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Resting-state synchrony between anterior cingulate cortex and precuneus relates to body shape concern in anorexia nervosa and bulimia nervosa

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ABSTRACT

Cortical areas supporting cognitive control and salience demonstrate different neural responses to visual food cues in patients with eating disorders. This top-down cognitive control, which interacts with bottom-up appetitive responses, is tightly integrated not only in task conditions but also in the resting-state. The dorsal anterior cingulate cortex (dACC) is a key node of a large-scale network that is involved in self-referential processing and cognitive control. We investigated resting-state functional connectivity of the dACC and hypothesized that altered connectivity would be demonstrated in cortical midline structures involved in self-referential processing and cognitive control. Seed-based resting-state functional connectivity was analyzed in women with anorexia nervosa ($N=18$), women with bulimia nervosa ($N=20$) and age matched healthy controls ($N=20$). Between group comparisons revealed that the anorexia nervosa group exhibited stronger synchronous activity between the dACC and retrosplenial cortex, whereas the bulimia nervosa group showed stronger synchronous activity between the dACC and medial orbitofrontal cortex. Both groups demonstrated stronger synchronous activity between the dACC and precuneus, which correlated with higher scores of the Body Shape Questionnaire. The dACC-precuneus resting-state synchrony might be associated with the disorder-specific rumination on eating, weight and body shape in patients with eating disorders.

1. Introduction

Anorexia Nervosa (AN) is characterized by intense fear of gaining weight and relentless pursuit of thinness (American Psychiatric Association, 2013). The term ‘anorexia (lack of appetite)’ is misleading, as individuals with anorexia nervosa are preoccupied with food and exhibit inappropriate eating rituals (Kaye et al., 2009). In addition, excessive cognitive control traits such as perfectionism, distorted body image, and obsessive–compulsive personality are predisposing factors and persist after clinical recovery (Anderluh et al., 2003; Johnson et al., 2006). By contrast, subjects with Bulimia Nervosa (BN) are known to lack of impulse control and experience intense food craving, which likely results in binge-eating episodes (Moreno et al., 2009). However, it has not yet been determined whether AN and BN share a primary disturbance of cognitive control and what neural correlates underlie their different clinical presentations (Brooks et al., 2012).

Cortical areas supporting cognitive control and salience demonstrate different neural responses to visual food cues in patients with eating disorders compared to healthy individuals (García-García et al., 2013). Functional brain imaging studies have reported abnormal prefrontal neural responses in patients with anorexia nervosa applying symptom-provoking paradigms (Cowdrey et al., 2011; Brooks et al., 2011a; Uher et al., 2004). Previously we reported that women with anorexia nervosa demonstrate greater activations within the dorsal anterior cingulate cortex (dACC) while watching high-calorie food images and proposed that the dACC activations represent excessive cognitive control effort to restrain appetite as well as the ambivalence toward food (Kim et al., 2012). This top-down cognitive control network, which interacts with bottom-up appetitive responses, is tightly integrated not only in task conditions but also in the resting-state (Cole and Schneider, 2007).

Here, we expanded our focus and investigated the resting-state functional connectivity of the dACC in patients with AN and BN.

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Resting-state functional connectivity is based on the observation that spontaneous blood oxygen level dependent (BOLD) signal fluctuations among brain regions reflects intrinsic interactions between functionally correlated regions (Biswal et al., 1995). Therefore, the resting-state functional connectivity is not a reaction to external stimuli, but represents intrinsic properties of functional brain organization (Raichle et al., 2001). The ACC is a part of the default network, which exhibits high baseline metabolic activity at rest and is proposed to be associated with self-referential mental activity (Gusnard et al., 2001). Converging evidence suggests that self-referential processing is mediated by cortical midline structures, such as the ventromedial prefrontal cortex, dorsomedial prefrontal cortex, and the posterior cingulate cortex/precuneus (Northoff et al., 2006). Recent studies showed that resting-state functional connectivity between these brain regions involved in self-referential processing and cognitive control were disturbed in participants recovered from anorexia nervosa (Cowdrey et al., 2012). Taken together, we hypothesized that the resting-state functional connectivity between the dACC and other cortical midline structures would be altered in women with eating disorders and underlie their ruminative preoccupation of body image and weight. We performed a region of interest (ROI) seed-based functional connectivity analysis in order to investigate the intrinsic dACC neural network in women with anorexia nervosa and bulimia nervosa.

2. Method

2.1. Participants

The study participants consisted of 58 women (aged 20–35): 18 had a current diagnosis of anorexia nervosa (AN), 20 had a current diagnosis of bulimia nervosa (BN) and 20 were healthy control age-matched women (HC) who were in normal weight range (Table 1). The patients were recruited from an outpatient eating disorder clinic; healthy controls were volunteers from the local community. All participants were administered the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorder (First et al., 1996) by a psychiatrist (J.L.) to exclude those with current or past psychiatric disorders, traumatic brain injury, neurological illness, and other substance use disorder except for caffeine or nicotine, relevant visual defects or any radiological contraindications for MRI scanning. All participants were right-handed and were asked to complete psychometric self-reports, including the Eating Disorder Inventory-2 (Garner, 1991) to assess eating symptoms, and the Body Shape Questionnaire (Cooper et al., 1987) to assess the body image and concerns about body shape. This study was carried out under the guidelines for the use of human participants established by the Institutional Review Board at Severance Mental Health Hospital, Yonsei University. Following a complete description of the scope of the study to all participants, written informed consent was obtained.

