Voxel-Based Morphometry Study of Gray Matter Abnormalities in Neurodegenerative Disease with Obsessive-Compulsive Behaviors

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ABSTRACT

Objectives : Obsessive-compulsive(OC) symptoms have yet to be directly studied in neurodegenerative conditions involving behavioral changes. To examine regional abnormalities in the brains of dementia patients with OC symptoms, we assessed the gray matter density using voxel-based morphometry(VBM).

Methods : We performed brain magnetic resonance imaging(MRI) with VBM analysis in 106 dementia patients with OC behaviors. In this study, OC behaviors were investigated in patients with neurodegenerative disease using the modified Manchester Behavior Questionnaire.

Results : The OC behavior scores were correlated with structural brain volume using VBM. The total OC symptom score correlated negatively with the volume of both putamens, the right middle orbitofrontal gyrus, both anterior cingulate cortices, and the left insula($p < 0.001$, uncorrected). No gray matter reductions were associated specifically with the OC symptom sub-categories.

Conclusions : Our results suggest that abnormalities in these brain regions may play an important role in the pathophysiology of OCD in neurodegenerative disease. This is the first lesion study to investigate the neural basis of OCD behaviors in neurodegenerative disease.

KEY WORDS : Dementia · Obsessive-compulsive symptoms · Voxel-based morphometry(VBM).

INTRODUCTION

Obsessive-compulsive disorder(OCD) is a disabling psychiatric disorder characterized by intrusive thoughts and ritualistic behaviors. Obsessions are persistent, intrusive, and inappropriate thoughts, impulses, or images that are distressing for the patient. Compulsions are repetitive behaviors or mental acts that a person feels driven to perform, which are generally aimed at reducing the distress caused by the obsessions.

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The pathophysiologic basis of OCD has not yet been clearly delineated. However, several studies have investigated the pathophysiology of OCD in relation to the frontal-subcortical circuits.[1)] In particular, the orbitofrontal and anterior cingulate regions have been hypothesized to play an important role in producing the symptoms associated with the disorder.[2-5)]

A recent study by Valente et al. reported increased gray matter volume in the orbitofrontal cortex(OFC) in patients with OCD,[6)] whereas Pujol et al. reported that the gray matter volume was reduced in the medial frontal gyrus, the medial OFC, and the left insulo-opercular region in these patients.[7)] Valente et al. also performed whole brain correlations between gray matter volume and symptom dimension scores and found significantly increased gray matter volume in OCD subjects relative to control subjects in posterior orbitofrontal and parahippocampal regions and decreased gray matter volume in OCD

patients in the left anterior cingulate cortex(ACC).[6] Functional neuroimaging studies have revealed that several brain structures in OCD patients have abnormal functional activity.

Obsessive-compulsive(OC) symptoms frequently appear in dementia, including Alzheimer's disease, frontotemporal lobar degeneration(FTLD), and corticobasal degeneration(CBD). However, there have been few studies examining the correlation between OC symptoms and dementia. Destee and colleagues have previously reported an association between OC behaviors and progressive supranuclear palsy(PSP).[8] OC behaviors have also been reported to have associations with a number of other neurologic conditions including Huntington's disease,[9] basal ganglia lesions,[10] and damage to the caudate nuclei.[11] We can presume that the OC symptoms in dementia arise from damage in the circuits that run through the striatum, ACC, and OFC, as OCD does. In frontotemporal dementia (FTD), for example, patients demonstrate repetitive, stereotyped behaviors such as motor mannerisms, repeated use of a phrase or saying, and complex behavioral routines.[12,13] A disease process such as FTD that involves the insula and OFC could lead to obsessive-compulsive symptoms via several mechanisms. Idiopathic OCD usually begins in adolescence and then has a waxing and waning course over the individual's lifetime, whereas the later onset of OCD should raise suspicion for an underlying neurodegenerative disorder.[9]

Voxel-based morphometry(VBM) is a neuroimaging approach that assesses differences in gray matter volume across the whole brain between groups of subjects.[14] There have been a few studies that have used VBM to assess whole brain regional gray matter volumes in OCD patients.[6,7,15] However, contradictory reports exist.[16]

In the present study, we applied VBM methods to investigate structural abnormalities associated with OC symptoms in patients with neurodegenerative disease. VBM methodology has permitted investigators to examine regional differences in gray matter density across the entire brain. We hypothesized that patients with OC symptoms would show volumetric abnormalities in specific regions, including the orbitofrontal and cingulate cortices, as well as in some subcortical areas.

