THE NEURAL CORRELATES OF BODY DISSATISFACTION IN PATIENTS WITH ANOREXIA NERVOSA

Examining the similarities in brain regions between diagnosis of anorexia nervosa and body dissatisfaction

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Abstract

Body dissatisfaction (BD) is a condition derived from negative thoughts and feelings about one's body and is a core symptom of the eating disorder anorexia nervosa (AN). Being dissatisfied with one’s body is highly present in women and to some extent men. This might be a result of a skewed ideal in combination with social influences. In recent year, research on neurobiological risk factors as well as neuroscientific and cognitive mappings of AN and BD have gained traction, particularly when it comes to studies using neuroimaging-techniques and cognitive tests. Studies have identified brain regions (insular cortex, anterior cingulate cortex, parietal cortex, amygdala, dorsolateral and orbitofrontal areas of the prefrontal cortex) associated with the processing of body shape as well as dysfunctional processing of self-image and body satisfaction. Structural imaging studies of AN patients using CT and MRI have, in many cases, found reduced cerebral volume, increased spinal fluid (CSF) and enlarged ventricles. Usually, food and water restriction has been seen as the cause, and structural deficits in AN patients have shown to improve with weight gain after long-term recovery.

Keywords: anorexia nervosa, body dissatisfaction, neurobiology, neuroimaging, mental health
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1. Introduction

Cultural and social pressure has long promoted an ideal of thinness in women in the Western world. In females, positive traits are often connected to a thin body whereas negative traits often are connected to an overweight body. The thin beauty expectation in women can lead to such consequences as the development of a negative body image. This is often expressed in terms of exaggerated self-evaluation of body weight and body shape and is considered to be a core symptom in anorexia nervosa (AN) (Stice, Maxfield, & Wells, 2003; Uher et al., 2005). Individuals suffering from AN are suggested to have higher levels of body dissatisfaction (BD) due to their over-valuation of their bodies (Friederich et al., 2010).

Among many symptoms, individuals diagnosed with AN are characterized by a fear of gaining weight, refusal to maintain normal body weight, and disturbance in their perception of body weight and size (Sachdev, Mondraty, Wen, & Gulliford, 2008). The prevalence of AN in the general female population is suggested to be 0.3-0.7% (Kaye, 2008). Due to disturbed body satisfaction, this patient group has been a substantial basis for studies of body-image and BD.

BD has been defined as “a person’s negative thoughts and feelings about his or her body” and as “the devaluation of physical appearance relative to an ideal” (Grogan, 2008, p. 2; Rosen, 2013, p. 161). It is suggested to be a cognitive-affective component of a broader multimodal construct of body-image (Yamamotova, Bulant, Bocek, & Papezova, 2017). The idealized body appearance is according to Grogan (2008) for women to look slim and shapely and for men to look slender and muscular. The perfect female body is suggested to have flawless skin, a thin waist, long legs, and well-developed breasts. This is often reflected as a lifelong project for women where the body is seen as the most important attribute, whereas for men the focus concerns the face or the whole clothed body (Groesz, Levine, & Murnen, 2002).

From a neuroscientific perspective, researchers have been interested in what functions and structures in the brain that are involved in the presence of a negative body image. Many studies have identified brain regions associated with the processing of body shape, although it is suggested that emotions and cognition also play a critical role in the presence of BD (Groesz et al., 2002; Friederich et al., 2007; Friederich et al., 2010).

In the current neuropsychological hypothesis of AN, cognitive dysfunction is suggested to mediate the disease. Specific personality traits have been linked to the onset, symptomatic expression, and maintenance of AN and are seen as neurobiological risk factors. This eating disorder is complex and in addition to avoidance of food, it also includes (1)
extremes of behavioral inhibition and disinhibition (2) psychological dysfunctions such as anxiety, depression and obsessive behaviors and (3) a negative body image and perfectionism. Since the existing research findings have not been able to provide a clear and coherent pathophysiology of AN, there is no highly effective treatment for adult women with the AN diagnosis. It has been suggested that there should be more focus on the identification of neural circuits, their function and relationship to behaviors in AN patients to develop more specific and effective treatments (Kaye, 2008; Kaye, Wierenga, Bailer, Simmons, & Bischoff-Grethe, 2013; Kaye, Wagner, Fudge, & Paulus, 2010; Kidd, & Steinglass, 2012; Zipfel, Giel, Bulik, Hay, & Schmidt, 2015).

Since both BD and AN are thought to be mediated by cognitive components and dissatisfaction with one's body appearance is considered a core symptom of AN, neurobiological investigations might lead to further insights in the relationship between the above-mentioned concepts. How does the neural basis of BD relate to the neural correlates in individuals with a diagnosis of AN? Further, I expect to find similarities in brain structures and functions of both conditions.

1.1 Aim

The aim of this literature review is to illuminate the neural correlates of body dissatisfaction (BD) in individuals with a diagnosis of anorexia nervosa (AN). The thesis will focus on each concept on its own, especially in examining neuroanatomy. Structural and functional similarities in the brain will be compared between BD and AN to investigate the neural correlates.

2. Methods

To answer and discuss the question above, I will first provide with relevant background information of AN, including diagnostic criteria, risk factors, prevalence, and treatments. This will be followed by a section providing background information of BD, including different definitions and views of the phenomena. Both concepts will then be described in relation to each other. Neuroscientific research of structural and functional neuroanatomy of AN and BD will be presented in separate sections. The thesis will conclude with a result section, discussion, a section of methodological problems and limitations followed by further directions.
To accomplish the aim, relevant literature of neuroscientific and psychological aspects of AN and BD will be used. Particularly, the chosen approach for the thesis is a literature review. Therefore, it will be limited to only include existing studies within the field and no data will be collected.

The scope of the subject will be restricted to adult women over eighteen years. Neither research of males nor children with BD and AN will be included in this thesis. The major reasons for this are the lack of research in men suffering from BD and AN, because the expression of BD and AN can differ between men and women (Grogan, 2008), while children's brains are not fully developed and might result in misleading findings.

Other research areas in AN that will be excluded from the content of the thesis are worth mentioning. A rare type of AN in children has been found that is suggested to be triggered by infection. This is the pediatric auto-immune neuropsychiatric disorders associated with streptococcus (PANDAS). The onset usually occurs rapidly before children reach puberty; in which streptococcal infection occurs at the same time as the eating disorder symptoms. Usually, this disease is treated with long-term antibiotics to remove the streptococcal infection (Johnson, 2014; Sokol, 2001).

There is also research investigating in microbiomes in AN. It is suggested that microorganisms may have an impact on the development and course of AN; in particular, microbiomes in the gut may have an effect on the central nervous system and immune system. Researchers called this the “gut-brain axis.” It is thought that one’s lifestyle and what one eats affects this microbiological system. In turn, the gut microbes promote anxiety, psychopathology and weight gain (Herpertz-Dahlmann, Seitz, & Baines, 2017).

These two perspectives on AN might contribute with intriguing insights. However, they are not clearly defined and might be too broad to fit into this literature review.

3. Anorexia nervosa

Anorexia nervosa (AN) is a serious mental disorder. It can affect individuals of all ages, sexes, sexual orientations, etc, but is to a higher degree diagnosed in adolescent girls and young women. AN is an eating disorder (ED) characterized by an unusual and salient nature: namely, refusal to maintain body weight, intense fear of gaining weight despite being underweight, and disturbance of how the shape or weight of the body is experienced. As a consequence, restricted eating behaviors and other weight-loss behaviors (such as using laxatives, forced vomiting, and excessive exercise) are motivated. The disorder is extremely dangerous and has mortality rates exceeding all other psychiatric disorders (Gaudio &
To give a definite diagnosis of AN, certain diagnostic criteria should be displayed. According to Zipfel et al. (2015), the classification of AN is (1) restriction of energy intake relative to requirements, which can lead to low body weight. The weight has to be significantly lower than minimally normal (less than 85% of expected body weight). (2) Intense fear of weight gain or becoming fat. (3) Disturbance in experience of body weight or shape, or lack of recognition of the seriousness of low body weight. Many females suffering from AN stop menstruating, even though it is not a criterion for being anorectic (Morrison, 2017.) The severity of the disease is based on the body mass index (BMI; kg/meter²). For adults, the severity is mild if the BMI is 17 or more, moderate if the BMI is 16-17, severe if the BMI is 15-16 and extreme if the BMI is under 15.

AN can be divided into two sub-groups: restricting type (ANR) and binge eating/purging type (ANB). The former has not recently engaged in purging or binging while the latter has (Cassin & von Ranson, 2005; Morrison, 2017).

