Archival Report

Anatomical Characteristics of the Cerebral Surface in Bulimia Nervosa

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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.

Key Words: Bulimia nervosa, eating disorders, frontal cortex, frontostriatal, MRI, surface morphology

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 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 at 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 correlation analyses with measures of surface morphology. Because the adult (3) and adolescent (4) fMRI participants performed different versions of the Simon task, those behavioral or fMRI data could not be used in these correlation analyses. We therefore used Stroop data, because the Stroop and Simon tasks elicit similar patterns of frontostriatal activations during the engagement of self-regulatory control in healthy individuals (21).

**Statistical Analyses**

We used general linear modeling to compare the participants with and without BN in cortical morphology. Each imaging measure (Euclidian distances or cortical thickness) was subjected to statistical modeling at each voxel of the template brain with age as a covariate. The p values were corrected for multiple comparisons with a false discovery rate of .05, color-coded and plotted for each voxel on the cerebral surface. In exploratory analyses, we assessed the significance of correlations of distances over the entire cerebral surface with BN symptom severity in the BN group while covarying for age and illness duration and compared groups in their patterns of correlations with age and with Stroop interference at each voxel across the cerebral surface.

**Results**

**Participants**

Analyses include data from 34 BN and 34 healthy participants, including 16 BN and 16 healthy adolescents (≤ 19 years). All were right-handed. The BN participants included five inpatients
scanned within 1 month of admission and eight outpatients; the remaining BN participants were not seeking treatment (n = 11) or no longer receiving treatment in our clinic (n = 10), but all were symptomatic. Six presented with subclinical BN, with <8 (2 x/week) objective bulimic episodes (n = 2), vomiting episodes (n = 2), or objective bulimic and vomiting episodes (n = 2) over the past 28 days before participation. None met criteria for major depressive disorder or attention-deficit/hyperactivity disorder. Ten had a prior diagnosis of anorexia nervosa. Twelve were taking selective serotonin reuptake inhibitors (SSRIs) at the time of scan.

Group Differences in Morphology of the Cerebral Surface

The WBV did not differ across the BN and control groups, either unadjusted (BN vs. control: 1291.7 ± 131.8 vs. 1310 ± 130.7 cm³, t_{66} = −5.7, p = .05) or adjusted for age and BMI (1289.9 ± 25.9 vs. 1312 ± 25.9 cm³, t_{66} = .52, p = .47). Nevertheless, the BN group had significant reductions in local volumes of bilateral middle frontal (MFG) and precentral gyri (PreCG), right postcentral gyrus (PoCG), and lateral superior (SFG) and inferior frontal gyri (IFG) of the left hemisphere (Figure 1). Analyses of white matter demonstrated that these reductions on the cerebral surface of the frontal lobe in the BN group derived primarily from reductions of underlying white matter (Figure 2). Reductions were also detected in temporoparietal areas, including bilateral inferior temporal gyrus, right superior parietal gyrus (SPG) and cuneus, as well as bilateral posterior cingulate cortices (PCC), left precuneus, and fusiform gyrus. In addition, enlargements were detected in bilateral middle/ inferior occipital and lingual gyrus and right inferior parietal lobule (IPL) in the BN versus control groups, deriving from enlargements in underlying white matter (Figure 2).

Group Differences in Cortical Thickness. Scattered reductions in cortical thickness in bilateral dorsal and lateral frontal, parietal, and posterotemporal cortices in the BN versus control groups (Figure S1 in Supplement 1) were consistent with the locations of group differences in cortical morphology.

