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Anatomical Characteristics of the Cerebral Surface in Bulimia Nervosa

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ABSTRACT

BACKGROUND: The aim of this study was to examine morphometric features of the cerebral surface in adolescent and adult female subjects with bulimia nervosa (BN).

METHODS: Anatomical magnetic resonance images were acquired from 34 adolescent and adult female subjects with BN and 34 healthy age-matched control subjects. We compared the groups in the morphological characteristics of their cerebral surfaces while controlling for age and illness duration.

RESULTS: Significant reductions of local volumes on the brain surface were detected in frontal and temporoparietal areas in the BN compared with control participants. Reductions in inferior frontal regions correlated inversely with symptom severity, age, and Stroop interference scores in the BN group.

CONCLUSIONS: These findings suggest that local volumes of inferior frontal regions are smaller in individuals with BN compared with healthy individuals. These reductions along the cerebral surface might contribute to functional deficits in self-regulation and to the persistence of these deficits over development in BN.

Keywords: Bulimia nervosa, Eating disorders, Frontal cortex, Frontostriatal, MRI, Surface morphology

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Bulimia nervosa (BN) typically begins in adolescence, primarily affects female individuals, and is characterized by recurrent episodes of binge-eating that are accompanied by a sense of loss of control and followed by self-induced vomiting or another compensatory behavior to avoid weight gain (1,2). Mood disturbances and impulsive behaviors are also common in persons with BN, suggesting the presence of pervasive difficulties in behavioral self-regulation (2).

Our previous functional neuroimaging findings from adult women with BN suggest that their failure to engage frontostriatal circuits might contribute to their impaired capacity for self-regulation (3). Our findings from adolescent girls with BN suggest that this circuit-based dysfunction arises early in the course of illness and is therefore unlikely to be an effect of chronic illness (4). We do not know, however, whether anatomical abnormalities in these circuits are associated with deficient frontostriatal functioning in BN or contribute to illness persistence.

Previous anatomical imaging studies of individuals with BN are sparse. Findings from voxel-based morphometric studies of adults with BN vary; some suggest larger gray matter volumes of the orbitofrontal cortex (5,6) and ventral striatum (6), and others suggest no differences in global or regional gray matter volumes (7) in BN compared with control participants. Finer-grained approaches to assess and spatially localize structural abnormalities, such as measures of cortical thickness and morphological assessment of the cerebral surface, have not been applied to anatomical data collected from individuals with BN. In addition, no prior studies have assessed brain structure in adolescents with BN.

With methods previously used to assess brain morphology in various psychiatric disorders (8–11), we compared morphological measures of the cerebral surface across adolescent and adult female subjects with BN and age-matched healthy participants. On the basis of our previous functional findings, we suspected that, relative to healthy participants, those with BN would show reductions in local volumes within the surface of the frontal lobe. In exploratory analyses, we assessed group differences in the age correlates of surface measures and whether abnormalities in the frontal regions of individuals with BN were associated with measures of BN symptom severity or with deficits in self-regulatory control, as measured by cognitive interference on a Stroop task (12) performed outside of the magnetic resonance imaging (MRI) scanner.

METHODS AND MATERIALS

Participants

The sample consisted of 34 adolescents and adults with BN and 34 age-matched control participants who participated in our functional magnetic resonance imaging (fMRI) studies (3,4). Those with BN were recruited through flyers posted in the local community and internet advertisements (e.g., craigslist.com and eating disorder-specific websites) and through the Eating Disorders Clinic at the New York State Psychiatric Institute, where they were receiving treatment. Control participants were recruited through flyers and internet advertisements. All participants were female subjects, group-matched

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by age and body mass index. Those with a history of neurological illness, past seizures, head trauma with loss of consciousness, mental retardation, pervasive developmental disorder, or current Axis I disorders (other than major depression for the patients) were excluded. Control subjects also had no lifetime Axis I disorders. Formal diagnoses of BN and comorbid neuropsychiatric diagnoses were established with standard adult and child measures (Supplement 1). All participants received monetary compensation for their participation. The Institutional Review Board of the New York State Psychiatric Institute approved this study, and all participants gave informed consent.

