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Supplemental Material  
Clinical Guidance

## Right Prefrontal Cortical Thickness is Associated With Response to Cognitive-Behavioral Therapy in Children With Obsessive-Compulsive Disorder

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**Abstract**

**Objective:** Cognitive-behavioral therapy (CBT) is considered a first-line treatment for obsessive-compulsive disorder (OCD) in pediatric and adult populations. Nevertheless, some patients show partial or null response. The identification of predictors of CBT response may improve clinical management of patients with OCD. Here, we aimed to identify structural magnetic resonance imaging (MRI) predictors of CBT response in two large series of adults and children with OCD from the worldwide ENIGMA-OCD consortium.

**Method:** Data from 16 datasets from 13 international sites were included in the study. We assessed which variations in baseline cortical thickness, cortical surface area and subcortical volume predicted response to CBT (percentage of baseline to post-treatment symptom reduction) in two samples totaling 168 children/adolescent patients (age range 5-17.5) and 318 adult patients (age range 18-63) with OCD. Mixed linear models with random intercept were used to account for potential cross-site differences in imaging values.

**Results:** Significant results were exclusively observed in the pediatric sample. Right prefrontal cortex thickness was positively associated with the percentage of CBT response. In a post-hoc analyses, we observed that the specific changes accounting for this relationship were a higher thickness of the frontal pole and the rostral middle frontal gyrus. We observed no significant effects of age, sex, or medication on our findings.

**Conclusion:** Higher cortical thickness in specific right prefrontal cortex regions may be important for CBT response in children with OCD. Our findings suggest that the right prefrontal cortex plays a relevant role in the mechanisms of action of CBT in children.

### Keywords

obsessive-compulsive disorder; neuroimaging; magnetic resonance imaging; cognitive-behavioral therapy; anxiety disorders

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## INTRODUCTION

Patients with obsessive-compulsive disorder (OCD) typically present with anxiety-inducing intrusive thoughts, images, or impulses (obsessions), and repetitive behaviors (compulsions). OCD has a lifetime prevalence of 2.3% in the general population<sup>1</sup>, and its chronic course leads to important socioeconomic costs<sup>2</sup>. Cognitive-behavioral therapy (CBT) is an effective treatment for anxiety-related disorders, and it is considered a first-line and well-established treatment for OCD in pediatric and adult populations<sup>3-5</sup>. Although response rates to CBT in patients with OCD (between 62% and 68%) are higher than those for placebo and other treatments<sup>6</sup>, there is still a significant number of patients showing partial or no response<sup>7</sup>. The identification of predictors of response to CBT is therefore of paramount importance to select the best candidates for this treatment and ultimately optimize the clinical management of patients. Magnetic resonance imaging (MRI) is currently widely available and provides information about brain function and structure using minimally invasive means; hence, it may help to identify brain circuits underpinning psychological processes relevant for CBT success.

To date, studies using structural and functional MRI to predict treatment response in OCD have been largely inconclusive. In functional studies, a wide variety of approaches have been employed, ranging from different methods for resting-state data analysis to task-based approaches using symptom provocation and other experimental paradigms. The variety of methods and the low statistical power of small-sampled studies have prevented a meaningful integration of findings and drawing clinically relevant conclusions<sup>8</sup>. Results of brain structural studies have also been heterogeneous, except for evidence that morphometric features in the prefrontal cortex may be useful predictors of treatment outcome. Hoexter et al.<sup>9</sup> reported that larger pre-treatment gray matter volumes (derived from a voxel-based morphometric analysis) in the subgenual cingulate cortex predicted greater symptom improvement, while Fullana et al.<sup>10</sup> found that lower cortical thickness in another part of the ventromedial prefrontal cortex (vmPFC), i.e., the rostral anterior cingulate cortex, predicted good response to CBT. Despite the apparent opposite direction of these findings, they may point to regulation by the vmPFC of subcortical activity (e.g., amygdala). In addition, smaller volume in other regulatory prefrontal regions, such as the dorsolateral prefrontal cortex (dlPFC), has also been related to poor CBT outcomes<sup>11</sup>.

