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Neural correlates of clinical symptoms and cognitive dysfunctions in obsessive–compulsive disorder

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Abstract

Although results from neuropsychological and neuroimaging studies have postulated the involvement of the frontal lobe and the subcortical brain regions in the pathophysiology of obsessive–compulsive disorder (OCD), neuroimaging studies have provided little evidence that cognitive abnormalities in patients with OCD are related to dysfunctions in these areas. This study was designed to determine whether the clinical features and cognitive deficits of OCD might be taken to reflect frontal-subcortical dysfunction. Fourteen patients with OCD and 14 case-matched normal subjects completed clinical and cognitive evaluation, including four sets of neuropsychological tests that assessed the executive functions and visual memory. Cerebral glucose metabolic rates were measured by using positron emission tomography (PET) with ¹⁸F-fluorodeoxyglucose. Behavioral and PET data were analyzed using statistical parametric mapping for group differences and behavioral–metabolic correlates. The right orbitofrontal cortex showed increased metabolic activity and the left parieto-occipital junction showed decreased metabolic activity in patients. Metabolism in the right hippocampus, the left putamen and the right parietal region was associated with the severity of obsessive–compulsive symptoms. Correlations between metabolic rates and neuropsychological test scores in the prefrontal cortex and the putamen occurred only in the patient group. These results suggest that patients with OCD have distinct features of brain metabolic activities for performing cognitive tasks as well as presenting obsessive–compulsive symptoms. In particular, the frontal–subcortical circuits might mediate not only symptomatic expression but also cognitive expression in patients with OCD.

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Keywords: Obsessive–compulsive disorder; FDG-PET; Voxel-based analysis; Cognitive dysfunction; Neural correlates; Frontal-subcortical circuits

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1. Introduction

Although obsessive-compulsive disorder (OCD) is still the subject of an etiologic controversy, a number of studies over the last 20 years have provided strong evidence that a wide variety of neural dysfunctions are implicated in the pathophysiology of this illness. In the majority of studies using positron emission tomography (PET), hypermetabolic rates have been found in the orbitofrontal cortex and/or the basal ganglia in a resting state (Baxter et al., 1987, 1988; Nordahl et al., 1989; Swedo et al., 1989; Benkelfat et al., 1990; Sawle et al., 1991; Baxter et al., 1992). Interventions that provoke OCD symptoms have also been found to activate similar brain regions (McGuire et al., 1994; Rauch et al., 1994; Breiter et al., 1996; Cottraux et al., 1996). Furthermore, metabolic rates in these areas were demonstrated to be lower after pharmacotherapy, especially amongst drug responders (Baxter et al., 1987; Swedo et al., 1989; Saxena et al., 1999), and after behavioral therapy (Baxter et al., 1992; Schwartz et al., 1996). Accordingly, it has been hypothesized that frontal-subcortical circuitry may mediate the symptomatology of OCD (Insel 1992; Saxena et al., 1998).

A number of neuropsychological studies have indicated that some cognitive deficits, including executive and visual memory dysfunctions, are associated with OCD (Christensen et al., 1992; Purcell et al., 1998; Savage et al., 1999). In general, researchers have also interpreted abnormal neuropsychological performance in OCD to reflect circuitual dysfunction, including the frontal lobe and subcortical brain regions (Savage et al., 1999; Galderisi et al., 1995; Veale et al., 1996; Schmidtke et al., 1998). However, to date neuroimaging studies have presented little evidence that defective cognitive functions as identified by neuropsychological studies are related to dysfunctions in the circuit. Martinot et al. (1990) studied correlations between regional cerebral glucose metabolic rates and neuropsychological tests that revealed impairments in memory and attention, but only the Stroop test subscores were observed to be negatively correlated with regional metabolic activities in some cerebral areas, including the prefrontal lateral cortex. It is believed likely that such limited

findings are a result of the region of interest (ROI) approach adopted.