METHODS

1. Subjects

A total of 106 patients diagnosed with one of six neurodegenerative diseases were recruited into the study from the University of California San Francisco Memory and Aging Center. Criteria for including patients were a diagnosis of dementia, the availability of modified Manchester Behavior Questionnaire (MBQ) data, and a high quality research magnetic resonance imaging(MRI) scan performed within six months of the modified MBQ assessment. The study subjects included 23 patients who met the Neary criteria for the FTD variant of FTLD,[17] 15 with the semantic dementia variant of FTLD,[18] and five with the progressive non-fluent aphasia(PNFA) variant of FTLD.[19] In addition to the FTLD patients, 45 subjects had Alzheimer's disease(diagnosed according to the National Institute of Neurological Disorders and Stroke-Alzheimer Disease and Related Disorders Association(NINDS-ADRDA) criteria),[20] 13 had CBD,[21] and five had PSP, diagnosed according to the Litvan criteria.[22] Patient diagnosis was made by a multidisciplinary team consisting of neurologists, neuropsychologists, psychiatrists, and nurses who performed extensive behavioral, neuropsychological, and neuroimaging assessments. Patients from diverse diagnostic groups with a variety of OC symptom scores and patterns of gray matter atrophy were included to provide variability in the sample and thus increase the power of the correlation analysis. All subjects and their informants/caregivers signed an Institutional Review Board-approved research consent form to participate in the study. Patients seen at the clinic represented a broad sample of the population in terms of ethnicity, sex, education level, and socioeconomic status, and an attempt was made to recruit all available consecutive patients for this study. Subjects' demographic characteristics can be seen in Table 1. Patients' mean age was 63.4 years[standard deviation(SD)=9.0], and they averaged 16(SD=2.6) years of education. There were 72 males and 51 females, and the patients' mean Clinical Dementia Rating(CDR) score was 0.9(SD=0.6). Variables such as age, sex, years of education, Mini-Mental State Examination(MMSE) scores, and total intracranial volume(TIV) were included as covariates in all analyses.

2. Obsessive-Compulsive(OC) symptom assessment

OC behaviors were assessed using the modified MBQ. The MBQ is a semistructured questionnaire covering the basic and social emotions, social behavior, responses to sensory stimuli, eating and other oral behaviors, wandering behaviors, sexuality, sleep patterns, repetitive behaviors, compulsions and rituals, environmental dependency, memory and spatially related behaviors, and delusions and hallucinations.[23] Seven subscales of the modified MBQ were selected for the assessment of OC behaviors in dementia. Each item has a description of the behavior to assist caregivers in their evaluations. Repetitive themes are described as "repeats or sticks to the same theme in conversation" ; adherence to daily routine is described as "sticks to a strict timetable for ordinary daily activities" ; counts objects as "counting things" ; aligns/arranges as "always arranges or sorts objects/belongings in a certain way" ; overconcern with cleanliness as "more/overly concerned

Table 1. Demographic and clinical characteristics of dementia patients with obsessive-compulsive symptoms

