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### Longitudinal examination of decision-making performance in anorexia nervosa: Before and after weight restoration

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#### ABSTRACT

*Background:* This study aimed to extend previous work on decision-making deficits in anorexia nervosa (AN) by using a longitudinal design to examine decision-making before and after weight restoration. *Methods:* Participants were 22 women with AN and 20 healthy comparison participants who completed the lowa Gambling Task (IGT). Decision-making was assessed both before and after weight restoration in a subset of 14 AN patients. Self-report and interview assessments were used to measure psychological correlates of decision-making performance including depression, anxiety, and eating disorder symptoms, and magnetic resonance imaging (MRI) scans were conducted to explore associations between brain volume in the orbitofrontal cortex (OFC) and decision-making in individuals with AN.

*Results:* Currently ill AN patients performed worse on the IGT compared to the control group. Although decision-making performance did not improve significantly with weight restoration in the full AN sample, AN patients who were poor performers at baseline did improve task performance with weight-restoration. When actively ill, lower body mass index (BMI) and decreased left medial OFC volume were significantly associated with worse IGT performance, and these associations were no longer significant after weight restoration.

*Conclusions:* Findings suggest that decision-making deficits in AN in the acute phase of illness are associated with low weight and decreased left medial OFC volume, but increases in brain volume and BMI may not have been sufficient to improve decision-making in all patients. Findings contribute to a model for understanding how some patients may sustain self-starvation, and future work should examine whether decision-making deficits predict relapse.

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#### 1. Introduction

Anorexia nervosa (AN) is a serious psychiatric illness associated with neuropsychological impairments that may be implicated in the etiology of the disorder (Tchanturia et al., 2005). In particular, research has begun investigating the role of decision-making in AN

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using the Iowa Gambling Task (IGT; Bechara et al., 1994) (e.g., Cavedini et al., 2006; Danner et al., 2012; Fagundo et al., 2012; Guillaume et al., 2010; Tchanturia et al., 2007). This task was developed to simulate decision-making under conditions of uncertainty, reward, and punishment and to capture deficits found in patients with known lesions in the ventromedial prefrontal cortex, a broad area that includes the orbitofrontal cortex. Poor decision-making performance in these patients reflects insensitivity to future negative consequences, despite intact general intelligence and problemsolving abilities (Bechara et al., 1994). Similarly, individuals with AN act in ways that may have positive short-term consequences (e.g., anxiety relief through food restriction) despite negative long-term





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consequences (e.g., health problems) (Brogan et al., 2010; Cavedini et al., 2004). Consistent with this idea, the majority of studies examining decision-making in AN using the IGT have documented worse performance in AN compared to healthy participants (e.g., Abbate-Daga et al., 2011; Cavedini et al., 2004, 2006; Danner et al., 2012; Garrido and Subirá, 2013; Tchanturia et al., 2007). This has led to models in which poor decision-making may contribute to the development and maintenance of symptoms in AN (Brogan et al., 2010; Cavedini et al., 2004; Chan et al., 2014).

Importantly, malnutrition causes cognitive impairment independent of the presence of an eating disorder (Keys, 1950). Thus, poor decision-making in patients actively ill with AN may reflect a consequence of illness rather than a premorbid underlying impairment in decision-making that contributes to vulnerability. Researchers have evaluated decision-making in weight-restored patients with AN in order to disentangle state versus trait impairments; however, mixed findings have emerged from such studies (Bosanac et al., 2007; Danner et al., 2012; Lindner et al., 2012; Tchanturia et al., 2007). Studies have found poorer (Danner et al., 2012), similar (Bosanac et al., 2007; Tchanturia et al., 2007), and even superior performance (Lindner et al., 2012) in individuals recovered from AN compared to healthy comparison participants. Importantly, all studies were cross-sectional, thus it is unclear whether decision-making performance in individuals with AN actually improves with increased weight, given that differences may or may not have been present during the acute phase of illness.

Another way to examine whether decision-making deficits are state versus trait characteristics is to examine patients longitudinally. To our knowledge, only one study has examined IGT performance in individuals with AN using a longitudinal design (Cavedini et al., 2006). Cavedini et al. (2006) found that IGT performance in inpatients with AN did not improve significantly from intake to discharge. Importantly, average body mass index (BMI) at discharge  $(BMI = 15.9 \text{ kg/m}^2)$  was below a minimally healthy threshold  $(18.5 \text{ kg/m}^2)$ , suggesting that most patients were still malnourished at discharge. Thus, it remains unclear whether poor IGT performance in AN is a consequence of low weight because no study has examined decision-making in AN patients longitudinally at the time of acute illness and again following weight restoration to a minimally healthy weight. The primary aim of this study was to examine changes in decision-making performance from intake to hospital discharge in patients restored to normal weight.