2.2. MRI data acquisition and preprocessing

The participants were instructed to abstain from eating for 6 h preceding the MR scanning session, which began between 600 pm and 700 pm. Participants underwent a 5 min passive-viewing block scan, instructed to fixate on a white crosshair in the center of a black background screen, and refrain from any cognitive, lingual, or motor tasks as much as possible. Functional images were acquired on a 1.5 Tesla MRI scanner (General Electric, Milwaukee, WI) by using a gradient echo-planar imaging sequence (TR=2.5 s; TE=14.3 ms; flip angle=90; field of view=240 mm; 64 × 64 × 30 matrix with 3.75 × 3.75 × 5 mm^3 spatial resolution; 30 axial slices; and slice thickness=5 mm). A high-resolution anatomical dataset was obtained for each subject by using a fast spoiled gradient echo sequence (TR=8.5 s, TE=1.8 ms, flip angle=12, field of view=240 mm, 256 × 256 × 256 matrix with 0.94 × 0.94 × 1.5 mm^3 spatial resolution, 116 axial slices, and slice thickness=1.5 mm). Spatial preprocessing and statistical analysis of functional images were performed using SPM8 (Wellcome Trust Centre for Neuroimaging; http://www.fil.ion.ucl.ac.uk/spm). The first 7 time points in all the time series data were discarded to allow for T1 equilibrium effects. Motion artifacts were assessed in individual subjects by visual inspection of realignment parameter estimations to confirm that the maximum head motion in each axis was less than 2 mm and absent any abrupt head motion. Functional images were realigned and registered to structural images for each subject. The anatomical volume was then segmented into gray matter, white matter, and cerebrospinal fluid. The gray matter image was used for determining the parameters of normalization onto the standard Montreal Neurological Institute (MNI) gray matter template. The spatial parameters were then applied to the realigned functional volumes that were finally resampled to voxels of 2 × 2 × 2 mm and smoothed with an 8 mm full-width at half-maximum kernel.

2.3. Region of interest

To identify a seed region, we selected the cluster within the dACC ($x=-11$, $y=17$, and $z=32$), which exhibited significantly stronger activations in the AN group in response to high-calorie food images in our previous study (Kim et al., 2012). We defined a 5-mm radius sphere as a dACC seed for further functional connectivity analysis.

2.4. Functional connectivity analysis

The assessment of cortical networks was performed using a ROI seed-based correlation approach. The preprocessed fMRI data were temporally band-pass

Table 1
Demographic and clinical variables of subjects.

	AN (N=18)	BN (N=20)	HC (N=20)	F (t)	P	
Age (y)	25.2 ± 4.2	22.9 ± 3.9	23.3 ± 1.8	2.463	0.095	–
Education (y)	14.9 ± 1.5	15.5 ± 1.0	15.8 ± 0.4	2.937	0.061	–
BMI	16.0 ± 1.7	21.6 ± 2.3	19.9 ± 1.9	39.761	< 0.001	AN < BN,HC
Duration of illness (y)	3.8 ± 2.6	3.8 ± 4.7	NA	0.003	0.998	–
EDI score						
Drive for thinness	13.6 ± 6.2	16.3 ± 4.4	3.6 ± 3.7	35.061	< 0.001	AN,BN > HC
Bulimia	11.7 ± 5.4	12.2 ± 5.7	1.5 ± 1.5	30.525	< 0.001	AN,BN > HC
Body dissatisfaction	10.8 ± 4.5	19.6 ± 6.2	11.4 ± 9.0	10.398	< 0.001	BN > AN,HC
Ineffectiveness	15.0 ± 7.2	10.8 ± 7.6	2.6 ± 2.6	18.342	< 0.001	AN,BN > HC
Perfectionism	6.7 ± 4.3	9.2 ± 4.6	4.2 ± 2.7	7.765	0.001	BN > AN,HC
Interpersonal distrust	7.9 ± 5.4	5.7 ± 5.5	2.1 ± 3.1	6.817	0.002	AN > BN,HC
Interoceptive awareness	16.1 ± 6.9	13.8 ± 6.5	2.3 ± 2.2	31.129	< 0.001	AN,BN > HC
Maturity fears	10.7 ± 6.7	10.6 ± 5.6	3.4 ± 3.4	10.883	< 0.001	AN,BN > HC
Asceticism	9.4 ± 3.5	9.4 ± 4.3	3.9 ± 2.6	14.261	< 0.001	AN,BN > HC
Impulse regulation	10.9 ± 6.3	7.4 ± 5.8	2.6 ± 3.9	10.537	< 0.001	AN,BN > HC
Social insecurity	10.0 ± 5.6	8.7 ± 5.1	2.1 ± 2.0	15.177	< 0.001	AN,BN > HC
BDI score	25.7 ± 8.8	18.8 ± 9.5	7.5 ± 5.7	24.621	< 0.0001	AN > BN > HC
BAI score	21.7 ± 12.9	16.6 ± 10.5	7.1 ± 6.3	10.913	< 0.0001	AN,BN > HC
BSQ score	129.5 ± 35.7	146.1 ± 27.6	89.4 ± 28.8	17.929	< 0.0001	AN,BN > HC

AN: anorexia nervosa, BN: bulimia nervosa, HC: healthy control, BMI: body mass index, EDI: eating disorder inventory, BDI: beck depression inventory, BAI: beck anxiety inventory, and BSQ: body shape questionnaire.