In fact, most of the earlier functional imaging studies employed the ROI approach and thus suffered from some methodological limitations. For example, the arbitrarily defined ROIs might be generally too large to reflect the functional unit of brain activities and, therefore, significantly increased metabolic activity in some neuronal field is likely to be obscured if surrounding areas within the same ROI show no changes or decreases in activity. There is a report that there existed both hyper- and hypo-functioning regions in the prefrontal area of patients with schizophrenia, which might account for the inconsistent findings of functional imaging studies using the ROI approach regarding so-called 'hypofrontality' in schizophrenia (Kim et al., 2000b).

Based on the consistent reports regarding the functional abnormalities of the frontal and subcortical regions in OCD, it can be hypothesized that the voxel-based approach, in which tiny functional units are examined without arbitrary delineation, would further highlight more precise localized positions of the abnormalities. In addition, we hypothesized that we could find evidence of the close relationship between cognitive dysfunctions and frontal-subcortical circuits in OCD if a voxel-based approach were applied. In the current study, we examined symptom severity and cognitive performance on tasks anticipated to be defective in patients with OCD, and measured regional brain metabolic activity using [¹⁸F]-2-fluoro-2-deoxyglucose (FDG) PET. Subsequently, results were analyzed using statistical parametric mapping (SPM) to examine the group differences in the metabolic activity between OCD and normal control subjects as well as the presence of any correlations between neuropsychological performance and frontal-subcortical activity.

2. Methods

2.1. Subjects

We studied 14 patients with OCD (10 men and 4 women) who were recruited from an OCD outpatient clinic at Seoul National University Hos-

Table 1
Subjects' demographics, clinical characteristics, and neuropsychological performance scores^a

Variable	Patients with obsessive–compulsive disorder (<i>n</i> = 14)	Normal subjects (<i>n</i> = 14)	<i>P</i>
<i>Demographic characteristics</i>			
Gender ratio (female/male)	10/4	10/4	NS
Age (years)	28.5 [8.4]	28.6 [7.1]	NS
Education (years)	14.1 [2.4]	15.1 [1.5]	NS
Handedness (right/left)	13/1	14/0	NS
<i>Clinical characteristics</i>			
Duration of illness (years)	10.4 [8.4]	–	
Yale-Brown Obsessive-Compulsive Scale	25.5 [8.2]	–	
Beck Depression Inventory score	16.2 [12.3]	–	
Beck Anxiety Inventory score	19.9 [15.1]	–	
<i>Neuropsychological performances</i>			
Estimated IQ	114.1 [7.8]	116.4 [8.2]	NS
Word fluency (total numbers)	32.6 [8.2]	43.5 [13.7]	< 0.05
Trail making B (spending time)	83.8 [21.3]	64.2 [18.6]	< 0.05
Wisconsin Card Sorting Test (perseverative errors)	13.8 [12.1]	23.4 [40.4]	NS
Rey–Osterrieth Complex Figures (immediate recall scores)	14.8 [6.6]	21.9 [6.7]	< 0.01

^a Data are given as mean (standard deviation), unless otherwise indicated.

pital and who fulfilled DSM-IV criteria (American Psychiatric Association, 1994) for OCD as diagnosed using the Structured Clinical Interview for DSM-IV (SCID-IV) (First et al., 1996). Exclusion criteria were the presence of significant medical illness and other major psychiatric disorders, such as substance abuse, schizophrenia and bipolar disorder. One of the 14 patients had a history of alcohol abuse but had remained sober for a period of 1 year, another had major depressive disorder and bulimia nervosa, and 12 had OCD as their sole diagnosis. There was no subject who had a history of tic disorder. Normal subjects consisted of 14 age- and sex-matched healthy volunteers (10 men and 4 women) who were recruited from the community through newspaper advertisements. Exclusion criteria for the normal subjects were any current or lifetime history of DSM-IV axis I disorder, as determined using the SCID-IV. This study was carried out under the guidelines for the use of human subjects, as established by the institutional review board. After the nature of the

study had been completely described to the subjects, written informed consent was obtained.