MRI Acquisition

The MRI scans were acquired on a GE Signa 3 Tesla whole-body scanner (GE Medical Systems, Waukesha, Wisconsin) with a body transmitter coil and an eight-channel head receiver coil. High-resolution, T1-weighted images were acquired with a fast spoiled gradient-recall three-dimensional pulse sequence: inversion time = 500 msec, echo time = 1.3 msec, repetition time 4.7 msec, 2 excitations, matrix size = 256 × 256, field of view = 25 cm, flip angle = 11, number of slices = 164, slice thickness = 1 mm encoded for sagittal slice reconstruction, providing voxel dimensions of .976 × .976 × 1.0 mm.

Image Processing

Morphometric analyses were conducted blind to participant characteristics and hemisphere (images were randomly flipped in the transverse plane before preprocessing) on Sun Ultra 10 workstations with ANALYZE 9.0 (Rochester, Minnesota).

Preprocessing. Large-scale variations in image intensity were corrected (13), and extracerebral tissues were removed by an automated tool (14) before connecting dura was removed manually on each sagittal slice and checked in orthogonal views.

Cortical Gray Matter Segmentation. Gray-scale values of "pure" representations of cortical gray and white matter were sampled bilaterally in frontal, temporal, occipital, and parietal regions with an 8 × 8 = 64 pixel array that was sufficiently large enough for statistical stability but small enough to avoid partial volume effects from other tissue types. These four values were averaged for each tissue type, and a threshold value (halfway between the gray and white matter values) was applied to each slice in the imaging volume to provide an initial classification of gray and white matter that was then hand edited in coronal and transverse views. The intraclass correlation coefficient, calculated with a two-way random-effects model (15) as a measure of reliability of our segmentation procedures, was .98.

Choice of Template Brain. We applied a rigorous two-step procedure to select template brain most representative of our control sample (16). We first selected as a preliminary reference the brain of a healthy participant who was representative of the control sample by age, weight, and height. The brains of the other control participants were coregistered to this preliminary template. Point correspondences on cortical surfaces were determined, and we computed the distance from the template surface for each of the corresponding points on the surfaces of the brains of all the other control participants. The brain for which all points across the surface were closest to the average of least squares distances was selected as the final template. Brains then underwent a second coregistration to this template. We used a single template rather than an averaged brain, because it has well defined-tissue interfaces (e.g., cerebrospinal fluid/gray matter or gray/white matter). Averaging images for a template would blur these boundaries, thereby increasing registration errors that could contribute to subtle group differences in morphology.

Morphological Maps of the Cerebral Surface. Detailed descriptions and validation of our methods used to analyze morphological features of the cerebral surface are provided elsewhere (16–18). Briefly, the random flips were first reversed to provide their correct left-right orientation. With a similarity transformation on the basis of mutual information of gray scale values, each brain was coregistered to the template brain such that the cerebral surfaces were moved to a close approximation of the template surface. We then applied to each brain a high-dimensional, nonlinear warping algorithm so that its gray scale intensities matched those of the template brain point by point across the entire cerebrum (11,16–18) providing a point-wise labeling of the correspondences of the cortical surfaces across all brains in the sample. The high-dimensional, nonlinear warp was then reversed, bringing the labels for point correspondences of the cerebral surface back to the close approximation established by the similarity transformation.

Surface Distances/Local Volumes. Signed Euclidian distances from corresponding points across the cerebral surfaces for each participant to corresponding points on the template surface were calculated and subjected to statistical modeling at each voxel. These distances were positive for outward deformations (protrusions) and negative for inward deformations (indentations) of the surface of each participant relative to the template. Thus, indentations or protrusions along the surface were interpreted as representing greater or smaller local volumes, respectively, of brain tissue along those surfaces.

Cortical Thickness. We masked out the cortical mantle from the coregistered brain of each participant. A three-dimensional morphological operator then distance-transformed each brain without the cortex from the same coregistered brain containing the cortex (19), calculating cortical thickness as the smallest distance of each point on the cortical surface from the outermost surface of white matter in the coregistered brain. Because these thicknesses were scaled for whole brain volume (WBV), the values inherently accounted for general scaling effects and interindividual differences in WBV.

Stroop Interference

Stroop interference, measured outside the scanner with the standard format of the task (20) (Supplement 1), was used for