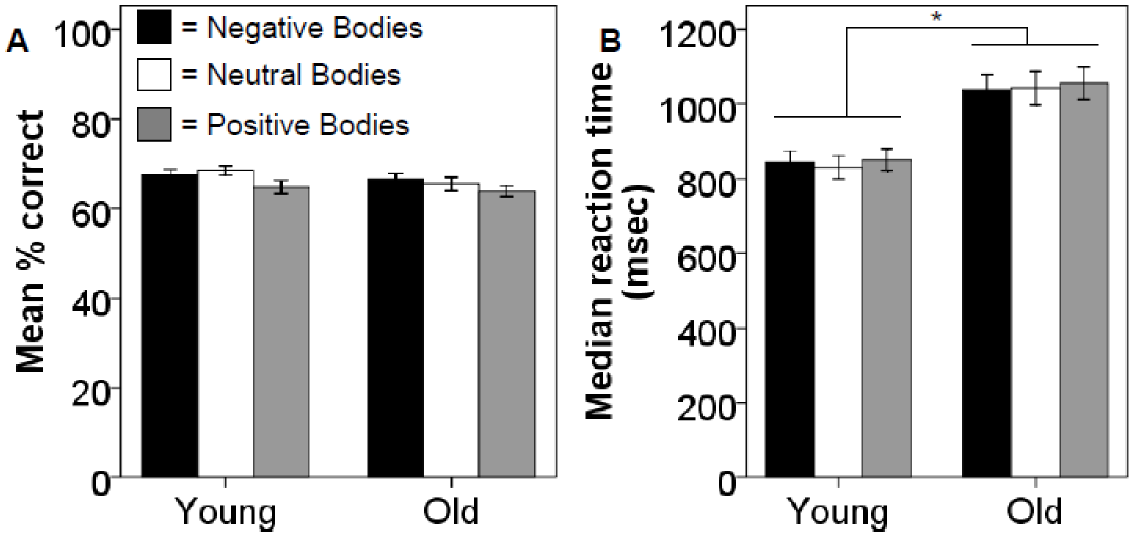

Figure 3. Working memory performance. (A) Viewing bodies rated as positive was more disruptive to working memory performance than viewing bodies rated as negative or neutral. There was no difference between younger and older women. Main effect when combining groups: Positive < Negative, Neutral. (B) Younger women were faster to make the arrow orientation decision than older women, but there were no effects of the valence category of the bodies on decision time. * = Older > Younger.

Table 1. Participant demographics.

	YOUNGER (*n* = 23)	OLDER (*n* = 27)
Age (years)	27.7 (25-32)	72.3 (65-80)
Education (years)	15.9 (14-19)	16.3 (10-21)
WAIS-R[a] Vocabulary raw scores	59.2 (44-69)	61.5 (46-68)
Geriatric Depression Scale	NA	2.3 (0-6)
Center for Epidemiologic Depression Scale	5.26 (0-13)	NA
Mini-Mental Status Examination	NA	29.2 (26-30)
Eating Attitudes Test-26	3.74 (0-12)	4.33 (0-14)
Body Mass Index[b]	**23.1** (19-28)	**25.0** (19-31)

[a] Wechsler Adult Intelligence Scale- Revised
[b] Younger < Older.
Note: Range is shown in parentheses.

Table 2. Questionnaires.

Questionnaire	Younger Mean (SE)	Older Mean (SE)
PANAS[a]		
Negative affect[b]	**18.4** (0.91)	**15.6** (0.72)
Positive affect	38.2 (0.84)	38.9 (0.89)
Cognitive control[c]		
Primary strategies[g]	5.20 (0.19)	4.98 (0.18)
Secondary strategies[g]	4.68 (0.15)	4.87 (0.13)
Body dissatisfaction[dg]	28.7 (1.76)	26.6 (1.63)
Drive for thinness[beg]	**18.3** (1.17)	**14.8** (1.08)
SATAQ-3 total score[bfg]	**86.3** (4.33)	**67.8** (3.99)

[a] Possible total per subscale = 50.
[b] Younger > Older women.
[c] Possible total per subscale = 7.
[d] Possible total =54 .
[e] Possible total = 42.
[f] Possible total = 150.
[g]BMI-adjusted means.

Chapter 3: Altered brain activation in response to bodies in women who have recovered from anorexia nervosa

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Abstract

Frontal lobe mediated regulation of emotion may permit women to recover from anorexia nervosa (AN) and decrease their affective response to bodies. fMRI was used to examine brain activity in women who had recovered from AN and control women when working memory was disrupted by viewing distracter stimuli that were bodies of varying sizes. The body stimuli were also rated for valence (negative, neutral, positive). Women who had recovered from AN were significantly faster to assign negative ratings to the body stimuli and categorized a higher percentage of body stimuli as negative than did control women. Working memory performance was similar in both groups, and viewing bodies rated as negative was more disruptive to working memory than viewing bodies rated as neutral or positive. The amygdala activated during the working memory task in women who had recovered from AN but not in control women, and the fusiform responded more in women who had recovered from AN than in control women. There was more suppression of medial prefrontal cortex activity in women who had recovered from AN than in controls when the distracter stimulus viewed during the working memory was a negative body. These results suggest that higher amygdala and fusiform activity in response to body stimuli occurs despite recovery. However, medial prefrontal suppression may permit functional recovery in the face of continued negativity towards bodies in women who had recovered from AN.

Key words: body image, recovery, anorexia nervosa, amygdala, prefrontal cortex, fusiform gyrus, fMRI, working memory

Body dissatisfaction refers to unhappiness with one's body shape or size. As discussed in the overall Introduction to this document, body dissatisfaction is more common in women and has a variety of potential causes. Healthy young women overestimate their actual body size (Thompson et al., 1989), and, in comparison to men, a smaller percentage of women find their body size socially acceptable (Rand et al., 2000). While both men and women recognize that they get heavier with age, women have a larger discrepancy than men between their perceptions of their current size and their ideal size (Altabe et al., 1993). In fact, 71% of women want to be thinner, but 73% of those women are already in a normal weight range (Allaz et al., 1998). There are several theories as to why body dissatisfaction occurs, including weight gain and body changes associated with puberty (Richards et al., 1990); perceived pressure to be thin from friends, family, and media (Stice et al., 2002b); and internalization of the stereotypical ideal female appearance (Stice et al., 2001), which is becoming increasingly thin (Byrd-Bredbenner et al., 2005). Collectively, these data suggest that body dissatisfaction is a pervasive issue among adolescent girls and women.

Anorexia nervosa (AN) differs from general body dissatisfaction and poor body image. This disorder is characterized by refusal to maintain a healthy body weight for one's age and height; intense fear of gaining weight or becoming fat; denial of the seriousness of one's low body weight; and undue influence of body weight and shape on self-evaluation (American Psychiatric Association, 2000). In women who are post-menarcheal but premenopausal, there is typically a cessation of menstrual cycles due to low body weight (Swenne, 2004), lowered metabolism (Sterling et al., 2009), and altered hormones (Mitan, 2004). Women with AN suffer many physical consequences due to their disorder, such as lower blood pressure and heart rate (Cong et al., 2004; Misra et al., 2004; Romano et al., 2003); muscle wasting (McLoughlin et al., 1998; Melchior, 1998); slowed digestion and constipation (Stacher, 2003); and high mortality rates. The crude mortality rate for women diagnosed with AN is 5.9% (Sullivan, 1995), which is more than 7 times higher than the crude mortality rate for the general adult population in the US (Zlotnik, 2009). Onset of AN typically occurs in teenagers or women in their early twenties. The lifetime prevalence for AN in women aged 18 and older is 0.9% (Hudson et al., 2007). Several factors have been proposed as potential causes of eating disorders. External factors include the influence of peers (Meyer et al., 2008) and family (Jacobs et al., 2009). Internal factors include high body dissatisfaction (Stice et al., 2002a), feeling lack of control over one's life (Williams et al., 1993), anxiety (Bulik et al., 1997), and, more recently, altered neurobiology (Kaye et al., 2009). This study expands on the current literature by exploring the neural basis of recovery from AN.

Recovery and relapse are significant issues for women with AN. A 7.5 year longitudinal study found that relapse occurs in 40% of women who have been diagnosed with AN and only 33% ever reach full recovery (i.e. complete absence of symptoms (Herzog et al., 1999). Recovery is usually defined as restoration of weight, initiation of menstrual cycles, and absence of restricting or purging behavioral symptoms (Uher et al., 2003; Klump et al., 2004; Casper, 1990). If we can understand what leads to biological and psychological recovery, perhaps better treatments can be developed for women who still suffer from this disorder. Women who have recovered from AN offer a unique opportunity to study persistent behavioral, psychological and neurobiological traits associated with AN (Casper, 1990; Bulik et al., 1997; Kaye et al., 2009) without the physical effects that starvation has on the body and brain (Swenne, 2004; Sterling et al., 2009; Matsumoto et al., 2006). Studying these women may suggest the key features that permit recovery.

Bodies are unique affective stimuli to women, especially to women with AN. Healthy women without an eating disorder rate fatter images of their own body as more unpleasant in comparison to their actual size (Kurosaki et al., 2006). In Chapter 2, women rated underweight, overweight, and obese bodies more negatively than normal weight bodies. Women with AN have higher aversion to under, over, and normal weight line drawings of bodies than healthy women, suggesting that women with AN are generally more sensitive to body stimuli than healthy women (Uher et al., 2005). However, women with AN also rate overweight bodies as more aversive than normal or underweight bodies, while healthy women rate underweight bodies as more aversive than normal or overweight bodies (Uher et al., 2005). Additionally, stimuli associated with weight are aversive stimuli to women with AN. They rate food stimuli as more disgusting and less pleasurable than healthy women, but women with AN do not differ from healthy women on ratings of non-food and neutral stimuli (Uher et al., 2004). Interestingly, women who have behaviorally recovered from AN do not differ from healthy women in their ratings of food, non-food, negative, or neutral stimuli and have less fear and less disgust in response to food stimuli than women with chronic AN (Uher et al., 2003). These data suggest that body image-related stimuli elicit strong negative emotional responses in women with AN and that with recovery the intensity of that emotional response declines.

The brain circuit that responds to bodies includes (but is not limited to) the fusiform gyrus. The fusiform region is typically associated with responding to faces and has been considered face-selective (Haxby et al., 2000; O'Craven et al., 2000), meaning that it responds more to faces than other types of stimuli. However, recent work has shown that the fusiform responds robustly to bodies (Peelen et al., 2005; Schwarzlose et al., 2005; Taylor et al., 2007);for review see (Peelen et al., 2007). Furthermore, the fusiform is sensitive to emotion in body stimuli. Hadjikhani & de Gelder (2003) created body stimuli with blurred faces that were posed in fearful or neutral positions. They found that the fusiform region had higher activation in response to the fearful body expressions than the neutral body expressions (Hadjikhani et al., 2003). This study examined the fusiform, in addition to the amygdala and PFC, as regions of interest due to this region’s activation in response to bodies and its sensitivity to emotion expressed in bodies.

Neuroimaging studies of women who suffer from AN and women who have recovered from AN suggest that higher prefrontal activity leads to more regulation of responses to body image-related stimuli. Women with restricting AN activate the amygdala in response to viewing fatter images of their own bodies versus images of their actual size, while women who have never had an eating disorder activate the amygdala in addition to the medial, dorsolateral, and ventrolateral PFC for the same comparison (Miyake et al., 2010). Region of interest analyses show that amygdala activation is the same between women with AN and healthy control women, but PFC activation is greater in control women than women with AN. This study suggests that women with AN and healthy control women both activate the emotion system in the brain in response to bodies, but the prefrontal activation may mean that healthy control women regulate those responses more. Interestingly, women who have recovered from AN have higher prefrontal activation in response to food versus non-food stimuli than both women who currently have AN and healthy control women (Uher et al., 2003), suggesting that recovery may be due to higher prefrontal regulation of responses to body image-related stimuli. Of note, women who recovered from AN did not differ from women who currently have AN or healthy control women in their brain activation to negative versus neutral scenes (Uher et al., 2003), suggesting that recovery is specific to body image-related stimuli and not a general change in emotional control. Taken together, this suggests that a higher prefrontal response to body image-related stimuli leads to regulation of responses to those stimuli and a healthier body image.

Studies of baseline cerebral blood flow (meaning not in response to any stimuli) suggest that there is less prefrontal activation (and thus potentially less regulation) in anorexia nervosa. In one longitudinal study, young women had higher prefrontal blood flow after behavioral therapy, as compared to before (Matsumoto et al., 2006). Additionally, women who have recovered from anorexia nervosa have similar prefrontal blood flow as women who never had an eating disorder (Frank et al., 2007). These blood flow studies suggest that restoring normal blood flow in the brain is a component of recovery. However, it is not the only factor affecting neural responses to body stimuli in women who have recovered from AN, because these women also have higher prefrontal activation in response to body image-related stimuli than healthy women (Uher et al., 2003). Therefore, it is not simply a restoration of baseline brain metabolism that changes neural and behavioral responses in women who have recovered from AN, but a prefrontal activation above and beyond that of controls.

One way to test the prefrontal regulation hypothesis would be to determine the effect of emotional body stimuli on a task that requires regulation and engages the PFC. Working memory refers to the ability to maintain and manipulate information during a cognitive task (Baddeley, 2010). Working memory taps prefrontal resources, as evidenced by lesion (Boisgueheneuc et al., 2006); for review see (Muller et al., 2006) and neuroimaging studies (D'Esposito et al., 1998; D'Esposito et al., 1999). Specifically, these tasks activate lateral prefrontal (Bunge et al., 2001; Gazzaley et al., 2004; Ungerleider et al., 1998) and suppress medial prefrontal brain regions (Drobyshevsky et al., 2006), which are similar to regions of the brain that are involved during the processing and regulation of emotion (Goldin et al., 2008; Levesque et al., 2003; Ochsner et al., 2002; Williams et al., 2006b). Furthermore, negative scenes are more disruptive to working memory performance than neutral scenes (Dolcos et al., 2006). This suggests that emotional stimuli can disrupt working memory performance and alter brain activation. Therefore, in this study, body stimuli that were previously rated as negative, neutral, or positive were used as distracters during the retention interval of a working memory task. If women were only viewing body stimuli, I would expect the amygdala to have higher activation in controls than women who had recovered from AN. This would be due to regulation of the emotional responses by the lateral PFC, which would decrease the intensity of the negative response to bodies in women who had recovered AN. Thus, amygdala activation would be lower than in controls but the lateral PFC activation would be higher. However, since women are also performing a working memory task at the same time, I predicted that women who had recovered from AN would have a harder time regulating their negative emotional responses to bodies. Therefore, I hypothesized that lateral PFC activation would still be higher in women who had recovered from AN than in control women, but amygdala activation in women who had recovered would increase too. The combination of these things would disrupt performance on the working memory task in women who had recovered from AN, such that they would have worse performance than controls when viewing body stimuli that they rated as negative. However, the two groups will have similar performance for bodies they think are neutral or positive, because those bodies will not require as much regulation. Finally, I predicted that fusiform activation would be similar between groups, although it would be more sensitive to negative than positive emotion.