As shown in Table 1, for the OCD and comparison group, the mean \pm S.D. age was 28.5 ± 8.4 and 28.6 ± 7.1 years ($t = 0.05$, d.f. = 26, $P = 0.96$), the mean years of education were 14.1 ± 2.4 and 15.1 ± 1.5 years ($t = 1.88$, d.f. = 26, $P = 0.07$), and the mean socioeconomic status (Hollingshead and Redlich, 1958) was ranked as 2.9 ± 0.7 and 3.0 ± 0.8 ($t = 0.25$, d.f. = 26, $P = 0.81$), respectively. Thirteen patients were right-handed and one was left-handed, whereas all normal subjects were right-handed. At the time of the study, patients had a mean duration of illness of 10.4 ± 8.4 years, ranging from 2 to 25 years. Five patients were drug-naïve, and nine had a history of anti-obsessional medication, but they had all been free of psychotropic drugs for at least 4 weeks.

2.2. Clinical and cognitive assessments

Clinical assessment included the Yale–Brown Obsessive-Compulsive Scale (Y-BOCS) (Good-

man et al., 1989) which measured the severity of OCD symptoms (obsessive symptoms, 13.4 ± 4.0 ; compulsive symptoms, 12.1 ± 4.5 ; total score, 25.5 ± 8.2). The Maudsley Obsessive Compulsive Inventory (Hodgson and Rachman, 1977) was self-reported by the patients for specifying OCD symptom subtype (checking, 4.0 ± 2.2 ; doubting, 3.7 ± 1.6 ; slowness, 2.7 ± 1.8 ; cleaning, 2.8 ± 2.4 ; total 13.3 ± 6.1). The Beck Depression Inventory (BDI) (Beck et al., 1961) and the Beck Anxiety Inventory (Beck and Steer, 1990) were also administered (16.2 ± 12.3 and 19.9 ± 15.1 , respectively).

To assess cognitive potential, the Korean version of the Wechsler Adult Intelligence Scale (KWIS) was administered to all subjects. Based on the previous findings that patients with OCD had some cognitive deficits (Christensen et al., 1992; Purcell et al., 1998; Savage et al., 1999), we chose four cognitive tests including word fluency, Trail-Making Part B (TMB), and the Wisconsin Card Sorting Test (WCST) for executive functions and the Rey–Osterrieth Complex Figure Test (RCFT) for visual memory (Crawford et al., 1992). Data from the tests were used to evaluate the potential relationship between regional glucose metabolism and cognitive performance. In terms of word fluency, which reflected the subjects' ability to devise a strategy as well as language production, as many words as possible beginning with three kinds of Korean letters were to be given within a minute for each, and the total number was counted. In TMB, assessing set shifting, the time needed for the test was measured. The WCST was administered to evaluate executive control, and perseverative errors were counted as a resulting variable. In the RCFT, the score for immediate recall was counted to assess visual memory. All tests were performed on the day of PET scanning.

2.3. PET procedures and imaging data analysis

All subjects were scanned at rest without ear plugs or eye pads, using an ECAT EXACT 47 scanner (Siemens-CTI, Knoxville, TN, USA), which had an intrinsic resolution of 5.2-mm-full width at half-maximum (FWHM) and simultaneously imaged 47 contiguous transverse planes with thickness of 3.4 mm for a longitudinal field of

view of 16.2 cm. Before the injection of the tracer, a 15-min transmission scan was performed using a triple Ge-68 rod source to correct for attenuation. Emission scanning started after the intravenous injection of 370 MBq (10 mCi) of [^{18}F]FDG and continued for 30 min. Stored data were reconstructed in a $128 \times 128 \times 47$ matrix with a pixel size of $2.1 \times 2.1 \times 3.4$ mm using a filtered back-projection algorithm employing a Shepp–Logan filter with cut-off frequency of 0.3 cycles/pixel.

Spatial pre-processing and statistical analysis were performed using SPM 99 (Institute of Neurology, University College of London, UK) implemented in Matlab (Mathworks Inc., USA) (Friston et al., 1995b). All reconstructed images were spatially normalized into the MNI (Montreal Neurological Institute, McGill University, CA) standard template to remove inter-subject anatomical variability (Talairach and Tournoux, 1988; Friston et al., 1995a). Affine transformation was performed to determine the 12 optimal parameters to register the brain on the template. Subtle differences between the transformed image and the template were removed by the nonlinear registration method using the weighted sum of the pre-defined smooth basis functions used in discrete cosine transformation. Spatially normalized images were smoothed by convolution using an isotropic Gaussian kernel with 16-mm FWHM to increase the signal-to-noise ratio and accommodate variations in subtle anatomical structures.

