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ALTERED REGIONAL HOMOGENEITY AND EFFICIENT RESPONSE INHIBITION IN RESTRAINED EATERS

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Abstract—Restrained eaters (REs) characterized by less efficient response inhibition are at risk for future onset of binge eating and bulimic pathology. Previous imaging studies investigating REs have been based on task-related functional magnetic resonance imaging (fMRI) and little is known about resting-state neural activity underlying restrained eating. To illuminate this issue, we investigated resting-state fMRI differences between REs ($n = 22$) and unrestrained eaters (UREs) ($n = 30$) using regional homogeneity (ReHo) analysis, which measures the temporal synchronization of spontaneous fluctuations. Samples were equated on body mass index (BMI) and caloric deprivation levels (i.e., 14 ± 2.1 h since last evening meal) before undergoing fMRI. Correlation analyses were performed between the ReHo index of identified regions and response inhibition based on stop-signal reaction time (SSRT) within each sample. Compared with UREs, REs showed more ReHo in brain regions associated with food reward (i.e., orbitofrontal cortex (OFC), dorsal-lateral prefrontal cortex (dlPFC)), attention (i.e., lingual gyrus, cuneus, inferior parietal lobule) and somatosensory functioning (i.e., paracentral lobule, anterior insula). In addition, ReHo values for the left dlPFC and left anterior insula, respectively, were negatively and positively correlated with SSRT among REs but not UREs. In concert with previous studies, these results suggest altered local synchronization may help to explain why dieting to maintain or lose weight often fails or increases risk for binge eating among REs.

Key words: restrained eating, resting-state fMRI, dieting, reward, inhibition, attention.

INTRODUCTION

Restrained eating (RE) refers to intentional, sustained restriction of caloric intake to lose or maintain body weight (Herman and Mack, 1975; Wadden et al., 2002). Recent studies show that restrained eaters (REs) characterized by less efficient response inhibition or impulsivity are particularly vulnerable to overeating (Guerrieri et al., 2008, 2009; Jansen et al., 2009; Jasinska et al., 2012). Furthermore, theory and associated research (Polivy and Herman, 1985; Stice, 2001; Wertheim et al., 2001; Johnson and Wardle, 2005; Neumark-Sztainer et al., 2006; Stice et al., 2008a), have linked RE to increased risk for the onset and maintenance of binge eating and bulimia nervosa, disturbances that have significant negative implications for health and functioning (e.g., Dingemans et al., 2002; Araujo et al., 2010; Wade et al., 2012; Kessler et al., 2013). Because approximately 50% of adolescent girls and young women report engaging in dieting behaviors (Field et al., 2010), investigating potential neural bases of RE may help to clarify why dieting to lose or maintain weight so often fails (Hetherington et al., 2000; Sysko et al., 2007).

Functional magnetic resonance imaging (fMRI) studies have revealed differences in the processing of food stimuli between REs and unrestrained eaters (UREs). Coletta et al. (2009) found that compared to UREs, REs show stronger activation in the orbitofrontal cortex (OFC) and dorsolateral prefrontal cortex (dlPFC) in response to food pictures when calorically deprived, although groups have similar activation patterns after consuming a meal. Burger and Stice (2011) found high scorers on the Restraint Scale (RS; Herman and Polivy, 1980) are also hyper-responsive in motivational and reward regions (right OFC, bilateral dlPFC) during food intake. Moreover, images of high-calorie, ''fattening'' foods may elicit stronger activation in the left amygdala, right thalamus, and occipital lobe (cuneus, lingual gyrus) in monozygotic RE twin pairs compared to URE identical twin pairs (Schur et al., 2012). Although

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Abbreviations: BMI, body mass index; dlPFC, dorsolateral prefrontal cortex; EPI, echo-planar imaging; FDR, false discovery rate; fMRI, functional magnetic resonance imaging; MNI, Montreal Neurological Institute; MTG, middle temporal gyrus; NA, Negative Affect; OFC, orbitofrontal cortex; PA, Positive Affect; RE, restrained eater; ReHo, regional homogeneity; ROI, region of interest; rsfMRI, resting-state functional magnetic resonance imaging; RT, reaction time; SDT, stop delay time; SSD, stop-signal delay; SSRT, stop-signal reaction time; SST, stop-signal task; URE, unrestrained eater.

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neuroimaging research on RE is still in its infancy, these findings suggest RE is related to heightened responsiveness of brain reward circuitry to food cues that increases risk for binge eating and overeating (Stice et al., 2010; Stice and Presnell, 2010).

