

# Decrease in Thalamic Volumes of Pediatric Patients With Obsessive-compulsive Disorder Who Are Taking Paroxetine

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**Background:** Thalamic dysfunction has been implicated in obsessive-compulsive disorder (OCD). While OCD frequently has its onset during childhood, to our knowledge, no prior study has measured neuroanatomical changes in the thalamus of patients with OCD near the onset of illness, and before and after treatment.

**Methods:** Volumetric magnetic resonance imaging studies were conducted in 21 psychotropic drug-naïve children, aged 8 to 17 years, with OCD and 21 case-matched healthy comparison subjects. Magnetic resonance imaging studies were also conducted in 10 of the 21 patients with OCD after 12 weeks of monotherapy with the selective serotonin reuptake inhibitor, paroxetine hydrochloride.

**Results:** Thalamic volumes were significantly greater in treatment-naïve patients with OCD than in controls

but declined significantly after paroxetine monotherapy to levels comparable with those of controls. Decrease in thalamic volume in patients with OCD was associated with reduction in OCD symptom severity.

**Conclusions:** Our findings provide new evidence of thalamic abnormalities in pediatric OCD and further suggest that paroxetine treatment may be paralleled by a reduction in thalamic volume. These reductions may, however, not be specific to paroxetine treatment and could be due to a more general treatment response, and/or spontaneous improvement in symptoms. Our findings are preliminary given the small sample size and our inability to measure discrete thalamic nuclei.

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**O**BSESSIVE-COMPULSIVE disorder (OCD) has a lifetime prevalence of 2% to 3%<sup>1-3</sup> with pediatric onset in as many as 80% of cases.<sup>4</sup> Investigation of the developmental neurobiology of the disorder is, therefore, best accomplished by studying early onset illness in childhood to minimize potentially confounding factors of long-term illness duration and treatment intervention.

Abnormalities in the thalamus, a sensory and motor gateway to the cortex, are believed to be involved in the expression and pathophysiological mechanisms most often implicated in the formation of OCD symptoms.<sup>5-7</sup> Neurosurgical interventions such as partial thalamotomy that decrease OCD symptoms in treatment-refractory patients with OCD provide indirect support for this hypothesis.<sup>5</sup> More direct evidence comes from functional neuroimaging studies in adult patients with OCD that demonstrate metabolic abnormalities within the thalamus that have been correlated with OCD symptom severity and subsequent treatment response.<sup>6,8-11</sup>

Serotonin is the neurotransmitter most implicated in the pathophysiology of OCD. Pharmacological treatment studies have demonstrated the effectiveness of the selective serotonin reuptake inhibitors (SSRIs) in the treatment of OCD.<sup>12</sup> This selective serotonergic response has led to the "serotonin hypothesis" of OCD.

The thalamus is a densely serotonergic region.<sup>13</sup> Serotonin is also a complex modulator of thalamocortical development and activity.<sup>14-19</sup> Chugani et al<sup>20</sup> reported high regional serotonin synthesis in the thalamus. Baxter et al<sup>21</sup> have reported decreases in thalamic metabolic activity in adult patients with OCD after SSRI treatment. The preferential therapeutic effects of SSRIs in OCD may arise principally from their potent actions on serotonin neurotransmission within thalamocortical circuits.<sup>22</sup>

Jenike et al<sup>23</sup> reported no thalamic volumetric differences between adult patients with OCD and control subjects. Most of these patients had long-term illness duration and had been treated with SSRIs and other central nervous system-active medi-

## SUBJECTS AND METHODS

### SUBJECTS

Twenty-eight right-hand dominant, psychotropic-naïve, pediatric outpatients with OCD, aged 8 to 17 years, and 28 healthy controls matched pairwise for age, sex, handedness, weight, height, and parental socioeconomic status<sup>24</sup> were studied. All patients recruited were referred to our child psychiatry outpatient clinic at Wayne State University, Detroit, Mich. Two patients with OCD refused to undergo MRI scanning; 5 patients with OCD and 2 controls were also excluded because of motion artifact and magnetic field inhomogeneities. Thus, 21 case-control pairs were analyzed (**Table 1**).