	% of symptoms	AD (n=45)	FTD (n=23)	SD (n=15)	PPA (n=5)	CBD (n=13)	PSP (n=5)	ALL (n=106)	Overall F(df)	p-value
Age		68.5±11.2	61.9± 9.2	66.5±8.0	70.6±11.2	69.9±5.8	73.2±2.6	67.3±9.9	5.072(5)*	0.003
M/F		28/17	12/11	7/8	2/3	5/8	4/1	58/48	χ^2=4.589(5)	0.468
Education		16.0±3.2	16.0±2.2	15.9±2.5	13.6±2.2	14.9±1.8	18.0±2.8	15.8±2.8	1.708(5)	0.140
MMSE		18.3±8.1	22.6±8.3	19.7±10.0	23.8±4.8	21.8±7.4	23.2±5.0	20.4±8.2	1.307(5)	0.267
OCD Total	82.1%(87/106)	4.7±4.7	10.4±8.5	7.9±6.4	4.6±4.8	7.7±6.9	3.6±1.3	6.7±6.5	3.594*(5)	0.015
M 67	48.1%(51/106)	1.2±1.6	2.8±1.7	1.8±1.8	0.6±1.3	1.2±1.7	0.4±0.9	1.5±1.8	4.115*(5)	0.002
M 71	46.2%(49/106)	0.7±1.2	2.5±2.0	1.8±1.6	1.8±2.0	1.1±1.7	1.4±1.5	1.4±1.7	3.325*(5)	0.026
M 72	13.2%(14/106)	0.1±0.5	1.1±1.8	0.7±1.5	0.4±0.9	0.2±0.8	0±0	0.4±1.1	N/A	N/A
M 73	34.9%(37/106)	1.1±1.7	1.2±1.6	1.1±1.7	0.4±0.9	1.4±1.4	0.2±0.4	1.1±1.6	2.679*(5)	0.046
M 74	18.9%(20/106)	0.2±0.8	0.7±1.3	0.3±0.7	0.4±0.9	0.8±1.0	0.2±0.4	0.4±0.9	0.858(5)	0.525
M 76	32.1%(34/106)	0.7±1.4	1.1±1.6	1.4±1.8	1.0±1.4	1.2±1.8	0.8±1.3	1.0±1.5	0.650(5)	0.662
M 77	30.2%(32/106)	0.7±1.3	1.2±1.7	0.7±1.4	0±0	1.8±2.1	0.6±0.9	0.9±1.5	N/A	N/A

Values are listed as mean ± standard deviation. Derived from Welch's ANOVA due to positive Levine's test suggesting inhomogeneity of variance. ∗ : $p<0.05$. AD : Alzheimer's disease, FTD : frontotemporal dementia, SD : semantic dementia, PPA : primary progressive aphasia, CBD : corticobasal degeneration, PSP : progressive supranuclear palsy, N/A : not applicable, M67 : repetitive themes describes as 'repeats or sticks to the same theme in conversation', M71 : adherence to daily routine describes as 'sticks to a strict timetable for ordinary daily activites', M72 : counts objects as 'counting things', M73 : aligns/arranges as 'always arranges or sorts objects/belongings in a certain way', M74 : overconcern with cleanliness as 'more/overly concerned about being neat and clean', M76 : excessive attention to detail as unnecessary attention to detail when carrying out tasks', M77 : excessive checking as preoccupied with checking things such as light switches, door locks, window locks'

about being neat and clean" ; excessive attention to detail as "unnecessary attention to detail when carrying out tasks" ; and excessive checking as "preoccupied with checking things such as light switches, door locks, window locks". In the original questionnaire, responses to each question are coded as 1 or 0, representing the presence or absence of notable changes from the premorbid state. In our study, however, caregivers were asked to rate the frequency of the behavior on a scale of 0 to 5. A score of 0 refers to "never" ; 1 to "had problem/not anymore"; 2 to "a few times a month", 3 to "a few times a week", 4 to "daily", and 5 to "incessant" in the modified MBQ. The patient's caregiver was asked to rate the patient's OC symptoms. For VBM analysis, OC symptoms were calculated by summing up all of the subscale scores. Disease severity was indexed using the patient's score on the MMSE, a widely used 30-item clinical instrument for grading cognitive state based on sampling from a number of different cognitive domains, where a lower score corresponds to reduced cognitive function.

3. Structural MRI

MRI scans were obtained on a 1.5T Magnetom VISION system(Siemens Inc., Iselin, NJ, USA) equipped with a standard quadrature head coil. A volumetric magnetization-prepared rapid gradient echo MRI(MPRAGE, TR/TE/TI=10/4/300ms) was used to obtain T1-weighted images of the entire brain, 15° flip angle, coronal orientation perpendicular to the double spin echo sequence, $1.0\times1.0mm^2$ in-plane resolution and 1.5 mm slab thickness.