Methods

Participants

Healthy women who had never had an eating disorder (Control; n=17) and women who had recovered from anorexia nervosa (RecAN; n=16) were recruited for this study. All women were recruited through our participant database, advertisements to the general public, and the patient contact database at Oregon Health & Science University (OHSU). Most women (n=28) had participated in a previous lab study involving the behavioral tasks presented here and were re-contacted to participate in this fMRI study as a follow up. The women were 25 years or older (see Table 1 for participant characteristics). Health histories were obtained via phone interview and confirmed in person. Exclusion criteria specific to the control group included depression as measured by scores greater than 16 on the on the Center for Epidemiologic Studies Depression

(CES-D) Scale (Radloff, 1977); self-report of previous or current diagnosis of an eating disorder; and use of medications for depression, anxiety, or any other psychiatric condition. Women who had recovered from AN had to meet DSM-IV criteria for AN in the past, but had to have a stable, healthy body weight for the past two years and regular menstrual cycles (at least 10 in the last year) if they were not post-menopausal (Uher et al., 2003). DSM-IV criteria for past AN included weight <85% expected for height and age (~BMI<=16); fear of gaining weight or becoming fat; and undue influence of body shape or weight on self-evaluation, or denial of the seriousness of their low body weight (American Psychiatric Association, 2000). Since co-morbidity with depression and anxiety is high in women who have AN (Hudson et al., 2007; Herzog, Nussbaum, & Marmor, 1996), women who had recovered from AN were permitted to be on anti-anxiety or anti-depressant medication. Women on anti-psychotic medication were excluded. These criteria were similar to those in another fMRI study of women who had recovered from AN (Uher et al., 2003). Women who have recovered from AN are rare and difficult to recruit. Therefore, we did not exclude one woman with a CES-D score of 21, who met all the other study criteria. Removing her did not change the overall pattern of results for the fMRI data. Exclusion criteria common to both groups included abnormal eating behaviors as shown by scores of scores greater than 21 on the Eating Attitudes Test-26 (Garner et al., 1982); major psychiatric disorders (e.g. bipolar disorder, schizophrenia, PTSD); a history of head trauma that resulted in an unconscious state for more than 15 minutes; a history of seizures, strokes, or other neurological illness; consuming greater than 3 alcoholic beverages per day; smoking cigarettes; and body mass index (BMI) less than 18 and greater than 30. This BMI range included "overweight" sizes, but was reflective of the average size of American women (McDowell et al., 2005). All women included here had never been unconscious for more than 15 minutes, but two women who had recovered from AN had been knocked unconscious for less than 15 minutes due to accidents that happened 20+ years prior to their participation in this study. Exclusion criteria specific to MRI included no in-dwelling magnetic metal and no claustrophobia. We also administered the first part of the EATATE Lifetime Diagnostic Interview (Anderluh, Tchanturia, Rabe-Hesketh, Collier, & Treasure, 2009) to women who had recovered from AN in order to characterize their history with the disorder (Table 2). One woman in the control group and one woman in the recovered AN group were excluded due to technical errors during fMRI data collection. Data from these two women were not included in the demographics or any study measures (final participants: n = 16 control women and 15 women who recovered from AN). Our final groups of women were matched for years of education and age-scaled scores on the Wechsler Adult Intelligence Scale Vocabulary Subtest-Revised (Wechsler, 1981). This study was approved by the Institutional Review Board of OHSU. All participants provided written informed consent and were paid for their time and involvement in the study.

Questionnaires

The Body Dissatisfaction and Drive for Thinness subscales of the Eating Disorder Inventory (Garner et al., 1983), the Body Shape Questionnaire (Cooper et al., 1987), and the Sociocultural Attitudes Toward Appearance Questionnaire-3 (Thompson et al., 2004) were used to characterize body image. The International Short-form of the Positive and Negative Affect Schedule (Thompson, 2007), the Beck Depression Inventory (BECK,

WARD, MENDELSON, MOCK, & ERBAUGH, 1961), and the Beck Anxiety Inventory (BECK, Epstein, Brown, & Steer, 1988) were used to characterize affect.

Stimuli

Detailed procedures for creating the body stimuli have been previously described in Chapter 1 (Pruis et al., 2010). In brief, these stimuli were made from photographs of real women that were morphed in 3.5% increments to be 35% fatter and 35% thinner than their actual size. The sizes of the body stimuli selected for this study ranged from underweight (BMI=16) to obese (BMI=33). Thus, women viewed morphed images of a broad size range of other women's bodies. Scrambled images of the bodies served as control stimuli. The scrambled images were created in Adobe Photoshop using a 5-pixel setting on the Scramble feature and then applying a 100% blur.

Valence Rating Task

We use the same method here as was used in a study of body image in aging. Detailed procedures for this task have been previously described (see Chapter 2). In order to use stimuli for the fMRI working memory task that were tailored to each woman's judgment of bodies, we selected stimuli based on each woman's valence ratings. In brief, women viewed 180 morphed bodies and had 3 seconds to assign each one a valence rating using a 9 point scale (1=most negative, 5= neutral, 9=most positive). Body stimuli that were assigned ratings 1- 3 were binned as negative, ratings 4- 6 were binned as neutral, and ratings 7-9 were binned as positive. In order to use each woman's most negative and most positive stimuli in the Working Memory Task, we selected the 36 lowest and highest scores from the negative and positive bins, respectively. Stimuli with ratings of 5 were used for the neutral body category. If more stimuli were needed to obtain 36 neutral bodies, then stimuli rated 4 or 6 were randomly selected until 36 stimuli were achieved. Outcome measures were mean valence ratings of the 180 body stimuli, median reaction time to assign valence ratings, and the percentage of body stimuli that fell into each valence bin.

Working Memory Task

Women performed the working memory task during fMRI data collection. We used an event-related design. During each trial, women viewed an arrow (1000msec), a distracter stimulus (4000msec retention interval), and then another arrow (2000msec). Each one was presented one at a time on the screen. Women were instructed to keep in mind the orientation of the first arrow while viewing the distracter stimulus, and then decide whether the second arrow was in the same or a different orientation as the first arrow (Figure 1). Women indicated their response using two response keys on a button box that they held on their torso (left key = same, right key = different). There was a 1000msec delay before and after the presentation of the distracter stimulus creating a total retention interval of 6000msec. Additionally, there was a jittered delay of 7000, 9000, or 11000msec between each trial for total trial lengths that ranged from 16-20s. A between-trial jitter was used to ameliorate expectancy effects on brain activity. Behavioral outcome measures for this task included percent correct and median reaction time for the response to the second arrow. Mean valence ratings of the bodies categorized as negative, neutral, and positive that were used in the working memory task (n=108) were also assessed to ensure that valence ratings were similar between groups.

There were four distracter types used during the working memory retention interval: body stimuli rated as negative, bodies rated as positive, bodies rated as neutral, and scrambled images. There were 36 trials for each distracter type for a total of 144 trials. These trials were split into 4 fMRI runs of 36 trials. Each run contained the same number of stimuli for each distracter type, which was shown in pseudo-random order. We took care to ensure that no more than 3 distracters of the same type were shown consecutively, so as not to induce a lasting affective state (see methods in Dolcos & McCarthy, 2006). Per other neuroimaging studies of working memory, only correct trials were used in the fMRI and behavioral analyses (Dolcos et al., 2006).

MRI data collection

MRI data were collected with a Siemens 3T TIM Trio scanner (Erlangen, Germany) and 12-channel head coil in the Advanced Imaging Research Center at OHSU. Subjects were positioned supine, headfirst in the scanner and wore earplugs to dampen the noise. Air conductance headphones were used to further dampen scanner noise and to communicate with the subjects from the control room. Structural images were acquired using a magnetization prepared rapid gradient echo (MPRAGE) T1 sequence with the following parameters: repetition time (TR) = 2300msec; echo time (TE) = 3.4msec; flip angle (FA) = 12 degrees; field of view (FOV) = 256mm; matrix= 256X256. Slices were: 1mm thick, 144 total, collected in a transverse orientation. Functional brain activity was measured using an echo-planar imaging, blood oxygenation level-dependent (EPI-BOLD) sequence with the following parameters: TR = 2000msec; TE = 30msec; FA = 90 degrees; FOV = 220 mm; matrix= 64X64. The 38 slices were 4 mm thick and collected in an oblique orientation (T > C -16.2).

MRI data processing

MRI data were processed and analyzed using Brain Voyager QX 2.1 (Brain Innovations; Maastricht, Netherlands). Functional data from all 4 runs of the working memory task were spatially smoothed with a Gaussian filter (FWHM = 8mm) and temporally corrected with a high pass filter and linear trend removal. Slice scan time and 3D motion corrections with sinc interpolations were applied to all functional data. Each run of the functional data was coregistered to the structural image, and both structural and functional data were transformed into Talairach space (Talairach & Tournoux, 1988). Activation that occurred during the 4000msec presentation of the distracter was modeled for subsequent whole brain and region of interest analyses. Thus, we examined brain activity for the period when the women were viewing the body and also holding in mind the orientation of the arrow.

Whole brain analyses

Comparison of whole brain activation between groups

All Talairach-transformed functional data from all subjects in both groups were concatenated using Brain Voyager's Multi-Run GLM function in order to create one data set for the between-subjects whole brain analysis. A contrast of all distracters versus baseline was used to show all potential areas of task activation for all distracter types (Table 4). We used a stringent statistical threshold ($p=0.00001$) to isolate only the most activated regions and applied a cluster threshold of 10 voxels. The center of mass of each cluster was assigned a hemisphere, region, and BA number using Talairach Daemon software (Lancaster et al., 2000). Between-group analyses that used a random effects mixed-model were performed on clusters of activation from Table 4. One cluster from the lateral prefrontal cortex (PFC) and another cluster from the medial PFC were chosen, because these were a priori regions of interest. Thus, cluster activation was compared between groups for bodies rated as negative, neutral, and positive and scrambled images.

Comparison of whole brain activation within groups

Within-group whole brain contrasts of the functional data were performed separately for each group. We averaged all runs of each individual across each group, and then applied a random effects general linear model. Contrasts were all body stimuli versus scrambled images (i.e. all body stimuli – scrambled images) and each emotion versus neutral (i.e. negative – neutral, positive – neutral). Since there were more trials with body stimuli than with scrambled images, Brain Voyager's balancing option was applied to the all body stimuli versus scrambled images contrast. A 22-voxel cluster threshold, as determined by Brain Voyager's Monte Carlo simulation (Goebel, Esposito, & Formisano, 2006), was applied at $p = 0.001$. Talairach coordinates for the center of mass of each surviving cluster were assigned a hemisphere, region, and Brodmann Area (BA) number using Talairach Daemon software (Lancaster et al., 2000).

A priori region-of-interest (ROI) analyses

In addition to the whole brain comparisons, separate voxel-wise ROI analyses were performed on the amygdala, the lateral PFC, the medial PFC, and the fusiform gyrus (FG). The amygdala of each subject was defined using a mask that was created based on Talairach boundaries (Figure 2A). This mask covered the entire human amygdala, as resolution of the anatomical scan was not high enough to accurately parse out amygdala subnuclei. What constitutes the lateral or medial PFC varies from study to study, so the functional data were used to define the prefrontal ROIs. Smaller, more focused regions of the large prefrontal clusters of activation that were found in the between group whole brain analyses were quantified using cubes. Therefore, the same contrast was used (i.e. all subjects, all stimuli vs. baseline, p=0.00001, cluster threshold=10). The centers of the lateral (Figure 6A) and medial (Figure 6B) prefrontal clusters were used to place the ROI cubes. Thus, the lateral PFC ROI was comprised of two 20mm cubes centered at +/-40, -2, 34 (Figure 2B) and the medial PFC ROI was comprised of two 10mm cubes centered at +/-10, 43, 30 (Figure 2C). Finally, the FG was a 10mm cube centered at +/-35, -55, -12 (Figure 2D), which is similar to other FG coordinates in the literature (Hadjikhani et al., 2003; Peelen et al., 2005).

Time courses for each type of distracter were extracted from Talairach-transformed data for each ROI. We used event-related averaging with one pre-stimulus, one stimulus onset, and eight post-stimulus onset time points (10 time points total). Each time point was equivalent to one TR, which was 2000msec in duration. Thus, the time courses were 20 seconds long. Each time point was calculated as percent signal change from baseline. The crosshairs between trials served as baseline. Time courses were averaged across all participants and all distracter types to determine an overall grand mean time course for each ROI. The grand mean time courses were used to determine where each time course differed from zero. Only those points that differed from zero were used to calculate mean percent signal change values for each distracter type in each ROI.

Only the peak time point (post-stimulus point 6) differed from zero for the grand mean time course for the amygdala (see asterisk in Figure 7A). Stimulus onset through post-stimulus point 4 (P4) differed from zero for the grand mean time course for the medial PFC (see asterisks in Figure 7C). The peak and stimulus onset through P4 were used to calculate mean percent signal change for the amygdala and medial PFC, respectively. The lateral PFC and the FG both had two peaks in their time courses (Figure 7B,D). Since the homodynamic lag takes approximately 4-6 seconds (Huettel et al., 2004), the first peaks occurred too quickly to be a response to the modeled stimuli. Thus, for the lateral PFC and FG ROIs, only the second peak was used to calculate mean percent signal change. The beginning of the second peak was determined as the time point on the grand mean time course with the lowest value after the first maximum (see Figure 7B,D). All points that were significantly higher than zero were included in the second peak (see Figure 7B,D). In order to account for the effects of the first peak on the second peak, the mean percent signal change of the second peak was adjusted for the first time point in the second peak. For example, in the lateral PFC, the second peak consisted of post-stimulus time points 2 through 5. Therefore, the mean for post-stimulus time points 2 through 5 was adjusted for post-stimulus time point 2. In the FG, the second peak consisted of post-stimulus time points 3 through 5. Therefore, the mean for post-stimulus time points 3 through 5 was adjusted for post-stimulus time point 3. Thus, statistics for average percent signal change in the lateral PFC and the FG were calculated on the adjusted means.

Data analysis

The working memory task, valence rating task, questionnaire outcome measures, and average percent signal change were analyzed using mixed-model ANOVA or mixed-model repeated measures ANOVA where appropriate (SPSS version 17.0). Outcomes measures for the working memory task were first analyzed for the effect of bodies versus scrambled images on performance and then analyzed with a separate ANOVA for the effect of body valence on performance. Control women had higher BMI ($F(1,29)=6.84$, $p=0.01$) and lower age ($F(1,29)=4.82$, $p=0.04$) than women who recovered from AN, so BMI and age were used as covariates for between group comparisons. Exploratory regression analyses were conducted to examine relationships among behavioral measures, questionnaires, and percent signal change. Some data did not fit a normal distribution. However, transforming the data did not improve normality, and non-parametric statistics yielded the same pattern of results for all measures except the Beck Depression Inventory. Thus, non-parametric statistics (Mann-Whitney U Test) were reported for the Beck Depression Inventory, but untransformed data and parametric statistics were reported for all other measures. Two-tailed significance level was set at 0.05 for all analyses. Post-hoc p-values were Bonferroni corrected, unless otherwise noted.