Correlations with Symptom Severity and Impulsivity. Within the BN group, we detected significant inverse associations of cerebral surface morphology with log transformed (22) objective bulimic and vomiting episodes in bilateral IFG, PreCG, and PoCG (Figure 3; Figure S2 in Supplement 1). Scatterplots of these associations suggested greater reductions of these areas in those who engaged in the most episodes within 28 days before scanning. Inverse associations with participant ratings of their preoccupation with shape and weight in bilateral IFG, right PoCG, and left MFG (Figure S3 in Supplement 1) suggested greater reductions in the most preoccupied BN participants. Impulsivity in the BN group, measured with three items targeting impulsivity on the attention-deficit/hyperactivity disorder rating scale, correlated inversely with surface morphology in left IFG and medial temporal gyrus (MTG) (Figure S4 in Supplement 1).

Effects of Age and Illness Duration. Significant diagnosis × interactions on cortical surface morphology were detected in MFG and IFG of the left hemisphere and in the PoCG of the right hemisphere (Figure 4). Scatterplots of these interactions indicated that age correlated significantly and inversely with local volume reductions in the BN but not the control group in these brain areas. Diagnosis × age interactions were also detected in bilateral IPL such that age correlated inversely with reductions in the control but not the BN group. Separate maps of age effects in each group revealed that age correlated inversely with reductions in right IFG and MFG in control subjects and in large expanses of bilateral inferior frontal/parietal regions in the BN group (Figure S5 in Supplement 1). Because age and illness duration were significantly intercorrelated in the BN group (r = .89; p = .001), we controlled for illness duration effects on surface morphology with a subgroup of 21 BN participants in whom age and illness duration were uncorrelated (r = .36; p = .10) and a subgroup of 18 age-matched control subjects. Diagnosis × age interactions remained in left IFG and MFG and were additionally detected in left PreCG, MTG, superior temporal gyrus (STG), right IFG, as well as right cingulate (CG) and left SFG (Figure S6 in Supplement 1) on the mesial surface; age correlated inversely with reductions in

![Figure 1](image1). Maps of group differences in morphological measures of the cerebral surface. The signed Euclidean distances between points on the surfaces of the cortex for each participant and corresponding points on a template brain were compared statistically between the bulimia nervosa (BN) and control groups with linear regression at each voxel on the surface while covarying for age. Warm colors indicate significantly larger distances (local enlargements, outward deformations) in the BN versus control group; cool colors (blue and purple) indicate reduced distances (local indentations, inward deformations) in the BN versus control group. The color bar indicates p values corrected for multiple comparisons with a false discovery rate of p < .05. The BN group brains were significantly reduced bilaterally in medial frontal (MFG) and precentral gyri (PreCG), in superior (SFG) and inferior frontal gyri (IFG) of the left hemisphere, the postcentral gyrus (PoCG) of the right hemisphere, and bilateral temporoparietal areas (p values = .01–.0001). Cu, cuneus; FG, fusiform gyrus; IPL, inferior parietal lobule; ITG, inferior temporal gyrus; LG, lingual gyrus; OCC, occipital cortex; PCC, posterior cingulate cortex; PreCG, precuneus; SPG, superior parietal gyrus.

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the BN but not the control subgroup in these areas. Age also correlated inversely with reductions in right IPL and positively with enlargements in right SFG in the BN but not the control subgroup (Figure S6 in Supplement 1). Illness duration in the BN subgroup correlated inversely with reductions in right IFG, bilateral MFG, IPL, occipital cortices, and CG (Figure S7 in Supplement 1).

Interactions of Diagnosis × Stroop Interference. The BN and control groups performed similarly on the Stroop task (Table S1 in Supplement 1). Nevertheless, significant interactions of diagnosis × Stroop interference scores on surface morphology were detected in the IFG, MTG, and STG on the lateral surface of the left hemisphere; Stroop interference correlated inversely with reductions in the BN but not the control group (Figure 5).

Medication and Comorbidity Effects. After including current SSRI treatment as an independent variable in a separate linear regression, local reductions in bilateral frontal cortices in the BN group remained unchanged from those depicted in Figure 1 (Figure S8 in Supplement 1), indicating that SSRI treatment did not have an appreciable effect on our findings. Likewise, neither a history of anorexia (Figure S9 in Supplement 1) nor current depressive symptoms (Figure S10 in Supplement 1) contributed to our findings.