Focusing on pediatric populations, a recent whole-brain study reported that thinner cortices in 9 fronto-parietal regions predicted clinical improvement after CBT<sup>12</sup>. Results in children should be interpreted differently from results in adults. In this population, it is important

to consider maturation-related changes<sup>13,14</sup>. Moreover, in children, CBT has been shown to modulate the development of specific regions of the prefrontal cortex, such as the orbitofrontal cortex, where volume increases were reported after CBT<sup>15</sup> and two years after treatment, especially in children between 8 and 12 years of age<sup>16</sup>.

The aim of this study was to identify structural MRI predictors of CBT response in adults and children with OCD. For this, we pooled data from multiple international sites participating in the worldwide ENIGMA-OCD consortium. This consortium provides the largest sample of patients with OCD with both imaging and clinical information (including response to CBT) available. Further, to aid in the interpretation of findings (i.e., to evaluate whether structural variations associated to CBT response did also differ from normative control values), we also compared regional brain measures of OCD patients with reference values from healthy controls (HC). We did not predict the specific location or the directionality of our findings, because previous research has reported both positive and negative correlations with CBT outcome involving different brain areas.

## METHOD

### Participants

We included in this analysis 16 datasets from 13 international neuroimaging institutes participating in the ENIGMA-OCD consortium (<http://enigma.ini.usc.edu/ongoing/enigma-oed-working-group/>). In total, we analyzed clinical, sociodemographic and structural imaging data from 1057 subjects: 489 patients with OCD (diagnosed with DSM criteria) (168 children and adolescent subjects, <18 years of age; and 318 adult subjects) and 571 healthy control subjects (HCs) free from any psychiatric, neurological or major medical condition (286 children and adolescent subjects, and 285 adult subjects) (Table S1, available online). Patients with OCD underwent CBT after the baseline MRI scan, and were clinically evaluated before and after treatment.

All participants, or their parents or legal guardians, signed an informed consent approved by the ethical committees in clinical research of their corresponding institutions.

### CBT characteristics and treatment response

From each site, we collected the following CBT variables: group or individual treatment, total number of sessions (as well as number of introductory/psychoeducational sessions, and of exposure/relapse-prevention sessions), duration of the therapy, frequency of sessions, and use of cognitive tasks or techniques. Treatment response was operationalized as the percentage of symptom reduction between baseline and post-treatment severity assessments:

$$\frac{(C)YBOCS_{pre} - CBT - (C)YBOCS_{post} - CBT}{(C)YBOCS_{pre} - CBT} \times 100$$

We also split patient samples into patients with positive response to CBT and patients with non-positive response to CBT using a symptom improvement cut-off of 35%<sup>17</sup>.

## Neuroimaging data acquisition and processing

High-resolution structural T1-weighted MRI brain scans were acquired at each site (Table S2, available online), and pre-processed locally in a harmonized way following a common pipeline, described elsewhere<sup>18,19</sup>. Briefly, images were parcellated using the fully automated and validated segmentation software FreeSurfer v5.3<sup>20</sup> following standardized ENIGMA protocols to harmonize analysis and quality control processes across multiple sites (<http://enigma.ini.usc.edu/protocols/imaging-protocols/>). For both hemispheres, thickness and surface areas were estimated from 68 (34 left and 34 right) cortical gray matter regions, which were parcellated based on the Desikan-Killiany atlas<sup>21</sup>. At this stage, the two whole-hemisphere measures were visually inspected and statistically evaluated for outliers. We also obtained the volume of seven subcortical regions of interest (bilaterally): nucleus accumbens, caudate, putamen, pallidum, amygdala, hippocampus, and thalamus.

## Statistical analyses

In line with previous work of the ENIGMA-OCD consortium<sup>22</sup>, individual level subject data were pooled for one merged adult sample and another children/adolescent dataset.

To better characterize our samples, we first contrasted differences in age, sex, and imaging variables between patient groups and healthy controls. Next, within patient samples, we contrasted sociodemographic, clinical and CBT-related variables between treatment positive response and those who non-achieve a positive-response. In all these analyses, we used independent sample *t* tests for continuous variables, and chi-squared tests for categorical variables.

