

An Investigation of Neuropsychological Functioning in Women Recovered From
Anorexia Nervosa

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Thesis Submitted in Partial Fulfillment
of the Requirements for the Degree of
Master of Arts
Clinical Psychology

Middle Tennessee State University
December 2015

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This paper is dedicated to every individual who has struggled, is struggling, or will struggle, at some point in his or her life, with an eating disorder. It is dedicated to those whose lives have been claimed by these devastating illnesses and to those who have survived and recovered from them, as well as their families and loved ones. It is my hope that through concerted efforts to increase our understanding of eating disorders through research studies such as this one, we can find better ways to treat and prevent them.

ACKNOWLEDGEMENTS

First, I would like to acknowledge my loving and supportive parents, Grace Renshaw and Randy Horick, who have always motivated and encouraged me to pursue my passions, and my sister, Allie Horick, who constantly reminds me of my strengths and capabilities and inspires me to bring my dreams and ideas to fruition.

I must also acknowledge my friends and classmates, who have listened patiently, offered their ideas, and served as guinea pigs for any neuropsychological tests that I needed to practice administering. Special acknowledgement must be given to my dear friend and roommate, Carly Hill, as she been an incredible source of support and encouragement throughout this process.

I would also like to acknowledge Kathleen Yabroudy and Courtney Grimes of the Eating Disorders Coalition of Tennessee, without whose willing generosity this study would not have been possible.

Finally, I would like to acknowledge those who have provided their instruction and mentorship during my graduate and undergraduate careers. I owe a great deal of gratitude to Dr. Kimberly Ujcich Ward, who has been a wonderfully kind, giving and patient mentor throughout the time that I've known her, and Dr. Paul Foster, who helped to foster my interest in neuropsychology (no pun intended). I would also like to thank my undergraduate instructors, Dr. Bryan Neighbors and Dr. Fay Guarraci, for imparting on me their knowledge and passion for research, and for inspiring me to pursue a career in psychology.

ABSTRACT

Research has shown that anorexia nervosa (AN) is characterized by structural and functional brain abnormalities. A distinct pattern of neuropsychological functioning has been observed in women with AN, characterized by poor performance on tasks assessing visuospatial and executive functioning, and normal-to-superior performance on verbal fluency tasks, compared with healthy women. This study sought to explore this phenomenon in women recovered from AN, using neuropsychological measures associated various brain areas. It was predicted that recovered AN women would perform more poorly than controls on tasks assessing right parietal, right frontal, and left parietal functioning, and similar or superior performance on a left frontal task. Recovered AN women outperformed healthy controls on neuropsychological measures, suggesting that they do not experience relative impairment in neuropsychological functioning. Whether these findings are the result of improvements in cognitive functioning in women recovered from AN or from methodological issues in the current study remains unclear.

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CHAPTER I

Literature Review

Anorexia nervosa (AN) is a potentially life-threatening condition characterized by an extreme preoccupation with weight and body size and fear of gaining weight, distorted body image, and strict adherence to routines or patterns of behavior in an attempt to maintain a low weight. Individuals with AN sometimes restrict their food intake to the point of emaciation, and some also engage in compensatory behaviors, such as vomiting, laxative use, and compulsive exercise. These compensatory behaviors distinguish between the two subtypes of AN: Restricting Type (AN-R) and Binge-Purging Type (AN-BP). AN is associated with many medical complications, such as osteoporosis, cardiac arrhythmia and metabolic abnormalities, as well as psychological problems such as depression, anxiety, and obsessive-compulsive symptoms (Klein & Walsh, 2004).

Treatment of AN is often unsuccessful, as AN patients tend to be resistant to treatment, and relapse is common. Full recovery from AN is considered uncommon, with fewer than half of those diagnosed with the disorder achieving full recovery (Klein & Walsh, 2004). Research has focused on personality traits, environmental and interpersonal factors, and sociocultural factors as etiological components of AN and has targeted these factors in treatment. More recently, however, some researchers have focused on identifying potential genetic and biological components of AN. Specifically, neurological components of AN have become a topic of increasing interest in AN research during the past few decades, with an emphasis on areas of brain differences in

individuals with AN. In the current paper, neurological and neuropsychological research on AN will be discussed, as well as the aims of the current study.

Neurological Functioning in AN

Neuroimaging studies have revealed structural abnormalities in the brains of women with AN. A comprehensive review of imaging studies on women with AN by Phillipou, Rossell, and Castle (2014) showed a consistent pattern of abnormalities in gray matter volume in women with AN compared with healthy control women across studies. Specifically, decreases in gray matter volume were found using magnetic resonance imaging (MRI) consistently in the anterior cingulate cortex (e.g., Amianto et al., 2013; Friederich et al., 2012; Gaudio et al., 2011), hippocampus and amygdala (e.g., Connan et al., 2006; Friederich et al., 2012; Giordano et al., 2001) as well as the frontal (Boghi et al., 2011) and parietal lobes (Boghi et al., 2011; Gaudio et al., 2011) in women with AN. Several studies cited in the review reported that gray matter volume in women with AN normalized following weight recovery (e.g., Cowdrey, Filippini, Park, Smith, & McCabe, 2012; Lázaro et al., 2013; Mainz, Schulte-Rüther, Fink, Herpertz-Dahlmann, & Konrad, 2012), whereas others reported persisting gray matter abnormalities in women recovered from AN (e.g., Frank, Shott, Hagman, & Mittal, 2013; Friederich et al., 2012; Roberto et al., 2011). These studies' findings suggest that women with AN experience alterations in their brain structure that could be related to the symptomatology of the disorder; however, structural imaging alone is not sufficient to make the connection between neurological abnormalities and AN symptomatology.

Functional neuroimaging techniques, which include functional magnetic resonance imaging (fMRI), electroencephalogram (EEG), and single-photon emission computed tomography (SPECT), have been used to assess women with AN in recent years, as they show levels of activity in specific brain areas, providing a clearer picture of neurological dysfunction in women with AN and how it may relate to their behavioral patterns. Functional neuroimaging studies (e.g., Amianto et al., 2013; Favaro et al., 2012; Sachedev et al., 2008) comparing AN patients to healthy controls have found abnormalities in brain activity in patients with AN, which have generally been consistent with the structural abnormalities found in the aforementioned studies. In these studies, brain activity in AN women has been observed during a resting state and while performing specific tasks. In one study, a group of patients with AN were given fMRI scans while in a resting state and were shown to have decreased connectivity between several neural networks, including the cerebellar-parietal network, and increased connectivity between the cerebellum and insula (Amianto et al., 2013). Favaro et al. (2012) evaluated both ill and recovered women with AN during a resting state using fMRI and observed decreased connectivity between left occipital and left temporal areas, and increased activation of the somatosensory network and left parietal cortex in the ill group, and observed decreased activation in the right frontal lobe in the recovered group (Favaro et al., 2012).

EEG studies also have proven helpful in localizing levels of brain activity to specific areas. Rodriguez et al. (2007) found that women with AN experience lower

alpha power (i.e., greater cortical activation) in temporal, parietal, and occipital areas during resting state compared to controls. Hatch et al. (2011), in their EEG study, found that a group of female adolescents with AN experienced increased theta power, which they suggested is indicative of increased cortical activation, in parietal-occipital areas when they closed their eyes, and that this increased theta power persisted after weight gain. Grunwald et al. (2001) used EEG to record brain activity levels in a group of adolescents with AN and healthy controls while performing a haptic visuospatial task and found that the AN group experienced significant reductions in theta power in the right parietal cortex compared to the control group, which also persisted after weight gain. These disparate findings suggest that women with AN experience altered levels of parietal activity while in a resting state and while performing cognitive functions.

SPECT studies have consistently shown decreased activity levels in temporal areas (e.g., Frampton, Watkins, Gordon, & Lask, 2011; Gordon, Lask, Bryant-Waugh, Christie, & Timimi, 1997; Key, O'Brien, Gordon, Christie, & Lask, 2006), parietal areas (e.g., Chowdhury et al., 2003; Kojima et al., 2005; Naruo et al., 2001), and the anterior cingulate cortex (e.g., Kojima et al., 2005; Naruo et al., 2001, Takano et al., 2001), as indicated by decreased regional cerebral blood flow (rCBF) in these areas, in women with AN compared with controls. In two of these studies, hypoperfusion, or reduced rCBF, in the temporal lobes persisted after weight gain (Frampton et al., 2011; Gordon et al., 1997).

Functional imaging studies have frequently been used to observe brain activity in women with AN while passively and actively engaging in cognitive tasks. Several studies have assessed brain activity in women with AN during passive viewing tasks. AN women showed increased right parietal activation when viewing images of ‘body checking’ versus neutral actions compared to controls (Suda et al., 2013). Both Castellini et al. (2013) and Mohr et al. (2010) found that women with AN showed increased temporal/insular activation compared to controls when viewing images of their bodies that had been digitally distorted to make them thinner than their actual bodies. Two other studies assessed brain activity in AN and control women when viewing images of their own and other women’s bodies and found that the AN group showed decreased activity in frontal, temporal, parietal and occipital areas and increased amygdala activity when viewing images of their own bodies (Sachedev, Mondraty, Wen, & Gulliford, 2008; Vocks et al., 2010). Women with AN showed increased insular and premotor activity and decreased activity in the anterior cingulate cortex when comparing their bodies with slim, idealized female bodies (Friederich et al., 2010). Interestingly, a couple of studies have demonstrated that viewing words related to negative body image elicits similar patterns of neurological activity as those elicited by images of women’s bodies. Miyake et al. (2010) found that negative body-image words resulted in greater amygdala activation in women with AN compared to women with bulimia nervosa (BN) and controls, and Redgrave et al. (2008) observed greater activity in frontal and temporal areas in women with AN when viewing “thin” words, and reduced prefrontal activity

when viewing “fat” words, compared to controls. These studies suggest that body image disturbance in AN is associated with abnormal patterns of brain activity in a variety of areas.

Women with AN also appear to show abnormal patterns of brain activity in comparison to healthy controls while performing various cognitive tasks. While performing a set-shifting task, women with AN showed reduced activation in prefrontal and parahippocampal areas compared to control women (Sato et al., 2013). A group of women with AN was assessed before and after weight recovery and showed increased temporal and parietal activation while completing a working memory task compared to controls. Following weight recovery, the AN group showed decreased activity in the anterior cingulate cortex, as well as temporal and parietal areas while completing the same task (Castro-Fornieles et al., 2010). Lao-Kaim, Giampietro, Williams, Simmons, and Tchanturia (2013) assessed brain activity in a group of women with AN using a working memory task similar to that of Castro-Fornieles et al. (2010), but used letters rather than numbers. Interestingly, they observed no difference in performance on the task between AN women and controls, and also observed no significant differences in brain activity between the two groups. It is further noteworthy that working memory performance differed between AN women and healthy women on a perceptual working memory task, but did not differ for a verbal working memory task. Based on the findings of these studies, it appears that cognitive dysfunction in AN may be related to neurological abnormalities. Whether this dysfunction results from abnormalities in brain

structure or from abnormal connectivity between neural networks, however, has yet to be elucidated.