Patients were diagnosed using DSM-IV<sup>25</sup> criteria using the Schedule for Affective Disorders and Schizophrenia for School-aged Children—Present and Lifetime (K-SADS-PL) versions.<sup>26</sup> All subjects and their parent(s) were interviewed by a board-certified child and adolescent psychiatrist (D.R.R.). Exclusion criteria for patients and controls were lifetime history of unipolar or bipolar disorder, psychosis, eating disorders, substance abuse or dependence, Sydenham chorea, Tourette syndrome and other tic-related conditions, conduct disorder, significantly debilitating medical or neurologic conditions, pervasive developmental disorders, mental retardation or learning disorders. Seven of the 21 patients had comorbid anxiety disorders, 2 had dysthymia, 2 had oppositional defiant disorders, 1 had attention-deficit disorder without hyperactivity, 1 had trichotillomania, and 10 had OCD as their sole diagnosis. There was no history of psychiatric illness in controls or in any of their first-degree relatives. Familial psychopathology was assessed using Family History Research Diagnostic Criteria.<sup>27</sup> The child's parents served as informants. Prior to all studies, legal guardians gave written informed consent, and all subjects provided written assent.

### CLINICAL ASSESSMENTS

The Children's Yale-Brown Obsessive Compulsive Scale (CYBOCS)<sup>28,29</sup> measured OCD symptom severity (obsessive symptoms, mean [SD] score, 14.10 [3.77]; compulsive

symptoms, mean [SD] score, 14.10 [3.45]; total mean [SD] score, 28.19 [5.99]). All patients with OCD had a pretreatment total CYBOCS score of at least 19. The 17-item Hamilton Depression Rating Scale<sup>30</sup> measured severity of depression (mean [SD] score, 9.57 [6.67]) and the Hamilton Anxiety Rating Scale<sup>31</sup> measured severity of anxiety (mean [SD] score, 10.24, [6.4]). Tic severity was measured with the Yale-Global Tic Severity Scale<sup>32</sup> (mean [SD] score 1.67, [4.12]). A neuropsychological screening examination assessed general intelligence,<sup>33</sup> cerebral dominance,<sup>34</sup> manual dexterity,<sup>35</sup> and attention.<sup>36</sup> No significant differences were noted between case-control pairs on any of these measures. One patient with OCD was unable to complete the neuropsychological screening examination because of severity of illness.

### MRI STUDIES

All volumetric MRI scans were conducted at the Children's Hospital of Michigan Imaging Center (1.5-T, Horizon 5.7; General Electric, Milwaukee, Wis). Image acquisition and analysis have been described in detail previously.<sup>37</sup> Briefly, image quality and clarity as well as patient head position and cooperation were determined with a sagittal scout series. A 3-dimensional spoiled gradient echo pulse sequence obtained 124 1.5-mm-thick contiguous coronal images (echo time = 5 milliseconds, repetition time = 25 milliseconds, acquisition matrix = 256 × 256 pixels, field of view = 24 cm, and flip angle = 40°). To facilitate image orientation, coronal slices were obtained perpendicular to the antero commissure-postero commissure line. Axial proton density and T2-weighted images were obtained to exclude structural abnormalities on MRI scans. National Institutes of Health image software (version 1.61)<sup>38</sup> was used to measure anatomical data. This technique yields valid and reliable neuroanatomical measurements with a semiautomated segmentation approach.<sup>39</sup>

Neuroanatomical boundaries were determined by reference to standard neuroanatomical atlases,<sup>40-42</sup> and detailed definitions (available on request) were adapted from previously published psychiatric neuroimaging studies of the thalamus.<sup>43-47</sup> Intracranial volume measurement has been described in our previous investigations.<sup>37</sup>

cations. To our knowledge, no prior study of patients with OCD has measured thalamic volume before and after treatment in childhood patients near illness onset. Thus, we performed a volumetric magnetic resonance imaging (MRI) study in the treatment-naïve children with OCD focusing on the in vivo neuroanatomy of the thalamus before and after treatment with the SSRI, paroxetine hydrochloride.