Imaging data were analyzed using a mega-analysis strategy with mixed-effects linear models with random intercept to account for cross-site differences. This approach provided lower standard errors and narrower confidence intervals in relation to meta-analytic approaches, while it also displayed better fit indices compared to linear regression methods<sup>22</sup>. We first assessed which sociodemographic, clinical and CBT-related variables were associated with CBT response, also using mixed linear models. The variables found to be associated with treatment outcome were subsequently used as nuisance covariates in all imaging analyses, along with total intracranial volume (TIV) for surface area and volume analyses. We also performed sensitivity analyses to explicitly evaluate the effects of age, sex, and medication (both previous and during CBT treatment) in our findings.

For cortical thickness and surface area analyses, cortical parcellations were grouped in 6 right/left regions (12 regions in total): sensorimotor strip, prefrontal cortex, temporal cortex, parietal cortex, occipital cortex, and limbic cortex (including the insular cortex). Subcortical volume analyses considered the 7 right/left subcortical regions described above (14 regions in total). These measurements were the focus of separate analyses, with a Bonferroni corrected threshold of  $P < 0.00416$  ( $0.05/12$ ) for cortical thickness and surface area evaluations, and  $P < 0.0036$  ( $0.05/14$ ) in subcortical volume analyses. All analyses were first performed considering treatment response as a quantitative variable (i.e., percentage of symptoms reduction) and then performed considering treatment response as a categorical variable (i.e., positive response vs. non-positive response). Effect sizes were presented as



Pearson's  $r$  for quantitative relationships and as Cohen's  $d$  for analyses of treatment response categories, following the equations described in<sup>23</sup>.

## RESULTS

### Demographic, clinical and CBT-related characteristics

Demographic and clinical characteristics of the overall adult and children samples are detailed in Table 1, and site-specific information are detailed in Tables S3 and S4, available online.

We did not observe differences between patients with OCD and HCs in mean age or sex distribution, neither in the child/adolescent nor in the adult sample.

CBT-related variables are presented in Table 2. Our sample of adult patients included treatment protocols that were administered individually, in a group, or using an intensive protocol, which can involve both individual and group sessions concentrated in a few days. In children, a large majority of patients were administered individual CBT. It is also important to highlight that cognitive strategies (including techniques such as cognitive restructuring, thought records or behavioral experiments), in addition to exposure and response prevention, were used both in adult and children/adolescent patients, although their use in adult patients was not as common as it was in children/adolescent patients.

### Brain structural differences between patients with OCD and Healthy Controls

These results are presented in Supplement 1 and Tables S5-S10, available online.

### Clinical and CBT-related variables in patients with positive response and in those with non-positive response.

After CBT completion, 61.6% of adult patients and 56.5% of pediatric patients showed a symptom reduction  $\geq 35\%$ . Tables S11 and S12 (available online) present the main clinical and CBT-related features in these groups for the pediatric and the adult samples, respectively.

### Mixed Linear models: Prediction of CBT response

**Pediatric sample**—The sociodemographic and baseline and CBT clinical variables associated with better CBT response were higher age at disease onset, lower current age, and no previous medication use (Table S13, available online). These variables were therefore controlled for in imaging analyses.

At the cortical level, we observed that right prefrontal cortex thickness was positively associated with the percentage of CBT response ( $t=3.25$  [ $r=0.25$ ];  $P=0.002$ , see Figure 1 (A) and Table 3). This same measurement was also significantly associated with the dichotomous categorical variable treatment response (positive response vs. non-positive response) ( $t=3.05$  [ $d=0.48$ ];  $P=0.003$ , see Figure 1 (B)). No further results were observed at the cortical level. At the subcortical level, we observed two trend level results: left hippocampal volume was positively associated and left accumbens volume negatively

associated with CBT response ( $t=2.84$  [ $r=0.22$ ] and  $t=-2.85$  [ $r=-0.22$ ], respectively;  $P=0.006$ ). These results are reported in Tables S14 and S15, available online. These results held when we additionally controlled for sex and medication use during CBT (current age and previous medication use were already included in the model).