Results

Questionnaires

Women who had recovered from AN had higher body dissatisfaction (Table 3; $F(1,27)=7.81$, $p=0.009$), higher body shape concern ($F(1,27)=9.27$, $p=0.005$), and experienced more societal influence on their appearance ($F(1,27)=5.38$, $p=0.03$) than women in the control group. There was a trend for women who had recovered from AN to have higher drive for thinness than control women ($F(1,27)=3.24$, $p=0.08$).

Women who had recovered from AN experienced more negative affect than control women ($F(1,27)=8.56$, $p=0.007$) and trended towards experiencing less positive affect than control women, as measured by the I-PANAS-SF (Table 3; $F(1,27)=3.21$, $p=0.08$) , but Beck Depression Inventory scores did not differ between groups (U=101.5, Z= -0.73, p=0.47). Beck Anxiety Inventory scores were higher in women who recovered from AN than in control women ($F(1,27)=9.67$, $p=0.004$).

Valence rating task

The 180 body stimuli to which women assigned valence ratings did not fall equally into each valence category ($F(2,58)=17.2$, $p<0.001$), which was modified by an interaction with group ($F(2,58)=7.71$, $p=0.001$). Women who had recovered from AN assigned negative valence ratings to a larger percentage of body stimuli than did control women ($F(1,29)=10.0$, $p=0.004$), while control women assigned neutral valence ratings to a larger percentage of body stimuli than did women who had recovered from AN ($F(1,29)=11.0$, $p=0.002$). The groups did not differ in the percentage of body stimuli to which they assigned positive ratings (Figure 3C; $F(1,29)=0.18$, $p=0.68$).

The valence ratings of the 180 body stimuli used in this task did not differ between women who had recovered from AN and control women ($F(1,27)=0.18$, $p=0.68$), but they did differ by valence category ($F(2,58)=1939$, $p<0.001$), as expected from the study design. Bodies rated as negative had lower valence ratings than bodies rated as neutral, which were lower than bodies rated as positive ($\text{Mean(SE)}_{\text{Negative}}=2.09(0.08)$; $\text{Mean\%(SE)}_{\text{Neutral}}=4.95(0.05)$; $\text{Mean\%(SE)}_{\text{Positive}}=7.59(0.05)$; $t(30)$'s>28.5, $ps<0.003$). There were no significant interactions with group.

When dividing the body stimuli into size bins based on BMI guidelines from the National Institutes of Health, there was a main effect of size bin (Obese < Underweight, Overweight < Normal; t(30)'s>3.96, ps<0.003) that was modified by an interaction with group (Figure 3a; $F(3,87)=3.99$, $p=0.01$). Women who had recovered from AN rated overweight bodies more negatively than did control women ($F(1,29)=4.85$, $p=0.04$). There was also a trend for women who had recovered from AN to rate normal weight bodies more negatively ($F(1,29)=2.97$, $p<0.10$) and underweight bodies more positively in comparison to control women ($F(1,29)=3.10$, $p<0.09$). Additionally, both control women (t(15)'s>6.05, *p*s<0.003) and women who had recovered from AN rated normal weight bodies more positively than all other sizes (t(15)'s>3.38, *p*s<0.01).

Reaction time to assign valence ratings to body stimuli did not differ between control women and women who had recovered from AN ($F(1,27)=1.08$, $p=0.31$) but did differ by valence category ($F(2,58)=56.6$, $p<0.001$). Women were faster to assign negative valence ratings to body stimuli than to assign positive valence ratings, which they were faster to assign than neutral valence ratings (negative < positive < neutral; Figure 3B; *t*(30)'s>3.11, *ps*<0.01). This was modified by a marginal interaction between group and valence category ($F(2,58)=2.96$, $p=0.06$). Women who had recovered from AN were faster to assign negative valence ratings to body stimuli than were control women ($F(29)=5.35$, $p=0.03$). Reaction time to assign neutral and positive valence ratings did not differ between groups.

Valence ratings of the stimuli used in the fMRI working memory task

The valence ratings of the 108 body stimuli (36 of each valence) that were used in the working memory task did not differ by group ($F(1,27)=0.87$, $p=0.36$), but they did differ by valence category ($F(2,58)=1526$, $p<0.001$), as expected per the study design. Body stimuli rated as negative had a lower valence rating than body stimuli rated as neutral, which was lower than body stimuli rated as positive ($\text{Mean(SE)}_{\text{Negative}}=1.64(0.11)$; $\text{Mean\%(SE)}_{\text{Neutral}}=4.98(0.03)$;

Mean%(SE)$_{Positive}$=7.78(0.07); *t*(30)'s>26.7, *ps*<0.003). There were no interactions with group, also per the study design. Therefore, the affective content of the stimuli for the fMRI study was similar between groups and based on each individual's subjective ratings of body stimuli.

Working memory task

Effect of viewing body stimuli versus scrambled images as distracters during the retention interval

Control women and women who had recovered from AN did not differ for percent correct for matching arrow orientation in the working memory task ($F(1,27)=0.26$, p=0.61). Viewing body stimuli versus viewing scrambled images was not differentially disruptive to working memory performance (Mean percent correct (SE)$_{Bodies}$=73.3(1.27); Mean(SE)$_{Scrambled}$=72.4(1.64)). There was no interaction between type of distracter and group.

Control women and women who had recovered from AN did not differ in their reaction time to match arrow orientation in the working memory task ($F(1,27)=0.50$, $p=0.49$). Reaction times did not differ when viewing bodies or scrambled images during the retention interval (Mean(SE)$_{Bodies}$=943(26.2); Mean(SE)$_{Scrambled}$=946(29.2)). There was no interaction between type of distracter and group.

Effect of viewing bodies rated as negative versus neutral versus positive as distracters during the retention interval

When only trials with body stimuli were considered, control women and women who had recovered from AN did not differ for percent correct for matching arrow orientation in the working memory task ($F(1,27)=0.51$, p=0.48). However, there was a main effect of valence category (*F*(2,58)=4.91, *p*=0.01). Post-hoc comparisons showed that viewing bodies rated as negative was more disruptive to working memory performance than viewing bodies rated as positive or neutral (Figure4A; *t*(30)'s>3.05, *ps*<0.02). Viewing bodies rated as positive and neutral did not differentially disrupt working memory performance. There was no interaction between type of distracter and group.

Control women and women who had recovered from AN did not differ in their reaction time to match arrow orientation (*F*(1,27)=0.50, *p*=0.49), but there was a main effect of valence category (*F*(2,58)=5.90, *p*=0.005). Women were slower to respond to arrows when they viewed body stimuli rated as positive during the retention interval than body stimuli rated as neutral or negative (Figure4B; *t*(30)'s>2.58, *ps*<0.05). Reaction time to arrows did not differ when women viewed body stimuli rated as neutral versus negative. There was no interaction between type of distracter and group.

Whole brain analyses

The contrast of all stimuli versus baseline yielded activation in the lateral PFC, the parietal cortex, the insula, and the midbrain (Table 4). There was suppression in the default network, which included the medial PFC, temporal lobe, and posterior cingulate. One lateral PFC and one medial PFC cluster were compared between groups for the all stimuli versus baseline contrast (see superscripts in Table 4). For both the lateral (*ps*>0.62) and medial PFC clusters (*ps*>0.12), activation to viewing bodies rated as negative, bodies rated as neutral, bodies rated as positive, and scrambled images did not differ between groups.

Within-group whole brain contrasts of all body stimuli versus scrambled images yielded temporal and parietal activation in control women and occipital, parietal, and frontal activation in women who had recovered from AN (Table 4). There were no regions for which viewing scrambled images elicited more activation than viewing body stimuli. Within-group whole brain contrasts of negative versus neutral body stimuli yielded significant thalamic activation in control women, but no significant activation in women who had recovered from AN. Within-group whole brain contrasts of positive body stimuli versus neutral yielded no significant activation in either group. There were no regions for which viewing neutral body stimuli elicited more activation than viewing positive or negative body stimuli.

ROI analyses

Effect of viewing body stimuli versus scrambled images as distracters during the retention interval

Mean percent signal change in the amygdala did not differ between control women and women who had recovered from AN ($F(1,27)=0.59$, $p=0.45$). There was no difference in activation bodies and scrambled images as distracters (Mean % signal change(SE)$_{Bodies}$=0.041(0.018); Mean % signal change(SE)$_{Scrambled}$=0.058(0.022)). There was no significant interaction between distracter type and group. Activity in the amygdala differed from zero (i.e. average percent sign change as compared to zero) for body distracters in women who had recovered from AN ($t(14)=3.36$, $p=0.005$, uncorrected) but not control women ($t(15)=0.62$, $p=0.55$, uncorrected). Conversely, activity while viewing scrambled images differed from zero in control women

($t(15)=2.30$, $p=0.04$, uncorrected) but not women who had recovered from AN ($t(14)=1.31$, $p=0.21$, uncorrected).

Mean percent signal change in the lateral PFC did not differ between control women and women who had recovered from AN ($F(1,27)=0.04$, $p=0.84$); however, the lateral PFC activated more when women viewed body stimuli during the retention interval than when they viewed scrambled images ($F(1,29)=0.59$, $p=0.003$; Mean % signal change$(SE)_{Bodies}=0.106(0.008)$; Mean % signal change $(SE)_{Scrambled}=0.080(0.009)$). There was no significant interaction between distracter type and group. Activity while viewing body stimuli or scrambled images was different from zero in both groups ($ts>5.34$, $ps<0.001$, uncorrected).

Mean percent signal change in the medial PFC did not differ between control women and women who had recovered from AN ($F(1,27)=0.23$, $p=0.64$). There was no difference between activation when women viewed body stimuli during the retention interval than when they viewed scrambled images (Mean % signal change $(SE)_{Bodies}=-0.059(0.008)$; Mean % signal change $(SE)_{Scrambled}=-0.067(0.003)$). There was no significant interaction between distracter type and group. Activity while viewing body stimuli or scrambled images was different from zero in both groups ($ts>3.96$, $ps<0.002$, uncorrected).

Mean percent signal change in the FG did not differ between control women and women who had recovered from AN ($F(1,27)=0.27$, $p=0.61$). The FG activated more when women viewed body stimuli during the retention interval than when they viewed scrambled images ($F(1,29)=22.2$, $p<0.001$). This was modified by an interaction between distracter type and group (Figure5A; $F(1,29)=4.41$, $p=0.05$). Women who had recovered from AN had marginally higher FG activation when they viewed body stimuli than did control women ($F(1,29)=3.92$, $p=0.06$), but the groups had similar FG activation when they viewed scrambled images ($F(1,29)=0.01$, $p=0.91$). Additionally, FG activation was higher when viewing body stimuli than when viewing scrambled images in women who had recovered from AN ($t(14)=6.24$, $p<0.003$) but not control women ($t(15)=1.59$, $p=0.13$). Activity while viewing body stimuli or scrambled images was different from zero in both groups (*ts*>6.71, *p*s<0.001, uncorrected).

Effect of viewing bodies rated as negative versus neutral versus positive as distracters during the retention interval

Mean percent signal change in the amygdala did not differ between control women and women who had recovered from AN when only trials with body distracters were included ($F(1,27)=2.60$, $p=0.12$). There was no effect of valence category on amygdala activity and no significant interaction between valence category and group. However, amygdala activity when viewing bodies rated as negative and neutral significantly differed from zero in women who had recovered from AN (Figure5B; *t*(14)'s>2.34, *ps*<0.04, uncorrected), while amygdala activity when viewing bodies rated as negative, neutral, and positive did not differ from zero in control women.

Mean percent signal change in the lateral PFC did not differ between control women and women who had recovered from AN when only trials with body distracters were included ($F(1,27)=2.60$, $p=0.12$); however, there was an effect of valence category ($F(2,58)=7.75$, $p=0.001$). Lateral PFC activation was higher when women viewed bodies rated as positive than when they viewed bodies rated as neutral or negative (Figure5C;

t(30)'s>2.56, *ps*<0.05). Activity did not differ when women viewed bodies rated as negative versus bodies rated as neural. There was no significant interaction.

Mean percent signal change in the medial PFC did not differ between control women and women who had recovered from AN when only trials with body distracters were included (*F*(1,27)=0.01, *p*=0.91). There was no effect valence category on medial PFC activation, but there was a significant interaction between valence category and group (*F*(2,58)=3.10, *p*=0.05). Viewing bodies rated as negative elicited a larger decrease in activation (i.e. suppression) in women who had recovered from AN than in control women (Figure5D; *F*(1,29)=5.72, *p*=0.02). Medial PFC suppression when viewing bodies rated as neutral and positive bodies did not differ between groups. Activity in the medial PFC was lower than zero for bodies rated as negative, neutral, and positive for women who had recovered from AN (*t*(14)'s>4.37, *ps*<0.001, uncorrected). Medial PFC activity in response to bodies rated as neutral and positive (*t*(15)'s>4.24, *ps*<0.002, uncorrected), but not bodies rated as negative (*t*(15)=1.75, *p*=0.10, uncorrected), was lower than zero in control women.

Mean percent signal change in the FG did not differ between control women and women who had recovered from AN when only trials with body distracters were included (*F*(1,27)=2.22, *p*=0.15). There was no effect of valence category on FG activity and no significant interaction.

Regressions

Since negative affect and anxiety differed between women who had recovered from AN and control women, regression analyses were used to examine whether or not this was related to valence ratings, performance on the working memory task, or ROI activation. Neither negative affect as measured by the I-PANAS-SF nor Beck Anxiety Inventory Scores predicted valence ratings, percent correct on the working memory task, or percent signal change in the amygdala, lateral PFC, or FG in either group. I-PANAS-SF negative affect scores did not predict medial PFC activation in either group; however, Beck Anxiety Inventory Scores predicted medial PFC activation in control women (b= 0.50, p<0.05) but not women who had had recovered from AN (b= -0.40, p=0.15).

Since we hypothesized that prefrontal regions control emotional responses to body stimuli, we explored the relationship between prefrontal brain activation and working memory performance. Percent signal change in the lateral PFC did not predict working memory performance when women viewed body stimuli nor when they viewed scrambled images in either group. However, percent signal change in the medial PFC predicted percent correct for the working memory task when viewing body stimuli in women who had recovered from AN (b= -0.59, p=0.02) but not control women (b= -0.06, p=0.82). Medial PFC activation did not predict percent correct when either group of women viewed scrambled images. Since the amygdala is extensively connected to the medial prefrontal cortex (Amaral & Price, 1984), we explored the relationship between medial PFC and amygdala activation. However, amygdala activation did not predict medial PFC activation when viewing body stimuli or scrambled images in either group of women. Finally, we examined the relationship between activation in the two prefrontal ROIs. Percent signal change in the lateral PFC did not predict percent signal change in the medial PFC when viewing body stimuli or scrambled images.

The relationship between the number of years recovered (4-36 years) and outcome measures that differed between groups was explored in order to see if this would illuminate what is a trait of AN versus a marker of recovery. A higher numbers of years recovered predicted higher amygdala percent signal change for only neutral distracters in women who had recovered from AN (b= 0.59, p=0.02). Number of years recovered did not predict FG activation when women viewed bodies or scrambled images or medial PFC activation when women viewed negative, positive, or neutral bodies. Additionally, number of years recovered did not predict valence ratings of normal weight bodies, reaction time to assign negative valence ratings to body stimuli, percentage of body stimuli categorized as negative, Beck Anxiety Inventory scores, negative affect scores on the I-PANAS-SF, or any body image questionnaires. Finally, number of years recovered did not predict lateral PFC activity. Number of years recovered was highly correlated with age (r= 0.74, p=0.002).