Discussion

Significant reductions in local volumes of the cerebral surface in individuals with BN predominated in frontal and temporoparietal

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**Figure 2.** Group differences in surface measures of white matter. Shown here are color-coded maps comparing surface distances of white matter at each corresponding voxel of the brain of each participant from the corresponding voxel of the white matter surface in the template brain. The pattern of differences across groups is similar to the pattern of statistical significance of those differences depicted in the maps of p values comparing surface measures on the cerebral surface across groups (Figure 1), particularly in frontal regions on the lateral surface. These analyses suggest that the observed regional reductions of the cerebral surface in the BN group derived primarily from reductions in underlying white matter. Abbreviations as in Figure 1.

**Figure 3.** Correlations of cerebral surface morphology with objective bulimic episodes in the BN group. Warm colors (red and yellow) indicate positive correlations, and cool colors (blue and purple) indicate inverse correlations between surface measures and objective bulimic episodes within the past 28 days before magnetic resonance imaging scan. Logarithmic transformations were used to reduce excessive skewness in this frequency variable. Surface distances (in millimeters from the corresponding point of the template brain), adjusted for age and duration of illness, are plotted on the y axis, and log transformed objective bulimic episodes are plotted on the x axis. The scatterplots show greater reductions (larger indentations) in bilateral IFG, PreCG, and PoCG with more severe symptoms. Abbreviations as in Figure 1.
regions, including bilateral MFG and PreCG, SFG and IFG on the lateral surface of the left hemisphere, and bilateral inferior temporal gyri on the ventral surface. On the medial surface, reductions were detected in right fusiform, SPG, and cuneus, left precuneus, and bilateral PCC. Greater reductions in bilateral inferior frontal cortices were detected in the BN participants who engaged in the most objective bulimic and vomiting episodes and in those who were the most preoccupied with shape and weight. Significant diagnosis × age interactions indicated that reductions in MFG and IFG of the left hemisphere and in the PoCG of the right hemisphere became more prominent with advancing age in the BN but not the control participants. Conversely, interactions with age in bilateral IPL indicated age-related volume reductions that were more prominent in the healthy than in the BN participants, consistent with the overall enlargement of the right IPL in the BN versus control group. Analysis of a BN subgroup revealed that reductions in right but not left IFG and in bilateral IPL and CG were associated with illness duration rather than age. Significant interactions of diagnosis with Stroop interference scores in IFG, MTG, and STG of the left hemisphere suggested that greater Stroop interference accompanied greater regional reductions, consistent with the interactions with age at these locations.

Our previous fMRI findings from adult (3) and adolescent (4) female subjects indicated deficient activation of frontal areas compared with age-matched control participants during performance of a self-regulatory task. The current findings suggest that morphological abnormalities, specifically reductions in local volumes of inferior frontal lobes, are associated with and might underlie these deficits in self-regulation that characterize individuals with BN and likely contribute to their impaired control over feeding and other behaviors. These reductions were detected in bilateral MFG and PreCG and left IFG, consistent with a previous report of significantly lower T1 relaxation times in BN versus control participants in inferior frontal gray matter (23). Inverse associations of objective bulimic and vomiting episodes with surface measures were detected in bilateral IFG, PreCG, and PoCG, suggesting that reductions in bilateral frontal cortices might be required for individuals to manifest the greatest loss of control over feeding behaviors and therefore the most severe BN symptoms. Inverse correlations of surface measures with

![Figure 4](image1.png)

**Figure 4.** Correlations of surface morphology with age in the BN versus control groups. Reductions in lateral IFG and MFG of the left hemisphere and PoCG of the right hemisphere correlated inversely with age in the BN but not the healthy participants, producing significant diagnosis × age interactions (p values = .01–.001). Reductions in IPL, bilaterally, correlated inversely with age in the healthy but not the BN participants, producing significant diagnosis × age interactions. Surface distances (in millimeters from the corresponding point on the surface of the template brain) are plotted on the y axis. Abbreviations as in Figure 1.