4. Voxel-Based Morphometry(VBM)

The VBM technique utilizes an image pre-processing step (segmentation, normalization, modulation, and smoothing), followed by statistical analysis. Both stages were performed using the statistical parametric mapping 5(SPM5) software package(Wellcome Department of Cognitive Neurology, London, UK ; http://www.fil.ion.ucl.ac.uk/spm) running on Matlab 7.1.0(MathWorks Inc., Natick, MA, USA). Unified segmentation provides a generative model of VBM preprocessing that combines tissue classification, image registration, and radio-frequency bias correction. To obtain high resolution results (voxel size : 1×1×1mm), the VBM5.1 tool included in the SPM5 software package was used. Standard tissue probability priors of the International Consortium for Brain Mapping (ICBM) were warped to T1-weighted MR images in an iterative manner to create spatially normalized gray matter, white matter, and cerebrospinal fluid(CSF) tissue maps. For gray matter volume analysis, all three tissue maps were modulated with the Jacobian determinants derived from the spatial normalization step. Spatially normalized, segmented, and modulated gray matter images were then spatially smoothed with a 12mm full width at half maximum(FWHM) isotropic Gaussian kernel to increase the validity of statistical parametric analysis. In unbalanced designs such as ours, with different numbers of subjects across groups, a kernel with at least 12mm FWHM should be used to avoid false positive results in statistical analysis. In all preprocessing steps, SPM5 default parameters were used, with the exception of the change of voxel size from 2×2×2mm to 1×1×1mm in the writing option.

5. VBM Analysis of OC symptoms

Covariates-only statistical models were used to show the re-

lationship between OC symptom scores and gray matter volume. Normal controls were not used for any VBM analysis, because by definition they were not expected to have significant variability in either brain volume or OC symptom scores, and thus could cause restriction of range in the VBM regressions. The total score for OC symptoms was used as a covariate, and the age, gender, years of education, and MMSE score for each subject were entered as nuisance covariates into all design variables. TIV was used as a global covariate to correct for individual differences in head size. The main effect of OC symptoms was tested using the total OC symptom score in a(−1) t-contrast, assuming that increasing severity of the OC symptoms would be associated with decreased gray matter volumes in this population. In order to investigate whether each of the OC subscale scores showed similar patterns of gray matter loss, we looked at the separate effects of each of the seven subscale scores, using seven different design matrices and performing a(−1) t-contrast. Regionally specific differences in gray matter volumes at each voxel were assessed using the general linear model, and the significance of each effect was determined using the theory of Gaussian fields. In all analyses of main effects, the statistical threshold was set at $p<0.001$(uncorrected) with a cluster threshold of 100 voxels for multiple comparisons. Region identification was accomplished by overlaying the T-maps on the Montreal Neurological Institute(MNI) single subject brain using the Automated Anatomical Labeling(AAL) and Brodmann's atlases included in the MRIcron software package(http://www.sph.sc.edu/comd/rorden/mricro.html). Locations of clusters were reported in the MNI reference space. For the visual display of the results, family-wise error(FWE) corrected($p<0.05$) T-maps were superimposed on multiple slices of the normal template image provided in MRIcron(Ch2.nii.gz).

RESULTS

Table 1 shows the characteristics of patients classified by diagnostic group. OC behaviors were observed in 87 patients (82.1%). Among the seven OC subscales, the most frequent item was "repetitive themes"(48.1%) and the least frequent item was "adherence to daily routine"(13.2%). The "repetitive themes"(No.67), "adherence to daily routine"(No.71), "counts objects"(No.72), "excessive checking as preoccupied with checking things"(No.77) and total OC scores were highest in FTD patients. No significant differences were found in age, sex, education, and MMSE scores among the six dementia groups. There were significant differences in the total OCD, No.67, No.71, and No.73 scores among the diagnostic groups ($p<0.05$).

Table 2 and Fig. 1 show the results of regional gray matter density assessment in dementia patients with OC symptoms. The total OC score negatively correlated with gray matter volume in the left and right putamens, right middle orbitofrontal gyrus, left and right ACCs, and left insula($p<0.001$, uncorrected). At a corrected significance threshold($p<0.05$), gray matter loss was significant in the putamen.

To explore whether a single diagnostic group made a significant contribution to a particular portion of the OCD circuit identified in our results, we evaluated unique brain regions associated with the OC total score according to the dementia subtype. Alzheimer's disease and FTLD, including FTD, semantic dementia, and PPA did not show unique regions associated with the OC total score($p<0.001$, uncorrected).