To date, associated imaging studies have relied on task-based fMRI. Given that brain activity in a resting state consuming 95% of total brain energy reflects the brain's baseline status (Biswal et al., 1995; Fox and Raichle, 2007), resting-state fMRI (rsfMRI) is a promising alternative route for identifying neural correlates of RE. Regional homogeneity (ReHo) analysis, a robust and reliable index (Zuo et al., 2013), can effectively evaluate resting-state brain activity (see Zang et al., 2004). Based on an underlying assumption that brain activity is more likely to occur in clusters than single voxels, ReHo is calculated using Kendall's coefficient of concordance (KCC) (Kendall and Gibbons, 1990), which evaluates similarities between the time series of a given voxel and its nearest neighbors. As such, ReHo reflects the local coherence of spontaneous neuronal activity (Wu et al., 2009). Additionally, increased ReHo corresponds to increased local synchronization of local field potential signaling and vice versa (Wang et al., 2012). Although rsfMRI studies have examined intrinsic activity in related groups including the obese (Garcia-Garcia et al., 2012; Kullmann et al., 2012), to our knowledge, extensions have yet to investigate RE.

Since task-based studies have consistently found increased activation differences in reward regions between RE and URE groups, differential activity within these areas in a resting state seems plausible. Furthermore, because RE is associated with attention biases toward food cues in some behavioral studies (Boon et al., 2000; Hollitt et al., 2010; Veenstra et al., 2010), it is possible that increased spontaneous activity differences between RE and URE groups are found in attention areas, such as cuneus, lingual gyrus, middle temporal gyrus (MTG) (Schur et al., 2012; Stice et al., 2013).

Food deprivation correlates with activation in regions implicated in attention, reward, and motivation in response to food cues, such as the OFC, thalamus, parahippocampal gyrus, caudate, dlPFC, cerebellum, middle temporal gyrus (MTG), cuneus, lingual gyrus (Tataranni et al., 1999; Porubska et al., 2006; Goldstone et al., 2009; Siep et al., 2009; Stice et al., 2013). In particular, skipping breakfast increases brain activity that drives eating (Goldstone et al., 2009; Leidy et al., 2011, 2013) and leads to poor long-term success among those who want to control weight through caloric restriction (Dansinger et al., 2007). Given that RE is related to differences in reward processing and desire to maintain or lose weight through caloric restriction, evaluation of differences in spontaneous brain activity between REs and UREs following food deprivation would be an especially salient condition for examining rsfMRI.

Inhibitory control – the ability to stop or suppress responses that are no longer required, inappropriate, or in conflict with current goals (Verbruggen and Logan, 2008) – may have a key role in maintaining a healthy diet (Jasinska et al., 2012). Accumulating evidence suggests deficits in inhibitory control predict binge eating and overeating (see Waxman, 2009 for a review). Consistent with this view, several experiments indicate RE is associated with less efficient response inhibition (measured by the stop-signal task (SST)) and vulnerability to overeating (Guerrieri et al., 2008, 2009; Jansen et al., 2009; Jasinska et al., 2012). However, little is known about response inhibition capacities of RE and URE after skipping consecutive meals. Researchers have implicated the inferior frontal gyrus, dlPFC, medial prefrontal cortex (MPFC), insula in inhibition control (Verbruggen and Logan, 2008; Chambers et al., 2009; Swick et al., 2011; Tian et al., 2012), but relations between altered resting-state spontaneous activity and response inhibition have not been examined among REs.

Consequently, the current study had two main goals. First, possible alterations of regional spontaneous activity patterns among REs and UREs were assessed using ReHo analysis within a food deprivation condition. Based on the literature reviewed above, we hypothesized that ReHo indices would differ between these groups in brain regions associated with food reward and attention. Specifically, REs were expected to show increased ReHo values in the thalamus, parahippocampal gyrus, caudate, OFC, dlPFC, MTG, and occipital lobe (cuneus, lingual gyrus). Second, we examine whether REs would also display altered regional spontaneous activity related to response inhibition relative to UREs based on SST performance. We expected response inhibition would show positive correlation with regional spontaneous activity of dlPFC and inferior frontal gyrus, and negative correlation with insula among REs but not UREs.

EXPERIMENTAL PROCEDURES

Participants

Participants were 52 undergraduate women from Southwest University (SWU), Chongqing, who comprised URE (n = 30) and RE (n = 22) groups. Respondents were selected on the basis of RS scores in a prescreening procedure administered to 107 volunteers two to three weeks before the imaging study. Only women were recruited because men and women differ in how and why they gain and lose their weight (Holm-Denoma et al., 2008). Volunteers in the RE and URE groups were eligible to participate if they scored above 15 or lower than 12, respectively, on the RS following other published accounts (Trottier et al., 2005; Jarry et al., 2006; Demos et al., 2011).

Open-ended queries assessed exclusion criteria including current neurological disease (i.e., central and peripheral nervous system diseases such as epilepsy, migraine and other headache disorders, multiple sclerosis or brain trauma), eating disorder diagnosis, or binge eating disturbances or a history of these concerns. Obese participants (body mass index (BMI) $\geqslant$ 30 kg/m^2) were also excluded because of potential neuro-anatomical differences that vary as a