In a post-hoc analysis, we explored which right prefrontal subdivisions were responsible for the significant association between right prefrontal thickness and CBT response. We observed that right frontal pole ( $t=3.58$  [ $r=0.27$ ];  $P=0.001$ ) and right rostral middle gyrus ( $t=3.04$  [ $r=0.23$ ];  $P=0.003$ ) thickness were positively associated with the percentage of treatment response. These results held when we additionally controlled for sex and medication use during CBT, and are presented in Figure 2A/B and Table S16, available online. We also observed that the right superior frontal gyrus ( $t=2.91$  [ $r=0.22$ ];  $P=0.004$ ) was associated with CBT response, but this result was no longer significant when controlling for sex and medication use during CBT.

These results were largely confirmed when repeating the analyses excluding OCD subjects from centers contributing with less than 10 participants ( $n=8$ , 1 center). Right prefrontal cortex findings remained significant ( $t=3.25$  [ $r=0.25$ ];  $P=0.002$  and  $t=3.74$  [ $d=0.61$ ];  $P<0.0005$  for quantitative and categorical analyses, respectively). Within the right prefrontal cortex, frontal pole findings also remained significant ( $t=3.38$  [ $r=0.26$ ];  $P=0.001$ ), but results from the rostral middle frontal gyrus were only significant at the trend level ( $t=2.75$  [ $r=0.22$ ];  $P=0.007$ ). Previous trend level findings involving left hippocampus and accumbens volumes also diminished their significance. These results are presented in Table S17, S18, S19 and S20, available online.

To better evaluate the potential effects of age in our findings, we split the pediatric sample into two groups: children ( $\leq 12$  years old) and adolescents ( $>12$  years old), akin to what has been done in previous studies<sup>16</sup>. Results did not differ between these age groups, and, indeed, we observed no regions significantly predicting CBT response in any of the groups because of the smaller statistical power.

In a final post-hoc analysis, we observed that none of the regional brain measures associated with CBT response significantly differed between patients with OCD and healthy controls.

**Adult Sample**—The sociodemographic and baseline clinical and CBT variables significantly associated with the percentage of symptom reduction after CBT were age of onset (the higher the age, the better the response) and type of CBT: intensive treatment, in comparison to individual and group treatment, was associated with a better response (see Table S21, available online). These variables were therefore controlled for in imaging analyses. None of the imaging assessments was associated with response to CBT after Bonferroni correction for multiple comparisons (see Tables S22, S23 and S24, available online), and these results did not change after controlling for age, sex, and use of medication prior to or during CBT. To evaluate whether the pattern of results in the adult sample differed between those with early vs. late age of onset, this sample was split in two groups ( $< 18$  years), and no differences regarding the association between morphometric variables and CBT response were observed.

## DISCUSSION

This is the largest study evaluating the anatomical predictors of CBT response in OCD. We explored two large multicenter pooled datasets of adults and children/adolescents with OCD, and we identified significant structural brain characteristics associated with positive CBT outcomes in the pediatric sample. Specifically, and controlling for all the sociodemographic and clinical variables also associated with CBT response, we observed that larger right prefrontal thickness predicted greater symptom improvement after CBT in children/adolescents. Moreover, within this region, we were able to more precisely locate our findings to the frontal pole and the rostral middle frontal gyrus. Our results, therefore, indicate that, in pediatric populations with OCD, responses to psychological interventions may be predicted by anatomical variability in specific brain areas. In adult populations, however, factors other than brain anatomy may more strongly moderate CBT response.

The positive association between right frontopolar cortex thickness and CBT response may be interpreted in relation to previous findings. Electrical stimulation of this region has been recently shown to increase safety learning in OCD, which may critically boost CBT effects<sup>24</sup>. Moreover, connectivity of the frontopolar cortex with emotion processing regions, such as the bed nucleus of the stria terminalis (BNST), is increased in adults with OCD<sup>25</sup>, and this can be interpreted as resulting from the control exerted by the frontopolar cortex over abnormally increased BNST activations underpinning sustained anxiety responses<sup>26</sup>. Partially concurring with these results, graph-based approaches have shown that functional connectivity of the frontopolar cortex with distant structures is disrupted in pediatric OCD samples<sup>27</sup>. Furthermore, in depression samples, the frontopolar cortex has been linked to specific cognitive processes targeted by CBT, such as negative cognition in ‘future thinking’<sup>28</sup>. CBT has indeed been shown to modulate frontopolar activity in these clinical samples<sup>29</sup>, which is germane to the present findings considering the highly prevalent use of cognitive techniques in our sample of children and adolescents with OCD, even though the findings from these two last studies were reported in adult samples.

