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Impaired neural processing of social attribution in anorexia nervosa

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ABSTRACT

Anorexia nervosa (AN) patients have been found to have problems in social cognition, including the process of thinking about other people's thoughts and feelings, often referred to as Theory of Mind (ToM). We examined neural correlates relating to thinking about social relationships in 17 women in recovery from anorexia (RAN) and 17 healthy women (CON) using a functional magnetic resonance imaging (fMRI) task. The task consisted of short videos of moving shapes that subjects viewed either in the context of performing a social decision related to how the shapes interacted: "People: All friends?" or in the context of performing a visuospatial task related to how the shapes moved after bumping into each other: "Bumper cars: Same weight?". The RAN participants showed reduced activation in the social cognition network, with the most robust differences in the right temporoparietal junction (RTPJ). There were no significant differences between the CON and RAN groups in regions more active during the visuospatial task. These neural correlates show differences in the processing of social knowledge in RAN subjects suggesting that biological impairments in social cognition may contribute to pathology in AN.

1. Introduction

Anorexia nervosa (AN) is a severe and complex psychiatric illness, characterized by the development of a distorted body-image, a fixed belief that one is overweight, and minimal food intake, leading to severe weight loss. Evidence for a strong genetic component indicates that biological factors are involved in the pathology (Bulik et al., 2007). Additionally, the distorted cognitive processes in AN demonstrate a psychological component of the pathology: the thoughts of people with AN are inordinately focused on food and body-image (Turner and Cooper, 2002; Zakzanis et al., 2010). Social and cultural norms can also change the prevalence of AN, demonstrating an environmental contribution (Pavlova et al., 2010). Social difficulties have long been reported in AN patients, including loneliness and shyness before the illness appears (Troop and Bifulco, 2002). Elevated levels of separation anxiety occur during the childhood in AN patients before eating symptoms emerge (Godart et al., 2000), and high levels of social phobia are present in AN patients before, during, and following the eating disorder (Nilsson et al., 1999; Godart et al., 2000; Wentz et al., 2001; Zucker et al., 2007). Recently, social cognition has become a focus of research that may provide linkages between the biological, psychological and social factors implicated in AN.

Social cognition refers to those components of intelligence that help people understand and relate to other people and behave appropriately in interactions with friends, family, coworkers, and acquaintances. This term encompasses a number of different dimensions, including the exhibition of appropriate social behaviors such as maintaining eye contact, conversational turn-taking, as well as understanding the thoughts and feelings of people (for review, see Lieberman, 2007). Social cognition can be studied quantitatively through psychological testing assessing one's understanding of particular situations and emotions. Theory of Mind (ToM) refers to the subset of social cognition that specifically describes the ability to reason about the mental states of other people, such as what another person knows about a particular situation (Frith and Frith, 2006). In more complex cases ToM extends to the interpretation of what others are feeling (emotional ToM), and inferring the reasons for their words and actions (cognitive ToM). Additionally, neuroimaging studies have enabled the identification of cortical regions, in particular the RTPJ, that appear to be critical for the performance of social cognition tasks (Pelphrey et al., 2004; Saxe and Wexler, 2005). However, biological evidence for social cognitive differences in AN has not previously been examined through neuroimaging of ToM.

1.1. Neuroimaging of ToM

ToM has been examined in healthy controls through fMRI and PET tasks incorporating story-telling, interpreting cartoons, and watching videos (Castelli et al., 2002; Pelphrey et al., 2003; Schultz et al., 2003; Pelphrey et al., 2004; Saxe et al., 2004; Saxe and Kanwisher, 2005; Frith and Frith, 2006; Perner, et al., 2006; Whitehead et al., 2009). These imaging studies have identified a set of core regions associated with social cognition that includes the medial prefrontal cortex

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(MPFC), the fusiform gyrus (FG), the inferior frontal gyrus (IFG), the precuneus (PreC), the temporal poles (TP), and the bilateral TPJ. The activity in the RTPJ, in healthy controls, has been most specifically linked to ToM function (Pelphrey et al., 2004; Saxe and Wexler, 2005; Young et al., 2010). More recently, neuroimaging paradigms for ToM have been applied to patient populations.

Problems in the development of ToM have been proposed to occur in autistic spectrum disorder (ASD), schizophrenia, borderline personality disorder (BPD), and eating disorders (Gillberg, 1983; Harrington et al., 2005; Zucker et al., 2007; Korkmaz, 2011). In ASD, diminished activity in the RTPJ has been reported using fMRI studies examining biological motion (Herrington et al., 2007; Kaiser et al., 2010). Biological motion refers to visual stimuli created by placing points of light on the limbs and joints of a person moving (walking, jumping); a healthy person viewing the trajectories of the points of light (not the person) will almost immediately recognize this motion as indicative of a human moving in a particular direction (for review, see Troje, 2002). These types of stimuli lead to the activation of social cognition regions, and have been particularly helpful to examine ToM in patient populations because the social percept generated by such stimuli emerges effortlessly in a healthy viewer (Pelphrey et al., 2003). Consistent behavioral deficits in ToM have been observed in schizophrenia, and both functional and structural neural differences in the frontal and temporal regions have been correlated with these impairments in ToM in schizophrenia (Brunet-Gouet and Decety, 2006; Benedetti et al., 2009). In contrast to both ASD and schizophrenia, BPD subjects have shown either no difference or improved performance on behavioral ToM tasks rather than impairments (Arntz et al., 2009; Fertuck et al., 2009; Ghiassi et al., 2010; Franzen et al., 2011). The only neuroimaging study examining ToM in BPD showed elevated activation of the RTPJ in BPD subjects compared to controls (Buchheim et al., 2008), consistent with the behavioral data suggesting that ToM may not be impaired in BPD. These neuroimaging studies in patients have supported the findings in healthy controls that the RTPJ is relevant to ToM.