## RESULTS

### VOLUMETRIC COMPARISONS BETWEEN TREATMENT-NAÏVE PATIENTS WITH OCD AND CONTROLS

Psychotropic-naïve patients with OCD had significantly larger thalamic volumes than controls ( $t_{40} = 2.71, P = .01$ ;  $F_{1,38} = 5.65, P = .02$ ; 16% difference between groups) (Table 2). A moderate effect size ( $d_f = 0.86$ ) for abnormality in tha-

lamic anatomy was observed in pediatric patients with OCD. Case-matched control pairs did not differ in intracranial volume ( $t_{40} = 1.26, P = .22$ ;  $F_{1,39} = 1.59, P = .21$ ). No significant correlations were observed between thalamic volumes and clinical or neuropsychological inventories, illness duration, or age of onset of illness.

### TREATMENT RESPONSE

After 12 weeks of paroxetine therapy, patients with OCD showed a significant decrease in OCD symptom severity as reflected by their total CYBOCS scores, obsessive subscale scores, and compulsive subscale scores (**Table 3**). Seven of the 10 subjects were considered treatment responders (>30% improvement on the CYBOCS score) and 3 nonresponders (<30% improvement on the CYBOCS score). There was a significant reduction in anxiety but no significant change in severity of depression or tics.

Separate measurements were obtained for the left and right thalami using a manual tracing technique. The mamillary bodies and interventricular foramen were used as the anterior boundaries. The internal capsule was considered the lateral boundary, the third ventricle the medial boundary, and the hypothalamus the inferior boundary. The posterior boundary was defined by where the thalamus merged under the crux fornix. The superior boundary was the main body of the lateral ventricle (**Figure 1**).<sup>43</sup> The number of coronal slices used to quantify the thalamus ranged from 14 to 20 slices, with an average of 17.5 slices.

Measurements were made by a single well-trained and reliable rater (A.R.G.). Pretreatment and posttreatment patients and controls were measured concurrently with the rater unaware of time or of the identity of MRI scans. Interrater (F.P.M. and A.R.G.) and intrarater reliabilities for thalamic measurements ( $r = 0.98-0.99$ ) and intracranial volume ( $r = 0.99$ ) were very high.

#### PAROXETINE TREATMENT

After completion of the clinical assessment and baseline volumetric MRI study, 13 of the 21 patients with OCD were given paroxetine hydrochloride, 10 mg/d. Eight of the 21 patients and their parents chose nonmedication therapy and/or rejected medication intervention. Paroxetine hydrochloride was titrated to a maximum of 60 mg/d (mean [SD] paroxetine hydrochloride dose,  $51.00 \pm 8.76$  mg/d; range, 40-60 mg/d). Patients were monitored for medication side effects and adverse experiences during the 12-week treatment trial. After 12 weeks of paroxetine therapy, 10 patients with OCD underwent a second follow-up MRI scan. Two patients refused the follow-up MRI scan and, in 1 patient, excess motion artifact precluded measurement. None of the patients had significant side effects during the 12-week paroxetine trial. The same clinical rating scales as those performed at baseline were repeated at follow-up assessments. All patients were treated with paroxetine only and were not receiving cognitive behavioral therapy or psychotherapy other than supportive therapy or family therapy. Patients with OCD were not enrolled in this part of the study if (1) they were unable to be maintained on paroxetine

monotherapy because of comorbid neuropsychiatric condition necessitating additional psychotropic medication, (2) they exhibited contraindication to paroxetine therapy, (3) there was a need for additional behavioral/psychosocial interventions, and (4) the patient's parents refused to consent to their child's taking psychotropic medication and/or the child psychiatrist (D.R.R.) determined that alternative treatment was indicated. Four of these 10 patients had comorbid anxiety disorders, 1 had dysthymia, 1 had oppositional defiant disorder, 1 had trichotillomania, and 3 had OCD as their only diagnosis.