The other subdivision of the right prefrontal cortex associated with the extent of CBT response was the rostral middle frontal gyrus. This finding resonates with previous studies on the neuroimaging correlates of CBT outcomes in patients with OCD and other psychiatric disorders, which have, however, emphasized different aspects of middle frontal gyrus function. First, this region, together with parietal lobe structures, is part of the dorsal attentional network, whose intrinsic connectivity has been shown to increase after CBT in anxiety disorders in parallel with clinical improvement<sup>30</sup>. Similarly, in pediatric OCD, increased connectivity of this fronto-parietal network has been shown to predict better CBT response<sup>31</sup>. These results may be framed within the attentional control theory, which suggests that there exists an inverse relationship between anxiety and attentional control<sup>32</sup>. Nevertheless, findings from the evaluation of the structural features of this fronto-parietal network have been opposite to our results, and thinner fronto-parietal cortices have been associated with CBT success<sup>12</sup>. Although this heterogeneity in findings motivates further research, we propose that the methodological differences between the studies, such as the different number of individuals assessed in each study, may partially account for these discrepancies.

Other studies have emphasized other roles of the rostral middle frontal gyrus beyond its participation in attentional networks. This region roughly corresponds to Brodmann areas 9 and 46, and may therefore be labeled as dorsolateral prefrontal cortex, the core area of executive functioning that optimizes information processing and response to external stimuli<sup>33</sup>. Van der Straten et al.<sup>34</sup>, for instance, observed excessive middle frontal gyrus activation in a pediatric OCD sample during an executive planning task – a finding that normalized after a CBT trial. In contrast with other areas involved in executive function, such as the anterior cingulate cortex or the superior frontal gyrus, the role of the middle frontal gyrus is probably more related to the processing and regulation of emotional information<sup>35</sup>. This is important because although regulation of amygdala activity in the context of CBT response in OCD has been related to ventromedial prefrontal cortex function<sup>12,36</sup>, other studies have shown that the connectivity between the right middle frontal gyrus and the left basolateral amygdala is increased in patients with OCD<sup>37</sup>. These notions dovetail with the conceptualization of CBT as an intervention aimed at modulating emotion regulation circuits and processes<sup>38</sup>, in which executive functions play a nodal role<sup>39</sup>. Our findings of a positive association between right middle frontal gyrus thickness and CBT response could be related to baseline variability in the emotion regulation capacity of children/adolescents. Interestingly, gray matter volume in the right middle frontal gyrus has been observed to increase after group CBT in young students with mild depressive symptoms<sup>40</sup>.

None of the regions described here to be associated with CBT response significantly differed from controls in our pediatric sample. This suggests that interventions such as CBT do not have to necessarily act upon regions with alleged baseline dysfunction (i.e., restoring their function), as could be expected if they showed abnormal brain volumes. Conversely, CBT may act through compensatory mechanisms by recruiting brain systems (e.g., attentional, top-down regulatory or mnemonic systems) which function may be at least partially independent from disorder's nuclear symptoms. Improving functioning of these brain systems may result in symptom improvement. These are indeed the principles of cognitive remediation therapy, which, despite the recent negative findings regarding its usefulness as main therapy in treatment protocols for OCD<sup>41</sup>, might help optimizing the success of CBT treatment strategies through modulation of relevant brain circuits.

Variability in the neural underpinnings of these systems, moreover, should be associated with treatment success and disorder evolution, although not necessarily with disorder severity, or the identification of OCD cases or subjects at increased risk for OCD by means of biologically-informed approaches. An additional implication of this is that regions linked to CBT response may be shared across different disorders, providing a neurobiological explanation to the trans-diagnostic efficacy of CBT<sup>42</sup>.