Discussion

Women who recovered from AN had more negative affect, higher anxiety, worse body image, and more negative affective responses to body stimuli than control women. However, their working memory performance did not differ from control women. In both groups, performance was more disrupted by negative than neutral or positive bodies. There were differences in amygdala, fusiform, and medial PFC activity between groups. Amygdala activity was greater than zero in women who had recovered from AN but not control women, FG activation was higher when viewing body stimuli in women who had had recovered from AN than in control women, and women who had recovered from AN had more suppression of medial PFC activation than control women when they viewed bodies that were rated as negative. Furthermore, larger medial PFC suppression predicted better working memory performance when body stimuli were distracters in women who had recovered from AN, but there was no relationship between working memory performance and brain activity in control women. Finally, the lateral PFC did not show group differences in activation, but did respond more when women viewed bodies rated as positive than bodies rated as neutral or negative.

Viewing negative bodies was more disruptive to working memory performance than viewing neutral or positive bodies. This is comparable to Dolcos & McCarthy (2006), who found that negative images are more disruptive to working memory performance than neutral images in healthy younger adults. However, viewing negative bodies was no more disruptive to working memory performance in women who had recovered from AN than control women. Even though women who had recovered from AN rated more body stimuli as negative and assigned negative valence ratings more quickly than control women during the valence rating task, viewing negative bodies was not subsequently more disruptive to performance on the working memory task. However, the brain activity that supported the similar behavioral performance differed between the groups in the amygdala, FG, and medial PFC.

The amygdala and FG activation during the working memory task suggested these regions were more sensitive to body stimuli in women who had had recovered from AN than in control women. Percent signal change in the amygdala was low. In fact, amygdala activation only differed from zero when viewing negative and neutral bodies in women who had recovered from AN but not in control women. The FG responded with more overall activation when women viewed bodies than when they viewed scrambled images, which was expected, based on work showing that the fusiform responds robustly to bodies- more so than to objects or other types of stimuli (Peelen et al., 2005; Taylor et al., 2007). However, activation while viewing body stimuli was higher in women who had recovered from AN than in control women. Overall, the activity in these two regions suggests that the brains of women who had recovered from AN were more sensitive to body stimuli than control women, possibly because women who have recovered from AN have a fear response to body image-related stimuli while controls do not (Uher et al., 2003). Furthermore, it is not likely that this was due to overall higher brain activation in women who had recovered from AN, because FG activation between the groups was similar for scrambled images.

Suppression of activity in the medial PFC was greater in women who had recovered from AN than in control women when they viewed bodies rated as negative. In fact, medial PFC activation while viewing negative bodies was different from baseline in women who had recovered from AN but not controls. The medial PFC is part of the default mode network in the brain (Raichle et al., 2001). The default network is active when the brain is "at rest" but is suppressed when the brain performs cognitive (i.e. goal-directed) tasks (for review see (Gusnard & Raichle, 2001), such as working memory (Drobyshevsky et al., 2006). "At rest" is a broad term, but is thought to include activities such as self-referential thinking (Johnson et al., 2002) and mind-wandering (Mason et al., 2007). The theory is that these types of activities need to be suppressed in order for the brain to perform more demanding tasks (Gusnard et al., 2001). In fact, some evidence suggests that the more demanding the task is, the more the default mode network is suppressed (McKiernan, Kaufman, Kucera-Thompson, & Binder, 2003; Singh & Fawcett, 2008). The medial PFC region activates during some aspects of emotion processing (Erk, Abler, & Walter, 2006; Williams et al., 2006b), particularly self-referential emotion (Fossati et al., 2003). Thus, it could be that suppression of the default mode network, including the medial PFC, normalized working memory performance in women who had recovered from AN, specifically when negative bodies were the distracters. The regression analyses offer some support for this idea. Larger suppression of medial PFC activity predicted better working memory performance when the distracters were bodies but not when they were scrambled images, and this only occurred in women who had recovered from AN. Additionally, the response by control women here was similar to healthy subjects in another study who showed that those with the lowest anxiety had the largest medial PFC suppression (Simpson, Jr., Drevets, Snyder, Gusnard, & Raichle, 2001). Taken together, these results imply that recovery from AN may not necessarily involve decreasing negative affect towards bodies but instead compensatory mechanisms that prevent negative responses to bodies from disrupting cognitive functioning.

The lateral PFC activation and the reaction time results from the working memory and valence rating tasks suggest that women deliberate more when viewing bodies they think are positive than bodies they think are negative, regardless of a history with AN. Activity in the lateral PFC is associated with working memory tasks (Bunge et al., 2001), but the lateral PFC is also involved in regulating emotion, particularly reappraisal of emotion (Goldin et al., 2008). It could be that viewing bodies rated as positive elicited more lateral PFC activation than bodies rated as negative or neutral because women were "reappraising" them. If a body was not immediately classified as negative, the women needed to deliberate about the qualities of the body to decide whether or not it was positive or neutral. This reappraisal takes time, and, in fact, women had a slower reaction time to positive and neutral bodies than negative bodies in the valence rating task. Furthermore, women were slower to make the arrow orientation judgment during the working memory task when they viewed bodies rated as positive during the retention interval than bodies rated as neutral or negative. This slower response could have been due to the “appraisal” process. Collectively, these results indicate that viewing bodies rated as positive elicited unique behavioral and functional responses in women that suggested utilization of the lateral PFC for reappraisal.

Women who had recovered from AN had more negative affective responses to body stimuli than control women. Women who had recovered from AN assigned negative valence ratings to a higher percentage of body stimuli, assigned negative ratings faster, and rated normal weight bodies more negatively than did control women. Although negative affect and anxiety were higher in women who had recovered from AN than control women, this did not predict valence ratings, suggesting that those differences were not responsible for the more negative affective responses in women who had recovered from AN. Overall, these data suggest that negative feelings towards body stimuli remain after women behaviorally recover from AN.

The higher anxiety and more negative affect in women who had recovered from AN were not surprising, given that anxiety (Bulik et al., 1997) and negative affect (Kaye et al., 2009) may be long lasting traits that precede AN, and that AN is co-morbid with anxiety and depression (Hudson et al., 2007; Herzog et al., 1996). Casper (1990) found that women who had recovered from AN had similar body dissatisfaction as control women but still had higher drive for thinness. Some evidence suggests that these factors may depend on how you define recovery (Bachner-Melman et al., 2006). Behavioral recovery is usually defined as restoration of weight, initiation of menstrual cycles, and absence of restricting or purging behavioral symptoms (Uher et al., 2003; Klump et al., 2004; Casper, 1990), while cognitive recovery requires that women no longer have a distorted body image or a fear of becoming fat (Bachner-Melman et al., 2006). Women who are behaviorally and cognitively recovered tend to match control women on measures of body dissatisfaction, societal influence on body image, drive for thinness, and mood or anxiety disturbances, while women who are only behaviorally recovered tend to have worse body image and more emotional or mood disturbances than control women, and they fall somewhere between control women and women who have an active eating disorder (Bachner-Melman et al., 2006; Bardone-Cone et al., 2010). Therefore, the women in this study match the profile of behavioral recovery, including higher anxiety and retention of poor body image, which may relate to the higher amygdala and fusiform sensitivity to body stimuli in this group.

Limitations

First, three of the women who had recovered from AN were using anti-depressant or anti-anxiety medication at the time of their study participation. Depression and anxiety are highly co-morbid with anorexia nervosa (Herzog et al., 1996), so the women in this study are representative of the population of women who develop and need treatment for AN. These medications could potentially affect brain activity, as seen in studies of healthy controls (Norbury et al., 2009; Paulus, Feinstein, Castillo, Simmons, & Stein, 2005), but so could unmedicated depression (Drevets et al., 1992) or unmedicated anxiety disorders (Shah, Klumpp, Angstadt, Nathan, & Phan, 2009). Some evidence suggests that anti-depressant medications normalize amygdala (Sheline et al., 2001) and prefrontal (Passero, Nardini, & Battistini, 1995) activity in depressed patients. Therefore, permitting women who use these medications into the study is likely not adding any more variation to the data than if they were unmedicated and depressed or anxious. Furthermore, removing those three women from the study did not change the overall pattern of results for that group. Second, we do not know the potential long term effects of malnutrition and starvation on brain activity in women with AN. However, evidence shows that baseline prefrontal blood flow returns to similar levels as controls after recovery from AN (Matsumoto et al., 2006; Frank et al., 2007). Additionally, women who had AN during adolescence do not differ from health controls for frontal grey and white matter volume (Chui et al., 2008). Only women who are not yet behaviorally recovered have larger ventricles (Chui et al., 2008). Collectively, these studies suggest that brain function and structure are restored after recovery from AN. Finally, there was a wide range in the number of years since recovery in the women who had recovered from AN. However, most study measures were not related to number of years since recovery. This suggests that the results here are due to long-lasting traits of these women and are not necessarily marker of recovery. On the other hand, it could be that behavioral or neural changes reach a plateau at a certain point after recovery, in which case they could be a marker of recovery but still not be related to number of years recovered.

Conclusion

These data suggest that the medial PFC suppression compensated for the higher negative affective responses to bodies in women who had recovered from AN in order to produce the same working memory behavior as control women. Women who had recovered from AN rated normal weight bodies more negatively and had more amygdala and fusiform activation in response to viewing body stimuli than control women. This study also confirmed the results in Chapter 2 that women were slower to categorize bodies as positive and extended this idea by showing that viewing these bodies increased activity in the prefrontal cortex. Taken together, these data suggest that recovery from AN may not necessarily involve decreasing negative affect towards bodies via the lateral PFC but instead via compensatory suppression of the default network.

In terms of treatment, this supports use of body exposure therapy for women with AN. During exposure therapy, women must confront their own bodies in a mirror (Key et al., 2002). This is usually in conjunction with cognitive behavioral therapy which teaches them to change the way they think about and react to their bodies (Grant & Cash, 1995). Evidence suggests that body exposure leads to sustained improvements in body dissatisfaction in women with AN (Key et al., 2002) by decreasing their negative emotions and thoughts in response to their bodies over time (Vocks et al., 2010). The data here suggest that the underlying neural mechanism for this may be suppression of the default mode network (more so than in healthy women) in order to allow enough cognitive resources to regulate their emotional responses to their bodies in addition to permitting normal cognitive functioning.

Acknowledgements

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Table 1. Participant demographics.

Characteristic	Control	RecAN
N	16	15
Age[a] (years)	**31.6** (26-59)	**39.0** (26-57)
Education (years)	15.7 (12-19)	16.5 (14-20)
WAIS-R[b] Vocabulary age-scaled scores	12.7 (8-18)	13.5 (10-17)
CES-D[c] Scale	7.19 (2-16)	7.67 (0-21)
Eating Attitudes Test-26	3.00 (0-9)	8.27 (0-21)
Body Mass Index[d]	**23.7** (20-28)	**21.5** (19-25)

[a] Control < RecAN.
[b] Wechsler Adult Intelligence Scale- Revised
[c] Center for Epidemiological Studies Depression Scale.
[d] Control > RecAN.
Note: Range is shown in parentheses. Bold = significant group difference (p<0.05).

Table 2. History with AN in women who had recovered from AN.

Characteristic	Mean (Range)
Age at onset (years)	16.1 (11-20)
Age at recovery (years)	22.8 (18-41)
Year recovered	15.4 (4-36)
# lifetime episodes	1.4 (1-2)

Table 3. Questionnaires to characterize body image and affect.

Questionnaire	**Control Mean[g] (SE)**	**RecAN Mean[g] (SE)**
Body dissatisfaction[a]	**24.3** (2.25)	**34.1** (2.33)
Drive for thinness[b]	16.7 (1.91)	22.2 (1.98)
Body shape concern[c]	**62.4** (5.96)	**90.8** (6.19)
SATAQ-3 total score[d]	**80.4** (4.27)	**95.9** (4.43)
Positive affect[e]	20.3 (0.69)	18.3 (0.72)
Negative affect[e]	**9.19** (0.89)	**13.3** (0.93)
Beck Depression Inventory[f]	3.63 (1.58)	8.40 (1.64)
Beck Anxiety Inventory[f]	**6.66** (1.94)	**16.1** (2.02)

[a] Possible total = 54.
[b] Possible total = 42.
[c] Possible total = 204.
[d] Possible total = 150.
[e] Possible total = 25.
[e] Possible total = 63.
[g]BMI- and age-adjusted means.
Note: Bold = significant group difference ($p<0.05$).

Table 4. Whole brain task activation and within-group contrasts.

	Left/right	Region	x	y	z[a]	BA	# Voxels
TASK ACTIVATION[b]	*All Stimuli > Baseline*						
	L	Posterior Cingulate	-4	-62	16	23	137863
	L	Midbrain	-1	-20	-2	NA	9733
	L	Insula	-32	17	6	13	3073
	L	Superior Frontal Gyrus	-26	48	-21	11	711
	R	Insula	32	18	5	13	4038
	R	Precentral Gyrus	42	0	31	6	3587
	R	Precentral Gyrus	27	-12	49	6	844
	R	Superior Frontal Gyrus	28	44	-21	11	387
	Baseline > All Stimuli						
	L	Cingulate Gyrus	-1	36	27	32	41711
	L	Superior Temporal Gyrus	-56	-19	2	NA	8755
	L	Posterior Cingulate	-4	-54	22	31	7480
	L	Middle Temporal Gyrus	-42	-71	25	39	1173
	R	Superior Temporal Gyrus	55	-7	-5	22	1791
	R	Middle Temporal Gyrus	46	-67	25	39	459
WITHIN GROUP[d]							
Control	*Bodies > Scrambled*						
	L	Fusiform Gyrus	-39	-77	-10	19	9097
	R	Fusiform Gyrus	38	-69	-9	19	19097
	R	Precuneus	27	-70	51	7	1254
	Negative > Neutral						
	L	Thalamus	-10	-32	17	NA	647
RecAN	*Bodies > Scrambled*						
	L	Inferior Occipital Gyrus	-44	-76	-6	19	8161
	L	Precentral Gyrus	-43	-11	39	6	801
	R	Inferior Occipital Gyrus	41	-72	-6	19	15310
	R	Postcentral Gyrus	42	-26	38	2	773

[a] Coordinates correspond to Talairach space.
[b] p = 0.00001, cluster threshold = 10 voxels, random effects model.
[c] Quantified in between-group cluster comparison.
[d] p = 0.001, cluster threshold = 22 voxels, random effects model.

Figure 1. Working memory task trial design. Participants viewed a memoranda arrow for 1000msec, a distracter for 4000msec during a 6000msec retention interval, and then a probe arrow for 2000msec. They decided whether the probe arrow was in the same or different orientation as the memoranda arrow. Each trial was followed by a jittered 7000, 9000, or 11000msec inter-trial interval during which time they viewed a crosshair. Distracters consisted of bodies rated as negative, neutral, and positive or scrambled images (36 of each), which were viewed in random order across and within the 4 runs.