1.2. Theory of Mind in AN

Concern for social cognitive problems in AN have been suggested from a number of clinical observations. Patients with AN have both premorbid social impairments (Rastam, 1992) and an increased incidence of social phobia (Nilsson et al., 1999). The onset of AN typically occurs in the presence of social stressors (Troop and Treasure, 1997), and less social support is correlated with more severe illness (Karatzias et al., 2010). Relationships between ASD, the psychiatric disorder with the most profound and specific social cognition impairments, and AN have also been described (Gillberg, 1983; Zucker et al., 2007; Gillberg et al., 2010). Specifically, AN patients show elevated scores on the autistic spectrum quotient questionnaire compared to healthy controls, with differences found on three subscales: social skills, attention switching, and imagination (Hambrook, et al., 2008); conversely ASD patients frequently have eating disturbances and low body weights (Råstam, 2008).

Additionally, both AN and ASD patients show a similar profile of cognitive neuropsychiatric impairments in executive-function (EF) tasks including problems in set-shifting (Roberts et al., 2010), central coherence (Lopez et al., 2009) and cognitive-flexibility (Steinglass et al., 2006). Correlations between EF and ToM have been observed in ASD (Hughes and Graham, 2002; Fisher and Happé, 2005). ToM, central coherence, and cognitive-flexibility have also been shown to be predictive of autistic behavioral traits in a general population of young adults (Best et al., 2008), suggesting that this pattern of neuropsychiatric function may reflect on a biological trait in the general population.

Recently, emotional recognition has been reported to be impaired in both recovered and currently ill AN patients in a number of studies using a variety of psychological tasks (Zonnevijlle-Bender et al., 2002; Katarzyna Kucharska-Pietura et al., 2004; Harrison et al., 2009; Harrison et al., 2010; Oldershaw et al., 2010). Emotional ToM has also been examined in AN in several studies using the Reading the Mind in the Eyes (RME) task. Each of these studies have reported differences in ToM in currently ill AN patients compared to controls (Harrison et al., 2009; Russell et al., 2009; Harrison et al., 2010; Oldershaw et al., 2010). Two studies also examined RME in recovered AN patients: Harrison et al. (2010) observed continued impairments in both AN groups whereas Oldershaw et al. (2010) found that fully recovered AN subjects had normal scores in RME although this group continued to show deficits in the recognition of positive emotions. These studies suggest that problems in emotional recognition and ToM may be traits related to stable cognitive characteristics of AN patient population rather than being a deficit emerging from the state of being ill with AN.

We examined the neural activity in the social cognition network in CON and RAN subjects using a fMRI social attribution task that used inanimate objects moving in ways to create both social and non-social stimuli, to test the hypothesis that ToM is altered in AN. This study was an exploration of whether biological differences in the social cognition neural network could be observed in AN, based on the behavioral differences reported in ToM tasks in AN (Harrison et al., 2009; Russell et al., 2009; Harrison et al., 2010; Oldershaw et al., 2010).

2. Methods

2.1. Participants

A total of 34 female participants, between 18 and 45 years of age, were recruited for this study. The participant groups consisted of 17 healthy controls (CON) and 17 individuals with a recent history of AN but currently in the process of recovering from AN (RAN). The RAN participants were recruited from local treatment providers in the Dallas, TX area. All participants had maintained a minimum body mass index greater than 17.5 and had menstrual cycles for at least 2 months, and had no reported binging or purging behaviors during the previous month. All RAN subjects had also met the full criteria for AN within the previous 2 years. Nine of the RAN subjects had maintained a stable weight with menses and BMI >19 for over 6 months. One of these subjects had had a relapsing–remitting course of AN for over 25 years and was currently obese; she had been in weight recovery for 18 months at the time of her scan. The other eight RAN subjects had maintained BMIs exceeding 17.5 for only 3–6 months. Eleven of the RAN subjects met criteria for the restricting subtype of AN and six had the binge–purge subtype of AN. We examined RAN patients for two main reasons. First, neuroimaging findings in currently ill AN patients are confounded with the physiological effects of current starvation. Second, the cognitive effects of AN (i.e. thoughts about body image and food) are known to lag the physical recovery from AN, by approximately 2 years (Strober et al., 1997).

Subjects provided written informed consent to participate in this study at an initial appointment. All subjects were then interviewed using the Structured Clinical Interview for DSM-IV disorders (SCID-RV) to confirm the history of AN in the RAN group, the absence of eating disorders in the CON group, and the absence of other current Axis I disorders, including current major depressive episodes (MDE), depression NOS, and dysthymia, in both groups. Participants were also screened for MRI compatibility. Some of the subjects had a history of recurrent Major Depressive Disorder (MDD) (1, CON; 7, RAN) but none had met symptom criteria for a MDE for at least 3 months prior to the neuroimaging. No participants had a current or past diagnosis of any psychotic disorders or bipolar disorder; no participants were currently taking mood-stabilizers, antipsychotics, or benzodiazepines. Participants on antidepressants were included (1 CON; 8 RAN). Current