Polivy and Herman (2002) state that identifying risk factors in eating disorders is a complex task. Only a few longitudinal studies exist to enable exact identification of risk factors in AN, and it has been difficult to differentiate between early symptoms of eating disorders and risk factors (i.e. food reduction or excessive exercise) (Bulik, Reba, Siega-Riz, & Reichborn-Kjennerud, 2005). In the following section, I will go through several suggestions of factors making individuals more vulnerable to developing AN.

Specific personality traits have been linked to the onset, symptomatic expression, and maintenance of AN. It is, however, difficult to draw etiological conclusions on personality in AN (Cassin, & von Ranson, 2005). Common personality characteristics and possible neurobiological risk factors seen in anorectic patients are perfectionism, obsession-compulsiveness, neuroticism, harm avoidance, anxiety, low cooperativeness, negative affect, self-directedness, low novelty seeking, high persistence and low self-esteem (Bulik et al., 2005; Cassin, & von Ranson, 2005). Negative affect is also considered to be a result of food restriction due to an imbalance between the serotonergic and dopaminergic system (Zipfel et al., 2015). Kaye (2008) highlights that premorbid traits such as obsessive-compulsiveness and social phobia exaggerates by malnutrition. Perfectionism has been shown to mediate the relationship between perceived criticism and restrictive dieting and might be a factor for individuals to regulate their appetite. Personality traits, as previously presented, have often been seen persisting long after recovery. Research has shown that the majority of AN patients...
have been perfectionistic and had a presence of anxiety symptoms since early childhood, before development of the disorder (Kaye, 2008; Kaye et al., 2013).

Looking at sociocultural factors, AN is more likely to occur in high-income countries where an abundance of food exists and idealization of low body weight is the norm (Polivy & Herman, 2002). Grabe, Ward, and Hyde (2008) have summarized findings from several studies showing that media exposure is linked to an increased endorsement of distorted eating behaviors, investment in appearance, and dissatisfaction with body appearance.

Genetic factors have been identified by looking at several twin studies using strategies to improve statistical power. The heritability for developing AN has been proposed to be approximately 50-80%. It is suggested that differentiating genetic from environmental effects could be done by comparing accordance for behavioral traits or the disorder between identical and fraternal twins. The genetic vulnerability might be expressed as behavioral traits and contribute to insights into the neurological underpinnings of AN (Bulik et al., 2006; Guisinger, 2003; Kaye, 2008; Kaye, Fudge, & Paulus, 2009; Kaye et al., 2013).

From an evolutionary perspective, AN is, according to Gatward (2007), a disease including many features that are hard to explain. Why are patients with AN ambivalent about the opportunity to recover, despite facing serious risks with their low body weight? How do some individuals function quite well despite being underweight?

A contemporary evolutionary theory suggests that food restriction is a result of the threat of exclusion. Gatward contends that the need for belonging to a group and competing within that group is strong in humans, which can lead to behaviors such as dieting and losing weight. Not belonging to a group is associated with less chance of survival and is therefore one of the most prominent human needs. Competing is important to keep value within the group and includes comparison of physical appearance. In turns, mass media could lead to more distinct contrasts of ideals as comparison among a large range of individuals is available (Gatward, 2007).

The fear of weight gain and recovery for females is explained by a female intra-sexual model which is described as “a response to manipulation by, a more socially dominant woman or women” (Mealey, 2000, pp.106). Weight loss removes individuals from competition for status, while gaining weight is associated with reentering the competition, making people vulnerable to be attacked by others and excluded from the group (Mealey, 2000). Guisinger (2003) suggests that AN is likely to occur in reactivation of old adaptive responses from the prehistoric past when humans occasionally had to migrate from famine
conditions and needed to eat as little as possible to survive. This view explains AN as a biological response to low body weight.

According to Zipfel et al. (2015), the lifetime prevalence of individuals suffering from AN has been estimated to be approximately 1% in high-income countries. Looking at females in the general population, the rate is suggested to be 0.3-0.7%. The group at the highest risk developing AN are young females in the age range fifteen to nineteen years (Hoek, & Van Hoeken, 2003; Kaye, 2008).

Three important aspects to keep in consideration when examining prevalence is that (1) even if the prevalence of ED is rare in the general population, they are relatively common among adolescents and young women, (2) cross-cultural studies have shown that AN is more common in Western than non-Western countries (3) a minority of individuals meeting the criteria for ED rarely seek help in mental health care, and the incidence of these individuals is difficult to measure (Hoek, & Van Hoeken, 2003).

Among treatments, studies have shown that the most effective therapies in adolescents are family-based treatment (FBT) or Maudsley family therapy (MFT). The names refer to the same three-phase treatment. In the first phase, parents try to un-identify themselves as the cause of the disorder and receive help to encourage the positive aspects of their parenting and how they can help their child to recover. In the second phase, parents get help to create food and weight control for their child and in the last phase the family work on a healthy relationship. Including family members and partners in the recovery process is suggested to be an effective component of treatment (Zipfel et al., 2015).

In adults, there have been studies showing moderate effects for treatment, especially with cognitive behavioral therapy (enhanced, CBT-E), focal psychodynamic psychotherapy (FPT), and the Maudsley model of AN in adults (MANTRA). CBT-E is a personalized psychological treatment. In the therapy, the patient gets an understanding of the person’s disorder, receives help to stabilize his or her eating pattern and to identify which factors that can maintain an eating disorder. This is followed by a stage where the therapist works with the patient regarding how he or she can deal with setbacks in the future. FPT is a psychodynamic-oriented treatment for moderately ill anorectic patients. It is divided into three phases where patients work with; (1) attitudes, behaviors, and self-esteem; (2) association between intrapersonal relationships and eating behavior, and (3) transfer from treatment to everyday life. MANTRA is a cognitive-intrapersonal treatment focusing on underlying obsessional and anxious personality traits of AN. The treatment helps patients to deal with fear of making mistakes, difficulties in emotional regulation, delusional beliefs of
how AN is helpful for the person and unhelpful behaviors towards close ones. Although treatment for adults is advancing, there is no approach that has shown superior effects (Zipfel et al., 2015).

The use of neuromodulation treatments has increased (usually for individuals with severe AN) as the understanding of neurocircuitry has improved. These treatments include deep brain stimulation (DBS), repetitive transcranial current stimulation (rTMS) and transcranial direct current stimulation (tDCS) (McClelland, Bozhilova, Campbell, & Schmidt, 2013; Zipfel et al., 2015). It is common for individuals suffering from AN to be fearful of and ambivalent about treatment, for this reason it is important to build trust and rapport with the patient (Zipfel et al., 2015). Kaye et al. (2013) argue that there are no proven treatments for AN, and therefore the disease has high rates of chronicity, relapse, and death. The authors suggested that more understanding of the neurobiological components of AN is important for developing adequate treatments.

4. Body dissatisfaction

ED is a common body-image disorder. In cognitive terms, it is often a result of the emergence of body dissatisfaction (BD). Being dissatisfied with one’s body originates from an evaluation of one's body image, a multidimensional construct. Perceptions, attitudes, and feelings about body size and shape, and related behaviors are involved in this evaluative process. The perceptual process involves an individual’s subjective expectation of body image, whereas the attitudinal dimension reflects a person's feelings about body appearance. Whereas body satisfaction has been linked to well-being and long-term mental health, BD has been linked to disturbances that affect psychosocial functioning and overall quality of life. The emergence of BD is suggested to occur when individuals fail to meet the physical appearance standards in one or more social or personal situations (Cash, Morrow, Hrabosky, & Perry, 2004; Riva, 2014; Yamamotova et al., 2017).

Grogan (2008), describes body image as a person’s perceptions, thoughts, and feelings about his or her body, whereas BD is described as a person’s negative thoughts and feelings about his or her body.

Rosen (2013) propose that BD is the devaluation of physical appearance relative to an ideal. This can result in evaluative thoughts about the whole body being too big, too wide or too heavy. Being dissatisfied with body parts is common as well and can lead to such negative thoughts as having too wide hips, too much flesh on the back of the legs, etc. The most notable finding in research on BD is that most women and girls today suffer from being
dissatisfied with their appearance. A common belief is that they weigh too much and need to lose weight.

According to Brooks, Mond, Stevenson, and Stephen (2016), body-size misconception is common among individuals as well and is a core symptom in ED. Many individuals that suffer from body-size misconception thinks that they are much fatter than they are. In contrast, many overweight individuals think that they are much thinner than they are. However, Stice and Shaw (2002) emphasize the importance of distinguishing BD from body-image distortion, as the former concerns a negative subjective evaluation of one's body and the latter concerns misconception of one's body size and shape.