2.4. Statistical analysis

The effects of global metabolism were removed by normalizing the count of each voxel to the total brain count (proportional scaling in SPM). Then, significant changes of regional cerebral metabolism in the 14 patients with OCD were estimated by comparing their PET images with those of the 14 normal subjects using a *t*-test at every voxel. For easy interpretation, *T*-values were transformed to *Z*-scores in the standard Gaussian distribution. Clusters of a minimum of 50 contiguous voxels with a threshold of uncorrected two-tailed $P < 0.005$ were considered to be significantly different.

To identify which regions correlated significantly with the severity of obsessive–compulsive

symptoms, a general linear model with the total score on the Y-BOCS as a variable was tested at each voxel, in which the total score of BDI was used as a nuisance variable to control for the effect of depressive symptoms. Separately from clinical symptom scales, total numbers in word fluency, time to complete the TMB, perseverative errors on the WCST, and immediate recall scores on the RCFT were used as covariates to identify the regions associated with the neuropsychological test performances for each group. The correlation coefficients were also transformed to Z-scores. Reflecting a need to apply stricter criteria because multiple correlations were performed, clusters of a minimum of 50 contiguous voxels with a threshold of uncorrected two-tailed $P < 0.001$ were considered to be a significantly correlated region.

3. Results

3.1. Neuropsychological performance

Mean IQ estimated by the KWIS was 114.1 ± 7.8 for the patients and 116.4 ± 8.2 for the normal subjects ($t = 0.74$, d.f. = 26, $P = 0.47$), demonstrating no significant difference in general function between the two groups. As shown in Table 1, however, in the cognitive tests selected to evaluate executive functions and visual memory, the patient group had poorer performances than the comparison group. The total numbers of words starting with three different Korean letters were significantly fewer in the patients than in the normal subjects ($t = -2.54$, d.f. = 26, $P < 0.05$). The time needed for the TMB was significantly longer in the patients than in the normal subjects ($t = 2.59$, d.f. = 26, $P < 0.05$). However, no significant difference was apparent in perseverative errors on the WCST in the two groups ($t = -0.86$, d.f. = 26, $P = 0.40$), though they tended to be fewer in the patients. The RCFT showed that scores for immediate recall were lower in the patients than in the normal subjects ($t = -2.87$, d.f. = 26, $P < 0.01$).

3.2. Cerebral metabolic differences between OCD and normal subjects

Areas of significant differences found by comparing the patients with OCD and the normal

Table 2

Comparison of regional glucose metabolic rates between OCD and normal subjects^a

Region	Coordinates			Highest Z-value	Voxel number
	x	y	z		
Increases in patients'					
right orbitofrontal	26	28	-24	2.99	147
left insula	-42	-8	4	3.03	233
Decreases in patients'					
left inferior parietal	-48	-54	56	3.01	77
left parieto-occipital	-10	-84	32	4.09	798

^a The threshold for significance was clusters of $P < 0.005$, two-tailed.

subjects are presented in Table 2. As shown in Fig. 1a, the central portion of the right orbitofrontal cortex appeared to have hypermetabolic rates in the patients. The left insula was another area with hypermetabolism in the patients. Contrastingly, significant hypometabolism in the patients was observed in the left inferior parietal cortex and the medial portion of the left parieto-occipital junction (Fig. 1b).

3.3. Obsessive–compulsive symptoms and glucose metabolic rates

All significant findings obtained by correlating glucose metabolic rates with clinical symptoms and cognitive performances in each group are summarized in Table 3, which excludes non-significant findings. Areas showing a significant positive correlation between glucose metabolism and obsessive–compulsive symptoms in the patients were found in the right hippocampus, the left putamen and the deep portion of the right parietal lobe (Fig. 2a), while no area with a significant negative correlation was observed.