Nunn, Frampton, Fugslet, Törzsök-Sonnevend, and Lask (2011) proposed, based on neuroimaging studies on AN, that AN is associated with disruption or impairment in a complex neural circuit centered around the insula, a region located within the temporal lobes with numerous connections to other regions and structures of the brain (including the frontal lobes, somatosensory cortex, parietal lobes, thalamus, hypothalamus, amygdala, hippocampus, and striatum). Disconnection within this neural circuit could, according to Nunn et al., explain the symptomatology of AN, including pathological behavior, emotional dysfunction, and biological and neurological abnormalities that characterize the disorder.

Overall, neurological studies on AN have provided information that has contributed to our understanding of the pathophysiology of AN. Studies performed with women recovered from AN have been particularly insightful in demonstrating that only some neurological abnormalities normalize following weight-restoration and recovery. However, these studies are unable to give insight into the specific nature of the cognitive, emotional and behavioral deficits that result from these neurological abnormalities; that is, they do not show which specific skills are impaired in the AN population as a result of their structural and functional neurological abnormalities. Fortunately, the field of neuropsychology has made such insight possible. Neuropsychological research on AN

provides data regarding functional impairment in AN, and the findings of this research have largely corroborated the findings of the neuroimaging studies previously discussed.

Neuropsychological Functioning in AN

Neuropsychological research expands on the findings of neuroimaging studies by clarifying how structural and functional neurological abnormalities in AN may be manifested behaviorally. The various skills assessed using neuropsychological methods correspond to neurological functioning and can be used to indicate dysfunction in particular brain regions. These skills are encompassed by several broad areas of neuropsychological functioning, which include visuospatial functioning, executive functioning, central coherence, and verbal fluency. The findings of neuropsychological studies with females with AN are subsequently described by area of functionality.

Visuospatial Functioning

Visuospatial functioning refers to the brain's ability to perceive and integrate visual and tactile stimuli. This perception and integration occurs in the parietal cortex and enables the mental rotation of two-dimensional and three-dimensional objects, the estimation of distance and depth, and the construction or reproduction of two-dimensional and three-dimensional objects, as well as the ability to estimate the body's boundaries and peri-personal space and to form a coherent representation of one's body (Nico et al., 2010). Some researchers have found a disturbance in visuospatial functioning in women with AN, which they have traced to dysfunctional processing mechanisms in the right parietal cortex by using neuroimaging in addition to

neuropsychological measures (e.g., Grunwald et al., 2001; Grunwald et al., 2002; Nico et al., 2010). These mechanisms may be related to body image disturbance and distortion in AN.

Grunwald et al. (2001) assessed visuospatial functioning in adolescent females with AN ($M_{\text{age}} = 15.9$ years) and healthy female controls ($M_{\text{age}} = 16.14$ years) using a haptic perception task, in which participants manually explored six sunken reliefs with their fingers and then reproduced them. Reproductions made by those in the AN group were less accurate than those of the control group, even after gaining weight ($M_{\text{age}} = 16.9$ years). These findings were consistent with their findings of reduced EEG theta power in the right parietal cortex in the AN group compared to the control group, and suggests a disturbance in visuospatial processing in AN. In a similar study, Grunwald et al. (2002) assessed right parietal functioning in a group of adolescent females with AN ($M_{\text{age}} = 15.31$ years) and a group of healthy controls ($M_{\text{age}} = 16.31$ years) using a haptic task that required them to adjust a lever to either parallel or mirror a visual display while blindfolded, thus utilizing the resources of both the left and right parietal cortices. They found that the AN group performed poorly in comparison to the control group only for tasks requiring adjustment of the right angle leg, which heavily utilized the resources of the right parietal cortex. These results suggest a functional disturbance in the right parietal cortex in women with AN. More recently, Nico et al. (2010) assessed visuospatial functioning in a group of female AN patients ($M_{\text{age}} = 23.4$ years), healthy controls ($M_{\text{age}} = 29.4$ years), and a group of four stroke patients with left (males, aged 36

and 57 years) and right parietal (one male, one female, aged 42 and 64 years respectively) lesions and age-matched female controls ($M_{\text{age}} = 54.5$ years) using a perceptual task in which participants judged the proximity and angle of an approaching visual stimulus to their bodies. The performance of AN patients on the perceptual task was significantly poorer than that of the control group, and was comparable to the performance of right parietal stroke patients in that they experienced difficulty in judging the trajectory of visual stimuli approaching the left side of the body. Patients with left parietal damage did not demonstrate impaired performance on the task, and their performance was similar to that of the control group. These findings suggest that distorted body image in AN may result from disturbances in right parietal functioning, rather than from malnutrition or emotional disturbance.

A number of studies have assessed visuospatial functioning in AN using the Rey Osterreith Complex Figure Test (RCFT), in which participants must copy a complex figure and then reproduce it from memory (e.g., Danner et al., 2012; Key et al., 2006; Stedal, Frampton, Landrø, & Lask, 2012). Key et al. found that a group of women with AN scored ($M_{\text{age}} = 27.65$ years) significantly lower than healthy controls ($M_{\text{age}} = 26.11$ years) on both the copy and recall tasks of the RCFT, indicating deficits in visuospatial skills and visual memory. Stedal, Frampton, et al. (2012) reviewed eight studies that assessed visuospatial functioning in patients with AN and healthy controls using the recall task of the RCFT, and they reported that, overall, patients with AN performed more poorly than controls, indicating a deficit in visual memory. However, Danner et al. did

not find any significant differences in performance on the RCFT copy and recall tasks between women with AN ($M_{\text{age}} = 25.3$ years), women recovered from AN ($M_{\text{age}} = 24.33$ years), and healthy control women ($M_{\text{age}} = 25.8$ years).

Rozenstein, Latzer, Stein, and Eviatar (2011) compared the neuropsychological performance of a group of women with eating disorders (including women with AN-R, AN-BP and BN, with mean ages of 23.22 years, 22.19 years, and 23.3 years, respectively) to that of their healthy biological sisters ($M_{\text{age}} = 23.86$ years) and healthy female controls ($M_{\text{age}} = 24.87$ years), and they found that the performance of healthy sisters of patients with eating disorders on a visuospatial bar graph task was similar to that of their affected sisters, but significantly different from that of healthy control women. The healthy sisters scored similarly to healthy controls on measures of psychopathology (i.e., depression, obsessionality, impulsivity) and eating disorder symptomatology, in contrast to the AN and BN patients, whose scores on these measures were higher. Based on these findings, Rozenstein and colleagues suggested that the relative visuospatial deficits seen in women with eating disorders and their healthy sisters may indicate a neurocognitive biomarker for eating disorders, whereas the emotional pathology observed to a greater extent in the three ED groups may represent nonheritable traits that increase an individual's vulnerability to developing an eating disorder. Rozenstein et al. also assessed differences in performance on the bar graph task among the AN-R and AN-BP subtypes and BN patients, finding that the AN-R patients performed more poorly than the other ED groups and that their relative impairment in

their performance on the task was independent of their lower weight. Interestingly, the performance of the AN-BP group on the bar graph task fell in between that of the AN-R and BN groups and did not differ significantly from either, suggesting that neuropsychological functioning in women with EDs can be described in terms of a continuum, with AN-R exhibiting the highest degree of cognitive disturbance and BN exhibiting the least.

According to Christman, Bentle, and Niebauer (2007), body image disturbance may also bear some relation to handedness. The authors assessed handedness and eating disorder symptomatology in a group of college men and women and found that those who demonstrated strong right-handedness experienced greater discrepancies between their actual and perceived BMI. They attributed this to the fact that right-handers have decreased access to areas of the right hemisphere of the brain, which is responsible for updating representations of their bodies. They also found that those who demonstrated strong handedness (regardless of the dominant hand) exhibited significantly higher levels of eating disorder symptomatology (particularly drive for thinness, interoceptive awareness, body dissatisfaction, and impulse regulation) than those who demonstrated mixed handedness. This study suggests that strong handedness, particularly strong right-handedness, may increase an individual's susceptibility to body image disturbance and to AN.

Executive Functioning

Executive functioning refers to a set of cognitive abilities involved in the planning, organization, and strategizing of behavior. These abilities include selective attention, reasoning, problem solving, set-shifting (i.e., the ability to switch from one cognitive task to another), goal-setting, response inhibition and working memory (Tenconi et al., 2010). Executive functions are regulated by the frontal lobes; in particular, the prefrontal regions of the frontal lobes have been implicated in executive functions (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005).

Neuropsychological studies tend to indicate impairment in executive functioning in AN, which may explain the rigid thinking patterns and perfectionism typically observed in individuals with AN. Danner et al. (2012) found, for example, that women with AN ($M_{\text{age}} = 25.63$ years) exhibited problems with set-shifting, as evidenced by their number of perseverative errors on Berg's Card Sorting Task. Similarly, Gillberg et al. (2010) found that a cohort of patients with AN ($M_{\text{age}} = 32$ years) performed more poorly on the Tower of London Test (TOL), a measure of executive functioning, than controls, and that this impaired performance was independent of the patients' BMI, current eating disorder diagnosis, or the length of their illness. It should be noted, however, that three out of the 51 participants in the study were male. Stedal, Frampton, et al. (2012) observed that AN patients took significantly more time than controls to complete the Trail Making Test (TMT), a measure of executive functioning involving set-shifting, or

switching from one cognitive strategy to another in response to environmental changes, which could possibly explain the rigid thought patterns typically observed in AN.

Tchanturia et al. (2004) compared the performance of women with AN ($M_{\text{age}} = 27.2$ years) and healthy controls ($M_{\text{age}} = 25.9$ years) on a variety of set-shifting tasks and found that the AN group performed worse than the control group (i.e., they took longer and made more perseverative errors) on tasks of attentional, perceptual haptic, and contextual set-shifting. Interestingly, the AN group did not show relative impairment on a verbal set-shifting task; in fact, they generated more words, on average, than the control group on the Controlled Oral Word Association Test (COWAT). The AN group's impaired performance on perceptual set-shifting tasks and normal-to-superior performance on verbal set-shifting tasks, relative to healthy participants, is suggestive of a weakness in set-shifting ability in the right hemisphere of the brain, and normal or heightened set-shifting ability in the left hemisphere, which is responsible for verbal abilities. Abbate-Daga et al. (2011) assessed set-shifting and decision-making ability in a sample of patients with AN ($M_{\text{age}} = 24.3$ years) and controls ($M_{\text{age}} = 24.67$ years). In their study, the AN group exhibited cognitive inflexibility in both verbal and nonverbal domains, suggesting an overall relative deficit in set-shifting. They also found that the AN group made significantly more disadvantageous decisions than the control group in the Wisconsin Card-Sorting Task (WCST) and the Iowa Gambling Task (IGT), which they attributed to poor strategy formation. An assessment of set-shifting ability using the WCST and the TMT by Tenconi et al. (2010) yielded similar findings, in that patients

with AN ($M_{\text{age}} = 26.2$ years) made significantly more perseverative and nonperseverative errors on these tasks than healthy controls ($M_{\text{age}} = 27.4$ years). No relative deficits, however, were observed in attention, visual tracking, or motor speed on either task. Difficulties in perceptual set-shifting in AN patients also were observed by Holliday et al. (2005). Billingsley-Marshall et al. (2013) assessed executive functioning in a group of inpatients with AN (M_{age} AN-R = 23.6 years, M_{age} AN-BP = 24.5 years) following treatment and found that nearly a third of their sample exhibited clinically significant impairment on one or more measures. Interestingly, greater impairment was associated with higher levels of anxiety, suggesting that anxiety may hinder cognitive flexibility in women with AN.