At an uncorrected significance threshold($p<0.001$), no gray matter reductions were associated specifically with the OC behavior subcategories, including repetitive themes described as "repeats or sticks to the same theme in conversation" ; adherence to daily routine described as "sticks to a strict timetable for ordinary daily activities" ; counts objects described as "counting things" ; aligns/arranges described as "always arranges or sorts objects/belongings in a certain way" ; overconcern with cleanliness described as "more/overly concerned about being neat and clean" ; excessive attention to detail described as "unnecessary attention to detail when carrying out tasks" ; and excessive checking described as "preoccupied with checking things such as light switches, door locks, win-

Table 2. Regional gray matter density changes in dementia patients with obsessive-compulsive symptoms, uncorrected for FWE across the whole brain at a significance level of $p<0.001$

Anatomical region	BA	Cluster size	Talairach coordinates			Z-score	FEW
			x	y	Z		
R Putamen		1,642	34	2	−2	5.20	0.000
R Frontal Mid Orbital	10	950	12	52	−4	4.33	0.000
R Anterior cingulum	32		14	40	6	4.23	0.000
R Insula		531	−32	−4	12	3.79	0.000
L Insula			−34	−12	24	3.46	0.000
L Putamen			−30	8	−2	3.77	0.000
L Ant cingulum	10	113	−12	46	0	3.48	0.000