3.4. Neuropsychological performance and glucose metabolic rates

In terms of correlations with neuropsychological performance, the patient group showed a characteristic pattern of results in which significant areas were found in the correlation with the test scores of poor performance (e.g. TMB and RCFT), but

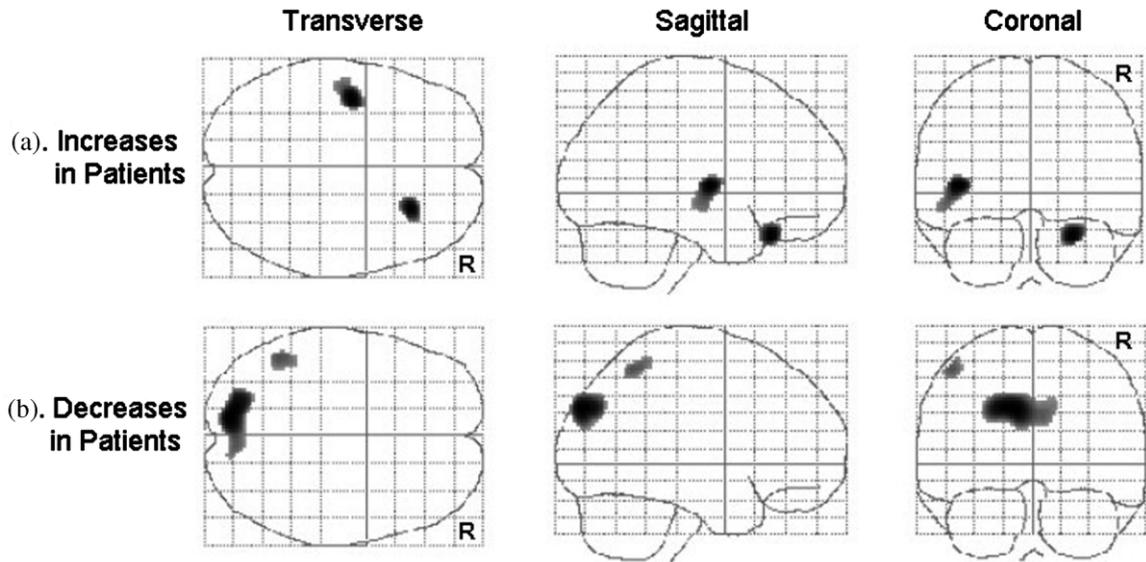


Fig. 1. Statistical parametric maps displaying differences in glucose metabolic rates between 14 patients with obsessive-compulsive disorder and 14 matched normal subjects. Significant group differences (two-tailed $P < 0.005$, $k > 50$) are shown on three orthogonal telescoped views. Note that the right orbitofrontal cortex shows increased metabolic activity in the patients (a), whereas the left inferior parietal cortex and the left parieto-occipital junction show decreased activity (b).

not in the correlation with the test scores of normal performance (e.g. the WCST). Areas where there were negative correlations with time to complete the TMB were evident in the left putamen (Fig.

2b). In the case of the correlations with immediate recall scores on the RCFT, multiple areas on both sides of the prefrontal cortex, such as the medial prefrontal, dorsolateral prefrontal and frontopolar

Table 3

Summary of the correlation analysis between regional glucose metabolic rates and severity of symptoms and neuropsychological performance

Region	Coordinates			Highest Z-value	Voxel number
	x	y	z		
Positive correlations with total score on the Yale–Brown Obsessive Compulsive Scale in patients					
Right hippocampus	38	–24	–6	3.90	179
Left putamen	–28	–10	2	4.09	298
Right parietal	32	–36	36	3.66	68
Negative correlations with time spent on the Trail-Making B test in patients					
Left putamen	–20	4	–4	3.84	167
Positive correlations with immediate recall score on the Rey–Osterrieth Complex Figure test in patients					
Right medial prefrontal	12	12	48	3.55	195
Right dorsolateral prefrontal	40	28	48	3.48	92
Left dorsolateral prefrontal	–22	34	36	3.51	113
Left frontal pole	–28	56	4	3.49	69
Negative correlations with immediate recall score on the Rey–Osterrieth Complex Figure test in patients					
Left cerebellum	–34	–40	–30	3.76	110