#### DATA ANALYSIS

Thalamic and intracranial volumes were analyzed using independent  $t$  tests as well as analyses of covariance (ANCOVAs) to test for differences between treatment-naïve patients with OCD and controls. Unpaired  $t$  tests were used to compare patients with OCD and controls on neuropsychological screening measures, age, height, weight, and parental socioeconomic status (Table 1). Paired  $t$  tests and ANCOVAs with intracranial volume as a covariate were then conducted to assess differences in thalamic volumes between patients with OCD before and after treatment. Paired  $t$  tests were used to compare intracranial volume in patients with OCD before and after treatment. Paired  $t$  tests compared pretreatment vs posttreatment CYBOCS, Hamilton Depression Rating Scale, Hamilton Anxiety Scale, and Yale Tic Severity Scale scores before and after paroxetine treatment. Pearson and partial correlations were used to determine the association between thalamic and intracranial volumes and age, clinical and neuropsychological inventories, and illness duration. Two-way sex by diagnosis ANCOVAs were conducted to delineate sex effects. Differences in left and right thalamic volumes were also examined using repeated-measures ANOVAs in which the main effects of side, diagnostic group, and group by side interaction were tested. Because no significant differences in laterality interaction effects were detected in case-control pairs, right and left thalamic volumes were pooled (**Table 2**). Two-tailed significance tests ( $P < .05$ ) are presented throughout.

**Table 1. Clinical and Demographic Characteristics of Pediatric Patients With OCD and Healthy Control Subjects\***

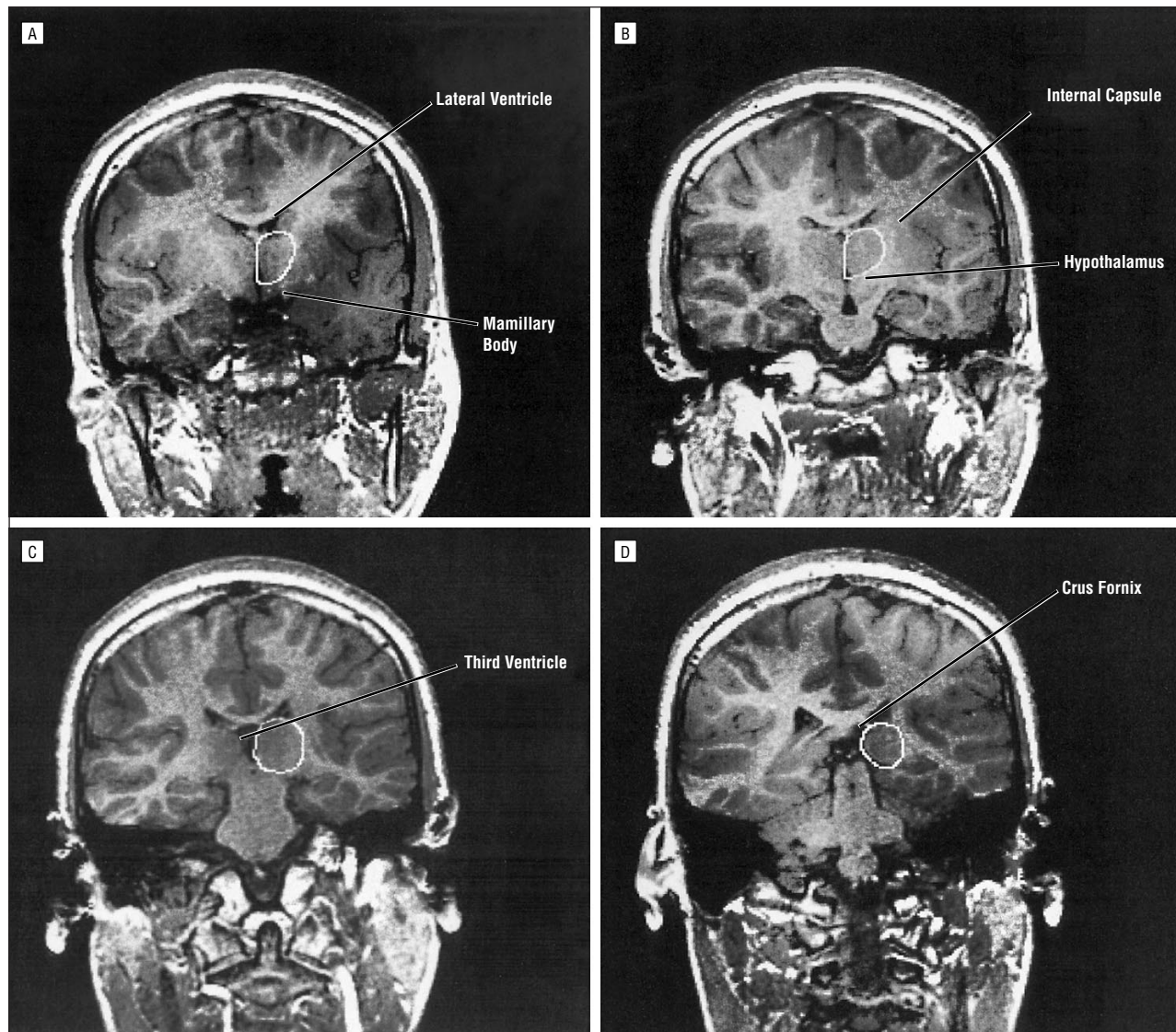
Characteristic	Patients With OCD (n = 21)	Healthy Control Subjects (n = 21)	t†	df‡	P
Age, y	12.35 ± 2.93 (8.08-17.33)	12.47 ± 2.64 (8.33 ± 17.17)	0.14	40	.89
Sex					
No. of males	7	7			
No. of females	14	14			
Weight, kg	43.83 ± 16.18 (17.27-79.55)	51.52 ± 15.56 (27.27-79.55)	0.65	40	.56
Height, cm	151.67 ± 12.58 (121.92-172.72)	155.06 ± 14.11 (121.92-180.34)	0.82	40	.42
Parental SES§	2.52 ± 0.75 (1.00-4.00)	2.71 ± 0.56 (2.00-4.00)	0.93	40	.36
Age of onset of first clinical presentation, y	10.49 ± 2.92 (5.25-15.33)	...	...	...	...
Duration of illness, y	1.86 ± 1.84 (0.25-7.00)	...	...	...	...