BA : Brodmann area, R : right, L : left, FEW : family-wise error

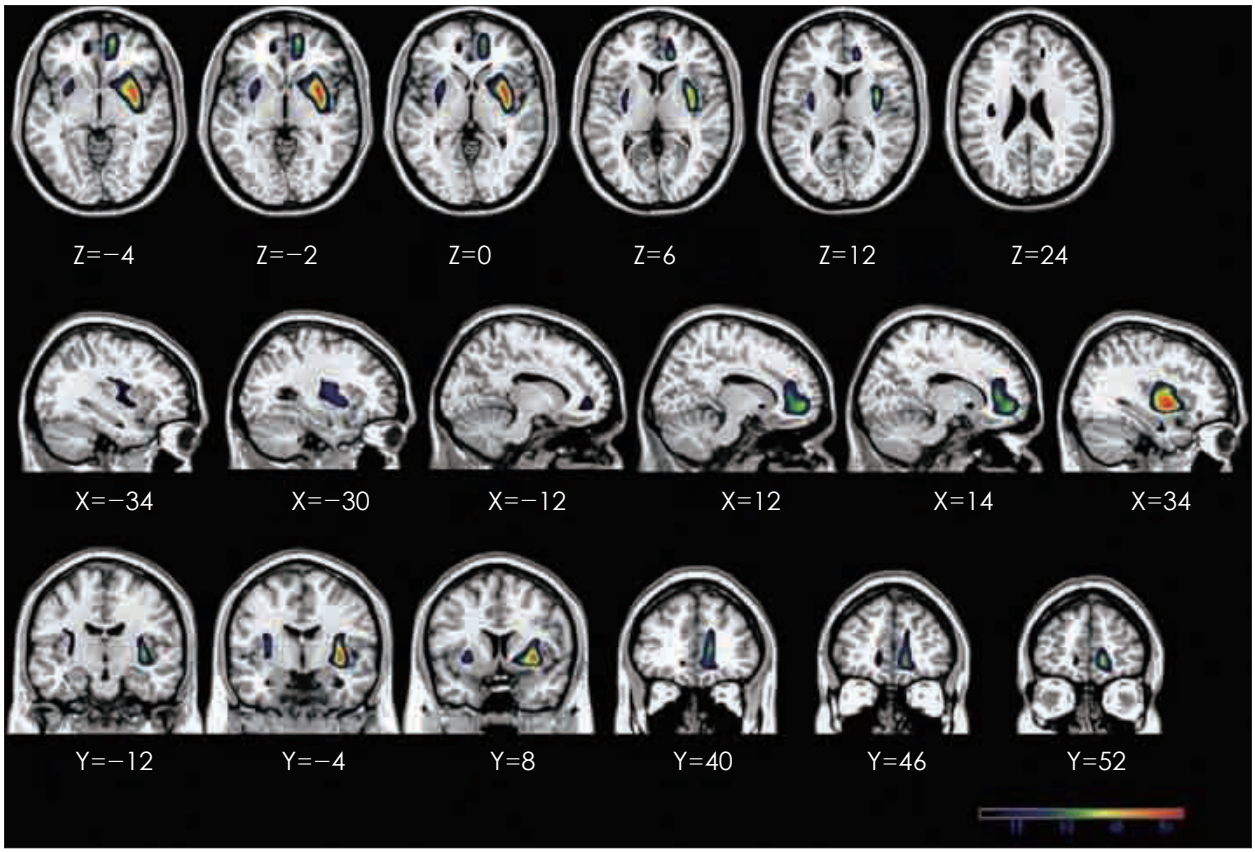

Fig. 1. Main effect of obsessive-compulsive disorder(OCD) total score, showing voxels significantly related to OCD total score at $p < 0.001$ uncorrected. The design matrix for this analysis contained only OCD total score, with sex, age, education, MMSE score and TIV included as nuisance covariates, and t-test was used. The brains of dementia patients with obsessive-compulsive symptoms showed reduced gray matter volume in left and right putamen, right middle orbitofrontal gyrus, left and right anterior cingulate, left insula($p < 0.001$, uncorrected).

dow locks".

DISCUSSION

This is the first structural investigation which evaluated the gray matter volume in dementia patients with OC symptoms. The volume changes found in this study may be implicated in the pathophysiology of OCD. Voxel-based mapping of structural brain alterations in dementia patients with OC symptoms showed significant reductions of gray matter volume in the right middle orbitofrontal cortices, both ACCs, both putamens, and the left insula. No specific patterns of gray matter atrophy were identified for any of the subscale scores, including repetitive themes, adherence to daily routine, counts objects, aligns/arranges, overconcern with cleanliness, excessive attention to detail, or excessive checking.

Although the pathophysiology of OC remains controversial, there is significant evidence to support a role for the frontal-subcortical circuitry in a neurobiological model of OCD.[24] Recent neurobiological models of the mediation of OC symptoms generally coincide in that the brain dysfunction involves the ventral striatum and functionally related orbitofrontal and cingulate cortices specifically.[25,26] In particular, orbitofrontal and anterior cingulate regions have been hypothesized to play an important role in producing the symptoms associated with the disorder.[3-5] The orbitofrontal-subcortical circuits are thought to connect regions of the brain that process information involved in the initiation of behavioral responses that are implemented with little conscious awareness.[27]

Several studies on OCD have suggested that the disorder involves abnormalities of the OFC, ACC, and basal ganglia.[7,28,29] However, structural brain alterations in OCD may be widely distributed,[30] and findings regarding increases or decreases in gray matter volume have been contradictory. Volume reduction in the OFC has been reported more frequently than that of other regions of the frontal-subcortical circuits.[31] Szeszko et al.[28] found reduced bilateral OFC volume in patients with OCD, suggesting that a degenerative process might be implicated in the pathophysiology of OCD. A recent VBM study reported significantly lower gray matter volume in the medial frontal cortex/Brodmann area 9 in adult OCD patients, although the medial frontal regions in that study were not identical to those in our findings.[7] Valente et al.[6] found increased gray matter in OCD subjects relative to control subjects in

posterior orbitofrontal regions. On the other hand, a parcellation study using semi-automated signal intensity histograms found no volumetric gray matter differences specific to the OFC in subjects with OCD.[32] Different study methods and heterogeneous samples among the studies could, in part, account for the conflicting findings. In our study, we found that OCD patients had significantly smaller OFC volumes. These results support the findings of aforementioned studies indicating that OFC volumes were reduced in OCD patients.

The OFC might play a potential role in inhibitory motor control.[33] Because it receives multimodal inputs from the temporal association cortex, amygdala, and hypothalamus as well as limbic components of the basal ganglia, it has been viewed as the highest integration center for emotional information processing.[34] Experimental and clinical studies have provided significant evidence that the OFC is involved in the mediation of emotional responses to biologically significant stimuli as well as in the inhibition of behavioral responses.[5] This may be of special importance given the compulsions present in OCD and the patients' attempts to resist performing these actions.[15] Patients with orbitofrontal damage have great difficulties in decision-making.[34] The OFC is involved in cognitive appraisal in determining the significance of stimuli and in integrating the subject's prior experience.[35] Thus, the OFC seems to play a predominant role in motivational aspects of decision-making.