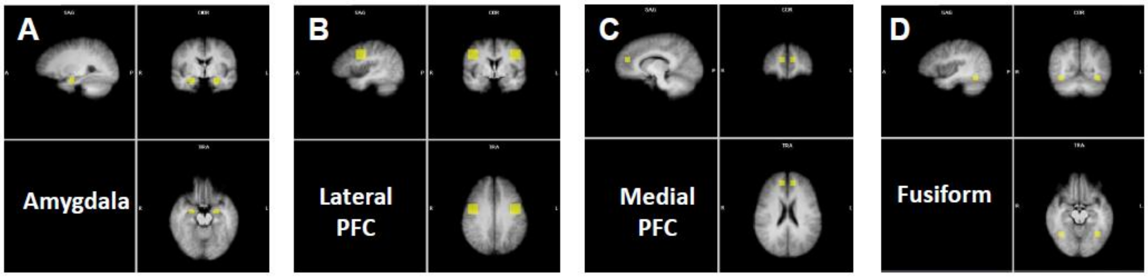


Figure 2. A priori regions-of-interest. (A) Amygdala. (B) Lateral PFC. (C) Medial PFC. (D) Fusiform gyrus.

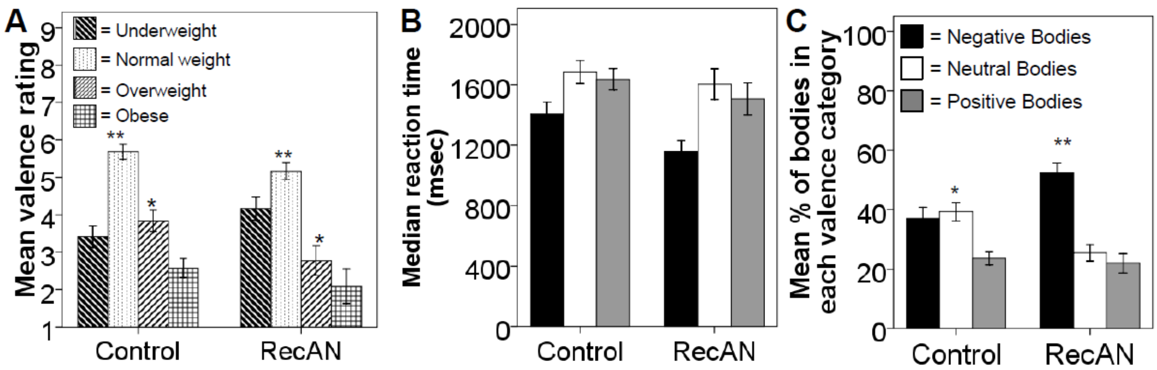


Figure 3. Valence rating task. (A) Women who had recovered from AN rated overweight bodies more negatively than did control women. There was a trend for women who had AN to rate normal weight bodies more negatively and underweight bodies more positively than control women. Both control women and women who had recovered from AN rated normal weight bodies more positively than all other sizes. * = Group difference. ** = More positive than all other size bins. (B) Women were faster to assign negative valence ratings to body stimuli than neutral or positive valence ratings, but women who had recovered from AN were faster than control women to assign negative valence ratings. * = RecAN < Control. (C) Women who had recovered from AN assigned negative valence ratings to a larger percentage of bodies than did control women, while control women assigned neutral valence ratings to a larger percentage of bodies than did women who had recovered from AN. * = Control > RecAN. ** = RecAN > Control.

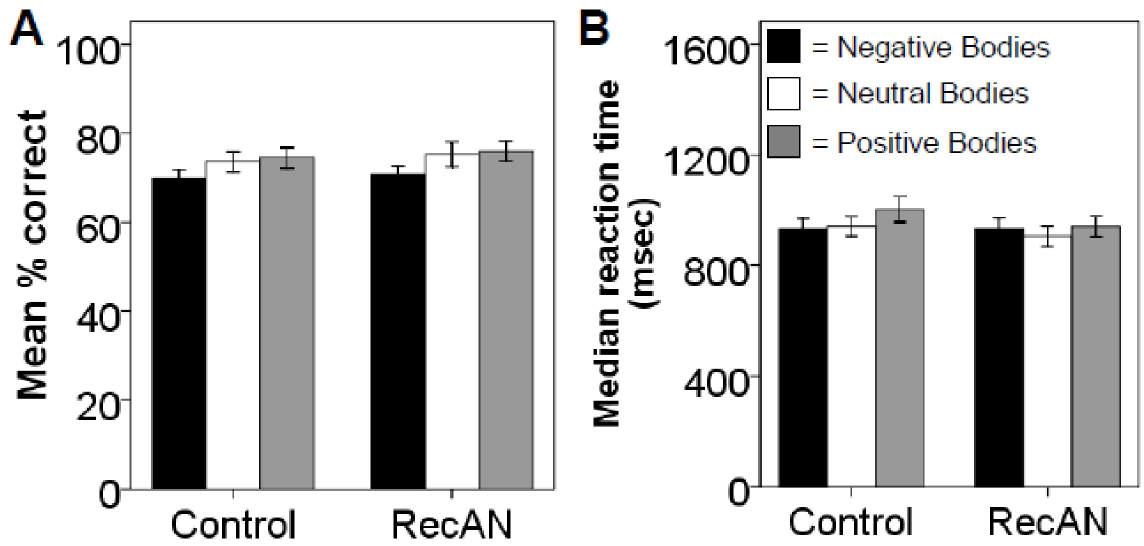


Figure 4. Working memory task. (A) Performance on the working memory task did not differ between groups. Viewing negative bodies was more disruptive to performance than viewing neutral or positive bodies. (B) Control women and women who had recovered from AN did not differ in their reaction times to arrows. Overall, women were slower to respond to arrows when they viewed bodies rated as positive during the retention interval than when they viewed bodies rates as neutral or negative (Main effect of valence: Positive > Negative, Neutral).

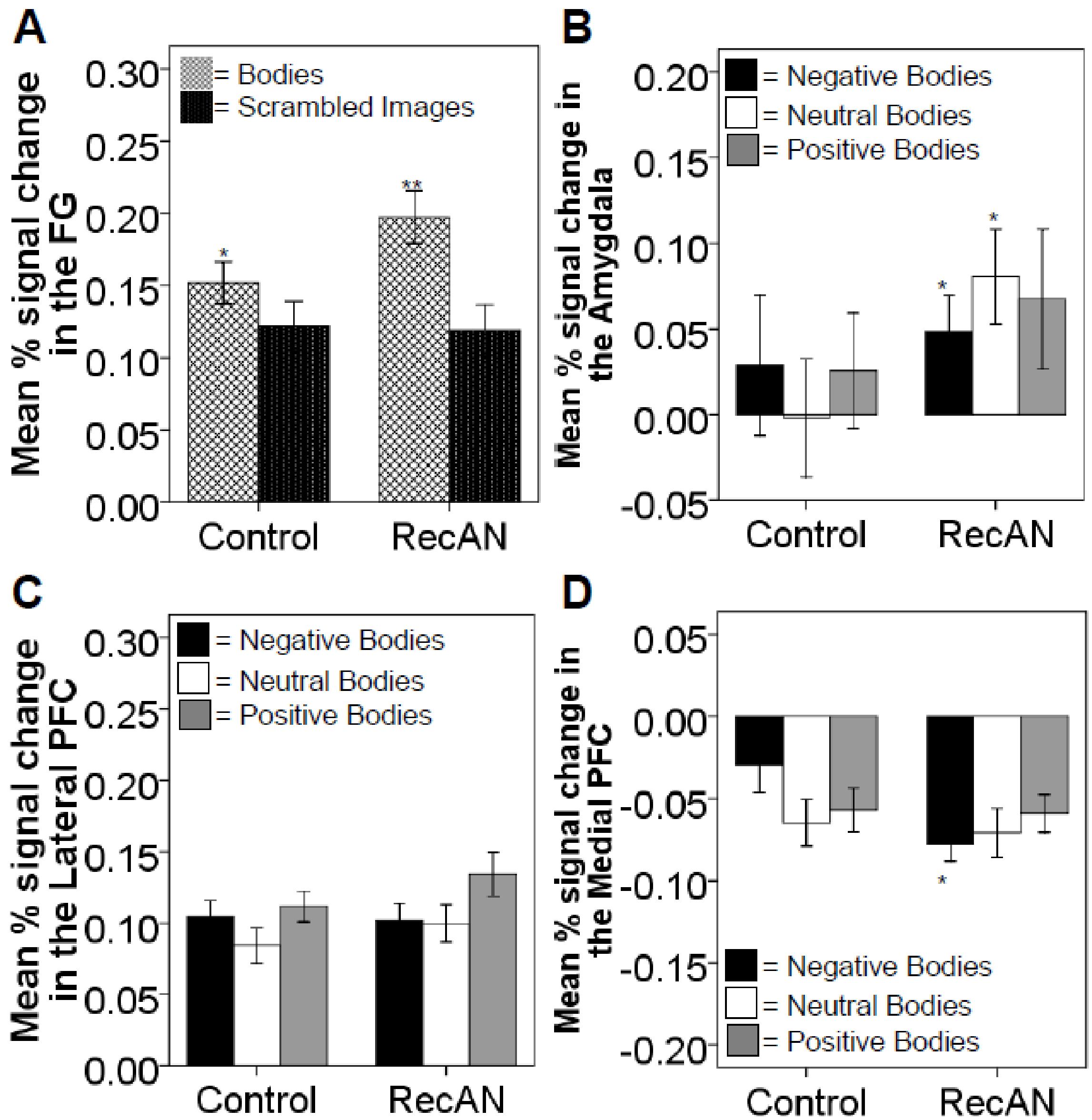


Figure 5. Average percent signal change in regions-of-interest. (A) Fusiform (FG) activation was higher when women viewed body stimuli than when they viewed scrambled images. This was modified by an interaction with group. Control women had less FG activation when viewing body stimuli than did women who had recovered from AN, but the two groups had similar FG activation when viewing scrambled images. FG activation differed when viewing body stimuli versus scrambled images in women who had recovered from AN but not control women. * = less than RecAN. ** = Greater than

scrambled images. (B) Amygdala activation did not differ between control women and women who had recovered from AN, and there was no effect of valence category and no interaction. However, amygdala activation when viewing negative and neutral body stimuli differed from zero in women who had recovered from AN but not in control women. * = Significantly different from zero. (C) Lateral PFC activation did not differ between groups; however, activation was higher when women viewed bodies rated as positive than when they viewed bodies rated as negative or neutral (Main effect of valence: Positive > Negative, Neutral). (D) Viewing bodies rated as negative elicited a larger decrease in activation in women who had recovered from AN than in control women. * = Less than Control.

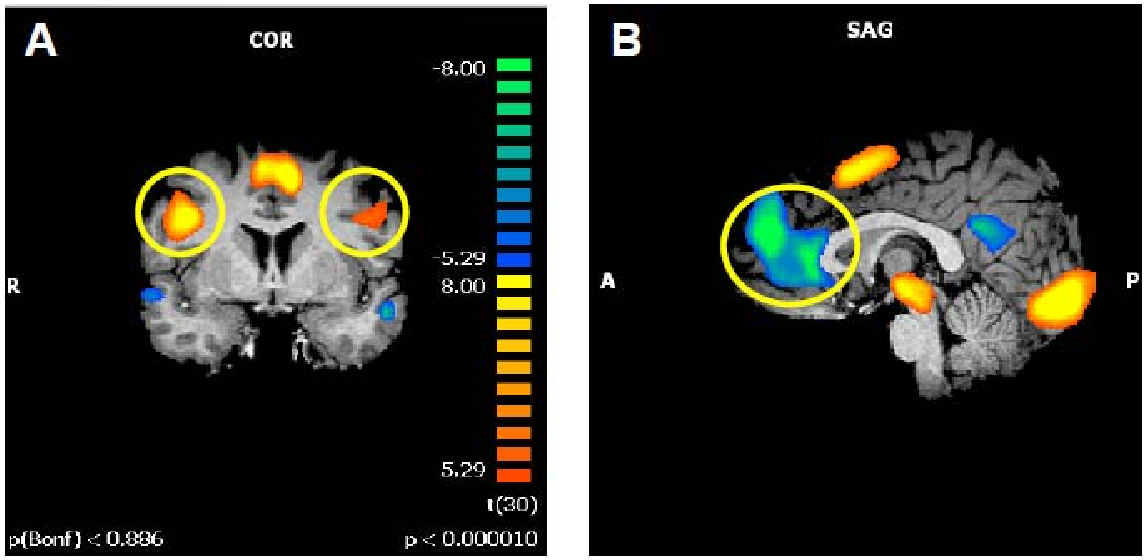


Figure 6. Whole brain contrast of all stimuli versus baseline for women who had recovered from AN and control women combined. This data was used to define the cubes for the lateral (A) and medial (B) PFC a priori regions-of-interest. This data corresponds to Table 4. Random effects model, $p<0.00001$, cluster threshold = 10.

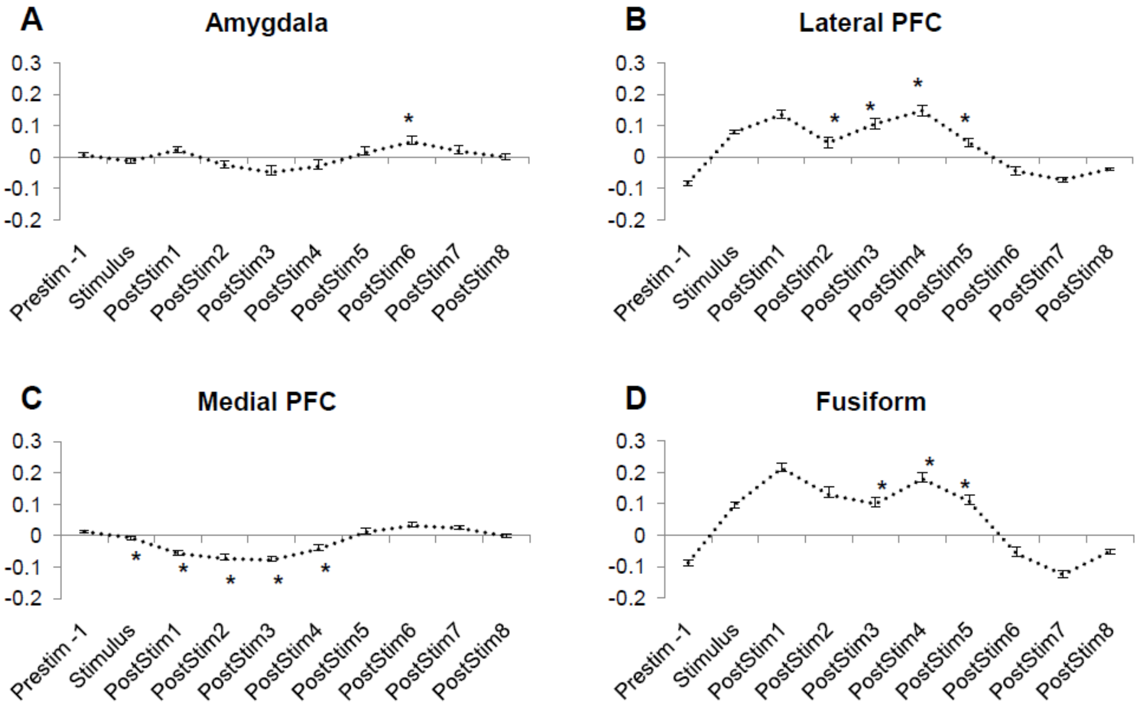


Figure 7. Grand mean time courses. (A) The amygdala time course was significantly higher than zero at its peak at post-stimulus time point 6. (B) The second peak of the lateral PFC time course was significantly higher than zero from post-stimulus points 2 through 5. (C) The medial PFC time course was significantly lower than zero from stimulus onset through post-stimulus point 4. (D) The second peak of the fusiform gyrus time course was significantly higher than zero from post-stimulus points 3 through 5. * = significantly different than zero and used to compute mean percent signal change for the region-of-interest analyses.