Importantly, decision-making deficits on the IGT have been identified in a range of mental illnesses (e.g., Cavedini et al., 2010; Jollant et al., 2007; LeGris et al., 2012); thus, in addition to examining associations between decision making and illness state, it is important to identify whether deficits found in AN may be explained by comorbid psychological factors rather than to AN. As such, a secondary aim of this study was to explore whether impaired decision-making is attributable to eating pathology or other psychological traits. Furthermore, the orbitofrontal cortex (OFC) is an important brain region for decision-making and the processing of rewards and punishments (e.g., Bechara et al., 1999, 2000; Kringelbach and Rolls, 2004; Kringelbach, 2005) and deficits in this region have been linked to eating disorders (Cavedini et al., 2004; Frank et al., 2013; Kaye et al., 2009; Uher et al., 2004). For example, differences in OFC volume have been found in individuals with acute and recovered AN and bulimia nervosa compared to control participants, and these differences have been linked to self-reported reward sensitivity (Frank et al., 2013). However, no study, to our knowledge, has examined whether OFC volume is a specific correlate of decision-making behaviors in AN and whether this association is independent of BMI. Thus, another secondary aim of this study was to evaluate whether OFC volume is associated with decision-making performance in AN patients.

#### 2. Methods

#### 2.1. Participants

Participants with AN (n = 22, female) were recruited from the inpatient eating disorder unit at the University of Iowa Hospitals and Clinics as part of a larger longitudinal study examining cognitive functioning. The AN diagnosis and subtype were determined by board certified psychiatrists using criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR; American Psychiatric Association, 2000). Fifteen patients met criteria for the restrictive subtype, and seven met criteria for the binge-purge subtype. Patients with AN were excluded if they had a diagnosis of illicit drug or alcohol abuse/ dependence within the past three months, had a concurrent diagnosis of a psychotic or bipolar disorder, had a history of DSM-IV diagnosis of bulimia nervosa prior to the onset of AN, had a history of significant brain damage or neurological problems, were currently pregnant, or had the presence of standard exclusionary criteria for magnetic resonance imaging (MRI) of metal objects in the body (e.g., a pacemaker). Healthy comparison participants (n = 20) were matched to AN participants on gender, age, and education. This comparison group was recruited through advertisements in the Iowa City area and did not have current or lifetime histories of any major psychiatric diagnoses, including eating disorders, as established through the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002).

#### 2.2. Procedures

All participants signed consent forms prior to participation. The AN participants completed a battery of assessments including demographic information, self-report questionnaires, interviews, neuropsychological tests and MRI scans. The IGT and MRI scans were completed as part of intake assessments, approximately 10 days after hospital admission (range 6–15 days). Fourteen patients (63%) completed second IGT and MRI assessments after weight restoration (BMI  $\geq 18.5 \text{ kg/m}^2$ ). At the time of the second assessments, patients had been weight-restored for at least one week. The healthy comparison group completed the demographic information and one IGT assessments in order to calculate BMI. All study procedures were approved by the University's Institutional Review Board.

MRI scans were obtained using a Siemens 3T Trio scanner (Siemens Medical Solutions, Erlangen, Germany). T1- and T2-weighted images were collected. T1 images were collected using a coronal 3D MP-RAGE sequence (slice thickness = 1 mm, TR = 2530 ms, TE = 2.8 ms, TI = 1100 ms, NEX = 1, number of echoes = 1, flip angle = 10°, FOV = 256 × 256 × 256 mm, Matrix = 256 × 256 × 256) whereas T2 scans were acquired using a coronal 2D TSE sequence (slice thickness = 1.5 mm, TR = 9910 ms, TE = 12 ms, NEX = 1, number of echoes = 10, FOV = 256 × 256 mm, Matrix = 256 × 256). Cortical reconstruction and volumetric segmentation was performed with the Freesurfer image analysis suite (v 5.1) (http://surfer.nmr.mgh.harvard.edu/). These procedures have demonstrated good test-retest reliability across scanner manufacturers and across field strengths (Han et al., 2006; Reuter et al., 2012).

The output of interest was total cerebral cortex gray matter volume and volume of predefined regions of interest (ROI), including the left and right medial and lateral OFC. The anatomical accuracy of each FreeSurfer ROI was visually inspected by independent reviewers who were blind to both diagnosis and IGT performance and modifications of abnormally parcellated scans were

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