There is little consistency across studies in the measurement of the ACC. The structural variability and complexity of this region make the identification and selection of boundaries difficult. Only a few studies have examined the structure of the ACC in patients with OCD, and to date no volumetric abnormalities have been reported.[32,36] However, Szeszko et al.[28] reported a significant effect by hemisphere, with larger ACC volumes in the right hemisphere in patients with OCD. Although our finding of decreased ACC gray matter in OCD patients contrasted with the pattern of increased volumes of the same structure in the MRI studies conducted by Szeszko et al.,[37] this result suggests that the volumetric reduction may related in some way to the OCD. This finding may provide a starting point for pathophysiological investigations of OCD. Previous neuroimaging studies have underlined the potential role of the ACC in the management of cognitive and emotional information.[38] It may be that some of the emotional symptoms observed in OCD such as non-specific anxiety involve the ACC. In addition, many neuroimaging studies indicate that the ACC is involved in a variety of cognitive processes such as attention, motivation, reward and error detection, working memory, problem-solving, and action-planning.[39]

In the present study, we found that dementia patients with OC behaviors had significantly smaller putamen volumes. The results of neuropsychological tests in patients with OCD have revealed frontal lobe dysfunction, whereas many investigators have postulated a role for the basal ganglia along with the cortical brain regions in the mediation of OC symptoms.[9,40] Our results confirm that the basal ganglia, particularly the putamen, may be involved in the abnormal process along the circuit of OCD. Correlation analysis between neuropsychological performance and regional metabolic rate shows that a variety of brain regions, including the prefrontal cortices and the putamen, are involved in the poor processing of executive control and visual memory that are observed in OCD patients.[24] These results suggest that the frontal-subcortical networks may be involved in the expression of cognitive deficits in OCD. Inconsistent with other studies of the caudate nucleus,[41] our investigation did not demonstrate any statistically significant differences in this area in patients with OCD.

The insular cortex was correlated with OC symptoms in our study. Symptom provocation in individuals with OCD has been shown to be associated with increased cerebral blood flow in the bilateral insular cortices.[42] Moreover, insular activity has been linked to OCD.[43] Several investigators have emphasized that the insular cortex may be central to our understanding of anxiety proneness. Specifically, Steins et al.[44] suggested that anxiety-prone individuals have bilaterally increased activation of the insula during emotion processing. The insular cortex connects to the OFC[45] and the information in the anterior insula is relayed to the ACC, which, as part of the central executive system, can generate an error signal that is critical for the allocation of attentional resources.[46]

There are some limitations to our study. First, the two pathologic conditions of dementia and OCD may affect brain pathology simultaneously because our subjects are patients with degenerative disease who display OC symptoms. Second, the modified MBQ scale used to assess OC behaviors is based on caregiver report rather than direct clinical observation. Even when assessed directly by an experienced clinician, it is difficult to quantify abnormal behaviors with accuracy. Third, the discrepancies among various structural studies may be attributable to the nature of OCD itself. Several studies have shown that OCD is a multidimensional and etiologically heterogeneous condition. Although there were no significant relationships between gray matter volumes and OC symptom dimensions in our study, the symptom dimensions of OCD may be useful in genetic, neurobiological, and treatment response studies.[47]

Using VBM with structural MR images, the anatomic substrates of OC symptoms were delineated in a group of patients with diverse patterns of cortical atrophy due to neurodegenerative disease. Clinicians should be aware of the variable presentations of neurodegenerative disorders and consider these

in the differential diagnosis when common psychiatric disorders such as OCD present with atypical features. In summary, our findings show that the right OFC, both putamens, both ACCs, and the left insula are regions associated with OC symptoms in dementia patients, but distinct gray matter abnormalities are not associated with the symptom dimensions of OCD. Taken together, our results suggest that abnormalities in these areas may play an important role in the pathophysiology of OCD in neurodegenerative disease.

Further research is necessary to verify the neuroanatomic mechanisms responsible for OC symptoms in patients with neurodegenerative disease. Future studies will require larger samples of patients to examine this question using whole brain methods of analysis and validated instruments.

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