\*Pediatric patients with obsessive-compulsive disorder (OCD) were psychotropic naïve. Data are presented as mean ± SD, unless otherwise indicated. Numbers in parentheses indicate reference ranges. Ellipses indicate not applicable.

†Indicates independent statistic using the paired  $t$  test.

‡df indicates degrees of freedom.

§Parental SES indicates parental socioeconomic status that assesses parental education and occupational functioning on a scale of 1 (highest) to 5 (lowest).<sup>24</sup>



**Figure 1.** Representative multislice composite series of coronal images demonstrating the boundaries delineating measurement of thalamic volume.

Significant differences in thalamic volumes were observed between treatment-naïve patients with OCD and case-matched controls ( $t_{18} = 2.19, P = .01, F_{1,16} = 6.19, P = .02; 10.10 \pm 1.86 \text{ cm}^3$  vs  $7.91 \pm 1.72 \text{ cm}^3$ , respectively). Thalamic volume decreased significantly in patients with OCD after paroxetine treatment ( $t_9 = 2.95, P = .02, F_{1,16} = 8.15, P = .01; 19\%$  reduction). A large effect size ( $df = 1.28$ ) was observed for reduction in thalamic volume after paroxetine treatment. Thalamic volume did not differ significantly between patients with OCD after paroxetine treatment and controls ( $t_{18} = .39, P = .70, F_{1,16} = 0.10, P = .76; 8.18 \pm 1.26 \text{ cm}^3$  vs  $7.91 \pm 1.72 \text{ cm}^3$ , respectively) (**Figure 2**). Intracranial volume did not differ significantly between patients with OCD before and after paroxetine therapy ( $t_9 = 1.37, P = .21; 1211.25 \pm 84.51 \text{ cm}^3$  vs  $1190.30 \pm 104.78 \text{ cm}^3$ , respectively). Reduction in thalamic volume was correlated with reduction in OCD symptom severity as measured by the CYBOCS ( $r = 0.74, P = .02$ ) (**Figure 3**). Change in thalamic volume was not associated with a change in depressive, anxiety, or tic symp-

tom severity. Paroxetine dosage was also not correlated with thalamic volume or change in thalamic volume after treatment.

To evaluate the significance of our findings, test-retest reliability of thalamic volumetric measurements were obtained in 8 healthy pediatric controls who received a baseline MRI scan and were then rescanned approximately 12 weeks later. Controls did not receive medication. The temporal stability of the *in vivo* measure of thalamic volume in healthy children was  $\pm 5.6\%$  of the initial measure on repeated scanning ( $7.70 \pm 1.84 \text{ cm}^3$  vs  $8.16 \pm 1.93 \text{ cm}^3$ , respectively). Thus, the observed differences in thalamic volumes between patients with OCD before treatment and controls and the decrease in thalamic volume seem to be statistically significant.