The thin body ideal is suggested to be derived from several factors: particularly social influences such as family, school, peer, and athletics. The most discussed factor for establishing the thin ideal of beauty is mass media: radio, magazines, television, posters, and billboards (Groesz et al., 2002). Stice et al. (2003) write that messages from mass media can take various forms: e.g., glorification of slim fashion models and direct commercial messages to lose weight. Women portrayed in the media today are thinner than in the past, thinner than the actual female population and often thinner than individuals with the criterion for AN, making the media's presentation of the female body skewed (Grabe et al., 2008).

Stice and Shaw (2002) have found that experience of the pressure to be thin, internalization of the thin ideal, and higher BMI numbers increase the risk for BD. The suggestion that BD increases the risk of establishing an eating pathology has got experimental support. These findings are consistent with the view that sociocultural pressures to look thin foster BD and increase the risk for ED. Karazsia, Murnen, and Tylka (2017) describe thin-oriented BD as the strongest predictor for development of an eating pathology, being associated with anxiety, depression, and sexual dysfunction. BD is usually associated with, and predictive for, low self-esteem (Mond et al., 2013).

A study was made to examine how physical attraction could give insight into how the thin ideal for women affects individuals. This was inspired by the evolutionary theory of physical attraction, which proposes that attraction is a mechanism to identify a healthy mate. Attractive individuals are hypothesized to reflect good physical health. However, studies have shown that the most attractive BMI for women today is significantly lower than healthy BMI for female health. Sociocultural standards are considered to be a possible influence determining the most attractive BMI for women and should be examined since it opposes the theory of physical attraction (Brierley, Brooks, Mond, Stevenson, & Stephen, 2016).
Frisén, Gattario, and Lunde (2014) describe how the appearance of one’s body can be taken to reflect happiness and success. Studies have shown that people attribute to individuals considered to be attractive positive traits such as healthy, intelligent, successful and socially competent. Both men and women have been reported to rank physical appearance as one of the most important traits when looking for a long-term mate, according to a study across 37 countries. These aspects illustrate how a person's physical attractiveness might have a significant impact on social experiences (Swami et al., 2010).

5. Anorexia nervosa and body dissatisfaction

Cultural and social pressure has long promoted an ideal of thinness in women in the Western world. As a consequence, a negative body image in terms of exaggerated self-evaluation of body weight and body shape can develop. This is considered to be a core symptom in AN - and a serious consequence of BD (Frisén et al., 2014; Stice et al., 2003; Uher et al., 2005). Being dissatisfied with one’s body image is more often seen as a correlate of eating disorders in females than males. Due to disturbed body image and body satisfaction for individuals suffering from AN, this patient group has been a substantial basis for study of these phenomena (Furnham, Badmim, & Sneade, 2002; Skrzypek, Wehmeier, & Remschmidt, 2001).

BD present in individuals with AN is associated with overestimation of body size. For females, exposure to media with thin idealized women, and comparison between self and other of body shape, is suggested to increase emotional distress and dissatisfaction with one's own body (Friederich et al., 2010).

A view that has been established for understanding the relationship between ED, body image and socio-cultural influences is provided by the objectification theory. This theory posits that the female body is socially constructed as an object, especially in Western countries - an object that should be evaluated based on body appearance. This perspective can lead to increased body monitoring for women and thereby increase shame, and anxiety, and diminish internal bodily awareness. The prevalence of sexual objectification can give rise to internalization for females of an observer's perspective on their own body. Although objectification does not affect all women equally, it is suggested that sexual objectification of the female body diminishes a woman’s well-being and can contribute to mental health issues such as ED. Although the theory was developed for explaining BD and body-image concerns in women, other researchers argue that it concern males’ BD and body image as well (Daniel, & Bridges, 2010; Fredrickson, & Roberts, 1997; Holland, & Tiggemann, 2016).
Another view, called the Allocentric Lock Hypothesis, includes both socio-cultural and cognitive-biological factors for understanding the relationship between BD and AN. The theory posits that individuals with AN are locked into an "objectified body" so that the egocentric sensory inputs are no longer able to update an allocentric representation of the body. “Egocentric” refers to the body as first-person experience, while “allocentric” refers to the body as an object in the physical world. In individuals suffering from AN, there exists a negative allocentric representation (negative memory) such that the individuals’ perception creating the egocentric parietal representation cannot be updated. However, there has been controversy whether this dysfunction is a result of disturbances in neural processes related to appetite and emotional regulation, or if it reflects a disturbance in the experience and memory processing of the body (Riva, 2012; Riva, & Gaudio, 2012).

In previous research, body-image disturbances in anorectic patients have been evaluated in two modalities. The first is concerns perceptual body size and shape distortion, the second concerns cognitive-evaluative dissatisfaction. In the perceptual dimension, anorectic patients tend to evaluate themselves as larger than they actually are; the cognitive-evaluative dimension reflects an anorectic patients’ feelings of being too fat or being misshapen (Groesz et al., 2002; Skrzypek et al., 2001).

6. The neural basis of anorexia nervosa

There is a large body of research in cognitive neuroscience regarding the subject of AN and associated cognitive abnormalities. Still, these findings have not been able to provide a clear and coherent pathophysiology for AN. According to current neuropsychological hypothesis, cognitive dysfunction mediates the disease. AN is a complex illness that, despite appetitive divergence, includes (1) extremes of behavioral inhibition and disinhibition; (2) psychological dysfunctions such as anxiety, depression and obsessive behaviors, and (3) a negative body image and perfectionism. More developed neurobiological investigations of AN might be crucial for understanding the complexity of symptoms and behaviors in AN (Kaye, 2008; Kaye et al., 2013; Kaye, Wagner, Fudge, & Paulus, 2010; Kidd, & Steinglass, 2012). In this section, I will provide descriptions of what brain structures have been associated with AN, then present an overview of cognitive dysfunctions that have been linked to AN, and end with monoamine associations with AN. The monoaminergic system includes dopaminergic, serotonergic and noradrenergic circuits, which interacts in several brain regions. They are suggested to have a substantial impact of mood, behavior and neuroendocrine functions (Carlsson, 2006; Kaye, Ebert, Raleigh, & Lake, 1984).
6.1 Neural structures associated with AN

It is important to acknowledge that brain structures are complex and do not act in isolation. Brain structures act through interconnectivity to produce different functional outputs and inhibit or facilitate other networks (Nunn, Frampton, Gordon, & Lask, 2008). To identify neural circuits and brain structures in AN patients, studies within cognitive neuroscience have primarily used computed tomography (CT) and magnetic resonance imaging (MRI) (Connan et al., 2006; Kidd, & Steinglass, 2012; Kornreich et al., 1991).

Structural imaging studies of AN patients using CT and MRI have, in many cases, found cortical atrophy in terms of reduced cerebral volume, increased spinal fluid (CSF) volume, and enlarged ventricles (Dolan, Mitchell, & Wakeling, 1988; Golden et al., 1996; Lambe, Katzman, Mikulis, Kennedy, & Zipursky, 1997). Usually, this has been identified as a consequence of food and water restriction (Gordon et al., 2001). However, structural deficits have been seen to repair along with weight gain after long-term recovery (Connan et al., 2006; Golden et al., 1996; Wagner et al., 2006).

In studying white, and grey-volume matter in AN patients, researchers have been able to investigate potential trait alterations. Friederich et al. (2012) studied morphometry of grey matter volume (GMV) in individuals with acute AN, long-term weight-restored anorexia nervosa (AN-WR) and healthy controls. To investigate GMV, they used structural MRI and analyzed the results through voxel-based morphometry (VBM) and brain-atlas based automatic volumetry competition (IBASPM). VBM is referred to as a method quantifying shape, mass, and volume of the brain. It involves comparison of voxels of GMV between subjects (Ashburner, & Friston, 2000). IBASPM is a method able to calculate volume of an identified structure of the brain with improved structural validity (Friederich et al., 2012).

They found that GMV was decreased in the whole brain in acute AN compared to healthy controls (p=.033), but not in AN-WR. Local GMV in the anterior cingulate cortex (ACC) (left: p=.013, right: p=.014), supplementary motor area (SMA) (p<.001), and subcortical regions such as amygdala and putamen was decreased in individuals with acute AN compared to controls. For AN-WR, the researchers found a decrease of GMV in the ACC (left: p=.034, right: p=.021) and SMA (p=.015), but not in the subcortical regions, compared to controls. The authors suggest that the decrease of GMV in the ACC and SMA serves as a trait in AN, as the results show that the decrease was independent of recovery for post-AN patients.
Regional decreases of GMV in the ACC were found in recovered AN patients in a study by Mühlau et al. (2007). The authors suggest that the region is directly linked to the severity of AN, although it is not clear whether the abnormality is a result of genetic or environmental factors.