Discussion

Summary of goals and results

The overall goal of this dissertation work was to: 1) characterize body image in younger versus older women and women who had recovered from AN versus control women, and 2) examine affective responses to bodies, and 3) examine how bodies affect prefrontal cortical function in the brain. My hypothesis was that emotional responses to bodies and body image are regulated by the prefrontal cortex, and that bodies would differentially disrupt prefrontal regulation based on the emotional response to body stimuli.

The goal of the study in Chapter 1 was to characterize body image in younger and older women. I found that younger and older women had similar body dissatisfaction, similar acceptable ranges of body sizes, and similar body shape concerns, but younger women had a higher drive for thinness and experienced more societal influence on their body image. Using images of one's own body did not result in different body dissatisfaction scores than the Figure Rating Scale line drawings in younger or older women. The results of Chapter 1 suggest that age affects some facets of body image, but not others, and that personalized measures provide the same information about body image in normal, healthy younger and older women .

The goal of the study in Chapter 2 was to assess the effects of bodies and body valence on working memory performance in younger and older women in an effort to examine age differences in regulation of responses to body stimuli. Older women experienced less negative affect than younger women. Younger and older women both rated normal weight bodies as most positive, were slower to categorize positive bodies than negative bodies, and categorized the smallest percentage of bodies as positive. Additionally, positive bodies were more disruptive to working memory performance than negative or neutral bodies in both younger and older women. The results from Chapter 2 suggest that bodies are affective stimuli to women and, depending on their valence, differentially disrupt working memory. However, despite older women experiencing less negative affect than younger women, these groups did not differ in their affective responses to or the disruption of working memory by bodies. This suggests that the positivity bias in aging does not extend to body stimuli in women.

The goal in Chapter 3 was to examine the effects of body stimuli on prefrontal function in women who had recovered from AN versus healthy controls. This was accomplished by studying the brain activity induced when body stimuli are used as distracters during the retention interval of a working memory task. Women who had recovered from AN experienced more negative affect, higher anxiety, worse body image, and had more negative affective responses to bodies in comparison to control women. Despite these differences, women who had recovered from AN and control women had similar working memory performance. Performance in both groups was more disrupted by negative than positive or neutral bodies. However, there were differences between groups in amygdala, fusiform, and medial PFC activity. Amygdala activation was higher than baseline in women who had recovered from AN but not controls, FG activation was higher to bodies in women who had recovered from AN than in controls, and women who had recovered from AN had more suppression of medial PFC activation than controls when the distracter was a negative body. Furthermore, larger suppression of medial PFC activity predicted better working memory performance when body stimuli were distracters in women who had recovered from AN but not control women. Finally, the lateral PFC did not show any group differences in activation, but did respond more when distracters were positive than when they were neutral or negative. The results from Chapter 3 suggest that recovery from AN was associated with continued negativity towards bodies, which did not disrupt working memory performance but did alter brain activation. Suppression in the medial PFC may have compensated for the negative affective feelings towards body stimuli during cognitive tasks in order to allow output of normal behavioral performance in women who had recovered from AN.

Characterizing body image in women

The questionnaire results from Chapters 1, 2, and 3 suggest that women are dissatisfied with their bodies and concerned about their body shape, weight, and appearance, regardless of their age or history with AN. However, the degree to which they are dissatisfied or concerned is affected by age and eating disorder status. Younger women, older women, and women who had recovered from AN experienced body dissatisfaction, body shape concern, drive for thinness, and societal influence on their body image. However, age attenuated the drive for thinness and societal influence on appearance. In contrast, having experienced AN increased them. The results on aging are supported by literature showing comparable body dissatisfaction in younger and older women (Webster et al., 2003) but less appearance-related anxiety (Tiggemann et al., 2001), lower drive for thinness (Lewis et al., 2001), and less societal influence on body image (Bedford et al., 2006) in older women. This suggests that body dissatisfaction persists throughout the lifespan, but the negative impact of such feelings may lessen with age (Peat et al., 2008). Since older adults prioritize emotional goals (Carstensen, Isaacowitz, & Charles, 1999) and allocate their cognitive resources towards focusing on positive emotions (Mather et al., 2005a), it may be that older women are more likely to accept their bodies as they are (Thompson et al., 1998) and focus other, perhaps more positive, experiences and roles in their lives in lieu of dwelling on their appearance (Keel, Baxter, Heatherton, & Joiner, Jr., 2007). Conversely, women who had recovered from AN had persistent negative body image, which suggested that the women in Chapter 3 were, as a whole, behaviorally but not cognitively recovered. Cognitive recovery may involve learning similar mechanisms that older women use. For example, older women are more likely to accept their body appearance (Thompson et al., 1998) and be less anxious (Tiggemann et al., 2001) about their appearance than younger women. If women who had recovered from AN employed similar emotion regulation techniques as older women, it might improve their negative body image. Overall, the work presented here suggests that simply being a woman means having some amount of body dissatisfaction and concern about body image, but the intensity and regulation of these feelings depends on age, experience with AN, and the type of recovery from AN.

Data from Chapters 2 and 3 suggest that bodies viewed as positive are unique for women, regardless of their age or history with AN. In Chapter 2, younger and older women were slower to assign positive and neutral ratings to bodies than negative ratings, and there were very few bodies assigned positive ratings (<25%). A similar result was seen in Chapter 3 in both women who had recovered from AN and control women. This finding was additionally supported by behavioral data from an unpublished study (not included in this dissertation) where younger and older women had to categorize fatter and thinner images of their own bodies using a two choice response, either "negative" or "positive". Here too, women were slower to assign positive than negative categorizations, and they categorized ~35% of bodies as positive (see Appendix Part 1 for data). This reaction time pattern is opposite of what is seen for other types of emotional stimuli. Younger adults have been shown to respond faster to positive than to negative scenes when they are new stimuli (Bradley, Greenwald, Petry, & Lang, 1992) or to have no significant difference in their reaction time to positive versus negative stimuli (Mather et al., 2003), while older adults have been shown to respond faster to positive than negative or neutral faces (Keightley, Winocur, Burianova, Hongwanishkul, & Grady, 2006). This suggests that bodies are different from other types of stimuli for women and lends support to the idea that body stimuli rated as positive are particularly unique or require more time to evaluate by women. In Chapter 2, I suggested that women, regardless of their age, take longer to decide that a body is positive than to decide that a body is negative, and that presentation of a positive body may initiate a deliberative process in the brain. Results from Chapter 3 suggest that this hypothesis be true, since the lateral PFC, which is involved in evaluation and reappraisal of emotional stimuli (Goldin et al., 2008), was more active in response to positive bodies than negative or neutral bodies in both women who had recovered from AN and control women. This leads to interesting speculations about what this means for body image in women. It may be that women have a "default" state of responding negatively to bodies and responding positively requires a cognitive override of that process, which takes longer and requires more lateral prefrontal activation. Alternatively, it could be that women are hesitant to assign a body a positive status because they have stricter criteria for positive than for negative bodies. For example, it may be that one "bad" feature immediately relegates a body to being negative, which would make the response faster. However, multiple "good" features may have to be satisfied before a body can be categorized as positive, which would require more time. Additionally, the process of "appraising" the body for these "good" features may require more lateral PFC activation and may dampen the affective response, which could explain the lack of amygdala response to positive bodies in either group of women in Chapter 3. Whatever the mechanism for the slow response to bodies rated as positive, the data here suggest that it is common across women, regardless of their age or history with AN.

Prefrontal regulation hypothesis in aging

In the Introduction of this document, I hypothesized that emotional responses to bodies and body image are regulated by the prefrontal cortex and that higher prefrontal regulation of emotional responses to body stimuli will yield less negative body image. I hypothesized that the bias towards positive emotional information in older adults (Mather et al., 2005a) would extend to body stimuli. Thus, older women would have less negative ratings of body stimuli and would be more disrupted by bodies rated as negative on a task that engages the prefrontal cortex than younger women. I hypothesized that this would occur because of the extra cognitive "effort" older women would put forth to regulate their emotional responses to the negative bodies. The results from Chapter 2 indicate that my hypothesis for older women was incorrect. Younger and older women had similar affective responses to bodies, and negative bodies were not differentially disruptive to working memory performance. This occurred despite less negative affect and better overall body image in older women. These results suggest that the positivity bias in aging does not extend to body stimuli, which in turn suggests that bodies are unique from other affective stimuli, at least for women. Additionally, in the Introduction of this document, I referenced a study showing that higher cognitive control may result in more or better regulation of emotion in older adults (Mather et al., 2005b). Cognitive control was also assessed, but not reported, in Chapter 1. I found that younger and older women did not differ in their use of cognitive control strategies and that both groups used persistence and positive reappraisal more than lowering their aspirations (see Appendix Part 2). Although Chapter 2 did not include a neuroimaging component, it is possible to speculate on brain mechanisms. The fact that all valence categories were not equally disruptive to working memory performance (negative was most disruptive) indicates that the emotional quality of body stimuli influences prefrontal function. The remaining question is whether or not this differs with age. On the surface, the behavioral data in Chapter 2 and Appendix Part 2 suggest that is does not. However, the data in Chapter 3 suggest that is it possible to have similar behavior in response to body stimuli between two groups but different underlying brain activation. Thus, it is possible that older women have different brain activation in response to negative bodies, but that there are compensatory mechanisms that produce the same behavior as younger women. One study of working memory found that older adults had similar performance as younger adults, but this was accompanied by higher lateral prefrontal activation in older as compared to younger adults (Cabeza et al., 2004). Furthermore, studies of emotion have shown that older adults, including older women, use the lateral PFC to regulate responses to negative emotion (Pruis et al., 2009; Roalf et al., 2009). Thus, older women in this study may have compensatory prefrontal activation that permits them to regulate their responses to negative emotional body stimuli in addition to performing a working memory task as well as younger women. Finally, it is likely that the older women who participated in this study were similar to other study populations of older adults, because they have similar body image and affect characteristics as reported in other studies of aging (Mroczek et al., 1998; Charles et al., 2001; Allaz et al., 1998; Lewis et al., 2001). Overall, my data would be consistent with the idea that lateral PFC is involved in regulating emotional responses to body stimuli in older women, and I propose that this is compensatory in nature, which is what permits older women to perform similarly to younger women on the behavioral measures.

Prefrontal regulation hypothesis in women who had recovered from AN

I hypothesized that part of recovery from AN involves decreasing the intensity of negative affective responses to bodies (i.e. regulating the negative responses) and that this occurs via a higher prefrontal response to body image-related stimuli. Results from Chapter 3 suggest that is partially true. Women who had recovered from AN had more negative responses towards bodies than control women. Despite this difference in their affective responses to body stimuli, working memory performance was the same between the two groups. However, women who had recovered from AN had different underlying brain activity while viewing bodies as distracter stimuli. The fMRI data from Chapter 3 suggested that larger suppression of the default mode network, which includes the medial PFC (Raichle et al., 2001), was required to have normal performance on a working memory task in women who had recovered from AN in comparison to control women when negative bodies were the distracters. Therefore, as stated in Chapter 3, recovery from AN may not necessarily involve decreasing negative affect towards bodies but using compensatory mechanisms that prevent negative responses to bodies (or body image-related stimuli) from disrupting cognitive function. This idea lends support to the use of cognitive-behavioral therapy. Part of cognitive-behavioral therapy involves learning to identify and change one's unrealistic thoughts about food and one's own body (McIntosh et al., 2005; Pike, Walsh, Vitousek, Wilson, & Bauer, 2003). Thus, women who recover from AN may suppress their self-referential thoughts about negative bodies to prevent their minds from "wandering" to negative body-related thoughts when they see negative bodies during a working memory task. This is then reflected in the larger suppression to negative bodies in comparison to control women. Additionally, these data also support the use of body exposure therapy for AN (Grant et al., 1995; Key et al., 2002), since this would give women practice changing and suppressing their negative responses to stimuli that have the potential to disrupt their cognitive functioning. Suppression of the default network increases as task difficulty increases (McKiernan et al., 2003; Singh et al., 2008); however, tasks that are practiced induce less suppression of the default network than tasks that are novel (Mason et al., 2007). This suggests that as women get better at regulating their negative responses to body stimuli, they should require less suppression of the default network to produce similar behavioral performance as control women. Overall, the data in Chapter 3 suggest that suppression of the medial PFC, which is a part of the default network, is a component of recovery from AN.

<u>Hypothesized body image circuits</u>

Hypothesized response in brains of healthy control women

The primary visual cortex is activated by the presentation of a stimulus (Poghosyan & Ioannides, 2007), in this case a body or a scrambled image (Figure 1). This activates the dorsal and ventral processing streams (Poghosyan et al., 2007) via projections that go through the visual cortex to the parietal and temporal lobes, respectively (Boussaoud, Ungerleider, & Desimone, 1990; Nakamura, Gattass, Desimone, & Ungerleider, 1993; Ungerleider & Desimone, 1986a; Ungerleider & Desimone, 1986b; Ungerleider, Galkin, Desimone, & Gattass, 2008). These streams then reconvene in the prefrontal cortex (Ungerleider et al., 1998).

The ventral stream is involved in the perception and identification of the stimulus (Goodale, 2001; Valyear, Culham, Sharif, Westwood, & Goodale, 2006), including recognition of the stimulus via the fusiform (Downing et al., 2006; Grill-Spector & Sayres, 2008), which was differentially activated to bodies versus scrambled images in women who had recovered from AN (Figure 1). The fusiform is anatomically connected to the amygdala via white matter tracts that extend from the occipital lobe to anterior temporal lobe (Catani et al., 2003). It also exerts feed-forward influence on the amygdala (Fairhall & Ishai, 2007). However, the amygdala may also get information about affective properties of the stimulus from other “short cut” pathways in the ventral visual stream (Rudrauf et al., 2008). There is evidence to suggest that maintaining information in working memory can dampen the amygdala response to emotion (Erk et al., 2006), which may explain why the amygdala was not significantly activated by the body distracters in the healthy control group in Chapter 3(Figure 1).