In contrast to what was observed in relation to prediction of CBT response, we observed more regions significantly differing between patients with OCD and controls in the adult than in the pediatric sample. Thus, while in children we only observed a thinner left parietal cortex, in adults, thinner cortices were observed in the bilateral parietal and the right prefrontal cortices. Moreover, in adults we observed larger left pallidal and smaller thalamic volumes. These findings are in overall agreement with previous studies<sup>18,19,43</sup>,

and suggest that maturation processes may play a role in the expression of morphometric brain alterations in OCD. Although the direct comparison between pediatric and adult samples is beyond the scope of this study, it is important to discuss why associations with CBT response have been exclusively observed in children. While it is true that initial reports described morphometric changes associated to response to CBT in adults with OCD<sup>9,10</sup>, more recent research has shown that region-specific prefrontal changes in relation to CBT response are probably more likely to be observed in pediatric samples<sup>12</sup>, whereas in adult patients, structural changes predicting CBT effects have been reported at the whole-brain network level, also encompassing posterior brain regions<sup>44</sup>. Despite findings are heterogeneous and therefore difficult to integrate with our present results, overall, it seems plausible that region-specific associations with CBT response may be more easily observed in developing brains, where differences in the degree of maturation of particular brain regions may relate to complex behavioral features, than in adult brains, where correlates of individual differences in complex behaviors are better captured by multimodal task-based functional measurements<sup>45</sup>. In any case, there may be other factors potentially related to the lack of findings in the adult sample, such as the higher variability observed in this sample in the methods of CBT delivery (individual, group and intensive) and other related variables (i.e., use of cognitive techniques and homework tasks).

Effect sizes of our findings fell between the small and medium labels. Although this may not be rare when associating very specific neuroimaging findings with complex behavioral and clinical data, a word of caution should be expressed regarding the immediate use of neuroimaging variables as biomarkers of treatment response. A further limitation of this study is that although multicenter studies of legacy data allow pooling together a large amount of information, this is typically at the cost of significant heterogeneity across the different data sources. In this study we have across-site variability both in technical aspects, such as those related to MRI acquisition, but also in some other aspects, such as patients' characterization, the criteria for CBT recommendation, and its methodology of application. Although our statistical approach (linear mixed models with random intercept) allowed us to partially control for these sources of variability and, on the pediatric sample, we did not observe significant effects on CBT response from any of the treatment related variables, this issue remains central to the interpretation of our findings. The heterogeneity in the methodology of CBT application may explain, for instance, the lower response rate observed in our study in comparison to the results of clinical trials<sup>3,46</sup>. The control of these different source of variability could ideally be accomplished in studies exploring large series of individuals with the same MRI scanner and using standardized protocols for patients' management, although such study is probably difficult to implement in practice.

In summary, in this study, pooling together data from 13 international centers, we identified significant structural predictors of CBT response in children/adolescents with OCD. These results should serve to better define the brain circuits relevant for CBT success, which modulation may potentially boost the effectiveness of this psychological intervention. Moreover, our findings suggest biologically-informed hypotheses about the mechanisms of action of CBT in pediatric samples, which may also apply to different clinical populations in which CBT is the treatment of choice.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Appendix