Studies in cortical atrophy have been inconsistent. Brooks et al. (2011) contrasts many of the studies of grey- and white-matter volume in AN. In an MRI study, they found no significant decrease in total GMV, although increased GMV in the right dorsolateral prefrontal cortex (DLPFC) was found (p<.002). They suggest that the increase is related to cognitive strategies for food restriction. However, the study included only fourteen individuals with AN and 21 healthy controls, which is a small sample (Brooks et al., 2011).

A study performed by Fuglset et al. (2016) was unable to find a significant difference in GMV, subcortical GMV, white-matter volume or lateral-ventricle volume between young females with AN and healthy controls. The authors discuss the limitations of the study and suggest that the results could be affected by the young age of the participants (17-23 years), as they have not suffered from malnutrition as long as older individuals suffering from AN; while some of the AN patients were partially weight restored, with a BMI variation of 13.5 to 20.7.

Frank, Shott, Hagman, and Mittal (2013) studied brain structure in relation to taste pleasantness and reward. They found no significant effect for differences of whole-brain volume between ED patients and a control group. They used structural MRI to measure white- and grey-matter volume and compared women with restrictive AN, women recovered from restrictive AN, women with bulimia nervosa and healthy controls. The groups underwent behavioral measures such as the revised sensitivity to reward and punishment questionnaire and a taste perception test. However, the researchers found a significant increase of gyrus rectus GMV (p=.003) in all of the ED groups. The researchers suggest that this area can predict taste pleasantness ratings. Moreover, they found increased GMV in the left orbitofrontal cortex (OFC) (p<.001) in all of the ED groups and increased antero-ventral insula GMV on the right side in both AN groups compared to controls. In all groups except AN, they found decreased GMV in the dorsal caudate (p=.001) and putamen (p<.001). Right putamen grey matter was positively correlated with sensitivity to reward in all ED groups. The researchers found both increased and decreased GMV, which they could not explain. They conclude that further research is needed.

The inconsistency of results has been highlighted: in particular, reported differences of cortical volume in various anatomical locations has been highly variable. It is suggested
that the varying results might reflect inconsistency between methods (Frank et al., 2013; Fuglset et al., 2016). In addition, Boghi et al. (2011) explain that because of the varying findings of cortical structures in AN patients, the interests of studying cognitive performances has increased.

### 6.2 Cognitive dysfunctions associated with AN

According to Nunn et al. (2008), abnormalities of brain function in various cortical areas such as the orbitofrontal cortex (OFC), somatosensory cortex and parietal cortex are reported in connection with AN diagnosis. Impairments of neural circuits in subcortical regions such as the amygdala, thalamus, hypothalamus, hippocampus, and striatum have also been reported. The authors hypothesize that the insular cortex is the primary region damaged by AN; it serves as a connection between the cortical and subcortical areas mentioned above. The insular cortex has been associated with several functions, such as sensorimotor processing, somatic processing, somatic sensation of pain, auditory processing, chemosensory function (i.e., processing the intensity, quality and value of taste stimuli) and vestibular function (i.e., balance and orientation). The insular cortex is found to be involved in socio-emotional processing and cognitive function: emotional experiences, risky decision-making, empathy, and social cognition are involved in the former, speech, attention and salience processing in the latter (Uddin, Nomi, Hébert-Seropian, Ghaziri, & Boucher, 2017). This region is one of the least understood due to limited access because of its location within the Sylvian fissure, a deep fissure separating the frontal and parietal lobe (Chi, Dooling, & Gilles, 1977; Uddin et al., 2017).

The insular cortex has been associated with AN in various studies (Kaye et al., 2013; Nunn et al., 2008; Wagner et al., 2008). With AN, all systems and regulations associated with the insular cortex are deregulated or otherwise disturbed from their normal functioning. Kaye et al. (2009) describe the role of the anterior insula and suggest that altered insula activity could be related to harm avoidance (reduced exposure of food) and a fundamentally and physiologically altered sense of self, with altered sensitivity to or integration of bodily signals.

As AN is related to restrictive food intake and maintenance of low body weight, studies on brain structures involved in food regulation have been of interest. Appetite is suggested to be a complex motivational drive dependent on several factors. Rewarding properties from food intake, homeostatic needs, and cognitive abilities are all components involved. Functions of the neural system are suggested to be disturbed in AN. Anterior insula
and frontal operculum are suggested to comprise the activity in the neural circuits involved in appetite regulation. This system is composed of cranial nerves, nucleus tractus solitarii, the thalamic ventroposterior medial nucleus, and primary gustatory cortex. The primary gustatory cortex and anterior insula have been shown to respond to food’s physical appearance and taste properties. In addition, neural reward processes are suggested to be linked to these structures. The ACC, amygdala, and OFC are other structures suggested to be involved in appetite regulation and are interconnected with the insula. The ACC has a significant role in autonomic and visceral control and is linked to conflict monitoring. According to Carter et al. (1998), the ACC is important for executive control of cognition; impairment in this region is linked to cognitive dysfunction, schizophrenia, and depression.

The OFC responds to the negative or positive value of external stimuli and is associated with flexible responses to changing stimuli (Kaye et al., 2009). Broberger (2005) describes the OFC as a higher-order taste cortex that determines the pleasantness of food and receives direct input from the insular cortex. Neural activity in the OFC decreases as one becomes satiated. In determining homeostatic appetitive needs, regions such as the anterior insula, ACC and OFC are important as they connect to the rostral ventral striatum, sending its inputs to compute behavioral repertoires (Kaye et al., 2009).

Specific subnuclei (clusters of neurons) of the amygdala are thought to play an important role in food-related behavior. The basolateral nucleus, the largest cluster in the amygdala, might link the motivational value of a stimulus to a goal-directed behavior, whereas the central nucleus controls the autonomic, gustatory and motoric functions in feeding behavior (Will, Franzblau, & Kelley, 2004). Moreover, the basolateral nucleus is associated with the involvement in spatial and motor learning and positive and negative affect (Davis & Whalen, 2001). Inactivation in the central nucleus of the amygdala has been shown to block the consumption of all food (Broberger, 2005).

The avoidance of food in AN is suggested to be mediated by the involvement of the DLPFC, parietal cortex, and posterior insular region. These structures are critical in cognitive functions such as planning and sequencing. These regions send inputs to dorsolateral striatum and might also overlap or interfere with the ventral striatal areas, suggested to be associated with food avoidance behavior (Kaye et al., 2009).

Ellison et al. (1998) has studied fear of high caloric food in patients with AN. They used functional magnetic resonance imaging (fMRI) to investigate the functional anatomy of fear of calories in six females meeting the criteria for AN and compared them to six healthy controls. They measured blood-oxygen changes while participants were shown pictures of
high vs. low-calorie drinks. They used a visual analog scale to measure how anxious the participants would be by drinking the high- vs. low-calorie drink by letting them rate their anxiousness on a ten-point scale. The results showed that the AN participants were significantly more anxious in comparison to the control group when shown the high-calorie drink (p<.001). In addition, the AN group showed a more intense signal change in the left insula, anterior cingulate gyrus, and left amygdala-hippocampal region compared to healthy controls. The authors suggest that the amygdala-hippocampal region mediates fear of high-calorie food whereas the anterior cingulate gyrus and the left insula might reflect autonomic arousal and attentional processes.

Investigations in the cognitive domain of individuals with AN have been of interest for researchers exploring the neurobiology of AN. Among others, neuropsychological tests have been useful to measure cognitive flexibility, cognitive rigidity, problem-solving skills and decision-making (Buzzichelli, Marzola, Amianto, Fassino, & Abbate-Daga, 2018; Cavedini, et al., 2004; Tchanturia et al., 2012). Tchanturia et al. (2012) used the Wisconsin Card Sorting Task (WCST), one of the most widely used and reported neuropsychological tasks. It integrates multiple measurements of executive processes. In this study, the researchers wanted to explore WCST performance and cognitive flexibility. Individuals with AN often exhibit inflexible behaviors around eating, daily routines and often experience difficulties to cope with problems. It is hypothesized that they have difficulties with cognitive flexibility and might be a maintenance factor for the disease.