![Figure 5](image2.png)

**Figure 5.** Correlations of surface morphology with Stroop interference scores in the BN versus control groups. Surface distances (in mm from the corresponding point on the surface of the template brain), adjusted for age, are plotted on the y axis. Reductions in the left inferior frontal gyrus (IFG) correlated inversely with Stroop interference scores in the participants with BN (r = -.7), producing significant diagnosis × Stroop interactions. Scatterplots suggest that greater interference was associated with greater reductions of these regions in the BN group. MTG, medial temporal gyrus; STG, superior temporal gyrus.
participant ratings of their preoccupation with shape and weight were detected in right PreCG, left MFG, and bilateral IFG, indicating the degree of reduction was related to the severity of the shape/weight concern characteristic of BN. The right IFG typically activates during successful response inhibition in healthy individuals (24–26) and is therefore implicated in supporting the capacity for self-regulatory control. Individuals with BN, however, either deactivate (4) or activate IFG less than control participants (3) during a task of self- regulatory control. Although the relationship between structure and function is far from clear, we suspect that both structural and functional deficits in this ventral (inferior frontal) attentional (27) and regulatory system are centrally involved in the pathogenesis of BN.

We also detected volume reductions in left precuneus, right cuneus, and SPG on the medial surface that derived primarily from reductions in underlying white matter, consistent with recent findings of reduced white matter in women with BN in right temporoparietal areas compared with control participants (5). Those findings were interpreted on the basis of insula-related brain circuitry in eating disorders, given the fiber paths that connect temporal areas with the insula and PFC (28). We did not assess insular morphology, but insula circuit-based abnormalities—including white matter reductions in connected temporal regions—might contribute to altered self-perceptions (29,30) of body image in BN. Both precuneus (31) and PCC are implicated in self-awareness and mental imagery about the self, constituting part of the default mode network (DMN) of brain areas that activate during engagement in internally driven thoughts (32).

We previously detected DMN deactivations in BN adolescents when performing a regulatory control task (4), a finding we attributed to their allocating attention to internally driven thoughts about eating or body image that preoccupy individuals with BN. Thus, volume reductions in these areas might contribute, in part, to excessive DMN deactivation during fMRI task performance and the tendency of BN adolescents to attend to internally driven thoughts. However, task-related deactivation of DMN is analogous to its activation when engaged in internally driven thoughts, so such thoughts would likely produce activity-dependent hypertrophy rather than the reductions in precuneus and PCC we observed in the BN group. In addition, ratings of preoccupation with shape/weight did not correlate with reductions in precuneus or PCC, a finding that would suggest hypoplasia rather than hypertrophy in those who engaged most in internally driven thoughts about their bodies. Thus, unlike our findings of reductions in inferior frontal cortices, reductions in precuneus and PCC are either unassociated with functional deficits in BN or, if associated, not detected herein.

Regional reductions of left MFG and IFG and right PoCG correlated inversely with age in the BN but not healthy participants (Figure 4). After controlling for illness duration in the BN group, these inverse age correlations remained in left IFG and MFG and were additionally detected in right IFG and CG, left PreCG, SFG, MTG, and STG (Figure S6 in Supplement 1). These reductions became more prominent with age in the BN but not the control group and might represent an abnormal developmental trajectory in BN, such as accelerated gray matter loss, axonal pruning, or reduced myelination. Illness duration was associated with reductions in bilateral occipital cortices and IPL and in right but not left IFG and CG. Reductions in left IFG, MTG, and STG correlated inversely with Stroop interference in the BN but not the control group, suggesting that these reductions might have functional consequences for individuals with BN, contributing to their inability to self-regulate their feeding and other behaviors. Stroop interference did not differ between the BN and control groups, consistent with previous behavioral findings (33–35). Thus, our interpretation of these brain–behavior associations were not confounded by group differences in performance (36). Right frontal activations during Stroop performance increased over development in healthy individuals (25), consistent with the late maturation of frontal cortex (37) and right hemisphere dominance over attentional control (38). Abnormal maturation of left but not right frontal cortex, perhaps due to reduced myelination, could therefore contribute to the inefficiency of these brain regions in the service of self-regulation over development in BN.