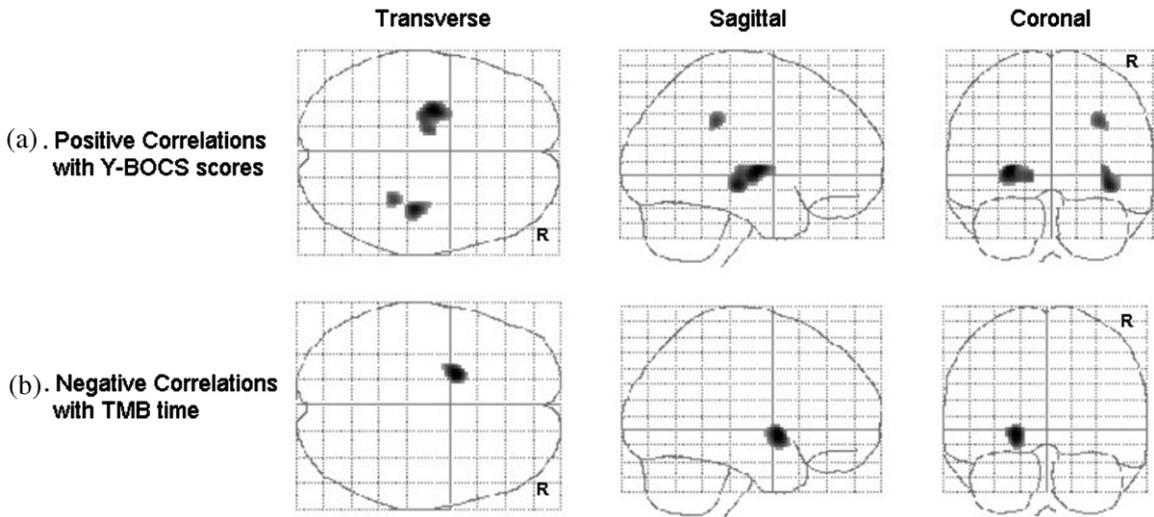


Fig. 2. Statistical parametric maps displaying correlations of cerebral glucose metabolic rates with total scores on the Yale–Brown Obsessive-Compulsive Scale (a) time spent on the Trail-Making Part B (b) in patients with obsessive–compulsive disorder. Significantly correlated areas (two-tailed $P < 0.001$, $k > 50$) are shown on just three orthogonal telescoped views. Metabolic activity in the left putamen is associated with the severity of obsessive–compulsive symptoms and cognitive dysfunctions.

regions, showed positive correlations, whereas a portion of the left cerebellum correlated negatively (Fig. 3). However, no significant areas were identified

in the correlations with word fluency and the WCST. In contrast to multiple findings in the patients, areas with significant correlations