To study cognitive flexibility, set-shifting abilities were examined. Set-shifting is described as the ability to modify behavior in response to changing goals. The test comprises matching stimulus cards with one of four categories. Participants need to be aware of color, shape, and number when matching cards. After sorting, the participant receives feedback on a screen with the text “right” or “wrong”. The test includes five rule shifts, which participants are not informed of to see how they respond. The process continues until all 128 cards have been sorted. The study included 542 participants divided into four groups: individuals with AN, individuals with BN, healthy controls and recovered AN (recAN) patients. The researchers discuss two possible errors: perseverative errors (responding to the wrong sorting rule) and non-per perseverative errors (errors that occur from other factors than the use of wrong sorting rule). The results shown that the AN and BN groups performed significantly worse than the control group (p<.001) in almost all categories of WCST. The recovered AN group performed worse on perseverative errors compared to controls, but significantly better than the AN group (p<.001).
The researchers suggest that, based on their results, the AN group showed poor cognitive flexibility, while individuals recovered from AN still had problems in some cognitive domains such as conceptual strategy and perseveration. The researchers propose that individuals recovered from AN have difficulty differentiating positive from negative feedback. The result show that the individuals with ED had more difficulties learning from the feedback provided than the control group, suggesting that it is harder for individuals with ED to learn from previous experiences.

The authors highlight the importance of studies such as these to develop better psychological treatments as they are dependent on learning from feedback. Understanding the mechanism by which feedback is used by AN patients might help them to learn new strategies and unlearn maladaptive strategies.

Buzzichelli et al. (2018) investigated the interaction between set-shifting and perfectionism in AN patients. Participants were given two self-report measures - the Eating Disorder Inventory 2 and the Beck Depression Inventory - to evaluate eating psychopathology and depression. Participants were given three neuropsychological tests - the WCST, the Trail Making Task (TMT A-B) and Hayling Sentence Completion task (HSCT) - to evaluate cognitive flexibility.

They found that the individuals with AN showed less cognitive flexibility - especially those with high perfectionism - compared to healthy controls. Individuals with high perfectionism were more ineffective compared to individuals with low perfectionism and healthy controls. Only in individuals with AN, perfectionism was shown to be associated with a drive for thinness (DT) (p=.001). However, when the researchers tested perfectionism as a mediator between DT and set shifting, the results were only significant when testing for the whole group (p=.031), but non-significant for the AN group. The authors conclude that there exists a complex and nonexclusive association between set shifting, eating psychopathology and perfectionism.

6.3 Monoamine functions associated with AN

Many medications used to treat psychiatric disorders act on monoamine functions and so many techniques focus on identifying and characterizing these neural substances. Serotonin (HT-5) and dopamine (DA) are examples of complex monoamine systems with multiple receptors, associated enzymes, transporters, etc. To study monoamine function in AN, research has generally used cerebral spinal fluid obtained through a lumbar puncture, positron-emission tomography (PET) brain imaging, single photon emission computed
tomography (SPECT) and related technologies. Studies have shown that HT-5 and DA systems are disturbed in individuals with AN, persisting after recovery (Bailer & Kaye, 2010; Kaye, 2008; Kaye et al., 2013).

HT-5 acts as a hormone and neurotransmitter, with broad functions in the human brain. Such functions include modulation of mood state, hunger, sleep, sex, anxiety, and emotions. HT-5 dysfunction is known to have a substantial impact on behavior, producing depressive symptoms, anxiety, refusal to eat, excessive exercise and impaired impulse control. These behavioral changes are common in AN. It has been suggested that increased activity of 5-HT systems could contribute to this psychopathological condition. The 5-HT system interacts with molecules, and neurotransmitters and involves fourteen or more receptors. Due to the complexity of the system, imaging technologies can only measure a few of these components. Studies investigating the functional activity of 5-HT are useful to measure potential state and trait differences between AN and healthy controls. Thus, examining 5-HT activity in relation to behaviors might help develop more effective treatments (Haleem, 2012; Kaye et al., 2003; Kaye et al., 2009). Levels of 5-HT can be studied by measure concentrations of its end product of 5-HT metabolism, 5-Hydroxyindoleacetic acid (HIAA-5), in the cerebrospinal fluid (CSF). Studies have found a reduction of CSF HIAA-5 in AN patients. Increased levels of CSF HIAA-5 levels have been found in individuals who have recovered from AN (Cen, Walther, Finkel, & Amato, 2014; Kaye, 2008).

Kaye et al. (2003) studied dysregulation of 5-HT in AN and found that a diet-induced reduction of tryptophan (TRP), a precursor of 5-HT that must be obtained through food, is associated with decreased anxiety in individuals with AN. The authors suggest that restrictive dieting may represent a mechanism in AN individuals that modulates dysphoric mood. Brain imaging studies have shown that individuals with ED or who have recovered from ED compared to controls have an elevated binding potential for postsynaptic 5-HT (1a) receptors and diminished binding potential for 5-HT(2a). In comparison, individuals with depression, social anxiety disorders, and panic disorders have decreased 5-HT (1a) binding potential (Kaye et al., 2013; Lanzenberger et al., 2007). Several studies have identified similar findings of 5-HT levels in AN patients and recovered AN, which supports the hypothesis that there might be trait-related alterations of 5-HT function in AN that might contribute to the pathogenesis of the disorder (Bailer et al., 2005; Kaye et al., 2009).

As mentioned, the DA system seems to be disturbed in AN patients. The DA system is complex and acts differently between brain regions due to their various DA receptors and
neurophysiological mechanisms. The function of the DA system has been seen to contribute to weight and feeding behaviors, pleasure, motivation, addictive processing, modulation of motor activity and reinforcement. Moreover, release of DA in the ventral striatum has a fundamental role in the reward process. It is suggested that actions of DA in the prefrontal cortex are associated with regulation of novel circumstances, whereas the involvement of DA in the striatum might be linked to expression of learned behaviors (Bressan & Crippa, 2005; Frank et al., 2005).

According to Kaye et al. (2009), individuals suffering from AN often exercise compulsively, have difficulty experiencing pleasure, and find little reward aside from their own weight loss. It is suggested that DA dysfunction in AN patients is linked to altered reward, affect, decision-making, and executive control and decreased consumption of food. Kaye, Frank, and McConaha (1999) explored altered DA activity in individuals recovered from AN by using lumbar puncture (LP) to measure CSF homovanillic acid (HVA), which is the end product of DA metabolism. In LP procedure, a lumbar needle is used to insert between vertebral bones of the lower back to collect CSF from the spinal canal (Gorman, Krummel, Webster, Smith, & Hutchens, 2000). HVA is used to measure brain DA neural production, usually found in body fluids. It is thought that neurotransmitter release is reflected by metabolic production in neurons (Amin, Davidson, & Davis, 1992).

Participants were divided into four groups: six individuals recovered from restrictive-type AN (rAN-R), thirteen individuals recovered from bulimic type AN (rAN-B), nineteen individuals recovered from normal weight bulimia nervosa (rNWB) and eighteen healthy controls. They found that CSF HVA in rAN-R was significantly reduced (p.<.05) compared to rNWB. When comparing the recovered ED groups while excluding the control group, the CSF HVA in r-ANR was significantly lower (p.<0.2) compared to rAN-B and rNWB. The authors suggest that disturbed DA metabolism persists after recovery of restrictive AN and that it might be possible that an altered DA metabolism contributes to the development of restrictive AN (Kaye et al., 1999).

Frank et al. (2005) studied D2/D3 receptors in recovered AN patients by using a PET scan to measure the radioligand [11C] raclopride, which is used as a radiotracer. [11C] raclopride is a selective DA D2/D3 antagonist which has a sensitive binding potential to DA concentrations and is often used to measure basal receptor availability and changes of receptor availability due to variations of DA concentrations (Yoder, Kareken, & Morris, 2008). In this study, the researchers used MR imaging to scan ten recovered AN female patients and twelve controls before using a PET scan to combine data from both scanners.
They found that individuals recovered from AN had a significantly higher [11C] raclopride binding potential in the anterior ventral-striatum compared to the control group (p=.028). This area is associated with modulation of reward, reinforcement, and addiction. No significant difference of [11C] raclopride binding potential was found in the ventral and dorsal putamen, neither in the middle or dorsal caudate. The study could not determine whether the results are due to increased D2/D3 receptors in AN patients, or increased binding caused by decreased intrasynaptic DA. The authors conclude that either increased density of D2/D3 receptors or decreased intrasynaptic DA concentrations are associated with AN and could contribute to an altered reward system, which could explain the dysphoric mood, ability to lose weight, and resistance to eating (Frank et al., 2005).