Cavedini et al. (2004) observed that patients with AN ($M_{\text{age}} = 22.8$ years) performed poorly in comparison to healthy controls ($M_{\text{age}} = 30.9$ years) on a gambling task, suggesting a deficit in decision-making that appears to be independent of illness severity or malnutrition. They paralleled the poorer performance of AN patients on decision-making tasks to their pathological eating behavior observed in real life, asserting that AN patients choose an immediate reward (i.e., they ignore or deny their hunger in order to ameliorate their fear of gaining weight) in spite of its negative long-term consequences (i.e., the deterioration of their physical health). Cavedini et al. also separately analyzed AN-R and AN-BP subtypes and noted that the two groups employed different strategies on the decision-making task. Whereas those with restrictive-type AN tended to make disadvantageous decisions on the task that hindered their performance in

the long-term, the strategy employed by those with binge-purge type AN was neither advantageous nor disadvantageous in the long-term. The authors speculated that the differences in strategies employed by the two AN subtypes could reflect their different strategies for reducing their body weight and size and maintaining a low weight – in the case of AN-R, self-starvation, and in the case of AN-BP, purging behavior.

Roberts, Tchanturia, Stahl, Southgate, and Treasure (2007) evaluated 15 studies in which set-shifting was assessed between patients with AN and healthy controls, and they concluded that AN patients consistently showed relative impairment on set-shifting tasks. Additionally, some memory impairment may be indicative of executive functioning deficits in AN. Key et al. (2006) found that AN patients ($M_{\text{age}} = 27.65$ years) performed poorly on both visual and auditory long-term memory tasks in comparison to controls ($M_{\text{age}} = 26.11$ years). Tenconi et al. (2010) examined set-shifting abilities in a group of AN patients ($M_{\text{age}} = 26.2$ years), their healthy sisters ($M_{\text{age}} = 27.5$ years), and nonrelated control women ($M_{\text{age}} = 27.4$ years) and found that both the women with AN and their sisters exhibited relative impairments in set-shifting. Specifically, they observed that both of these groups made significantly more perseverative and nonperseverative errors on the WCST, indicating an overall relative deficit in executive functioning. Galimberti et al. (2013) also compared the performance of patients with AN ($M_{\text{age}} = 24.1$ years) and their healthy first-degree relatives (i.e., mothers and sisters, $M_{\text{age}} = 43.79$ years) to that of unrelated controls ($M_{\text{age}} = 28.62$ years) and their first-degree relatives ($M_{\text{age}} = 43.31$ years) on both set-shifting and decision-making tasks, and found that the AN women and

their healthy relatives performed more poorly than controls on both types of tasks. Thus, weaknesses in executive functioning may also represent an endophenotype for AN. The results of these studies suggest that relative impairment in executive functioning, and specifically in set-shifting and decision-making, may represent an endophenotype of AN.

Central Coherence

Central coherence can be described as the ability to integrate incoming sensory information into something contextually meaningful, such as visual information into a picture or verbal information into a story (Frith, 1989, as cited by Kemps, Lopez, & Tchanturia, 2011). Lopez et al. (2008) describe the concept of weak central coherence, which was initially used in the context of autism spectrum disorders, but has been identified more recently as a cognitive feature of eating disorders as well. Weak central coherence, defined by Lopez et al. (2008), is “a cognitive style in which there is a bias towards local or detailed-focus processing of information over the natural tendency to integrate information into a context” (p. 143). Based on this notion, a handful of studies have examined central coherence in eating disorders. Lopez and colleagues (2008) observed that AN patients ($M_{\text{age}} = 28.4$ years) used a more detail-focused strategy to construct the complex figure in the RCFT, which hindered their performance on the recall task. In contrast, healthy control participants ($M_{\text{age}} = 26.3$ years) employed a more global approach and had higher scores on both the copy and recall tasks. However, the AN group in their study exhibited superior performance on the Embedded Figures Test (EFT), a task that requires detail-focused processing, in comparison to healthy controls.

On tasks measuring verbal coherence, the performance of the AN group was more comparable to that of the control group, although patients with AN hesitated more on the Hayling Sentence Completion Task. Tenconi et al. (2010) confirmed these previous findings, observing that women with AN ($M_{\text{age}} = 26.2$ years) and their healthy biological sisters ($M_{\text{age}} = 27.5$ years) exhibited weak central coherence relative to controls on several perceptual tasks; specifically, the AN patients in their study demonstrated poor global processing in comparison to healthy controls ($M_{\text{age}} = 27.4$ years). The findings of Danner et al. (2012) were inconsistent with those of previous studies assessing central coherence in AN, in that they did not observe weak central coherence in the AN group in their sample compared to the control group; however, they did find that weak central coherence was strongly associated with poor set-shifting in AN women.

Although relatively few studies have examined central coherence within the neuropsychological literature on AN, the studies that have assessed central coherence in AN suggest that a bias toward local processing at the expense of global processing represents a characteristic cognitive feature of AN. This type of cognitive processing style in women with AN could potentially explain various aspects of its symptom presentation, particularly obsessive-compulsive behaviors. Furthermore, weak central coherence in AN would be consistent with other types of cognitive deficits identified in AN, in that visuospatial impairment suggests a disturbance in functioning in the right hemisphere, which is responsible for sensory integration and global processing. Local or detail-focused processing, which has been shown to be superior in AN patients, is

governed predominantly by the left hemisphere (Gable, Poole, & Cook, 2013). Thus, the findings in the literature with regard to central coherence could be explained by right hemisphere dysfunction. Dysfunctional or disrupted processing in the right hemisphere in women with AN could also explain their lack of insight into the severity of their illness when acutely underweight and malnourished. Such lack of insight could be the result of anosognosia, or lack of awareness of deficits in functioning, which has been linked to lesions in the right hemisphere – more specifically, to the right parietal cortex (van Kuyck et al., 2009).

Verbal Fluency

Verbal fluency refers to the ability to retrieve specific verbal information from memory. Executive functioning is involved with verbal fluency, as various executive functions, such as selective attention, inhibition, and cognitive flexibility, are important for retrieval. Two primary domains of verbal fluency are semantic fluency, or the ability to generate words that fit into a particular category, and phonemic fluency, or the ability to generate words that begin with a particular letter of the alphabet (Stedal, Landrø, & Lask, 2013). In neuropsychological studies, verbal fluency is typically assessed using the COWAT as a measure of phonemic fluency, and Animal Naming as a measure of semantic fluency. The left frontal cortex has been implicated in phonemic fluency, whereas the left temporal cortex has been implicated in semantic fluency (Baldo, Schwartz, Wilkins, & Dronkers, 2006).

Neuropsychological studies of AN have consistently indicated normal-to-superior performance on verbal fluency tasks in women with AN. Tchanturia et al. (2004) did not find significant differences in performance on the COWAT between women with AN and healthy controls; in fact, the AN group generated slightly more words, on average, than their healthy counterparts, although they also made slightly more perseverative errors. Stedal, Frampton, et al. (2012) reviewed 6 studies that assessed verbal fluency in AN using the Verbal Fluency Test (VFT) and observed that AN patients performed significantly better than healthy control women on the task. In a more recent study, Stedal et al. (2013) administered the VFT to a group of female adolescents with AN ($M_{\text{age}} = 18.7$ years) and healthy female controls ($M_{\text{age}} = 14$ years) and analyzed the patterns of phonemic clusters, as well as switching between clusters, in each group. They found that, after controlling for age and verbal IQ (i.e., scores on the vocabulary subtest of the Wechsler Adult Intelligence Scale-IV, or WAIS-IV), the patient group not only generated more words than the control group, but they also switched to different phonemic clusters with significantly greater frequency than the controls, which suggests that verbal set-shifting abilities may be intact in AN women, whereas their nonverbal set-shifting abilities are impaired relative to healthy women. Consistent findings of superior performance by AN women on verbal fluency tasks led Stedal, Frampton, et al. (2012) to suggest that AN is associated with a distinct neuropsychological profile, characterized by relative deficits in executive and visuospatial functioning, weak central coherence, and normal-to-superior verbal fluency.

Neuropsychological Profile of AN

Overall, neuropsychological studies on women with AN have consistently found that AN patients exhibit relative deficits in visuospatial skills, executive functioning, and central coherence, and intact verbal fluency. The findings of this research suggest a distinct neuropsychological profile for AN that aligns with its unique symptom presentation, as well with personality characteristics observed in individuals with AN. Based on this notion, a group of neuroscientists at the Eating Disorders Research Society meeting held in Ravello, Italy, in 2004 developed a neuropsychological test battery, known as the Ravello Profile, to assess cognitive functioning specifically in AN (Rose, Davis, Frampton & Lask, 2011). The Ravello profile consists of a number of well-established, psychometrically sound neuropsychological instruments, which are described by Rose et al. (2011). These instruments include the RCFT as a measure of visuospatial skills, the Delis Kaplan Executive Functioning System (which includes a Verbal Fluency Test, a Stroop test, the TMT, and the TOL) as a measure of executive functioning abilities, the Brixton Spatial Completion Test as a measure of visual coherence, the Hayling Sentence Completion Test as a measure of verbal coherence, and the Vocabulary and Matrix Reasoning subtests from the WAIS-IV as an abbreviated measure of overall intellectual ability. Stedal, Rose, Frampton, Landrø, and Lask (2012) administered the full Ravello profile to a group of 155 patients with AN ($M_{\text{age}} = 17.13$), and have yielded findings consistent with those of previous studies (it should be noted, however, that 7 of the 155 patients included in the study were men).

Neuropsychological studies on AN (e.g., Grunwald et al., 2001; Grunwald et al., 2002; Nico et al., 2010) have indicated that women with AN tend to perform poorly in comparison to healthy women on tasks requiring visuospatial processing. Neuroimaging studies, however, have found increased levels of parietal activity in AN women while at rest (e.g., Rodriguez et al., 2007; Hatch et al., 2011), which is suggestive of enhanced visuospatial processing. The findings of neuropsychological studies with regard to visuospatial functioning are, therefore, inconsistent with those of neuroimaging studies on AN. The neuropsychological literature on AN also has indicated that AN women exhibit poorer performance compared to healthy women on tasks of executive functioning, particularly set-shifting and decision-making tasks. These findings are largely consistent with those of neuroimaging studies that have found decreased activity in frontal areas of the brain, which are known to govern executive functions. It should be noted, however, that executive functions encompass a wide range of skills that involve processing in both the left and right frontal lobes. The tasks in which AN women exhibit the poorest performance are those that use nonverbal or perceptual stimuli, which are processed in the right hemisphere. The same impairment has not been shown on verbal executive tasks, which involve processing in the verbal left hemisphere, consistent with the findings of an fMRI study showing no differences in brain activity between AN women and healthy controls during a verbal working memory task (Lao-Kaim et al., 2013). A majority of the neuropsychological studies evaluating central coherence have found that AN women exhibit relative deficits in global processing, although it is again

noteworthy that these deficits were less pronounced on verbal coherence tasks and more so on tasks assessing visuospatial coherence. Finally, neuropsychological studies have consistently found that the performance of AN women on verbal fluency tasks is comparable or superior to that of their healthy counterparts, which is consistent with findings of similar patterns of brain activity between these two groups while performing verbal tasks. On the whole, the findings of neuropsychological studies on AN have been consistent with those of neuroimaging studies, with the exception of neuropsychological studies assessing visuospatial skills. The performance of AN women on visuospatial tasks is inconsistent with the patterns of brain activity that have been shown in neuroimaging studies, which suggests that some other neurological mechanism could underlie the relative visuospatial deficits experienced by AN women.