The dorsal stream includes parietal regions (Ungerleider et al., 1998), where the spatial qualities of the stimuli are processed (Sack, 2009), including coding the location of (McCrea, 2007) and spatial relationship among (Corradi-Dell'Acqua et al., 2008) body parts. The parietal lobe shares reciprocal projections with lateral and medial regions in the prefrontal cortex (Cavada & Goldman-Rakic, 1989; Petrides & Pandya, 1984). These regions in the PFC are engaged during working memory tasks (Bunge et al., 2001; Drobyshevsky et al., 2006) and during the processing of emotion (Levesque et al., 2003; Williams et al., 2006b; Ochsner et al., 2002; Ochsner et al., 2004). My data suggest that the lateral PFC ROI is engaged in evaluating stimuli, since this region activated to both bodies and scrambled images (Figure 1). However, the activation was higher to bodies than to scrambled images, suggesting that perhaps the bodies were more complex or logical or had higher emotional content than scrambled images. Alternatively, it could also be that the parietal cortex responded more to bodies than to scrambled images, which could have subsequently increased activation in the lateral PFC, since these two regions are interconnected. If positive bodies require more appraisal in order to be classified, then this may induce activation of the lateral PFC ROI more than negative or neutral bodies. This happens in concurrence with other parts of the PFC maintaining the arrow orientation in working memory.

As previously discussed, the medial PFC is a component of the default mode network (Raichle et al., 2001), which is suppressed in order to allow performance of cognitive (i.e. goal-directed) tasks. In addition, increasing task difficulty increases suppression of this network (McKiernan et al., 2003; Singh et al., 2008). Therefore, the medial PFC in healthy control women was suppressed as part of the default mode network to allow performance of the working memory task. However, suppression for negative bodies did not differ from baseline, suggesting that negative body distracters did not make the working memory task more demanding for these women.

Hypothesized response in brains of women who had recovered from AN

In women who had recovered from AN, the function of the circuit is similar to healthy women up to the point of stimulus recognition via the fusiform. For this group, the fusiform was more activated by bodies than by scrambled images, and fusiform activation was to bodies was higher in women who had recovered from AN than in control women (Figure 1). Amygdala activation to negative and neutral bodies was significantly greater than baseline in this group but not in controls (Figure 1; Table 1). This amygdala activation occurred despite information being held in working memory, suggesting that cognitive demands do not fully dampen amygdala activation in AN women. In terms of activation in the dorsal stream, the lateral PFC activation was similar to that seen in healthy control brains (Figure 1; Table 1), suggesting that the mechanism of stimulus evaluation by the brain is similar between women who have had AN and control women, even though they do not necessarily rate the same bodies in the same way. Finally, the medial PFC in women who had recovered from AN was suppressed as part of the default network to allow normal performance of the working memory task when distracters were negative bodies (Figure 1; Table 1), suggesting that negative body distracters made the task more demanding for women who had recovered from AN than for control women. The medial PFC response to negative body stimuli could have been influenced by the amygdala activation in response to negative bodies, since there are reciprocal projections between the amygdala and medial PFC (Amaral et al., 1984; Carmichael et al., 1995) and other evidence to suggest that these two regions act in concert to process emotion (Shin, Rauch, & Pitman, 2006; Koenigs & Grafman, 2009). Therefore, the suppression in the medial PFC to negative bodies may function to overcome the amygdala activity and higher negative responses to bodies in this group and produce similar behavioral performance as healthy women.

Two peaks in lateral PFC and FG region-of-interest time courses

There were two peaks in the time courses of the lateral PFC and FG regions-of-interest. I propose that the first peak in the lateral PFC ROI could have been due to maintaining arrow orientation in working memory and then adding the activation from the distracter to that. The first peak in the FG ROI could have been due to processing the memoranda arrow, since this region activates in response to objects (Downing et al., 2006; Grill-Spector et al., 2008), in addition to its robust activation to bodies (Hadjikhani et al., 2003) and faces (O'Craven et al., 2000). There is a 4 to 6 second lag between the presentation of a stimulus and the peak of the hemodynamic response in the brain (Huettel et al., 2004). The first peaks in these time courses reached their maximum at 2 seconds after the onset of stimulus presentation, making it unlikely that the first peaks were due to the distracter stimuli. By the time women viewed the distracter, they had already viewed the memoranda arrow, making it likely that their activation was already above baseline, and this could account for the first peak. Therefore, only the second peak was used to calculate percent signal change for those regions. A control run that looked at brain activation in response to body stimuli separate from the working memory task would resolve the issue of whether or not the first peak in the lateral PFC and FG is due to viewing the memoranda arrow. If there were one peak in response to viewing a body alone, this would suggest the first peak was due to the memoranda arrow. If there were still two peaks, this would suggest there are dual processes performed by the lateral PFC in response to viewing bodies. Finally, I did not see two peaks in the amygdala or two troughs in the medial PFC. The amygdala responds most robustly to emotional stimuli (Zald, 2003). Since the arrows do not contain obvious emotional content, I would not expect those stimuli to activate the amygdala. The medial PFC is part of the default network (Raichle et al., 2001), which is suppressed to allow performance of cognitive tasks (Gusnard et al., 2001), particularly as those tasks get more difficult (McKiernan et al., 2003; Singh et al., 2008). My hypothesis is that the working memory task did not get difficult enough to suppress the medial PFC until the distracting body stimuli were viewed, which is why there is only one trough. In the future, I will reanalyze the fMRI data from Chapter 3 to model the entire time course of activation for each trial, so I can determine if my hypotheses regarding two peaks are true.

<u>Conflicting working memory results between Chapters 2 & 3</u>

The pattern of behavioral results for the working memory task differed between the studies in Chapter 2 and Chapter 3. In Chapter 2, positive bodies were more disruptive to working memory performance than negative or neutral bodies. In Chapter 3, negative bodies were more disruptive to working memory performance than positive or neutral bodies. The same stimuli, outcome measures, and overall task design were used in both experiments; however, the timing and the environment differed.

In order to adapt the working memory task for use in an fMRI study, it was necessary to increase the length of the trials and the amount of time that some of the stimuli were viewed. Memoranda presentation time increased from 750msec to 1000msec, distracter presentation time increased from 2000msec to 4000msec, the delay before and after the distracter presentation increased from 500msec to 1000msec, and the inter-trial interval increased from 1000msec to 7000-11000msec. One explanation for the difference in the pattern of results is that the length of time permitted for processing a stimulus affects how disruptive that stimulus is to working memory. In Chapter 2, the distracter stimuli were closer in time to the probe stimuli than in Chapter 3 (500 vs. 1000msec). The reaction time to rate positive bodies during the valence rating tasks in Chapters 2 and 3 and the higher lateral PFC activity to positive bodies during the working memory task in Chapter 3 suggest that it takes longer for women to evaluate, or "appraise", positive bodies. Therefore, positive bodies may have been more disruptive to working memory performance in Chapter 2 because women were still trying to appraise them when they needed be making a decision about arrow orientation. In Chapter 3, women had more time to view the stimulus and a longer delay after the stimulus, totaling an extra 2.5 seconds. This may have allowed the women the extra time they needed to appraise the positive bodies, making them less disruptive to working memory performance. One possibility is that negative stimuli are typically more disruptive to cognitive function than positive stimuli, and that this outcome can be viewed as the "normal" outcome. Meaning, that when there is enough time to process all stimuli, negative stimuli will be more disruptive than positive stimuli. There is some support for the "normal" outcome hypothesis. It has been suggested that there is a "negativity bias" or "negativity dominance" in the way younger adults experience or remember affective events or stimuli (Rozin & Royzman, 2001). In some instances, negative stimuli are better remembered than positive stimuli (Charles et al., 2003) and are more disruptive to working memory performance than neutral stimuli (Dolcos et al., 2006). Therefore, the shorter time frame in Chapter 2 may have caused a deviation from the normal outcome because there was not enough time to appraise the positive bodies, indicating that stimulus processing time affects the pattern of working memory results.

Another explanation for the difference in the pattern of working memory results could be the change in environments. In Chapter 2, the working memory task was performed at a computer on a desk in a quiet testing room with a comfortable chair. In Chapter 3, the task was performed in an MRI scanner, which means lying on one's back on a small table in a loud room. Psychosocial stress (Jelici, Geraerts, Merckelbach, & Guerrieri, 2004) and administration of cortisol (Buchanan & Lovallo, 2001) enhance memory for emotional and arousing stimuli, respectively, suggesting that stress may enhance the salience of emotionally arousing stimuli. There is some evidence to suggest that scanning can be stressful or anxiety-inducing (MacKenzie, Sims, Owens, & Dixon, 1995), even in healthy volunteers (Chapman, Bernier, & Rusak, 2010). If the negative bodies in Chapters 2 and 3 were more arousing to the women than the neutral or positive bodies, this could have created a situation where the negative stimuli were more salient because of the more stressful environment of the MRI scanner in comparison to the testing room. This higher salience could have made the negative bodies more disruptive to working memory performance. However, we would need arousal ratings of the bodies to confirm this hypothesis. Women who had recovered from AN had higher anxiety than control women, suggesting that effects of scanner anxiety could have been worse in women who had recovered from AN. However, one would expect that this would affect all distracter types equally and, therefore, would not explain differential effects of valence found in this study. Thus, stress is a potential but unconfirmed option for the increased disruption of working memory by bodies that were rated as negative in Chapter 3.

The pattern of behavioral results also differed between Chapters 2 and 3 for the body stimuli versus scrambled images comparison. In Chapter 2, scrambled images were more disruptive to working memory performance than were body stimuli. In Chapter 3, scrambled images and body stimuli were equally disruptive to working memory performance. In Chapter 2, it was suggested that the infrequent presentation of scrambled images made them more surprising, and, thus, more disruptive to performance. In Chapter 3, it may be that the extra time during the retention interval permitted women to recover from their “surprise”, such that scrambled images were no more disruptive to performance than body stimuli.

<u>Self versus other images used in tasks to assess responses to bodies</u>

There was a switch from using each participant’s own body in Chapter 1 to using stimuli of other women’s bodies in Chapters 2 and 3. However, the use of “self” versus “other” bodies did not appear to matter. First, the results of the Figure Rating Scale in Chapter 1 did not change when using images of the participants’ own bodies versus the line drawings of bodies. Second, the pattern of results for affective responses to bodies did not change when the body stimuli were morphed images of one’s own body (self) or morphed images of other women’s bodies (other). Appendix 1 shows unpublished data that were not included in Chapters 1 through 3. These reaction time and percent categorization data were based on fatter and thinner images of each woman’s own body. Younger and older women were slower to assign positive ratings to body stimuli than to assign negative ratings, and they categorized more body stimuli as negative than as positive. Thus, using “self” body stimuli yielded the same pattern of results as using “other” body stimuli, as was seen in Chapters 2 and 3. This lends support to the idea that “self” versus “other” bodies did not affect the results seen in younger and older women. Faces were blurred in all of these tasks so as not to distract attention from the bodies and not to cause face-related brain activation; however, this could also have made it easier for younger and older women to dissociate themselves from the “self” bodies, which may have contributed to the similar results between using “self” versus “other” bodies. However, I did not specifically test whether or not women identified each body as “self” in Chapter 1, although they were informed that they would be viewing morphed images of their own bodies.

Based on the study design used here, it is not possible to know whether or not using “self” versus “other” bodies would have changed the results for women who had recovered from AN. However, some behavioral and neuroimaging studies suggest that it would. For example, women with AN had a wider range of sizes that they considered obese for themselves than for other women (Smeets, 1999). Additionally, women with AN activate frontal regions to images of other women’s bodies but not to images of their own bodies, while women without an eating disorder activated frontal regions to both (Sachdev, Mondraty, Wen, & Gulliford, 2008). Another study found that control women activated frontal regions more than women who had AN in response to viewing images of their own bodies, while women who had AN activated prefrontal regions and the amygdala more than controls in response to viewing other women’s bodies (Vocks et al., 2010). These neuroimaging studies suggest that women with AN would have had less activation to their own bodies than to “other” bodies. However, it is unclear how these behavioral and neuroimaging results in women who actively have an eating disorder would translate to women who have recovered from AN. The fact that the women here retained higher negative affective responses towards body stimuli of other women and that they had worse body image than controls, suggests that they would have had an even greater negative response towards their own bodies than the "other" bodies that they saw. For example, this could manifest as lower valence ratings, even fewer bodies categorized as positive, and perhaps even longer response time to decide that their own body is positive. Thus, I would expect a similar pattern of results with even more medial PFC suppression and higher amygdala activation. However, these hypotheses are merely speculative, as this study was not designed to examine "self" versus "other".

Other factors affecting body image

Effects of ethnicity and culture on body image

Evidence suggests that ethnicity and culture affect susceptibility to body dissatisfaction and internalization of the thin ideal. Although greater than 50% of black and white teenage girls want to be thinner, black teenage girls report less body dissatisfaction than white teenage girls, even when they fall into similar BMI percentiles, and white girls report body dissatisfaction starting at a lower BMI than black girls (Banitt et al., 2008). Similar results are seen in adults. In one study, white women reported similar body dissatisfaction as black and Hispanic women, even though their BMI was lower (Fitzgibbon et al., 2000). On average, white women reported body dissatisfaction when they fell into the normal weight BMI range, while black and Hispanic women did not report body dissatisfaction until their BMI was in the overweight range (Fitzgibbon et al., 2000). Western culture may have a significant effect on body dissatisfaction.

Younger Amish women living separate from Western industrialized society do not report body dissatisfaction and do not over- or under-estimate their body size (Platte, Zelten, & Stunkard, 2000), and younger Muslim women who wear non-Western clothing , such as head veils, report lower drive for thinness and lower pressure to attain a thin ideal than women who wear Western clothing or do not wear veils (Dunkel, Davidson, & Qurashi, 2010). Additionally, higher exposure to western media predicts higher body dissatisfaction and endorsement of smaller body sizes as “most attractive” in a study of women and men from 26 countries in 10 regions across the world (Swami et al., 2010). Collectively, these results suggest that ethnicity and culture affect body dissatisfaction in women and girls. However, this ended up not being an issue for the series of studies completed here, since less than 3% of the study participants identified with an ethnicity other than white Caucasian. However, if the sample included more black or Hispanic women, I would predict lower mean body dissatisfaction scores on the Figure Rating Scale in Chapter 1 and the Eating Disorder Inventory subscale used in Chapters 1 through 3.