7. The neural basis of body dissatisfaction

As a negative body image in terms of exaggerated self-evaluation of body weight and body shape is considered a core symptom in AN, researchers have been interested in what functions and structures in the brain that are implicated in the presence of pathological body image. Studies on BD have in many cases used patients suffering from AN or other EDs as subjects (Friederich et al., 2010; Mohr et al., 2010; Pollatos et al., 2016).

Negative body image in AN patients has been evaluated in two modalities. The first concerns perceptual body-size and shape distortion, the second cognitive-evaluative dissatisfaction (Groesz et al., 2002; Skrzypek et al., 2001). As mentioned earlier, behavioral research suggests that body image is a multidimensional construct (Banfield, & McCabe, 2002) and BD is suggested to be a cognitive-affective component of this (Karazsia et al., 2017). Although current research is insufficient, many studies have shown interesting results, contributing to deeper understanding. I will describe what neural structures have been associated with BD and continue with neural functions associated with BD.

7.1 Neural structures associated with BD

As described earlier, studies of cortical structures in patients with AN is often associated with cortical atrophy. However, only a few correlational analyses have been made for evaluating BD and brain structures in AN patients.

Kohmura et al. (2017) investigated GMV in AN patients and evaluated relationships between regional cortical volume changes in the brain and symptoms of BD and DT. The study included 52 females, seven with a restrictive type of AN (AN-R), thirteen with a
purging/binge-eating type of AN (AN-BP), three nonspecific ED patients (ED-NOS), and 29 healthy controls. Kohmura and colleges used structural brain scan MRI to collect images of grey matter, white matter, and cerebral spinal fluid for each participant. Before scanning, all participants completed self-report questionnaires: the Beck Depression Inventory (BDI) and the Eating Disorder Inventory II (EDI-II) which evaluated DT and BD. The researchers estimated the quantitative relationship between regional GMV and levels of BD and DT. Mean intensity for volume of interests (VOI) was obtained with MRI to make a correlational analysis between VOI, BD, and DT. Because malnutrition and dehydration could be counted as the cause for the results, BMI was considered a covariate when identification of cortical regions was made, to avoid misleading results. Age was treated as a covariate as well.

The researchers found decreases of GMV for the whole brain in patients with AN (p<.01). The researcher found decreased GMV in the right superior temporal gyrus (STG) and right middle temporal gyrus (MTG) after eliminating the confounding variables of age and BMI. The STG has been seen to be involved in emotional processing and body perception. The authors found a correlation between the decrease of GMV in STG and BD. They suggest that the decrease of GMV in STG related to BD is mediated by altered visuospatial perception. However, the correlation was only found in the control group (p=.011). The authors suggest that AN patients have impaired emotional processing due to the large decrease of GMV compared to healthy controls. They suggest that visual dysfunction is a result of disturbances in both STG and MTG, as the former is considered to be included in body recognition and the latter in face recognition.

Suchan et al. (2010) looked at the association between reduced GMV (especially in the extrastriate body area [EBA]) in AN patients and their difficulties in body processing. Body processing is described as a cognitive phenomenon that involves brain circuits processing perceptual, visual and other body-related information. Together, these are suggested to process body-image. Before participants underwent MRI, they completed the Contour Drawing Rating Scale (Thompson & Gray, 1995) to rate their body image. The researchers found a significant reduction of GMV in AN patients in the lateral occipital cortex, which they refer to as the left EBA, compared to control subjects. The authors explain that the EBA is specialized in visual processing of the human body. They found a decrease of GMV in STG in AN patients - an area also shown to be involved in body processing. Performing a correlational analysis of EBA and body size misjudgment in AN, Suchan et al. found that results was close to a significant negative correlation (r= .38; p=.08) between these variables. The researchers suggest that structural alterations in the EBA might result in
distorted body image in AN. They conclude that the causality is unclear, whether the reduced GMV in EBA is involved in the onset of AN or whether it is a consequence of the disorder.

7.2 Neural functions associated with BD

The functional neuroanatomy of BD is not well known, although studies have identified brain regions associated with the processing of body shape. Several studies on normal and pathological body image have identified activations in the lateral occipital lobe comprising the EBA and fusiform body area (FBA), PFC, insula, ACC, amygdala and parietal cortex (Friederich et al., 2010; Gaudio & Quattrocchi, 2012; Suchan, et al., 2013; Uher et al., 2005; van de Riet, Grezes, & de Gelder, 2009).

Downing, Jiang, Shuman, and Kanwisher (2001) describes the EBA as a region selectively involved in visual processing of the human body. The area is located in the right lateral occipital cortex and has been shown to be strongly activated when individuals are shown human bodies and body parts (not faces) rather than objects. Another area involved in processing the human body is the FBA. It is located in the posterior fusiform area and is suggested to respond to the whole body rather than to body parts. It appears that the FBA is involved in recognition of familiar and unfamiliar bodies (Minnebusch, & Daum, 2009).

The PFC is suggested to play a critical role in cognitive control in terms of ability to accomplish actions and pursue thoughts in accordance with internal goals (Miller & Cohen, 2001). Activation of the dorsolateral PFC has been seen in a functional neuroimaging study by Friederich et al. (2007) when individuals compared their own bodies to bodies of slim fashion models. The researchers suggest that activation of this area occurred due to automatic thoughts about slimness and inhibition of negative emotions. The dorsolateral PFC is thought to be involved in the general processing of body shapes. The ventrolateral PFC has been shown to be involved in anxiety processing and basic emotions such as sadness and anger (Friederich et al., 2007). Grimm et al. (2006) suggest that this area and the dorsolateral PFC are involved in emotional judgments, mediating the subjective experience in emotional processing.

Major neuroscientific research on BD and body image has according to Gaudio and Quattrocchi (2012), been unidimensional and usually focused on visual perception and body schema. The authors argue that research should proceed from a behavioral view where body image is considered a multidimensional construct involving perceptive, affective and cognitive components. They suggest that (1) the perceptive component in a dysfunctional body image is mainly linked to alterations in the precuneus and inferior parietal cortex (2) the
affective component is mostly linked to alterations in the PFC, insula, and amygdala; (3) the cognitive component is but weakly explored, and further research is needed to investigate the neural alterations that are components of a distorted body image.

Similar results have been seen in a study by Mohr et al. (2010), who stress the importance of distinguishing body satisfaction from body-size estimation. They investigated neural correlates of two perspectives of body image: body-satisfaction ratings and size estimation. Sixteen AN patients (with mean BMI of 15.9) and sixteen healthy controls had their whole bodies photographed to use in a computer program that manipulated the image of each participant's body. Body parts were changed in degrees; 31 images were obtained with different body sizes compared to the original pictures. Fifteen pictures imagined a fatter body compared to the original (+1% to +15%) and fifteen pictures imagined a thinner body (-1% to -15%). Simultaneously as the participants underwent fMRI, they were shown the photographs randomly to rate them in relation to their own body image. This was done to rate their body-size estimation. Each picture was shown for 4000ms; participants had to rate them in relation to their own body size as (-2) = extremely distorted, (-1) = moderately distorted, (+1) = nearly realistic, and (+2) = realistic and not distorted. Misperception of body size was then calculated as the difference between the perceived body and real body.

The participants were given a second task where they had to rate their satisfaction in the same way as in the previous task. This time they rated how much the picture was in accordance with their ideal body image. They could choose between (-2) = image is not identical at all, (-1) = image is not identical, (+1) = image is nearly identical, (+2) = image is identical. Body satisfaction was then calculated as the difference between ideal and existing body shape. Participants completed a questionnaire to get a more detailed picture of their body image and body awareness.

The ratings of body satisfaction in the AN group showed a trend of lower body satisfaction compared to the control group (p=.08). The AN group tended to strive for thinner ideal body size in relation to their perceived actual size, in contrast to the control group. The AN group had a more negative rating of their actual body-size image when they compared to their ideal body size image, compared to the controls (p<.05). Mohr et al. (2010) found increased activation in the insula (p<.01) and anterior middle frontal gyrus (p<.05) for the AN group when shown thin self-images in the satisfaction task. The authors suggest that activation of the insula is associated with stronger experiences of emotions in the AN group when thinner self-images are presented. The activation in the lateral anterior PFC is hypothesized to be related to a higher affective value of thinner self-images in AN patients.
Regarding body-size estimation, there was a significant difference between the groups. Individuals with AN overestimated their actual size (p<.05) and rated the presented fatter self-images as more realistic than controls did (p<.05). The right precuneus was found to be more activated in the control group in the estimation task when they were shown the fatter self-images (p<.01), whereas there were no activation differences in the patient group between the levels of distortions. It is thought that this area could have a direct impact on the differentiation between thinner, real, and fatter self-images. The hypothesis that individuals with AN suffer from deficits in brain regions responsible for body size estimation could be maintained.