Neuropsychological Functioning in Women Recovered From AN

An even smaller body of research has examined neuropsychological functioning in recovered AN women. The purpose of this research has been primarily to determine whether neuropsychological impairment in AN is the result of malnourishment or whether it represents a consistent pattern of cognitive functioning that may heighten an individual's vulnerability to AN.

A number of studies have assessed neuropsychological functioning in weight-restored AN women to determine whether the relative neuropsychological impairment seen in ill AN patients is a consequence of severe malnourishment or, rather, if cognitive dysfunction in AN could result from a preexisting neurobiological predisposition.

Grunwald et al. (2001) assessed visuospatial functioning, using a haptic reproduction task, in a group of female adolescent AN patients before ($M_{\text{age}} = 15.9$ years) and after ($M_{\text{age}} = 16.9$ years) undergoing inpatient treatment (the mean interval between pretreatment and posttreatment testing was 14.5 months), and compared their performance with that of a group of healthy adolescent controls ($M_{\text{age}} = 16.14$ years). Their findings indicated that the haptic reproductions produced by the AN group were significantly poorer in quality in comparison to those of the control group, even after weight gain and completion of inpatient treatment. They suggested that impaired somatosensory integration of visuospatial information in AN is independent of nutritional state or weight status, i.e., that it is trait rather than state-related. Bosanac, Norman, Burrows and Beaumont (2005) compared a group of underweight women with AN ($M_{\text{age}} = 28.94$ years) with a group of AN women who had been weight-recovered for at least three months ($M_{\text{age}} = 28.92$ years) and healthy control women ($M_{\text{age}} = 23.81$ years) and found that the weight-recovered group showed significant impairment on an immediate word recall task compared to the other groups, whereas the underweight AN women showed relative impairment on several attentional tasks in which reaction time and vigilance were measured.

Several studies have also assessed long-term recovered AN women in an attempt to determine whether neuropsychological dysfunction persists after healthy weight has been restored and maintained for a long period of time (i.e., one year or more). Danner et al. (2012) compared performance on tasks measuring executive functioning and central

coherence in a sample of women recovered from AN ($M_{\text{age}} = 24.3$ years) to a sample of women currently ill with AN ($M_{\text{age}} = 25.6$ years) and healthy control women ($M_{\text{age}} = 25.8$ years), and found that the recovered group made significantly more perseverative errors on the Boston Card Sorting Task than the control group, exhibiting set-shifting problems similar to those of the ill AN group. The recovered AN women in their sample also made more disadvantageous decisions than those in the control group on the IGT, suggesting relative deficits in executive functioning that persist after recovery. Danner et al. also noted that the recovered group scored higher than control group, but lower than the currently ill group, on measures of harm avoidance and punishment sensitivity, which are components of decision-making. Their findings suggest that high harm avoidance and punishment sensitivity are characteristics that may be heightened during illness but also may be trait-related. The recovered group also scored similarly to the ill group on measures of OCD symptoms and anxiety, suggesting that these characteristics are also trait-related and may play a predispositional role in AN, in addition to neuropsychological characteristics. Lopez, Tchanturia, Stahl, and Treasure (2009) assessed central coherence in a group of women recovered from AN for one year ($M_{\text{age}} = 25$ years) and healthy control women ($M_{\text{age}} = 26$ years) and found that recovered group performed more poorly than healthy controls on both visuospatial and verbal tasks requiring global processing, but exhibited superior performance on the EFT, which requires local processing, in comparison to controls. These findings, according to Lopez et al. (2009), are suggestive of weak central coherence, which was also seen in women

currently ill with AN (Lopez et al., 2008). Weak central coherence, therefore, appears to persist after recovery, and may, therefore, be an endophenotype for AN.

Tchanturia et al. (2004) examined verbal and perceptual (i.e., visuospatial) set-shifting abilities in a group of female inpatients with AN ($M_{\text{age}} = 27.2$ years), women who had been recovered from AN for at least one year ($M_{\text{age}} = 28.4$ years), and healthy control women ($M_{\text{age}} = 25.9$ years), and found that both ill and recovered AN women showed significant impairment, compared to the control group, on perceptual set-shifting tasks, with the inpatient group exhibiting the poorest performance and the recovered group performing better, but similarly, to the ill AN group. Tenconi et al. (2010) assessed both set-shifting and central coherence in currently ill, weight-restored, and long-term recovered AN women (i.e., weight-recovered for at least three years with regular menses and absence of disordered eating), as well as healthy control women, and found that all three AN groups performed poorly in comparison to controls on set-shifting tasks (i.e., the WCST and the TMT) and central coherence tasks (i.e., the RCFT). The finding of impaired set-shifting and weak central coherence in long-term recovered AN women compared to healthy women with no history of an eating disorder provides compelling evidence of a neuropsychological endophenotype for AN.

Overall, it appears, based on the research previously discussed, that weight-restored and recovered AN women present with a similar neuropsychological profile to that of women acutely ill with AN. The persistence of neuropsychological dysfunction following recovery from AN, relative to normally functioning women, in visuospatial

functioning, executive functioning, and central coherence, is suggestive of a preexisting pattern of cognitive functioning rather than illness-induced cognitive deficits. Studies using longitudinal designs, such as that of Gillberg and colleagues (2010), are particularly insightful, as they have shown that relative cognitive deficits in AN persist in the long-term. The insight offered by Gillberg et al., however, is limited by methodological problems; the study's participants are not separately analyzed by their state of illness and the sample included several male participants. In spite of the helpful and interesting findings that such studies have yielded, they also suffer from major shortcomings in that they are not consistent in their definitions of recovery from AN. Jarman and Walsh (1999) assert that outcome studies on AN are limited not only by the lack of consensus among researchers on how recovery should be defined, but also by the variation in measurement tools used to evaluate recovery. In a majority of the studies previously discussed, recovery is considered to be synonymous with weight restoration, along with the return of regular menses – an indicator of sufficient body fat. Some also operationalized recovery as an absence of behavioral symptoms of AN (i.e., no restricting, bingeing or purging) in addition to normal weight status. However, recovery is considered by many practitioners, as well as patients themselves, to have a psychological or emotional component in addition to a physical one. Jarman and Walsh point out that AN patients' subjective views of their recovery are rarely considered in outcome studies, and that measurement tools assessing recovery tend to emphasize the absence of eating disorder symptomatology as indices of recovery, ignoring “qualitative

changes in the person's psychological functioning which go beyond reduced concerns about body weight and shape" (p. 778). Furthermore, weight restoration can be stressful and anxiety provoking for patients, who are, by nature of their illness, highly fearful of and resistant to weight gain; thus, the neuropsychological functioning of AN patients assessed immediately following weight restoration could be affected by their heightened state of anxiety related to recent weight gain. Although a couple of the aforementioned studies evaluated both physical and psychological aspects of recovery (Danner et al., 2012; Tenconi et al., 2010), the research literature on recovered AN as a whole lacks consistency and fails to address the emotional components of recovery. The current study seeks to address this gap in the research by using recovery criteria that encompass physical, behavioral and psychological/emotional aspects of recovery to assess neuropsychological functioning in a group of women recovered from AN.

Overview of the Current Study

The pattern of neuropsychological functioning consistently observed in women with AN can be explained through several theoretical models. According to these models, the brain functions as a modulator of activity in various regions in order to maintain homeostatic balance. Denny-Brown (1956) proposed that the brain seeks to maintain a balance of activity between the frontal and parietal regions, such that a reduction in activation of one region will yield an increased activation, or transcortical release of activity, in the other, and vice versa. Tucker (1981) proposed a model of hemispheric balance in which increased activation in one hemisphere yields a decreased

activation in the other, and vice versa. These two models can be integrated to form a single model in which the brain is divided into four quadrants: left frontal, right frontal, left parietal, and right parietal. According to this integrated “quadrant model,” increased activation in one quadrant will yield decreased activation in the two adjacent quadrants (i.e., the adjacent quadrant in the same hemisphere and the adjacent quadrant in the opposite hemisphere) and increased activation in the diagonally located quadrant. This integrated model of brain activity and functioning is described in detail by Foster, Drago, Webster, Harrison, Crucian, and Heilman (2013).

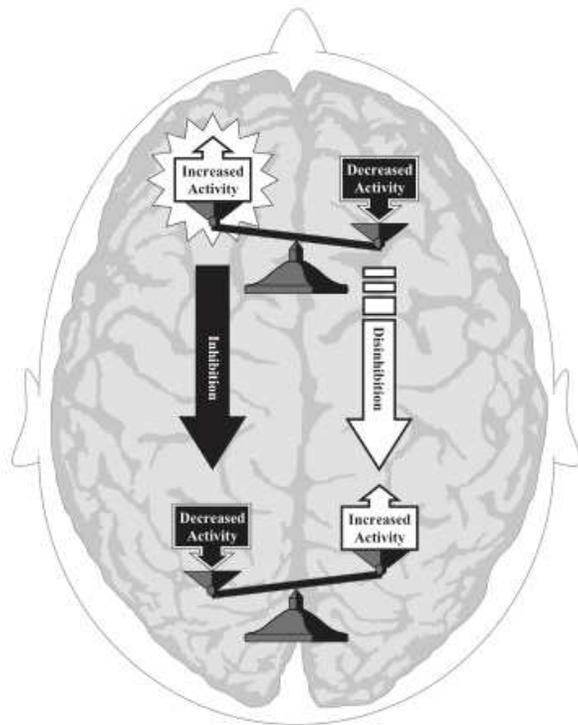


Figure 1. The effects of right parietal activation on cerebral activity according to the interactive quadrant model (Foster et al., 2013).

In the current study, neuropsychological functioning in women with AN is conceptualized using this integrated model of brain functioning. As body image disturbance is one of the most prominent features of AN and typically precedes onset of the disorder (Uher et al., 2005), it is suspected that abnormalities in body image processing - an ability governed by the right parietal region - set off the chain reaction of activation and deactivation that gives rise to the distinct pattern of neuropsychological functioning observed in women with AN. Increased activation in the right parietal lobe, which has been shown by both MRI and EEG studies on women with AN (e.g., Hatch et al., 2011; Suda et al., 2013; Wagner et al., 2003), would trigger a decrease in activation in the right frontal region, which would in turn yield increased activation in the left frontal region and decreased activation in the left parietal region. This model can explain the enhanced verbal fluency in women with AN, as verbal fluency (i.e., phonemic fluency) is associated with left frontal function, as well as impaired perceptual executive skills, as these are most associated with right frontal functioning. However, the quadrant model cannot adequately explain visuospatial deficits in women with AN, as increased right parietal activation should logically translate to enhanced visuospatial processing. Another model, proposed by Kinsbourne and Hicks (1978), can provide an explanation for this inconsistency. Kinsbourne and Hicks proposed a model of functional cerebral space, postulating that a particular cognitive task requires a certain amount of functional space in the area of the brain responsible for the processing involved in that task. The brain's functional cerebral space is limited, however, such that when a person

simultaneously performs two or more tasks that involve processing within the same brain area, performance in the more cognitively demanding task will suffer. In the case of women with AN, it is speculated that constant concern over and evaluation of their bodies results in an increase in right parietal activation. Therefore, visuospatial tasks, which are more cognitively demanding than body evaluation, compete for functional cerebral space and overtax the resources of the right parietal area, resulting in an impaired performance on visuospatial tasks.