#### SEX

Comparable ages were observed in male (mean  $\pm$  SD age,  $11.13 \pm 1.49$  years) and female patients ( $11.42 \pm 3.19$  years) with OCD. Age of onset of illness did not differ between

**Table 2. Volumetric Results for Treatment-Naïve Patients With OCD and Healthy Control Subjects\***

Region	Volume, cm <sup>3</sup>		95% Confidence Interval of Difference Between Groups (Range)
	Treatment-Naïve Patients With OCD (n = 21)	Healthy Control Subjects (n = 21)	
Intracranial volume, cm <sup>3</sup>	1179.95 ± 115.42	1129.61 ± 122.90	-46.3393 (-120.669 to 28.02)
Thalamus			
Total	9.17 ± 2.00	7.68 ± 1.52	-1.4837 (-2.5915 to -0.3759)†
Right	4.65 ± 1.05	3.87 ± 0.74	-0.7717 (-1.3365 to -0.2070)‡
Left	4.52 ± 1.01	3.81 ± 0.88	-2.430 (-1.3042 to -0.1199)§

\*Data are given as mean ± SD. OCD indicates obsessive-compulsive disorder.

†P = .01 by paired t test.

‡P = .009 by paired t test.

§P = .02 by paired t test.

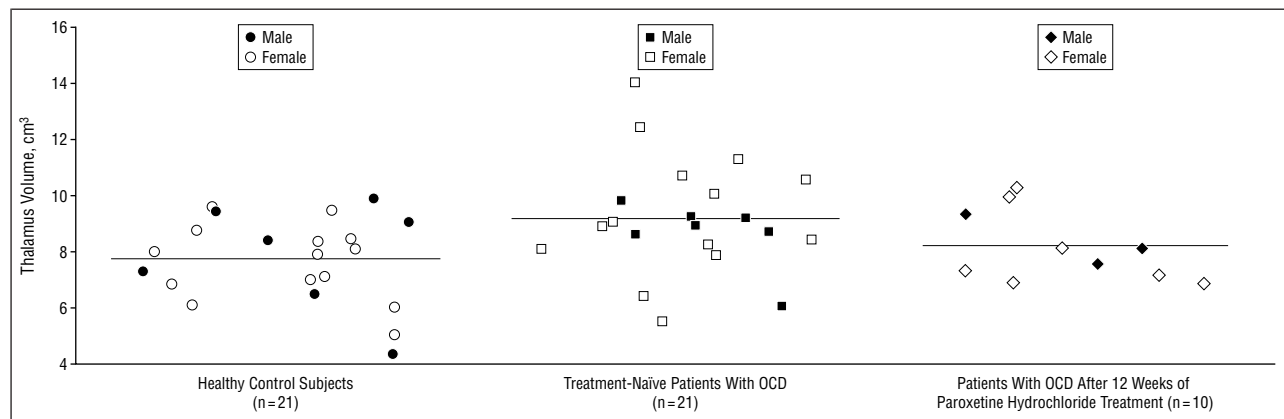
**Table 3. Clinical Assessment Data From Nondepressed, Psychotropic Medication-Naïve Pediatric Patients With OCD Before and After Paroxetine Treatment\***

Instrument	Patients With OCD†		t‡	P
	Before Treatment	After Treatment With Paroxetine Hydrochloride		
Total score CYBOCS	31.30 ± 4.37	20.60 ± 5.87	4.31	.002
Obsessive subscale score	15.30 ± 1.70	10.20 ± 2.74	5.92	<.001
Compulsive subscale score	16.00 ± 2.91	10.30 ± 3.60	3.19	.01
HAMA	10.24 ± 6.40	3.80 ± 2.97	2.50	.03
HDRS	9.57 ± 6.68	3.90 ± 3.81	1.85	.10
YGTS	1.48 ± 4.09	0.40 ± 0.97	0.97	.36

\*OCD indicates obsessive-compulsive disorder; CYBOCS, Children's Yale-Brown Obsessive Compulsive Scale; HAMA, Hamilton Anxiety Rating Scale; HDRS, Hamilton Depression Rating Scale; and YGTS, Yale Global Tic Severity scale. Data are presented as mean ± SD.