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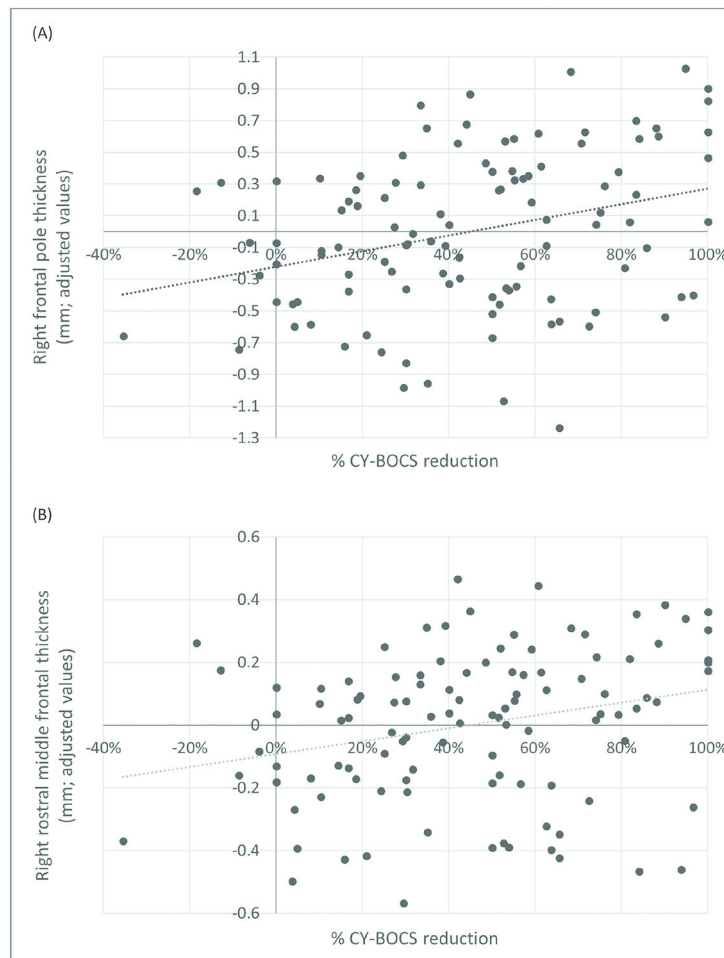
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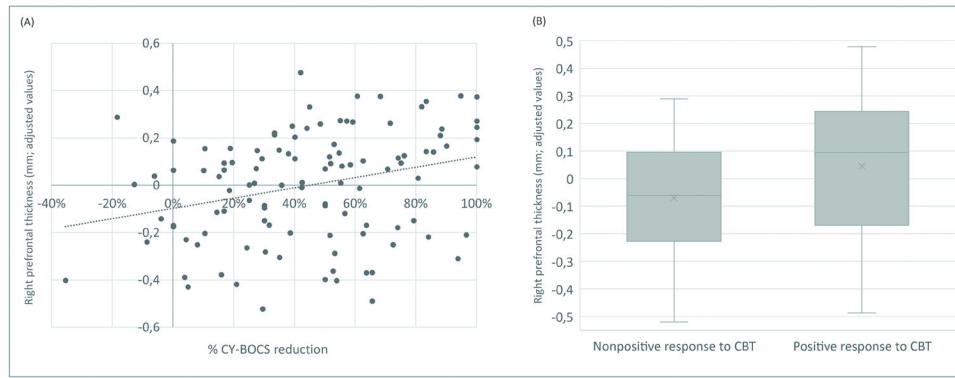
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**FIGURE 1.**

Association Between Right Prefrontal Cortex (r-PFC) Thickness and Cognitive-Behavioral Therapy (CBT) Response in Pediatric Patients With Obsessive-Compulsive Disorder (OCD)

**Note:** (A) Scatter plot depicting the positive correlation between cortical thickness of the right prefrontal cortex (r-PFC) and exposure therapy outcome as measured by the percentage of CY-BOCS reduction. (B) Box plot depicting r-PFC values in patients with positive response to CBT (  $\geq$  35% symptom reduction), and patients with a non-positive response to CBT. Patients with positive response showed a significantly thicker r-PFC in comparison to those with non-positive response.



**FIGURE 2.**

Association Between Right Frontal Pole And Rostral Middle Frontal Cortex Thickness With Cognitive-Behavioral Therapy (CBT) Response In Pediatric Patients With Obsessive-Compulsive Disorder (OCD)

**Note:** (A) Scatter plot depicting the positive correlation between right frontal pole thickness and exposure therapy outcome as measured by the percentage of CY-BOCS reduction. (B) Scatter plot depicting the positive correlation between right rostral middle frontal gyrus thickness and exposure therapy outcome as measured by the percentage of CY-BOCS reduction.