To date, no study has assessed neuropsychological functioning in AN using this type of theoretical model. The current study is unique in that it seeks to explain the distinct pattern of neuropsychological functioning in AN by evaluating performance of a recovered population and a typically functioning population on neuropsychological tasks that are associated with the functioning of particular brain regions, rather than various domains of cognitive functioning. Specifically, it was predicted that women recovered from AN would exhibit significantly poorer performance on measures of right parietal, right frontal, and left parietal functioning, and superior performance on a measure of left frontal functioning, than healthy control participants. It was also predicted that the pattern of neuropsychological functioning exhibited by women recovered from AN would follow in accordance with the interactive quadrant model previously discussed. This model postulates that heightened right parietal activity in women with AN while at rest sets off a chain reaction of increased and decreased activation in other areas of the brain – specifically, heightened right parietal activity results in decreased in right frontal

activity, increased left frontal activity, and decreased left parietal activity. Such patterns of activity would be suggestive of relative impairment on tasks of right frontal and left parietal functioning, and enhanced performance on tasks of left frontal functioning. Heightened right parietal activity is suggestive of strong performance on visuospatial tasks; however, in the case of women with AN, it appears that right parietal resources may be overtaxed during visuospatial tasks, resulting in relative impairment compared to healthy women.

CHAPTER II

Method

Participants

Participants consisted of 30 women between the ages of 22 and 47 years. Fifteen women who had recovered from AN and 15 healthy women (i.e., college women with no history of an eating disorder) participated. Recovery from AN was defined as having maintained a healthy weight status (i.e., a BMI of at least 18) and regular menses for the past year, an absence of restricting and/or bingeing-purging behaviors for the past year, and scores on the EDI-3 Eating Disorder Risk index that fall below the clinical range. Participants for the recovered AN group were recruited from the Psychology Research Pool at Middle Tennessee State University and from the Eating Disorders Coalition of Tennessee, an organization located in Nashville, TN.

Fifteen healthy female college students served as control participants. Data for these control participants were from an existing data set from Ujcich Ward, Peterson, Lyles and Foster (2013). These data were collected through the Psychology Research Pool and included all college women.

Participants were excluded from the current study if they had ever received a diagnosis of BN, reported any brain trauma or neurological condition, or were taking any antipsychotic medication at the time of the study. Table 1 summarizes the demographic variables and eating disorders risk factor scores by group.

Table 1

Descriptive statistics for demographic and clinical variables per group (recovered AN women and healthy control women) as well as group differences

| | AN Recovered (n = 15) | | | Control (n = 15) | | | <i>t</i> | <i>p</i> |
|------------------|--------------------------|----------|-----|---------------------|----------|-----|----------|----------|
| | <i>M (SD)</i> | Min | Max | <i>M (SD)</i> | Min | Max | | |
| Age | 31.93 (7.63) | [22, 47] | | 22.40 (4.76) | [19, 37] | | 4.10 | 0.000** |
| Years Education | 17.20 (1.57) | [14, 20] | | 14.40 (1.35) | [13, 16] | | 5.24 | 0.000** |
| EDI-3 Risk Index | 40.27 (8.92) | [29, 53] | | 40.50 (10.80) | [28, 57] | | -0.32 | 0.749 |
| EDI-3 DT T-score | 40.33 (8.72) | [29, 58] | | 41.53 (11.41) | [29, 58] | | -0.64 | 0.95 |
| EDI-3 B T-score | 46.07 (4.72) | [39, 55] | | 46.27 (7.83) | [39, 61] | | -0.09 | 0.93 |
| EDI-3 BD T-score | 42.20 (10.77) | [28, 60] | | 39.50 (9.83) | [27, 55] | | 0.70 | 0.49 |
| BDI-II Total | 7.67 (5.97) | [0, 20] | | 13.93 (10.86) | [2, 37] | | -1.96 | 0.06 |

* $p < .05$. ** $p < .01$.

Measures

Demographics

Demographic information, including age, ethnicity, education level, and a history of psychological or neurological problems were obtained from all participants prior to neuropsychological assessment (see Appendix A).

Eating Disorder Recovery Questionnaire (EDRQ)

The EDRQ is a 17-item self-report questionnaire developed by Pettersen, Thune-Larsen, and Rosenvinge (2012) will be used to evaluate recovery from AN. These 17 items encompass physical, behavioral, cognitive/emotional, psychosocial, and sociocultural dimensions of recovery. This questionnaire demonstrated adequate internal consistency, with an alpha coefficient of .69, when administered to a large sample of women with EDs who were undergoing treatment, as well as a sample of female clinicians and healthy women without a history of an ED. A factor analysis of the items

yielded two primary factors: psychosocial factors and specific symptom factors, both of which were shown to have high internal consistency, with alpha coefficients of .82 and .71, respectively. The items also demonstrated face validity as a measure of recovery, as clinicians, patients, and healthy women in the general population were strongly in agreement that the 17 items represented characteristics of recovery from eating disorders. In the current study, the EDRQ will be used as a brief assessment of recovery for participants recruited to participate in the recovered AN group (see Appendix B). Specifically, four critical items will be used in assessing recovery from AN: item 1 (normal weight), item 2 (absence of restricting or binge-purge behaviors), item 3 (regular menstruation), and item 4 (improved attitude to body and appearance). Each of the 17 items will be ranked on 7-point Likert scale, with a score of 7 representing the highest degree of improvement in a particular area of functioning or greatest decrease in eating disorder symptomatology. To be considered recovered from AN, participants must score a 5 or higher on each of these critical items. Participants whose self-reported ratings of recovery on any of these items were below 5 were excluded from participation in the current study.

Judgment of Line Orientation (JLO; Benton, Varney, & Hamsher, 1978)

The JLO is a measure of visuospatial functioning that has been shown to assess right parietal functioning. The JLO consists of 30 items, each of which shows two stimulus lines that are oriented in different directions, originating from a central point. On a page below the two lines is a key showing 11 numbered lines that originate from a

central point. The participant's task is to choose which of the numbered lines correspond to the two stimulus lines. A score is derived by adding up the number of items in which both stimulus lines were correctly identified, with the maximum possible score of 30. The JLO has been shown to have high reliability for adults, with internal consistency coefficients ranging from .84 to .91 (Strauss, Sherman & Spreen, 2006) and a test-retest reliability coefficient of .90 (Benton, Sivan, Hamsher, Varney, & Spreen, 1994). It also has been shown to have strong validity as a measure of visuospatial skills, as JLO scores were highly correlated with subtests on the Wechsler Adult Intelligence Scale-IV (WAIS-IV) requiring visuospatial processing (Trahan, 1998), and patients with right parietal damage were shown to perform worse on the JLO than patients with left parietal damage (Benton et al., 1994). Participants' corrected scores on the JLO were used in the current study to assess right parietal functioning.

Ruff Figural Fluency Test (RFFT; Ruff, 1996)

The RFFT is a measure of perceptual fluency consisting of five parts/pages, each of which contains 35 five-dot matrices. The matrices are configured differently on each part – the first page contains a simple five-dot pattern, the second and third parts include distracting elements, and the fourth and fifth parts contain different patterns of dots. The participant's task is to generate as many unique designs as possible by connecting the dots in various patterns, with a one-minute time interval for each part. Each unique design generated is scored one point, and repeat designs within the same part are scored as perseverative errors. An error ratio can be calculated by dividing the total number of

unique designs generated by the total number of perseverative errors, which provides a measure of planning efficiency (Ruff, 1996). The RFFT has been shown to have acceptable to high test-retest reliability for total scores, with alpha coefficients ranging from .71 to .88 in various studies, and high interrater reliability for total scores and perseverative error scores (Strauss et al., 2006). In validity studies, the RFFT has been modestly correlated with other figural fluency tests, and RFFT scores have been shown to be affected by frontal lobe damage or dysfunction; specifically, two studies linked performance on the RFFT with right frontal activity (Bartolic, Basso, Schefft, Glauser, & Titanic-Schefft, 1999; Foster, Williamson, & Harrison, 2005). In the current study, the RFFT was used to assess right frontal lobe functioning.

Controlled Oral Word Association Test (COWAT; Strauss et al., 2006)

The COWAT is a well-established measure of verbal fluency (specifically, phonemic fluency). The participant's task is to generate as many words that begin with a particular letter of the alphabet as possible in a 1-minute time interval – the letters given typically are F, A, and S. A score is derived by summing the total number of words generated for the three letters given, and any proper names or repeat words with different endings (e.g., “sit” and “sitting”) are not given credit and do not count towards the participant's total score. The COWAT has been shown to have high internal consistency, with an alpha coefficient of .83 for the FAS task (Tombaugh, Kozak & Rees, 1999), as well as high test-retest reliability, with alpha coefficients exceeding .70 in a number of studies reported on by Strauss et al. (2006). In terms of validity, scores on the COWAT

are positively correlated with Verbal IQ scores, ranging from .44 to .87 (Henry & Crawford, 2004). The COWAT also has been validated as a measure of left frontal functioning, as a number of studies cited by Strauss et al. (2006) have found that patients with left frontal lesions show impairment on the FAS task. In the current study, the COWAT was used to evaluate left frontal functioning in women recovered from AN and healthy control women.

Animal Naming (AN; Strauss et al., 2006)

Animal Naming is a measure of category fluency, or semantic fluency, which is often administered in conjunction with the COWAT to assess verbal fluency. The participant is asked to generate as many names of animals as possible within a 1-minute interval, and a score is derived by summing the number of names generated, not counting any repeated names. Test-retest reliability coefficients for AN were acceptable, although considerable practice effects were noted by Bird, Papadopoulou, Ricciardelli, Rossor, and Cipolotti (2004) in a sample of healthy adults who were retested after a 1-month interval. Scores on AN have been moderately correlated with scores on the Boston Naming Test (BNT), with correlations ranging from .57 to .68. Additionally, two studies have linked performance on semantic fluency tasks with left temporal functioning, finding that such tasks activated left temporal structures more so than left frontal structures and that nonfrontal left hemisphere lesions were associated with impaired performance on semantic fluency tasks (Gourovitch, Krikby, Goldberg, & Weinberger, 2000; Henry & Crawford, 2004). In the current study, total raw scores on AN, as well as the number of

perseverative errors committed, will be used to assess left parietal functioning in women recovered from AN and healthy controls.