Effects of marital and parental status on body image

In some cases, marital and/or parental status affects how women feel about their bodies. Being single predicts intense dieting in women over 26 years of age (Vogeltanz-Holm et al., 2000), and over 85% of engaged women want to lose weight prior to their weddings (Prichard & Tiggemann, 2009). On the other side of the coin, married women place lower importance on changing their bodies to fit the ideal body than single women (Tom, Chen, Liao, & Shao, 2005). Married women and men also place less importance on their spouses having ideal bodies than single women and men place on their dates

(Tom et al., 2005). Additionally, a 20-year longitudinal study found that being married and having children predicted a decrease in eating disorder symptoms, such as drive for thinness (Keel et al., 2007). In women who had given birth, being married was also associated with less body shape concern nine months post-partum than being single (Gjerdingen et al., 2009). However, not all studies agree that marriage improves body image. One survey including over 16,000 participants found that body dissatisfaction was similar between married and single individuals, even after controlling for gender, age, BMI, and self-esteem (Friedman, Dixon, Brownell, Whisman, & Wilfley, 1999). Furthermore, controlling or abusive partners can contribute to and sustain eating disorders in middle-aged women (Kally et al., 2008). Divorce is a common trigger for disordered eating in this age group (Kally et al., 2008). Overall, these data suggest that a healthy marriage may improve body image. This idea is further supported by a study that found a significant correlation between low marital satisfaction and higher body dissatisfaction (Friedman et al., 1999). Marital and parental statuses were not assessed in the studies presented in Chapters 1 through 3. However, I predict that women in healthy marriages with children would likely have lower mean body dissatisfaction scores, while single women or women in unhealthy marriages would likely increase those scores. Anecdotally, there were more married older women than younger women, so marital and parental statuses are probably larger issues for the studies in Chapters 1 and 2. Without quantifying these factors, it is not possible to parse out the effects of marriage and children on body image versus the effects of age. However, as referenced in the Introduction to this document and Chapter 2, older adults prioritize emotional goals (Carstensen et al., 1999) and have a bias for positive emotional information (Mather et al., 2005a). Thus, it may be that marriage and family are some of the positive aspects in life that older women chose to focus on in lieu of their aging bodies.

Conclusions

I set out to characterize body image in younger and older women and women who had recovered from AN and healthy controls, to examine affective responses to bodies, and to examine how exposure to bodies affects prefrontal cortical regulation. Regarding the characterization of body image, I found that younger and older women had similar body dissatisfaction, but other than that older women had a more positive body image, as assessed by other quantitative measures. I also found that women who had recovered from AN still had worse body image than control women. I found that younger and older women had very similar affective responses to body stimuli, while women who had recovered from anorexia are more negative than control women. However, all women had similar (slower) responses to positive bodies, suggesting that these are unique affective stimuli to women. However, negative affective responses to bodies are dependent on history with AN but not age. Regarding brain activity, there was different underlying amygdala, fusiform, and medial PFC activation in women who had recovered from AN. This suggests that similar behavior relies on differential prefrontal regulation and that these compensatory mechanisms that involve the default network permit the production of "normal" cognitive function in the face of affective challenge.

Future directions

These data provoke many questions regarding body image in women. Future questions of interest concern the manipulation of medial prefrontal suppression, task difficulty, and appraisal of positive bodies.

Manipulation of medial prefrontal suppression

One important question regarding the medial prefrontal suppression in women who had recovered from AN and controls was whether this was a trait of AN or part of the state of recovery. I hypothesized that this was part of the state of recovery. A within-subject design examining brain activity before treatment and after recovery in women with AN would answer this question more directly. If the medial PFC suppression was a trait of AN, I would expect the pattern of medial prefrontal suppression while viewing body distracters during a working memory task retention interval to be the same in women before treatment and after recovery, and that this pattern would differ from controls in the same way it did in the fMRI study here (i.e. more suppression to negative bodies in RecAN than control women). If the medial PFC suppression was part of the state of recovery, I would expect women with AN to have less suppression in response to negative bodies in comparison to after they had recovered. In fact, I might expect women with AN to have a fear response to bodies that overrides the necessity to perform the working memory task, in which case they might have medial prefrontal activation.

Women find few bodies to be positive, but the degree of negativity assigned to bodies may vary from woman to woman based on her history with AN. Therefore, it would be useful to know if there is a threshold of negativity that must be reached to elicit the medial prefrontal suppression during a working memory task. A working memory task with mildly, moderately, and extremely negative bodies as distracters would be one way to answer this question. I would expect that there is a threshold that must be reached to elicit suppression in women who have recovered from AN. I would also expect a higher (i.e. more negative) threshold to elicit suppression in control women. For example, mildly negative bodies may elicit medial PFC suppression in women who have recovered from AN, but extremely negative bodies may be required to elicit medial PFC suppression in controls. Furthermore, this could be used to test whether or not there is a point at which bodies become so negative that the medial PFC cannot compensate for the emotional response, and working memory performance for trials with negative bodies becomes worse in women who have recovered from AN than in control women. The negative bodies used in the fMRI study in chapter 3 were equated for negative valence ratings, so it was not possible to address this issue parametrically with the design that was used.

Another important issue to address is which qualities make a body negative. One hypothesis is that women who have recovered from AN have a fear response to the bodies that needs to be suppressed in order to perform the working memory task. Thus, it would be useful to know the effect of bodies rated as fearful versus not fearful on medial PFC suppression during the retention interval of a working memory task. I would expect that bodies that elicit equal fear ratings would elicit more medial PFC suppression in women who have recovered from AN than in control women. Furthermore, it would be useful to know whether or not behavioral and neural fear response can be modulated pharmacologically. This would provide information about potential underlying mechanisms (e.g. which receptors the drugs act on) and potential treatments to improve recovery from AN.

Task difficulty

Working memory tasks can encompass maintenance processes, where information has to be held in mind in the state it was encoded, and manipulation processes, where information that was encoded has to "operated on" in some way (D'Esposito, Postle, & Rypma, 2000). The working memory task used here falls under maintenance processes. Using a manipulation paradigm instead of a maintenance paradigm would activate more regions of the lateral PFC (D'Esposito et al., 2000) and, presumably, make the task more difficult. Increasing task difficulty would be useful in determining whether or not there is a ceiling for medial PFC suppression in response to body stimuli. More specifically, a design parametric for task difficulty could be used to test whether or not there is a point at which the working memory task becomes so difficult that the valence of the body does not matter, and women who have recovered from AN and control women have similar suppression simply because the task is difficult. In terms of recovery from AN, it would be useful to know whether these women are more distracted by negative bodies than are control women no matter how difficult the task at hand, or if distraction by bodies is only an issue for tasks of easy or moderate difficulty tasks.

Lateral prefrontal evaluation

To determine whether or not the lateral PFC activation was due to evaluation of positive bodies, I propose doing something similar to the valence rating task during fMRI data collection. Women would be instructed to view each body and decide whether they thought it was negative, positive, or neutral (simple three-choice categorization). With this design, one would be able to know (instead of speculate) that women are, in fact, evaluating the body, so it would be possible to more definitively attribute lateral prefrontal brain activity to that process (e.g. higher lateral prefrontal activation to bodies rated as negative than to bodies rated as positive or neutral).

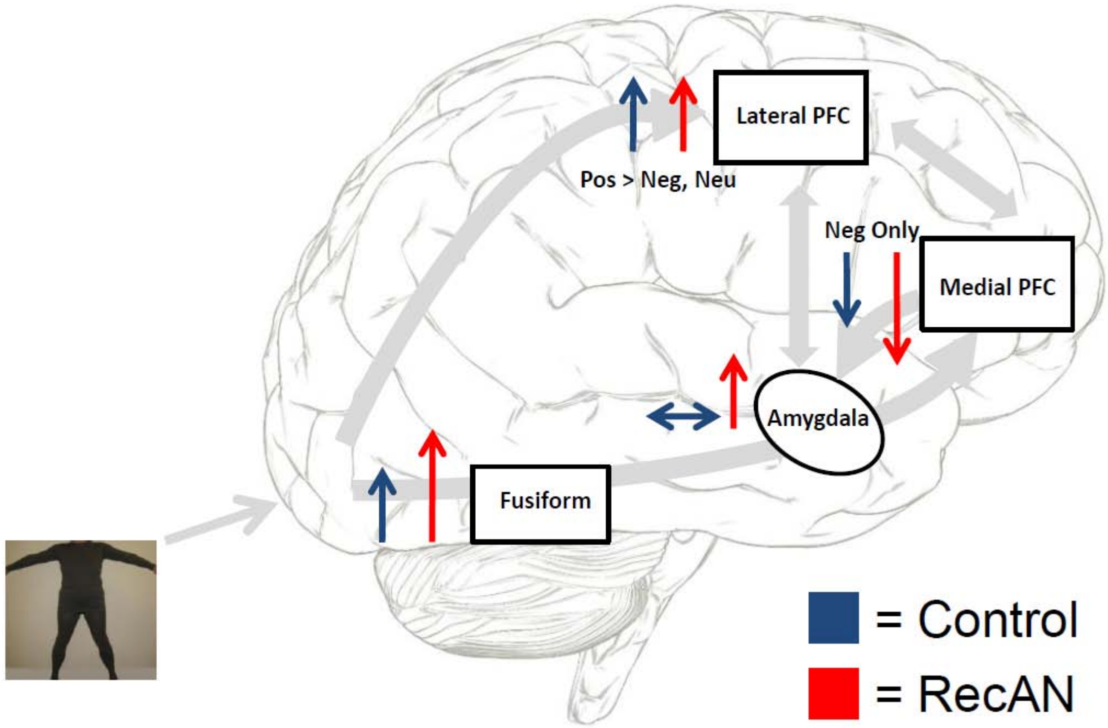


Figure 1. Regulation of emotional responses to body stimuli viewed as distracters during a working memory task. The fusiform and amygdala were more sensitive to bodies in RecAN than in control women. However, the lateral PFC was not regulating this response, because the pattern of activation was the same between groups: positive bodies elicited more activation than neutral or negative bodies. Finally, the medial PFC was more suppressed in women who recovered from AN than in controls when women had to view a negative body and hold something in working memory at the same time.

Table 1. Activation of ROIs in hypothesized body image circuits in brains of women who had recovered from AN and healthy control women.

Brain Region	Control	RecAN
Fusiform	↑ Bodies, ↑ Scr	↑ ↑ Bodies, ↑ Scr
Amygdala	↔ Bodies	↑ Bodies
Lateral PFC	↑↑ Bodies, ↑ Scr	↑↑ Bodies, ↑ Scr
	↑↑ Pos Bod, ↑ Neg Bod, ↑ Neu Bod	↑↑ Pos Bod, ↑ Neg Bod, ↑ Neu Bod
Medial PFC	↓ WM	↓ WM, ↓↓ Neg Bod WM

↑ or ↓ = increased or decreased from baseline

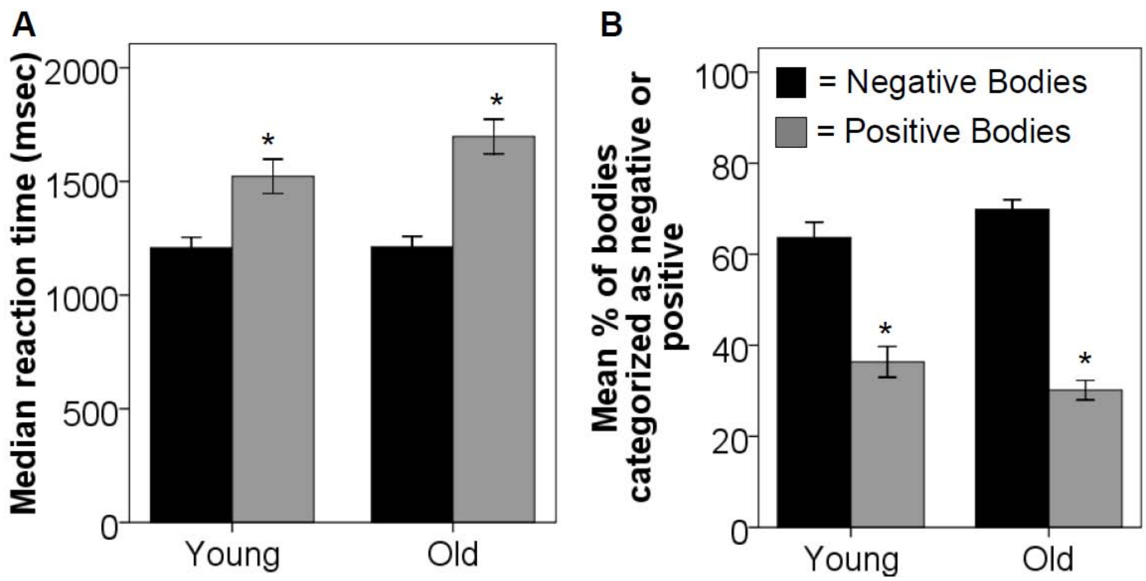
↑↑ = increased more than the other stimuli in that cell

↔ = no change from baseline

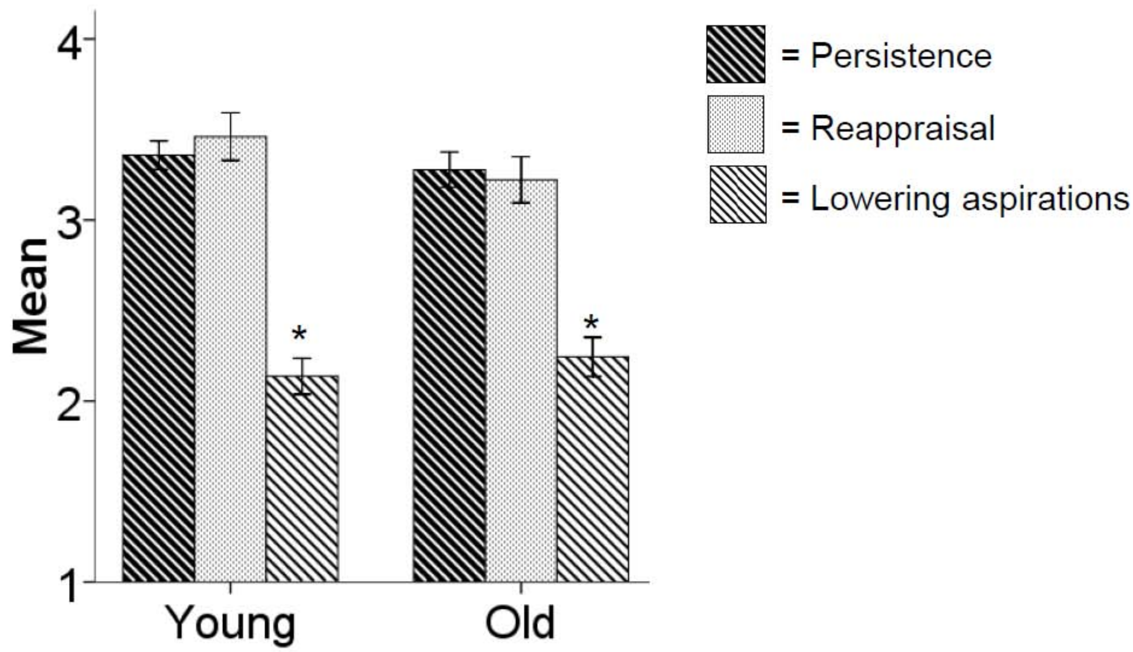
↓↓ = decreased from baseline more than control women

WM = Working memory maintenance

Appendix



Appendix Part 1. Unpublished data for reaction time and categorization of negative and positive bodies. (A) Younger and older women were slower to categorize bodies as positive than as negative in two-choice categorization task. * = Positive > Negative. (B) Younger and older women categorized more bodies as negative than as positive in a two-choice categorization task. * = Positive < Negative.



Appendix Part 2. Unpublished data on cognitive control in younger and older women from Chapter 1. This measure assesses three types of general (i.e. not body image specific) cognitive control strategies: persistence, reappraisal, and lowering aspirations. Younger and older women did not differ for their endorsed use of any cognitive control strategy; however, both groups endorsed using persistence and reappraisal more than lowering aspirations. * = Less than Persistence and Reappraisal.

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