We previously speculated that deficient frontostriatal activation in individuals with BN might contribute to their general impulsivity and inability to regulate feeding and other impulsive behaviors (39,40), such as substance abuse (41) and self-harm behaviors (42). Impulsivity correlated inversely with surface morphology in left IFG and PreCG and bilateral MFG (Figure S4 in Supplement 1). Healthy individuals engage both right (24–26) and left (43) IFG during successful response inhibition on fMRI measures of impulsivity in healthy individuals. Our fMRI findings suggest that both adolescents and adults with BN fail to activate right IFG, but adolescents deactivate left IFG during successful response inhibition. Perhaps functional and anatomical abnormalities in left inferior frontal cortices arise early in the course of BN and are associated with the greater impulsivity in BN versus healthy adolescents (44), consistent with the effects of illness duration detected in right IFG. These effects were also detected in right MFG and CG (Figure S7 in Supplement 1), suggesting that additional reductions in right frontal regions might be due to chronic illness. Future longitudinal imaging studies of adolescents with BN, beginning at illness onset, are required to further disentangle the effects of age and illness duration on the structural and functional maturation of frontal cortices in BN.

Magnetic resonance imaging cannot directly inform our understanding of the cellular changes (e.g., synaptic pruning, myelination) that contribute to brain development. However, our additional analyses of white matter suggested that the reductions in frontal brain volumes in the BN group derived primarily from reductions in underlying white matter (i.e., the reductions in frontal volumes [Figure 1] were detected in the same locations as those detected on white matter [Figure 2]). Healthy brain development involves both increases in synaptic pruning and myelination over adolescence and young adulthood (45). Greater synaptic pruning over development in BN compared with healthy individuals would manifest as greater reductions in frontal gray matter with increasing age in BN and more efficient processing. More axonal pruning or less myelination, in contrast, would contribute to reductions in white matter with increasing age in BN and less efficient processing, consistent with fMRI findings from these BN participants. Future longitudinal diffusion tensor imaging studies could confirm the presence of age-related reductions in white matter and offer an additional explanation for impaired self-regulation during development in BN, because myelination is thought to enhance the speed of the transmission of information and, hence, age-related improvements in cognition (45).

Although the largest anatomical study and only study of the morphological features of the cerebral surface in individuals with BN to date, this study is limited nevertheless by a modest sample size and cross-sectional design. In addition, our BN sample was heterogeneous in symptom severity, and participants were at differing stages of treatment. Moreover, we did not account for...
menstrual status, which can affect neural functioning in women (46), but we have no reason to suspect that menstrual status differed systematically across the BN and control groups to confound our findings.

Future longitudinal studies comparing brain development in BN and healthy adolescents, beginning at illness onset, are required to determine whether our cross-sectional findings of age-related reductions in inferior frontal volumes represent neurodevelopmental abnormalities in BN or effects of chronic illness on brain structure. Inclusion of a group of individuals with anorexia nervosa in such a study would allow assessment of how brain maturation differs across eating disorders. Identification of atypical neurodevelopmental trajectories in the structure/function of inferior frontal cortices in BN would then warrant development of early interventions aimed at bolstering their functioning. Finally, future studies should analyze the surface morphology of striatal structures in BN to determine whether reductions or enlargements in the dorsolateral putamen, for example, could contribute to functional abnormalities in habit learning (47), thereby explaining why the binge-eating behaviors in BN tend to crystalize into maladaptive habits.

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