Friederich et al. (2010) studied self/other body-shape comparison in healthy individuals and AN patients establish neural correlates of BD. Seventeen participants with AN and eighteen healthy controls were scanned with fMRI simultaneously as they were shown 72 images of body-shape images of slim fashion models and 72 control images of creative interior designs or furniture. Pictures were shown in six blocks (6x12 images) and participants were told to compare their own body shape/home with what they saw in the pictures. After twelve pictures of the first type were presented, participants rated their anxiety from 0-10. The procedure was then repeated. The researchers found that AN patients, compared to controls, had higher BD and anxiety from the self/other comparison (p=.02). However, there was no close relation between anxiety levels, body comparison and BD ratings. Alterations in the patient group were observed with more activations in the insula and premotor cortex and less activation in the ACC, compared to controls. These regions are thought to be involved in interoceptive awareness and own-body representation. The results were only found in the body-shape self-comparison condition.

Preston and Ehrsson (2016) investigated negative feelings about the body in relation to body perception. They used multisensory illusions (prerecorded video stimuli) to create a way for individuals to possess realistically slim and obese bodies from a first-person perspective. The study included sixteen healthy females and sixteen healthy males with no history of psychiatric or neurological disorders. In the slim condition, the BMI for males was 20.4 and 18.4 for females. The models in the obese condition had a BMI of 36 for males and 32.2 for females. The videos captured a view from a point above the models’ eyes pointing down at their bodies when they laid down on a bed. In the videos, the experimenter used a stick to attach to the models’ bodies for creating tactile stimuli. This was also done to the subjects in the experiment.
The subjects had to lie down in an MR scanner and then watched the videos. There were three blocks of the four conditions: obese synchronous, obese asynchronous, slim synchronous and slim asynchronous. Participants received touches in synchronization with touches in the video in the synchronous condition, whereas no touch was given the asynchronous condition. After each video trial, participants had to answer how satisfied they were with their body and rate the level of their ownership of the body stimuli. The question about body satisfaction was asked before each trial to collect a baseline measure.

Preston and Ehrsson found that individuals rated ownership higher in the synchronous compared to the asynchronous conditions (p<.001). The ownership of an obese body resulted in lower body satisfaction (p=.013) compared to baseline measures. BD was higher in females than males (p=.043). No reduction of body satisfaction was observed in the slim condition in females or males. From fMRI data, brain activation in conjunction with the illusion of body ownership was found in the bilateral ventral premotor cortex (p=.01), left precentral gyrus (p=.02) and right intraparietal sulcus (p=.013). Affective responses to the obesity ownership illusion were also evaluated. The authors found that the right anterior insular cortex had increased activation compared to the slim condition (p=.016). They suggest that this area plays a critical role in BD. They hypothesized that the anterior cingulate cortex should have increased activity as it has been found to be involved in emotional processing, and the grey matter in this area is decreased in AN patients. Their results did not confirm this hypothesis when including both sexes but did for the female group (p=.045).

When evaluating functional interactions of illusionary obesity, increased connectivity between the right intraparietal cortex, right anterior insular cortex (p=.033), dorsal ACC (p=.026), and rostral ACC (p=.014) was found. Preston and Erhsson explain that the posterior parietal cortex is involved in perceptual experience of the body. They claim that this finding of increased connectivity provides evidence for functional interactions between perceptual and affective body representations. They suggest that feelings of BD are related to neural processing in the insular cortex and ACC. These regions are suggested to be functionally connected to perceptual body representations in the posterior parietal cortex.

8. Results

In this section, I will present a summary of the studies included in the thesis. Several brain regions have been distinctly related to AN and BD. Dysfunction in the insular cortex has, in several cases, been related to an anorectic condition. As a potential mediator between various cortical and subcortical regions, an impaired insular cortex has been associated with
subsequent impairments in the orbitofrontal cortex, somatosensory cortex, parietal cortex, amygdala, thalamus, hypothalamus, hippocampus, and striatum. The DLPFC is thought to be involved in avoidance of food and the ACC in appetite regulation, conflict monitoring and executive control of cognition.

There are only a few studies investigating BD and brain structures. Current studies have found that grey matter volume (GMV) decreases in regions such as the STG, MTG, and EBA in individuals suffering from BD. Functional neuroimaging studies of BD have illustrated the importance of the EBA, FBA, PFC, insula, ACC, amygdala and parietal cortex in functions such as body-shape recognition, processing of bodily information, and emotions.

Since BD is a common symptom in AN, anorectic patients are often considered appropriate participants for studies exploring brain structures and functions relating to the negative body image. Comparing results from the studies included in this thesis, the brain regions that seem to be important for both BD and AN are the insular cortex (involved in socio-emotional processing and cognitive functions), ACC, parietal cortex, amygdala, and dorsolateral and orbitofrontal areas of the PFC. One could suggest that investigation of these regions in anorectic individuals could result in a better understanding of the disease. The findings can also help find the role of neurobiology in understanding AN and related cognitive-affective issues (i.e. idealizing thinness or comparing one's body to others).

9. Discussion

The aim of this thesis was to investigate neural correlates of body dissatisfaction (BD) in individuals with a diagnosis of anorexia nervosa (AN). Each concept on its own is highly complex. Neither causation nor consequences are clear when it comes to the effect AN has on neurobiology nor cognitive processes, and vice versa. Through recent brain imaging studies, the identification of neuroanatomy involved in symptoms of BD and AN has just begun to be mapped out. In this section, I will provide an in-depth discussion.

Surprisingly, the studies of BD included in the thesis did not mention the primary somatosensory cortex, which is related to soma-perceptual processing and interacts with body-surface locations (body schema) (Longo, Azañón, & Haggard, 2010). However, as BD has mostly been seen as a cognitive-affective problem, investigations of body perception might not be the primary focus. That said, dysfunctions of this region seems to be linked to body-image disturbance in anorectic individuals.

It has been shown that adolescents suffering from AN recover grey matter volume and recover from AN more easily than adults. Adolescent cortical structures are different from
adult ones and are more susceptible to change. Although, further investigations of risk factors associated with AN should be investigated to promote preventive strategies.

AN is in a way fascinating when comparing patients experienced advantages of anorectic behaviors compared to the actual consequences of the disease. How can the strive for losing weight become stronger than the strive for protecting oneself from bodily harm? Why are individuals with AN often afraid of recovery? As described earlier in the thesis, there are possible biological and social explanations that may have an impact of why harmful anorectic behaviors can be maintained. These explanations mean that cognitive dysfunction, impaired monoamine system, specific personality traits, genetic factors, and sociocultural pressures might play a critical role in AN. Moreover, evolutionary theories suggest that weight gain can be associated with vulnerability of being attacked by others, being excluded by the group, and that AN serves as an old adaptive response to famine. A contradiction to patients’ experienced advantages of AN is that starving can lead to somatic symptoms such as reduced bone density, higher risks for bacterial infections, amenorrhea in women, cognitive deficits, fatigue, etc. Almost every organ is argued to be affected by malnutrition and the mortality rate is the highest among all mental disorders (Zipfel et al., 2015). There are no clear answers to the questions previously mentioned and the cause of AN still needs to be further explored.

The beginning of this thesis mentioned two other perspectives on AN: PANDAS and the microbiomes view. The former diagnosis is made when streptococcal infection occurs at the same time as eating disorder symptoms; the latter suggests that microbiomes affect the brain along certain axes. The standard treatment of PANDAS is long-term antibiotics; a possible interpretation is that regular consumption of antibiotics would interfere with the healthy microbiomes in one’s gut. Francino (2016) write that many studies have confirmed that use of antibiotics can result in disturbance in composition and function of microbiomes. Long-term use of antibiotics is suggested to indirectly affect health. Although, PANDAS is a relatively new diagnosis, and the microbiome view has so far only been weakly explored. Further research exploring whether treatment methods of PANDAS might contradict treatment of the microbiomes view, might be necessary to strengthen each of these perspectives.

Women, in comparison to men, are to a greater extent diagnosed with BD and AN, making this group an appropriate focus for this literature review. A possible reason for this gender difference might be that women's bodies are presented more frequently in the media, often with a much thinner and elusive ideal than the ideal presented for men; although
recently, media forms such as video games and superhero movies have also featured more male-centric thinness and fitness ideals.