Line Bisection Task

Line bisection tasks are used frequently in neuropsychological assessment as detectors of hemispatial neglect, a condition typically associated with right parietal damage or dysfunction (Fox, McCourt, & Javitt, 2003). In a horizontal line bisection task, the participant is given a horizontally oriented sheet of paper containing a central horizontal line and asked to draw a mark on its central point. Once the participant has completed the task, the researcher finds the actual central point of the line and measures the distance, in millimeters (*mm*) between the actual central point and the participant's mark. Neurologically healthy participants tend to exhibit a slight leftward bias in bisecting horizontal lines, particularly in the case of right-handed individuals. Horizontal line bisection tasks have been shown to have moderate test-retest reliability, with a correlation of .64 between test and retest (Kinsella et al., 1995, as cited by Plummer, Morris, and Dunai (2003), as well as convergent validity with the star cancellation task ($r = -.40$), another test used to detect hemispatial neglect (Marsh & Kersel, 1993, as cited by Plummer et al., 2003).

Radial line bisection tasks are used to evaluate anterior-posterior dominance and are also used in assessing right parietal dysfunction. In a radial line bisection task, the participant is given a vertically oriented sheet of paper, which is laid flat on a table or other surface, containing a central vertical line and asked to draw a mark in what he or

she perceives to be the center. As with the horizontal line bisection task, the radial line bisection task is scored by measuring the distance in *mm* between the actual center and the participant's perceived center of the line. Neurologically healthy individuals tend to exhibit a distal bias in radial line bisection tasks, bisecting the line slightly farther away from themselves than its actual midpoint. In the current study, a horizontal line bisection task was used to evaluate lateral dominance and a radial line bisection task was used to evaluate anterior-posterior dominance. Each task consisted of five trials, and the deviations for the five trials were summed and averaged for each task, yielding a mean deviation from the center of the line horizontally and radially.

Eating Disorder Inventory-3 (EDI-3; Garner, 2004)

The EDI-3 is a self-report instrument used to assess eating disorder symptomatology in women from 13 to 53 years of age. It consists of 91 items that comprise 12 subscales: Drive for Thinness, Body Dissatisfaction, Bulimia, Low Self-Esteem, Personal Alienation, Interpersonal Insecurity, Interpersonal Alienation, Interoceptive Deficits, Emotional Dysregulation, Perfectionism, Asceticism, and Maturity Fears. Each of these subscales is given a score from 0 to 4. From these subscales, six composite scales are derived: Eating Disorder Risk, Ineffectiveness, Interpersonal Problems, Affective Problems, Overcontrol, and General Psychological Maladjustment. The first three subscales comprise the Eating Disorder Risk composite, which is often used to assess an individual's risk of eating disorder symptomatology and identify individuals whose symptoms fall within a clinical range. In studies on patients with

eating disorders, the Eating Disorder Risk (EDR) composite has been shown to have excellent internal consistency, with alpha coefficients ranging from .90 to .97, as well as test-retest reliability, with an alpha coefficient of .98 (Clausen, Rosenvinge, Friborg, & Rokkedal, 2011). Clausen et al. (2011) performed a factor analysis on the individual subscales of the EDI-3 and found that they possessed high reliability for both eating disorder patients ($\alpha = .75 - .92$) and healthy control women ($\alpha = .59 - .91$) in a large Danish sample. The EDI-3 also has been shown to have acceptable validity (Cumella, 2006). In the current study, the Eating Disorder Risk composite scale of the EDI-3 was used to evaluate eating disorder symptomatology.

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

The BDI-II is a 21-item self-report instrument used to assess depressive symptoms. For each item, the respondent is instructed to select one of four choices, which are scored from 0 to 3, which most closely describes his or her emotional and physical functioning during the past two weeks. Scores are derived by summing the scores for all 21 items, and are then classified as representing minimal, mild, moderate, or severe levels of depressive symptomatology. Strauss et al. (2006) reported that, among psychometric studies of the BDI-II, internal consistency coefficients are high (.84 to .93), and test-retest reliability coefficients over short time intervals range from adequate to high (.74 to .96). Validity studies have demonstrated that the BDI-II can be used as a diagnostic tool for major depression and is particularly useful as a screening tool, as BDI-II scores correlated highly with those of other instruments used to measure depression

(Strauss et al., 2006). BDI-II scores were used in the current study as a covariate in analyses, as depressive symptoms have been shown to affect cognitive functioning.

Procedure

Approval was obtained from the Institutional Review Board at Middle Tennessee State University prior to recruiting participants. Consent was obtained from each participant prior to testing (see Appendix C), and then each participant was individually assessed for approximately 1.5 hours. Participants completed the self-report paper-pencil measures, which included a demographic survey, the BDI-II, the EDRQ and the EDI-3. Then, the neuropsychological assessment tools were administered in random order to control for order effects.

CHAPTER III

Results

Group differences on demographic variables were assessed using independent samples *t*-tests. The recovered AN group and the control group differed significantly in both age, $t(28) = 4.12, p < .001$ and years of education, $t(28) = 5.24, p < .001$. Therefore, age and years of education were included as covariates in the analyses. The two groups did not differ significantly on any of the eating disorders risk variables, scoring similarly on subscales of the EDI-3 and the EDI-3 Risk Index, $t(27) = -0.06, p = 0.95$. Recovered AN women and healthy controls differed in their scores on the BDI-II, with control participants reporting higher levels of depressive symptoms than recovered AN participants, $t(28) = -1.96, p = 0.06$; however, the difference in BDI-II scores between the two groups did not reach statistical significance. Nevertheless, BDI-II scores also were included as a covariate in ANCOVA analyses due to the previous correlation between BDI-II scores and neuropsychological assessments.

Group Comparisons

One-way ANCOVAs were used to assess differences between the two groups on neuropsychological measures of right parietal (JLO), right frontal (RFFT), left frontal (COWAT), and left parietal (Animal Naming) functioning. A familywise alpha of .05 was used for all analyses, yielding an alpha level of .0125 for each *F* test.

The recovered AN group scored significantly higher than the control group on the JLO, $F(1, 25) = 19.13, MSE = 16.57, p < .001, \eta_p^2 = 0.43$. They also outperformed the

control group on the RFFT, $F(1, 24) = 14.93$, $MSE = 541.82$, $p = .001$, $\eta_p^2 = 0.38$; however, the two groups did not differ on RFFT perseverative errors, $F(1, 24) = 1.94$, $MSE = 0.075$, $p = 0.176$, $\eta_p^2 = 0.08$. The recovered AN group performed significantly higher than the control group on the COWAT, $F(1, 25) = 7.26$, $MSE = 129.56$, $p = .012$, $\eta_p^2 = .23$, but the two groups did not differ on COWAT perseverative errors, $F(1, 25) = 2.88$, $MSE = 3.16$, $p = 0.10$, $\eta_p^2 = 0.10$. The two groups performed similarly on Animal Naming, $F(1, 25) = 2.75$, $MSE = 19.40$, $p = 0.11$, $\eta_p^2 = 0.10$. ANCOVA results are shown in Table 2.

A one-way ANCOVA was used to evaluate differences between the recovered AN group and the control group on their performance on the horizontal and radial line bisection tasks. The two groups performed similarly on the horizontal line bisection task, $F(1, 25) = 0.57$, $MSE = 8.042$, $p = 0.457$, $\eta_p^2 = 0.022$. Performance on the radial line bisection task also was assessed; however, the results cannot be interpreted, as only 8 of the 15 participants in the recovered AN group completed the task. ANCOVA results for the horizontal and radial line bisection tasks are shown in Table 2.

Recovered AN Group Correlations

Pearson correlations were used to assess relationships between scores on the neuropsychological measures within the recovered AN group. Scores on the RFFT and Animal Naming were found to be positively related, $r = 0.61$, $p = 0.017$. Additionally, scores on the COWAT and RFFT were positively related, $r = 0.72$, $p = 0.003$, and scores on the COWAT and Animal Naming were positively related, $r = 0.68$, $p = 0.006$. No

relationships were found between any of the other neuropsychological measures within the recovered AN group. Pearson correlations for neuropsychological variables for the recovered AN group are displayed in Table 3.

Table 2
Descriptive statistics and group differences for neuropsychological variables

| | AN Recovered (n = 15) | Control (n = 15) | <i>p</i> |
|----------------------------|--------------------------|---------------------|----------|
| | <i>Mean (SD)</i> | <i>Mean (SD)</i> | |
| JLO | 29.13 (2.83) | 20.60 (4.78) | 0.000** |
| RFFT | 106.00 (24.97) | 63.79 (21.71) | 0.001** |
| RFFT Perseverative Errors | 0.60 (0.06) | 0.21 (0.38) | 0.075 |
| COWAT | 44.67 (12.62) | 29.00 (10.18) | 0.012* |
| COWAT Perseverative Errors | 0.47 (1.06) | 2.00 (2.20) | 0.103 |
| Animal Naming | 22.27 (5.44) | 18.47 (3.20) | 0.110 |
| Horizontal Line Bisection | -1.48 (3.03) | -2.75 (2.45) | 0.457 |
| Radial Line Bisection | 4.60 (4.43) | 3.32 (5.64) | 0.954 |

* $p < .05$. ** $p < .01$.

Table 3
Pearson correlations (two-tailed) between neuropsychological performance scores for recovered AN group

| | JLO | RFFT | COWAT | Animal Naming |
|---------------|-----|------|--------|---------------|
| JLO | | .224 | .190 | .053 |
| RFFT | | | .717** | .605* |
| COWAT | | | | .674** |
| Animal Naming | | | | |

* $p < .05$. ** $p < .01$.

CHAPTER IV

Discussion

In the current study, several hypotheses were evaluated. It was predicted that women recovered from AN would perform more poorly than healthy college women on measures of right parietal (JLO), right frontal (RFFT), and left parietal (Animal Naming) functioning, and similarly or better on a measure of left frontal functioning (COWAT) when controlling for depression, age, and years of education. The findings obtained through the ANCOVA analyses did not support this hypothesis, with the exception of the two groups' scores on the COWAT. Women recovered from AN significantly outperformed healthy control women on the JLO, which suggests that women recovered from AN may experience superior right parietal functioning in comparison to healthy control women. The recovered AN group also significantly outperformed the control group on the RFFT, which is suggestive of superior right frontal functioning relative to controls. The recovered AN group also made fewer perseverative errors on the RFFT than controls; however, the difference in the two groups' average error ratio scores was nonsignificant. The two groups performed similarly on Animal Naming, which was not concordant with the prediction of poorer performance on the task by the recovered AN group. This finding suggests that women recovered from AN may not experience relative deficits in left parietal functioning, as previous studies have suggested.

It was also predicted that, among participants in the recovered AN group, scores on neuropsychological measures would be correlated with one another in accordance

with the quadrant model postulated previously. Thus, it was predicted that scores on the JLO would be negatively related to scores on the COWAT, that scores on the RFFT would be negatively related to scores on the COWAT and positively related to scores on Animal Naming, and that scores on the COWAT and Animal Naming would be negatively related. Contrary to these predictions, scores on the JLO were not related to scores on the COWAT. Scores on the RFFT were related to scores on the COWAT; however, contrary to predictions, this relationship was positive. Scores on the RFFT were positively correlated with scores on Animal Naming, in accordance with the hypotheses. Scores on the COWAT and Animal Naming were positively correlated as well, contrary to predictions. These findings do not support the interactive quadrant theory as a model through which patterns of neuropsychological functioning can be accurately predicted in women recovered from AN. Rather, the findings of these correlational analyses suggest that some other mechanism may underlie patterns of neuropsychological functioning in women who have achieved a significant degree of recovery from AN.