†There were 10 pediatric patients with OCD studied before and after 12 weeks of paroxetine treatment.

‡Paired t test.



**Figure 2.** Data are presented as mean (±SD) values for the 3 groups. OCD indicates obsessive-compulsive disorder.

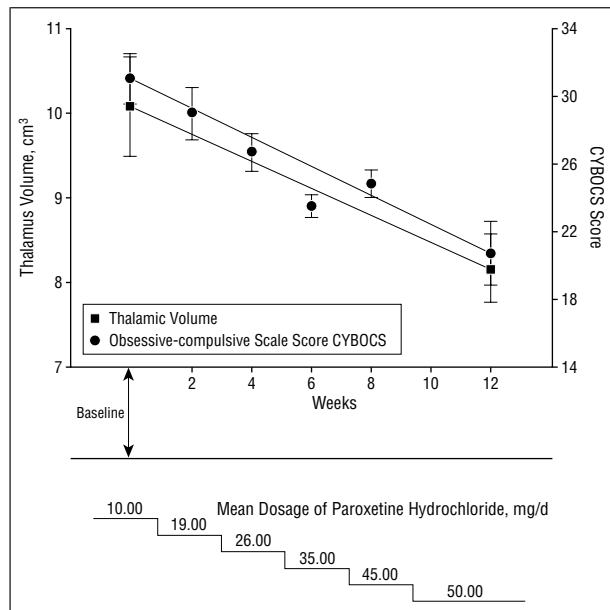
male and female patients with OCD ( $t_8 = .643$ ,  $P = .54$ ;  $10.64 \pm 1.43$  years vs  $9.83 \pm 1.93$  years, respectively). No sex-related differences were noted in thalamic and intracranial volumes between patients with OCD before and after treatment or controls.

**COMMENT**

To our knowledge, this is the first neuroimaging study of treatment-naïve patients with OCD to demonstrate increased thalamic volumes that decrease following treat-

ment with the SSRI, paroxetine. Our results suggest that abnormalities in thalamic anatomy may represent a central neurobiological deficit in this illness and may be reversible with effective paroxetine treatment. Reductions in thalamic volume may, however, not be specific to paroxetine treatment and might be the result of a general treatment response or spontaneous improvement.

While most studies of pediatric patients with OCD report an approximately 2:1 prevalence of males to females,<sup>48</sup> twice as many female subjects were enrolled in this study. Tic-related OCD is especially common in young



**Figure 3.** Decrease in thalamic volume associated with reduction in obsessive-compulsive score of the Children's Yale-Brown Obsessive Compulsive Scales (CYBOCS).

males<sup>48</sup> so this may have skewed our sample. This was also a small sample so that perhaps with additional recruitment, the male-female ratio would more closely approximate the typically reported pattern.

Serotonergic pathways play a crucial neuromodulatory role in thalamocortical development and activity.<sup>14-17,19</sup> Serotonin agonists decrease brain glucose metabolism in animals.<sup>49</sup> Increased thalamic volumes in psychotropic-naïve patients with OCD may be consistent with prior reports of hypermetabolism and increased regional cerebral blood flow in the thalamus of adult patients with OCD<sup>6,8,10,50</sup> that decreased after SSRI intervention.<sup>21</sup> This may, in part, explain the finding of Jenike et al<sup>23</sup> of no thalamic volumetric differences between adult patients with OCD and controls. Most of the patients they studied had been treated with psychoactive medications, particularly SSRIs. This underscores the importance of controlling for treatment intervention as well as illness duration and comorbidity when measuring brain anatomy.

The increased thalamic volumes in psychotropic-naïve patients with OCD are consistent with previous findings in a similar sample of patients with OCD and case-matched controls studied at the University of Pittsburgh Medical Center<sup>51</sup> and elsewhere<sup>23,52</sup> demonstrating increased ventral prefrontal cortical volumes in patients with OCD. Increased metabolic activity in ventral prefrontal cortex has also been reported in patients with OCD.<sup>21,50,53</sup> Ventral prefrontal cortex sends dense efferent projections to the thalamus and caudate nucleus.<sup>5</sup> While caudate volumetric abnormalities were not observed between patients with OCD ( $7.69 \pm 1.31 \text{ cm}^3$ ) and controls ( $7.49 \pm 1.10 \text{ cm}^3$ ) in our study, metabolic activity in ventral prefrontal cortex is very closely coupled with that in the caudate nucleus and thalamus in patients with OCD.<sup>21</sup> The thalamus serves as the final subcortical input to frontal cortex and as such stimulates cortical out-

put when released from the inhibitory tonic influence of the striatum.<sup>5</sup> As such, the thalamus may be exquisitely sensitive to SSRI intervention resulting in the volumetric changes observed in the present study.