The overrepresentation of women in AN diagnoses and BD might be due to differentiation in how men and women express their BD and AN. Researchers may have not begun to take into account how men express ED in diagnostic criteria. According to Grogan (2008), men have been reported to equally strive for thinner and bigger body ideals. The author explains that there are cultural preferences of body ideals for men, with a general consensus that ideal men should have muscular arms, chests, and shoulders, and slim waists and hips. According to the author, the male ideal is ubiquitous in the Western culture, linked to traits such as strength, power, and aggression. Griffiths, Murray, and Touyz (2015) link this ideal with traits such as sexual success, confidence, dominance, and physical and emotional self-control. They suggest that the muscular ideal might put men at risk of developing BD and ED. The number of men suffering from AN is unclear. Strother, Lemberg, Stanford, and Turberville (2012) believe that approximately 10% of all individuals suffering from AN and bulimia are men; Hudson, Hiripi, Pope Jr, and Kessler (2007) report 15%. The problem might be an issue of under-diagnosis as men rarely tend to seek help in the same degree as women (Strother et al., 2012). Although there are fewer studies of men suffering from these conditions, it is also important to include them for a comprehensive understanding of BD and AN.

9.1 Methodological problems and limitations

The major studies of AN patients have relatively small sample sizes and use methods that might be difficult to replicate. The results provided are more likely to show trends toward significance rather than actual significant findings. This might lead to difficulties of interpreting the results and decrease the statistical power.

In previous brain-imaging studies of AN, researchers have come up with varying results. Several studies of cortical volume thickness have found cortical atrophy in AN patients compared to healthy individuals (Dolan et al., 1988; Friederich et al., 2012; Golden et al., 1996; Lambe et al., 1997). These findings are, however, inconsistent. Non-significant results of decreased global cortical volume, enlarged ventricles and increased cerebral spinal fluid have been reported in several studies by contrast (Brooks et al., 2011; Frank et al., 2013; Fuglset et al., 2016). The appearance of inconsistency might reflect a differing of approaches and small sample sizes. In regards to recovered anorectic patients, it has been found that the
brain seems to repair since increases of GMV have been reported after weight gain (Wagner et al., 2006). It appears then that most of the lost cortical brain tissue can be regained.

The definition of BD within psychology and cognitive neuroscience has been somewhat disputed. Grogan (2008) and Stice and Shaw (2002) emphasize the need for a clear distinction between BD and body-size misconception whereas Friederich et al. (2010) associates BD in patients with AN with body-size misconception, and perceptual disturbances. Karazsia et al. (2017) suggests that being dissatisfied with one’s body is derived from a cognitive-affective component of the multidimensional construct framing body image. Body-image disturbance is a term commonly used within studies of anorectic patients. Thompson and Stice (2001) describe it as consisting of subjective unhappiness with one’s appearance, with internalization of the thin ideal as a risk factor for developing a body-image disturbance. Brooks et al. (2016) describe body satisfaction, perception of ideal body size, and judgment of actual body size and shape as be negatively influenced by social pressure to be thin. Preston and Ehrsson (2016) who studied negative feelings of the body and how they relates to body perception, conclude that is it not clear whether perceived body size has a direct effect on body satisfaction.

This twisted view of BD might be problematic. One could suggest that the implication of giving different meanings to BD could lead to inconsistency of results due to varying experimental designs. In regards to investigations of body image, functional imaging studies have mostly focused on visual and perceptual components (Gaudio & Quattrocchi, 2012), although BD is suggested to include cognitive-affective components. Only a few imaging studies exist that explore the structural and functional neural associations of BD, which might be affected by a disputed definition. Since BD is an abstract concept, it could be important to determine what variables exactly should be measured to improve the statistical analysis and replication possibility.

9.2 Further directions

To build a better understanding of BD in AN, both conditions need a foundation in valid research of their own. As mentioned, many studies of AN used small sample sizes, and attempts to increase sample size might improve the reliability, and generalizability of the results. As more brain-imaging and genetic studies of AN are suggesting that the condition is trait related, it might be of value to investigate heritability and further explore neural correlates in relation to AN-related behaviors. By developing a more biological paradigm for AN, one might be more clear how and to what extent BD is related to ED. Only a few
longitudinal studies investigating risk factors for AN currently exist (Bulik et al., 2005). More longitudinal studies might contribute to a better understanding of how BD relates to AN and contribute to preventive treatments.

Today, most research on BD involves participants suffering from a clinical condition that includes symptoms of a negative body image (Friederich et al., 2010; Mohr et al., 2010; Pollatos et al., 2016). Individuals suffering from ED or body dysmorphic disorder (characterized by a preoccupation with imagined or slight physical defects in appearance) (Rief, Buhlmann, Wilhelm, Borkenhagen, & Brähler, 2006), can have symptoms and medical conditions affecting the neural structure or function of the brain. Confounding effects from malnutrition (Friederich et al., 2010), use of medication or comorbidity (Frank et al., 2013) might be difficult to control for in brain-imaging studies of BD. Future research might benefit from including more non-clinical groups to decrease the risk of potential cofounders. I suggest that it is of great importance to do so, to understand the non-clinical nature of BD in the cortex.

The definition of BD between different disciplines and researchers might benefit from a uniform definition. An established definition could facilitate the process of replicating functional and structural imaging studies of BD. It might also reduce the risk of inconsistent results. Research into BD might benefit from exploring the neural correlates of individuals having a positive body image to get further insights when comparing brain structures and functions in both conditions.

The studies exploring monoamines in AN presented in his thesis revealed altered patterns of serotonin and dopamine functions (Bailer et al., 2005; Bailer & Kaye, 2010; Frank et al., 2005; Kaye, 2008; Kaye et al., 1999; Kaye et al., 2003; Kaye et al., 2009; Kaye et al., 2013). However, studies of monoamines in relation to BD barely exist; a section on monoamine functions of BD had to be omitted from this thesis. Since these hormones are critical to anxiety, pleasure, motivation, and modulation of mood states, it might be a potential contribution for research to explore these hormones in relation to BD. As the cognitive component of BD has been only weakly explored, I would suggest that well-developed cognitive tasks, such as Wisconsin Card Sorting Task (WCST), should be examined in both clinical and non-clinical BD to broaden the view of the neural network involved. This might create a better understanding of how BD relates to AN, as individuals with AN have been found to perform worse on cognitive tasks compared to healthy controls.

By investigating environmental factors that may play a role in developing a negative body image in children, this might contribute to further development in preventative
strategies for ED. Since children’s brains are not fully developed, early experiences and environmental influences are important for brain-development (Belsky & de Haan, 2011). Research on BD in children could serve as a foundation for developing an intervention program for young individuals. The content of this program would proceed from relevant research and needs to be well tested. If done properly, this may possibly reduce the risk for individuals to develop ED and BD. I further suggest that this program could be used by parents, in school and created as a mobile application available to use at different devices. Varying exercises adjusted for children might be effective to create positive experiences of self, one’s body, and to teach one to be critical to socio-cultural pressures.

Furthermore, I suggest that research investigating BD might benefit from using virtual reality (VR). This technology is described as a tool simulating contexts that are experienced as real. It relies on a selection of specific visual cues that can activate emotions (Diemer, Alpers, Peperkorn, Shiban, & Mühlberger, 2015). By creating conditions of possessing an obese body and an underweight body for individuals suffering from BD, this might be helpful to explore the emotional reactions related to perception of the body. I would suggest taking this further to investigate whether an obese body compared to an underweight body might have an impact on the performance in different cognitive tasks. This might lead to insights of the cognitive component in BD.

10. Conclusion

This thesis aimed to answer how the neural correlates of BD relates to the neural correlates in individuals with a diagnosis of AN. Based on relevant neuroscientific literature, the underlying neural correlates of body dissatisfaction in anorexia nervosa is suggested to be underpinned by the insular cortex, ACC, parietal cortex, amygdala, and dorsolateral and orbitofrontal PFC. Although, an issue of research in AN is the common use of small sample sizes and use of specific methods that might be difficult to replicate. The results are less likely to be actually significant findings. The definition of BD is disputed between researchers and may contribute to inconsistency of results. BD (which is suggested to reflect negative emotions and thoughts of body appearance) incorporates cognitive-affective components of body image, although, studies of body image have mostly focused on perceptual components. Further research is needed to investigate the true relationship between the behavioral, social and biological aspects of AN and BD.
11. References