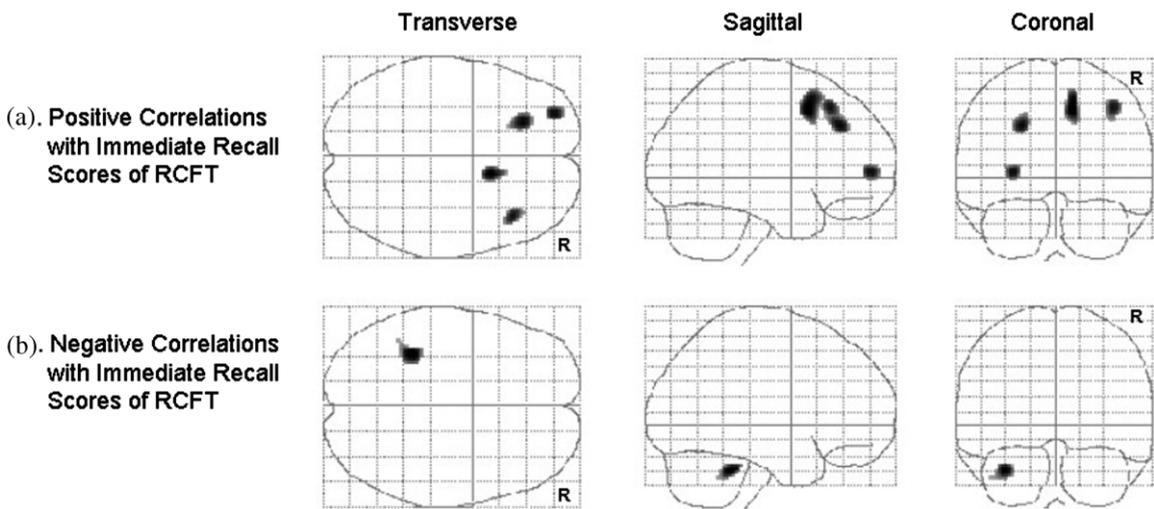


Fig. 3. Statistical parametric maps displaying correlations of cerebral glucose metabolic rates with immediate recall scores on the Rey–Osterrieth Complex Figure Test in patients with obsessive–compulsive disorder. Significantly correlated areas (two-tailed $P < 0.001$, $k > 50$) are shown on three orthogonal telescoped views. Multiple areas in the dorsolateral prefrontal cortex and an area in the left cerebellum may be involved in the impaired processing of visual memory.

between metabolic rates and cognitive performance were seldom found in the normal subjects.

4. Discussion

To confirm the a priori functional changes in the frontal-subcortical regions in patients with OCD, we analyzed data using a voxel-based approach rather than an ROI approach. Consistent with previous findings obtained with ROI-based methods, the patients with OCD in the current study were found to have a hypermetabolic area in the central portion of the right orbitofrontal cortex when compared with the normal subjects. The orbitofrontal cortex, particularly on the right side, had been found to be activated by the provocation of obsessive–compulsive symptoms (McGuire et al., 1994; Rauch et al., 1994; Breiter et al., 1996), suggesting that this area may be involved in mediating the active expression of obsessive–compulsive symptoms. Experimental and clinical studies have provided much evidence that the orbitofrontal cortex is involved in the mediation of emotional response to biologically significant stimuli as well as in the inhibition of behavioral responses (Zald and Kim, 1996). Furthermore, preferential metabolic decreases have been found in the orbitofrontal cortex in response to pharmacotherapy (Benkelfat et al., 1990; Saxena et al., 1999), suggesting that ‘hyperfrontality’ in OCD as a state marker can be modified by the therapeutic interventions.

The left inferior parietal and parieto-occipital junction in the current study, in contrast with the orbitofrontal cortex, was observed as a hypometabolic area in the patients as opposed to the normal subjects. Although low activity in this area was observed in other previous studies (Nordahl et al., 1989; Lucey et al., 1995), its importance was not emphasized. There were also reports of significant correlations between symptom intensity and blood flow in similar cerebral regions such as the left cuneus and precuneus (McGuire et al., 1994). These extrastriate areas have been activated by cognitive tasks related to visual imagery in some PET studies (Kosslyn et al., 1993; Mellet et al., 1996). It may be in turn related to visuo-spatial processing and visual memory deficits in some

patients with OCD (Zielinski et al., 1991; Purcell et al., 1998). Taken together with the previous reports, the finding of decreased parietal metabolic rates in the current study suggests a possibility that parietal dysfunction may underlie defective visual cognitions in patients with OCD.

Baxter et al. (1987) originally reported an increase in the glucose metabolic rate in the orbitofrontal cortex and the caudate nucleus. The former finding has been generally consistent in the following replication studies, whereas the latter finding has been controversial across studies. Subcortical areas showing hypermetabolism in patients with OCD have differed in different studies: the caudate nucleus (Baxter et al., 1988), the putamen (Perani et al., 1995), and the thalamus (Swedo et al., 1989; Perani et al., 1995). One study found no significant changes (Nordahl et al., 1989). In the current study, ratings of obsessive–compulsive symptoms were correlated with metabolic activity in the parietal cortex, hippocampus and putamen, but not in the orbitofrontal cortex. The results of neuropsychological tests and the efficacy of psychosurgery have suggested possible frontal lobe dysfunction, whereas many investigators have postulated a role for the basal ganglia along with the cortical brain regions in the mediation of OCD symptoms, which was based on observations of obsessive–compulsive symptoms among patients with lesions of the basal ganglia (Frankel et al., 1986; Cummings and Cunningham, 1992). The present finding confirms that the basal ganglia, particularly the putamen, may be involved in the abnormal process along the circuit, which exists in the symptomatic state.