Although our findings are consistent with serotonin-mediated thalamic involvement in OCD, our findings are preliminary given the limitations of our study. One major confound of this study was our inability to distinguish specific regions of the thalamus to identify volumetric changes within a particular thalamic target field. The dorsomedial nucleus of the thalamus may be especially relevant to the study of OCD.<sup>5</sup> Fitzgerald et al<sup>54</sup> have also identified abnormalities in the putative neuronal marker *N*-acetyl-aspartate, localized to medial and not lateral thalamus. Indeed, localization of abnormalities in other brain regions in patients with OCD has been observed with ventral prefrontal cortex more affected than dorsal prefrontal cortex<sup>51</sup> and putamen more affected than caudate.<sup>37</sup>

In this study, we chose to treat patients openly with paroxetine. A double-blind, placebo-controlled study would have been superior for delineating the specificity of neuroanatomical change in relation to paroxetine therapy. Since maximal anti-OCD treatment intervention effects may in some cases be delayed several months,<sup>12</sup> volumetric assessment after 12 weeks of paroxetine therapy is indicated.

Paroxetine was administered in a flexible dosage design since we were measuring treatment response not the dose-response curve. There is no known single optimal dose for paroxetine in treating OCD.<sup>12,55</sup> Paroxetine dosage was unassociated with posttreatment thalamic volumes or with reduction in thalamic volumes.

We were also unable to ethically give healthy pediatric comparison subjects paroxetine for 12 weeks. We believe that the critical study questions were addressed without our administering an SSRI to children who did not need medication. Thalamic volumetric reductions may be due to a general effect of paroxetine although reduction in thalamic volumes was associated with the reduction in OCD symptom severity. The changes in thalamic volume after paroxetine treatment also did not seem to reflect scan-rescan effects.

Together, our findings suggest that serotonergic abnormalities in patients with OCD may lead to volumetric abnormalities in the thalamus that may be reversible with effective SSRI treatment. Alternatively, it is possible that the observed thalamic changes with paroxetine treatment are epiphenomena of the underlying neuropathology and treatment intervention. The observed change could, for example, be secondary to hemodynamically mediated medication treatment effects. Second, paroxetine also has dopamine-blocking effects, ie, extrapyramidal side effects including tardive dyskinesia. Therefore, other neurotransmitter alterations such as those in the dopaminergic system may also be related to the observed neuroanatomical changes. While, to our knowledge, direct evidence for a dopamine-blocking effect of paroxetine treatment is lacking, there may be an indirect effect of serotonin causing dopamine inhibition.<sup>56</sup> These preliminary findings must be viewed with caution but demonstrate how volumetric MRI can be used

for the in vivo, noninvasive measurement of the impact of psychotropic medication on brain neuroanatomy in OCD.

Acute studies earlier in treatment and longitudinal studies of patients beyond 12 weeks are critical to identify mechanisms of response to SSRIs in OCD and their relationship to thalamic volumetric measures. Future neuropathological and in vivo neuroanatomical studies before and after SSRI treatment in brain regions other than the thalamus, ie, ventral prefrontal cortex and striatum, are indicated. For example, neuroleptics increase caudate nucleus volumes in patients with schizophrenia.<sup>57,58</sup> Baxter et al<sup>21</sup> also found that metabolic relationships between ventral prefrontal-striatal-thalamic circuits were altered after fluoxetine treatment. Recent functional MRI studies in adult patients OCD<sup>59</sup> suggest the potential feasibility of noninvasive investigation of corticostriatal-thalamic function in pediatric patients with OCD. Such studies must control for volumetric differences in these circuits between patients with OCD and controls as well as treatment-induced neuroanatomical changes.

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