TABLE 1

Demographic (Age, Sex) And Clinical (Age of Onset, Illness Duration, Medication Users During Cognitive-Behavioral Therapy (CBT) Trial, Comorbidities, Baseline Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS) Severity, Post-CBT CY-BOCS, % of Patients With Positive Response) Data From Pediatric Samples

	Pediatric sample		Adult sample	
	HC	OCD	HC	OCD
Male subjects (%)	49.3	55.4	42.8	49.4
Age, years ( <i>mean ± SD</i> )	13.41 ± 2.74	13.10 ± 2.81	30.5 ± 9.55	31.63 ± 9.65
	OCD		OCD	
Age of onset, years ( <i>mean ± SD</i> )	10.43 ± 3.39		16.5 ± 8.60	
Illness duration, years ( <i>mean ± SD</i> )	3.10 ± 2.54		15.5 ± 10.85	
Dimensions, yes (%)				
Agg. and check	68.5		75.7	
Cleaning	64.3		67.3	
Sex. and rel.	29.2		50.3	
Hoarding	31.5		26.4	
Ordering	64.9		57.9	
Medication us at MRI time, yes (%)	20.8		65.7	
Medication us during CBT, yes (%)	30.4		66.7	
	<i>SSRI</i>	25.6	<i>SSRI</i>	37.7
	<i>Combination</i>	1.2	<i>Tricyclics</i>	2.8
	<i>Other</i>	3.6	<i>Combination</i>	15.1
			<i>Other</i>	20.4
Comorbidities, yes (%)				
Hx. of anxiety	30.4		31.8	
Hx. of depression	6.5		36.5	
Cur. anxiety	42.3		30.2	
Cur. depression	7.7		23	
Baseline C/YBOCS severity ( <i>mean ± SD</i> )	24.83 ± 5.21		26.29 ± 4.58	
Post-CBT C/YBOCS severity ( <i>mean ± SD</i> )	14.32 ± 8.67		15.45 ± 6.96	
% C/YBOCS reduction ( <i>mean ± SD</i> ) / % Patients with positive response	43.19 ± 32.43/ 56.5		40.79 ± 25.29/ 61.6	

Note: Agg and check = Aggressive and checking; Cur = current; Hx = history; OCD = obsessive-compulsive disorder; MRI = magnetic resonance imaging; Sex and rel = sexual and religious; SSRI = selective serotonin reuptake inhibitors.

**TABLE 2**  
Cognitive-Behavioral Therapy (CBT) Characteristics in Pediatric and Adult Sample

	Previous CBT trial, yes (%)	Total n° of CBT sessions (mean ± SD)	Duration of CBT, weeks (mean ± SD)	N° psychoeducational/introductory sessions (mean ± SD)	N° exposure/relapse prevention sessions (mean ± SD)	Type CBT: Group/individual/combination (intensive) (%)	Use of cognitive techniques <sup>a</sup> , yes (%)	Homework tasks, yes (%)
<b>Pediatric sample</b>	36.3	14.61 ± 3.25	16.77 ± 6.43	2.35 ± 2.62	12.96 ± 3.19	Group: 14.3 / Individual: 85.1	94.0	98.8
<b>Adult sample</b>	5.3	15.45 ± 6.33	12.15 ± 9.84	2.26 ± 1.36	12.67 ± 6.23	Group: 28 / Individual: 15.4 / Intensive: 55.7	64.5	70.8

Note: n° = number

<sup>a</sup>They include cognitive restructuring, thought records, behavioral experiments and others.

**TABLE 3**

Cortical Thickness Predictors of Clinical Response Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS decrease) in Pediatric Patients (n= 168)

	Standard error	<i>t</i>	Sig.	95% confidence interval	
				Inferior	Superior
Left prefrontal	15.507	1.530	0.134	-7.637	55.089
Right prefrontal	11.483	3.249	<b>0.002<sup>a</sup></b>	14.546	60.065
Left temporal	12.556	0.423	0.674	-19.753	30.365
Right temporal	13.194	-0.278	0.782	-30.059	22.281
Left central	18.579	0.631	0.531	-25.570	49.002
Right central	17.703	0.857	0.394	-20.074	50.415
Left limbic	16.049	-0.681	0.497	-42.813	20.948
Right limbic	15.437	0.130	0.897	-28.635	32.651
Left parietal	19.291	1.742	0.086	-4.832	72.056
Right parietal	17.295	0.604	0.549	-24.364	45.272
Left occipital	24.860	-0.869	0.387	-70.875	27.668
Right occipital	25.179	0.756	0.451	-30.895	68.966

Note:

<sup>a</sup>Significant after Bonferroni correction for multiple testing