Finally, it was predicted that recovered AN women would perform significantly more poorly on horizontal and radial line bisection tasks than healthy controls, exhibiting a rightward bias on the horizontal bisection task and a proximal bias on the radial bisection task. The results of this task were not in accordance with this prediction, as the two groups scored similarly on both tasks. The results of the radial bisection task cannot be interpreted, as only half of the recovered group completed the task, yielding too small

of a sample for interpretation. The results of the horizontal bisection task, however, suggest that women recovered from AN do not experience deficits in right parietal functioning relative to healthy women, in that both groups' average scores on the horizontal bisection task fell slightly to the left of the true center of the line. This performance is not suggestive of cognitive dysfunction, but rather of a phenomenon called pseudoneglect, which is often observed in neurologically healthy individuals, particularly right-handed individuals.

Overall, the results of the neuropsychological tasks suggest that women recovered from AN perform comparably or superior to healthy women without a history of an eating disorder. Previous neuropsychological studies on women recovered from AN have suggested that this population experiences relative deficits in various domains of cognitive functioning, including visuospatial and executive functioning, and central coherence. The results of the current study, however, contradict previous findings in that, on tasks assessing visuospatial and executive functioning, recovered AN women actually outperformed their healthy counterparts. They also outperformed healthy control women on tasks assessing verbal fluency, both phonemic and semantic. Previous studies have shown that both ill and recovered AN women tend to exhibit comparable or superior performance to that of healthy women on verbal fluency tasks; the findings of the current study on verbal fluency tasks are therefore consistent with those of previous studies.

A number of factors could account for the inconsistency in these findings. One possibility is that the women in the recovered group have experienced improvement in

their cognitive functioning over the course of their recovery. A majority of previous studies conducted with recovered AN women equated recovery with weight restoration and did not take into account emotional and psychological factors that play a crucial role in recovery from AN. In the current study, psychological and emotional factors of recovery from AN were measured in the EDRQ, and the recovered AN group participants' responses to these questions indicated that their physical and emotional well-being, attitudes towards their body and appearance, and social and occupational functioning had improved since their state of illness. Improvement in psychological and emotional functioning is associated with enhanced cognitive functioning (Crocker et al., 2013); thus, the performance of the recovered AN group on the neuropsychological tasks could be the result of actual improvement in their cognitive functioning. However, it is unknown whether or not the performance of the recovered AN group represents improvement, as there are no baseline data with which compare these results.

The findings of the neuropsychological tasks in the current study are not suggestive of a neurobiological endophenotype for AN. Several studies comparing women with AN to their healthy biological sisters and healthy, unrelated female controls found that neuropsychological performance did not differ between women with AN and their unaffected sisters (e.g., Galimberti et al., 2013; Rozenstein et al., 2011; Tenconi et al., 2010), but was significantly poorer than that of healthy controls. These studies suggested that AN may have neurobiological underpinnings that make certain individuals more susceptible to developing AN, in the presence of certain personality traits (e.g.,

perfectionism and obsessionality) and environmental triggers. If, in fact, there is a neurobiological endophenotype for AN, then the relative neuropsychological deficits observed in women with AN would be expected to persist after recovery, as they presumably were present before the onset of AN symptoms. The performance of recovered AN women on neuropsychological tasks in the current study, however, suggest otherwise. A possible explanation for the discrepancy in the current study's findings and those of previous studies is that effortful cognitive restructuring over the course of treatment and recovery from AN produces cognitive resilience in the long-term and ameliorates the relative cognitive deficits that have characterized the performance of AN women on neuropsychological tasks in the research literature. Another possibility is that the obscurity of these findings stems largely from limitations of the current study, which will be discussed.

Additionally, the pattern of neuropsychological functioning observed in recovered AN women in the current study did not follow the pattern of cognitive functioning predicted by the interactive quadrant model. This model employed the brain activity balance models of Donald Tucker and Derek Denny-Brown, and Kinsbourne's theory of functional cerebral space. Although this integrated model was supported by findings from previous neuropsychological and neuroimaging studies on women with AN, it was not supported by the findings of the current study. Whether the model's failure to support the current findings is the result of inaccuracy of the model itself or of actual

neurocognitive differences between the recovered AN group in the current study and women with AN assessed in previous studies remains unclear.

Strengths and Limitations of the Current Study

A major strength of the current study is the inclusion of emotional and psychological components of recovery from AN as indices of recovery. A majority of previous studies seeking to assess recovered populations have conceptualized recovery from AN in terms of physical (i.e., weight restoration, return of menses) and behavioral (i.e., absence of food restriction or binge-purge episodes) components of recovery. The consideration and evaluation of psychological, emotional, and social aspects of recovery from AN are an important step in the progression of neuropsychological research on AN, as these components typically occupy a substantially greater period of the recovery process than physical or behavioral components.

The current study is also unique in that neuropsychological functioning was examined according to the area of the brain that a particular neuropsychological task was associated with, placing greater emphasis on the interaction of different brain areas. Observing interactions of various areas or structures within the brain allows the observation of neurocircuits and could yield insight into how neurocircuits are formed and how they are related to behavioral patterns observed in individuals with AN. A greater understanding of the neurocircuitry underlying pathological behavioral patterns in AN could have important implications for treatment approaches such as cognitive

remediation therapy, which has demonstrated possible efficacy in a number of studies (e.g., Tchanturia, Lloyd, & Lang, 2013; Dahlgreen & Rø, 2014).

Several major limitations also exist in the current study. The greatest of these limitations is its small sample size. Although adequate for statistical purposes, the sample is small nonetheless, and a larger sample could provide greater insight into the questions investigated in the current study. Also, it is unclear whether the performance of the recovered AN group represents an improvement from their neuropsychological functioning during their state of illness or following weight restoration, as there are no baseline data available for comparison.

Another major limitation is differences in characteristics between the recovered AN group and the control group. The two groups differ from each other demographically in that nearly half of the participants in the control group (i.e., 7 of the 15 participants) were African American and one participant reported her ethnicity as Other, whereas all of the recovered AN participants reported their ethnicity as Caucasian. Although other demographic variables, such as age and years of education, were controlled for in analyses, differences in ethnicity between the two groups could have had an effect on the outcome of the neuropsychological measures. Significant differences have been observed previously between Caucasians and African Americans on measures of IQ, a factor that was not measured or controlled for in the current study. Although overall IQ scores are not highly predictive of performance on neuropsychological measures such as the JLO and RFFT, Verbal IQ scores on the WAIS-IV tend to be positively correlated

with scores on the COWAT and Animal Naming (Henry & Crawford, 2004). Potential limitations of the current study, therefore, include the fact that IQ was not measured or controlled in statistical analyses and that the groups varied by ethnicity.

Another major issue that may have impacted the results of the current study is the performance of some of the participants in the control group. A close examination of participants' raw scores and z-scores on the neuropsychological tasks indicated that several of the participants in the control group scored within the Borderline or Impaired range on one or more neuropsychological measures, and a few scored in the clinical risk range on the EDI-3 (indicating the occurrence of risk factors for eating disorder, though not diagnostic), suggesting that this group does not represent a neurologically healthy female college population and therefore may not be an adequate comparison group for the current study. Whether the poor performance by some of the participants in the control group on neuropsychological tasks stems from actual cognitive dysfunction or from some other cause is unclear. It also is possible that differences in motivation could have played a role in the differences in neuropsychological performance observed between the two groups. The participants in the control group were all college students who received extra credit in an introductory psychology course as a reward for their participation, whereas the participants in the recovered AN group were recruited from the community and did not receive any compensation for their participation. The fact that the control group was a college-based sample and the recovered AN group was a

community-based sample leads to concern with regard to differences in motivation for participating in the current study.

Another concern with regard to characteristics of the sample in the current study is that 2 participants in the control group and 1 participant in the recovered AN group reported a history of a concussion, a neurological condition that can significantly affect cognitive functioning. Three participants in the recovered AN group were left-handed, which is also associated with differences in brain functioning. Future studies seeking to assess neuropsychological functioning in women recovered from AN would benefit from matching participants according to multiple variables, including age, education level, ethnicity, IQ, and handedness.

Another methodological issue in the current study is that, within the recovered AN group, nearly half of the recovered AN participants (i.e., 7 of the 15 participants) had also received a diagnosis of BN. Each participant who endorsed the BN item on the demographic questionnaire was subsequently questioned about her BN diagnosis, and all seven of the participants who had been diagnosed with BN stated that they developed symptoms of BN after having achieved weight restoration from AN. It appears, then, that these women may have developed symptoms of BN in response to weight gain during treatment for AN, perhaps as a way to cope with anxiety or distress over weight gain when restriction was (presumably) no longer a viable option. In fact, Eddy, Dorer, Franko, Tahlilani, Thompson-Brenner, and Herzog (2008) found that roughly one third of women with AN evaluated over a 7-year period experienced what they referred to as a

“diagnostic crossover” to BN. Neuropsychological studies on BN have suggested that women with BN exhibit a distinct neuropsychological profile from women with AN; thus, the recovered AN group in the current study may not accurately represent the typical population of women recovered from AN-R. A majority of neuropsychological studies on AN have focused on AN-R, as this population has been shown to exhibit the highest degree of impairment on neuropsychological tasks, relative to healthy women. Participants in the current study were not asked to specify which subtype of AN they had been diagnosed with; it is possible, therefore, that some of the participants in the recovered AN group were diagnosed with AN-BP, which has been associated in previous research with less pronounced relative neuropsychological impairment than AN-R. Perhaps future studies should investigate neuropsychological functioning in women who develop BN symptoms in the aftermath of their weight recovery from AN to elucidate whether their neuropsychological performance is more similar to that associated with AN-R, BN, or falls somewhere in between (i.e., AN-BP). The findings of the current study also suggest that perhaps the neuropsychological profile that has been suggested by previous studies (e.g., Rose et al., 2011; Stedal et al., 2012) is only valid for women with AN-R who do not experience any sort of diagnostic crossover.

It should be noted that a history of concussion and a diagnosis of BN were previously mentioned as exclusionary criteria from the current study. However, due to difficulties with the recruitment of participants recovered from AN, some of the women who served as participants in the recovered AN group were included in the current study

in spite of having characteristics that would have barred them from participating in the current study had more ideal candidates been available.