As expected, the overall performance profile for the neuropsychological tests shows that the executive and visual memory dysfunctions are present in our subjects with OCD. Although such poor neuropsychological findings are in agreement with those of previous reports (Christensen et al., 1992; Purcell et al., 1998; Savage et al., 1999), there are difficulties in generalizing them for all patients with OCD due to our small sample size. Nonetheless, they are more informative when combined with metabolic data. That is, correlation analysis

between the neuropsychological performance and regional metabolic rate reveals that a variety of brain regions, including the various prefrontal cortices, the putamen and the cerebellum, are involved in poor processing of executive control and visual memory in the patients. On the contrary, such correlations are not observed in the comparison group with normal cognitive function. These results suggest that the frontal-subcortical networks can be involved in the expression of cognitive deficits in OCD.

It is noteworthy that all of these areas are parts of abundant prefrontal-subcortical-cerebellar connections, which have been suggested to play a role in coordinating the complex mental and non-motor higher cognitive functions (Andreasen et al., 1998; Schmahmann and Pandya, 1997; Kim et al., 1999). Recently, impairment in this circuitry has been postulated to be an underlying factor in a variety of clinical symptoms and cognitive deficits in schizophrenia (Kim et al., 2000b; Andreasen et al., 1998). Our results suggest that this circuitry may also play an important role in the manifestation of cognitive deficits in OCD.

However, it is not conclusively known whether these identified regions are specific for each task and can be assigned as definitive neuroanatomic correlates for cognitive dysfunctions in OCD. Significant correlations emerged during two tasks, namely, the TMB and the RCFT, in which the patients were behaviorally impaired compared to the normal subjects. In general, patients with OCD tend to perform poorly on timed tests. Consequently, the greater variance in the patients on the neuropsychological tests could have been responsible for the observed correlations with metabolic rates, and the variance in the healthy subjects could have been too small to allow correlations to be observed. As shown in Table 1, however, the standard deviations of the patients, when compared with those of the normal subjects, are not larger. Therefore, the significant results limited to the patients do not seem to have arisen from such chance effects. In addition, it is important to consider that differences in the observed neural correlates may reflect the patients' impaired ability to perform the tasks rather than specific illness processes associated with the disorder. Indeed, on

the WCST the patients performed comparably to the normal subjects, and there were no group differences in the correlates. It is apparent, nevertheless, that patients with OCD show nonspecific but characteristic patterns of distributed brain circuits, which differ from those in healthy subjects.

Despite the interesting results, it may be questioned the resting metabolic rates correspond to the neuropsychological result, because of the time lag between PET scanning and neuropsychological testing in the current study. They are still informative, however, because the neuropsychological performances are considered to be stable over time in that they reflect enduring cognitive deficits. Well-designed cognitive activation paradigms can be helpful to resolve this issue. A PET study of implicit sequence learning, for example, suggested that cortico-striatal dysfunction was implicated in OCD (Rauch et al., 1997).

Our study suggests that the voxel-based approach can provide informative findings regarding the brain metabolic activities in OCD. Another study demonstrated that this approach was also useful to analyze regional cerebral blood flow in OCD (Busatto et al., 2000). However, since this approach relies on the linear proportional scaling system of the Talairach atlas (Talairach and Tournoux, 1988), it can be problematic in that it fails to reflect interindividual and interhemispheric morphological variability. MRI-based parcellation of the brain subregions may provide greater accuracy in standardizing ROIs across subjects (Crespo-Facorro et al., 2000; Kim et al., 2000a). Such more refined ROI approaches, may permit us to precisely detect regional functional changes.

In summary, our overall findings demonstrate that patients with OCD show distinct features of brain metabolic activity for performing cognitive tasks, as well as for presenting obsessive–compulsive symptoms. These abnormal features are particularly apparent in the frontal-subcortical circuits and are also possible in the parietal–subcortical circuits. We should emphasize that the frontal-subcortical circuits might be involved not only in the symptomatic expression of OCD but also in the expression of cognitive deficits in OCD.

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