Also, some of the participants in the recovered AN group did not meet the established cutoff score of 5 out of 7 on the Likert scale for some of the items on the EDRQ. All participants in the recovered AN group met the cutoff score for item 1 (maintaining a healthy weight), but for each of the other 3 critical items (regular menses, cessation of restriction/binge-purge behavior, and improved attitude towards body and appearance), several participants endorsed 4 or lower on the Likert scale. The 3 participants who reported on the EDRQ that they did not have regular menses were subsequently questioned - 2 of these 3 participants reported that their menses had been irregular due to pregnancy, and 1 participant reported that her lack of regular menses was an effect of an oral contraceptive. Six participants failed to meet the cutoff score for item 2 (no dieting, binge-purge behavior, or over-exercising to lose or maintain weight), and 3 failed to meet the cutoff score for item 4 (improved attitude towards body and physical appearance). Although the EDRQ adequately captures the multidimensionality of recovery by including items pertaining to cognitive, emotional and social functioning, it has not been empirically validated as an assessment tool for recovery from eating disorders. Further research is necessary to establish the validity of these items in evaluating recovery.

Finally, various factors regarding the recovery process of the participants in the recovered AN group were not measured or taken into account. These factors include age

of onset of AN symptoms, length of time spent in recovery, the occurrence of relapse or number of relapses experienced, type of treatment administered (e.g., cognitive, behavioral, inpatient, etc.), length of time spent actively in treatment, and length of time passed without the presence of eating disorder symptoms. Such information could provide insight into the performance of the recovered AN group on the neuropsychological tasks administered in the current study. For example, could the superior performance of the recovered AN group compared to the control group on the JLO and RFFT be attributable to improvements in cognitive functioning achieved through cognitive remediation? Future studies on recovered AN women should attempt to gather more thorough, detailed information about recovery so as to more fully understand which variables, if any, are associated with cognitive improvement and through what mechanism such improvement is achieved.

Implications and Future Directions

The results of the current study suggest that women recovered from AN do not exhibit impairment on measures of neuropsychological functioning relative to healthy women without a reported history of an eating disorder. They also suggest that the pattern of cognitive functioning observed in women recovered from AN may not be consistent with the neuropsychological profile that has emerged from previous studies assessing ill and weight-restored women with AN. Due to the limitations previously discussed, however, the results of the current study are somewhat unclear, and further investigation is therefore warranted. Future studies should seek to address the issue of

recovery from AN, expanding upon the efforts of the current study to encapsulate psychological, emotional and social components of recovery in their measures and evaluations of overall recovery from AN, along with physical and behavioral components. Future researchers also should strive to gather a more thorough and complete picture of recovery from AN by incorporating and analyzing variables such as length of time spent in recovery, length of time spent in treatment, type of treatment received, number of relapses, comorbid diagnoses, and other related variables, using a larger sample and comparing it with a sample of control women matched according to age, education level, ethnicity and IQ. Ideally, a longitudinal study could assess women with AN during a state of acute illness, following weight restoration, and at various points in recovery, so as to track and quantify their improvement during the course of treatment and recovery.

In conclusion, the current study is a step in broadening and deepening our understanding of neuropsychological functioning in women recovered from AN; however, it leaves a wide margin for advancement in the neuropsychological research literature on AN. Inconsistencies in researchers' and clinicians' definitions of recovery, the overlap of symptom presentation and diagnoses, and the paucity of long-term longitudinal studies assessing neuropsychological functioning in women with AN have left holes in our understanding of the neurobiology of AN and how neurocognitive functioning translates into behavioral manifestations of AN. Further investigation of cognitive functioning in women who have recovered from AN is necessary in order to

develop a clearer picture of how brain functioning changes during the course of recovery from AN, which factors play a role in these changes, and whether or not there is compelling evidence of a neurobiological endophenotype that may predispose certain individuals to developing AN. Gaining deeper insight into these questions could ultimately lead to the development of screening tools and preventative measures that could be used to identify women who are highly susceptible to developing AN and halt the onset or progression of the disorder.

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APPENDICES

APPENDIX A

Informed Consent

Principal Investigators: Kelsey Horick, B.A., Kim Ujcich Ward, Ph.D., BCBA-D

Study Title: Neuropsychological functioning following recovery from Anorexia Nervosa

Institution: MTSU

Name of participant: _____ Age: _____

The following information is provided to inform you about the research project and your participation in it. Please read this form carefully and feel free to ask any questions you may have about this study and the information given below. You will be given an opportunity to ask questions, and your questions will be answered. Also, you will be given a copy of this consent form.

Your participation in this research study is voluntary. You are also free to withdraw from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research study or your willingness to participate in it, you will be notified so that you can make an informed decision whether or not to continue your participation in this study.

For additional information about giving consent or your rights as a participant in this study, please feel free to contact the MTSU Office of Compliance at (615) 494-8918.

1. Purpose of the study:

You are being asked to participate in a research study because we are interested in how your body image may be related to how you work on different kinds of tasks, such as visual, verbal, and tactile kinds of activities.

2. Description of procedures to be followed and approximate duration of the study:

Participation in this study will take about 1.5 hours. During this time you will be asked to complete several questionnaires about your thoughts, feelings, and behaviors that are related to body image and body management. You also will participate in some neurological tasks that involve looking at objects and answering various types of questions verbally.

3. Expected costs:

There are no known costs to your participation in this study.

4. Description of the discomforts, inconveniences, and/or risks that can be reasonably expected as a result of participation in this study:

There are no known risks to participating in this study.

5. Compensation in case of study-related injury:

No injuries are expected in the course of participation in this study. MTSU will not provide compensation in the case of study related injury.

6. Anticipated benefits from this study:

a) The potential benefits to science and humankind that may result from this study are that we may develop a better understanding of how the brain works and how its functioning may be related to the way we perceive our bodies. Further, we may learn something about how body image distortions and body dissatisfaction are influenced by brain function and how eating/body image disorders may develop.

b) The potential benefits to you from this study are that you may receive research credit or extra credit in your psychology class. You are also contributing to our scientific understanding of body image and brain functioning.

7. Alternative treatments available:

No treatments are involved in this study.

8. Compensation for participation:

Your participation will be compensated by your receiving research credits for your psychology class.

9. Circumstances under which the Principal Investigator may withdraw you from study participation:

If it appears as though you are not being honest or putting forth effort during the study, your data may be withdrawn from the sample. If at any point during the study you become disruptive, you may be asked to leave and your data will be withdrawn from the sample.

10. What happens if you choose to withdraw from study participation:

You can choose to withdraw from the study at any time without any negative consequences. You also can choose not to complete any tasks or not to answer any questions with which you are uncomfortable.

11. Contact Information. If you should have any questions about this research study or possible injury, please feel free to contact Dr. Ujcich Ward, 615-898-2188 or Kimberly.ward@mtsu.edu, or Kelsey Horick, keh5d@mtmail.mtsu.edu.

12. Confidentiality. All efforts, within reason, will be made to keep the personal information in your research record private but total privacy cannot be promised. Your information may be shared with MTSU or the government, such as the Middle Tennessee State University Institutional Review Board, Federal Government Office for Human Research Protections, if you or someone else is in danger or if we are required to do so by law.

13. STATEMENT BY PERSON AGREEING TO PARTICIPATE IN THIS STUDY

I have read this informed consent document and the material contained in it has been explained to me verbally. I understand each part of the document, all my questions have been answered, and I freely and voluntarily choose to participate in this study.

Date

Signature of patient/volunteer

Consent obtained by:

Date

Signature

Printed Name and Title

APPENDIX B

Demographic Information

Please answer each of the following questions.

1. My current age is: _____ yrs
2. I am: _____ Male _____ Female
3. My ethnicity can best be described as (circle one):
 - a. African American
 - b. Caucasian
 - b. Hispanic
 - c. Other: _____
4. Currently I am a _____ at MTSU (circle one):
 - a. Freshman
 - b. Sophomore
 - c. Junior
 - d. Senior
 - e. Not Applicable
5. I have _____ years of education.
6. I am _____ handed. (circle one):
 - a. Right
 - b. Left
 - c. Both
7. Are you currently taking any antipsychotic medication?
 - a. Yes
 - b. No

8. During the past year, have you maintained a healthy weight (i.e., a BMI of ≥ 18)?
- a. Yes
 - b. No
9. During the past year, have you had regular menstrual periods?
- a. Yes
 - b. No
10. During the past year, have you restricted food intake in order to maintain or lose weight?
- a. Yes
 - b. No
11. During the past year, have you binged, purged (i.e., vomited or used laxatives) or over-exercised in order to maintain or lose weight?
- a. Yes
 - b. No

For each of the following conditions, please put a mark beside any that you have personally experienced or have been diagnosed with at any time in your life (check all that apply):

- _____ Concussion
- _____ Diabetes
- _____ Epilepsy/Seizure Disorder
- _____ Anorexia Nervosa
- _____ Bulimia Nervosa
- _____ Head Injury with a loss of consciousness
- _____ Stroke

Other neurological condition: _____

APPENDIX C

Eating Disorder Recovery Questionnaire

The following items describe various aspects of recovery from eating disorders. For each item, rate the degree to which you feel the statement describes your current level of functioning. Please choose and circle a response option for each item.

1. I have achieved a healthy weight.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

2. I do not diet (i.e., restrict food intake), binge, purge (e.g., vomiting, using laxatives), or over-exercise to maintain or lose weight.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

3. I currently have regular menstrual periods.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

4. My attitude towards my body and physical appearance has improved.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

5. My quality of life has improved.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

6. I understand why I got an eating disorder.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

7. I am able to recognize thoughts and feelings that lead to symptoms of an eating disorder.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

8. I am confident about my feelings.

| | | | | | | |
|--------------------------------|---|---|--------------------------|---|---|------------------------------|
| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
| Does not describe me at all | | | Somewhat describes me | | | Very closely describes me |

APPENDIX D

IRB Approval Letter

11/13/2014

Investigator(s): Kelsey Horick, Kimberly Ujcich Ward, Ph.D.

Department: Psychology

Investigator(s) Email: keh5d@mtmail.mtsu.edu; kimberly.ward@mtsu.edu

Protocol Title: "Neuropsychological Functioning in Women Recovered From Anorexia Nervosa "

Protocol Number: 15-069

Dear Investigator(s),

The MTSU Institutional Review Board, or a representative of the IRB, has reviewed the research proposal identified above. The MTSU IRB or its representative has determined that the study poses minimal risk to participants and qualifies for an expedited review under 45 CFR 46.110 and 21 CFR 56.110, and you have satisfactorily addressed all of the points brought up during the review.

Approval is granted for one (1) year from the date of this letter for 50 participants.

Please note that any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615) 494-8918. Any change to the protocol must be submitted to the IRB before implementing this change.

You will need to submit an end-of-project form to the Office of Compliance upon completion of your research located on the IRB website. Complete research means that you have finished collecting and analyzing data. Should you not finish your research within the one (1) year period, you must submit a Progress Report and request a continuation prior to the expiration date. Please allow time for review and requested revisions. Failure to submit a Progress Report and request for continuation will automatically result in cancellation of your research study. Therefore, you will not be able to use any data and/or collect any data. Your study expires 11/13/2015.

According to MTSU Policy, a researcher is defined as anyone who works with data or has contact with participants. Anyone meeting this definition needs to be listed on the protocol and needs to complete the required training. If you add researchers to an approved project, please forward an updated list of researchers to the Office of Compliance before they begin to work on the project.

All research materials must be retained by the PI or faculty advisor (if the PI is a student) for at least three (3) years after study completion and then destroyed in a manner that maintains confidentiality and anonymity.

Sincerely,
Kellie Hilker
Institutional Review Board
Middle Tennessee State University