Title: Structural and Functional Abnormalities of the Dorsal Anterior Cingulate Cortex in Obsessive-Compulsive Disorder

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HIGHLIGHTS

- Although recent neuroscience has implicated the dorsal anterior cingulate cortex (dACC) as a key hub of cognitive control, little research has explored systematic alterations within the dACC in obsessive-compulsive disorder (OCD), a disease largely defined by cognitive control dysfunction.
- We demonstrate structural and functional abnormalities within the dACC in OCD, which further support the hypothesis that dACC dysfunction is central to the neurobiology of OCD.

INTRODUCTION

Dysfunction within neural systems for cognitive control is thought to be central to the pathophysiology of obsessive-compulsive disorder (OCD). Recent developments in neuroscience suggest that the dorsal anterior cingulate cortex (dACC) acts a key hub for cognitive control within a network of frontal regions that enable adaptive decision making. Historically, cingulotomy has been used with some success to treat refractory OCD. Taken together, these results raise the possibility that dACC dysfunction may be central to the neurobiology of OCD. We sought to test this hypothesis by examining the relationship between dACC structure/function and OCD.

METHODS

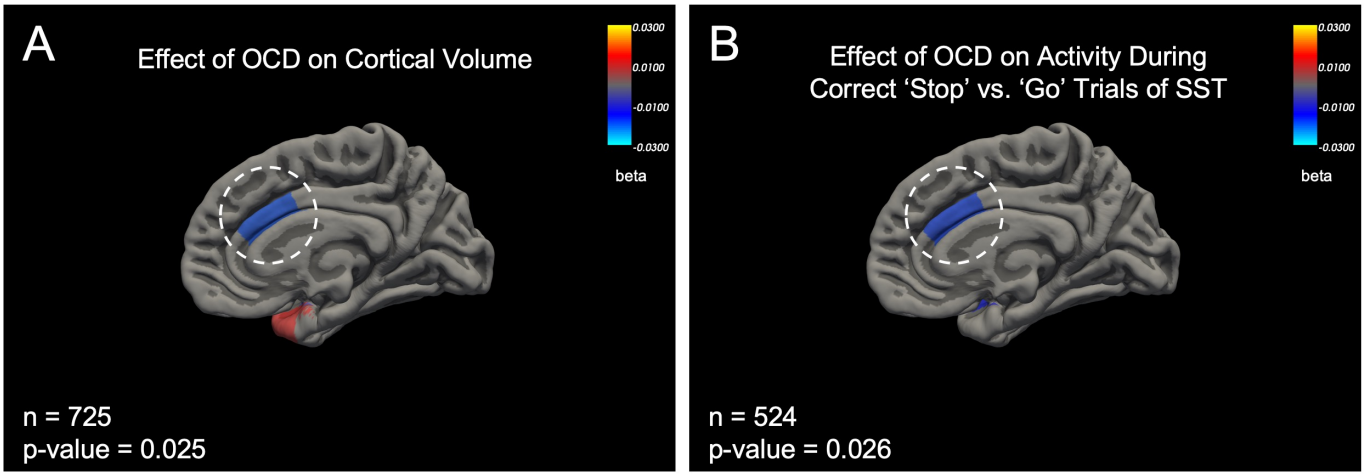
Using data from the Adolescent Brain and Cognitive Development (ABCD) study of 12,000 typically developing adolescents, subjects meeting criteria for OCD were identified based on the Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS-5). Using multivariate linear mixed-effects models, we examined differences between OCD subjects and matched controls in regional cortical volume and fMRI activity during the 'stop-signal task' (SST), an assessment of cognitive control and impulse inhibition. Using the Child Behavior Checklist OCD T-score, we further examined the effect of OCD symptom severity on dACC cortical volume and task-based fMRI activity. Lastly, we examined how resting-state fMRI (rsfMRI) connectivity across 13 resting-state networks (Gordon, 2014) differed in OCD subjects and matched controls.

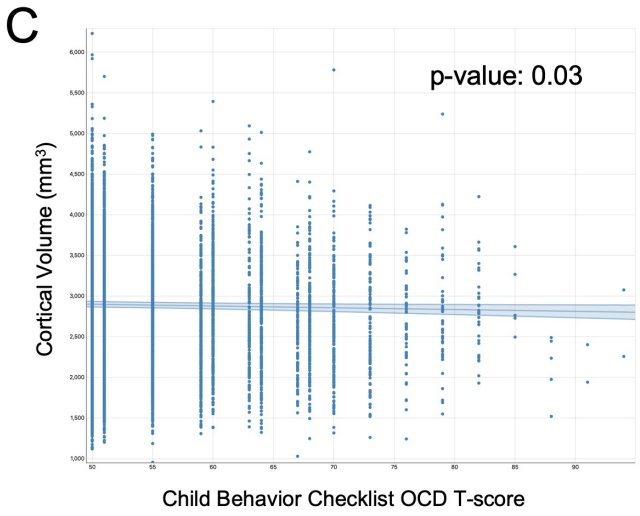
RESULTS

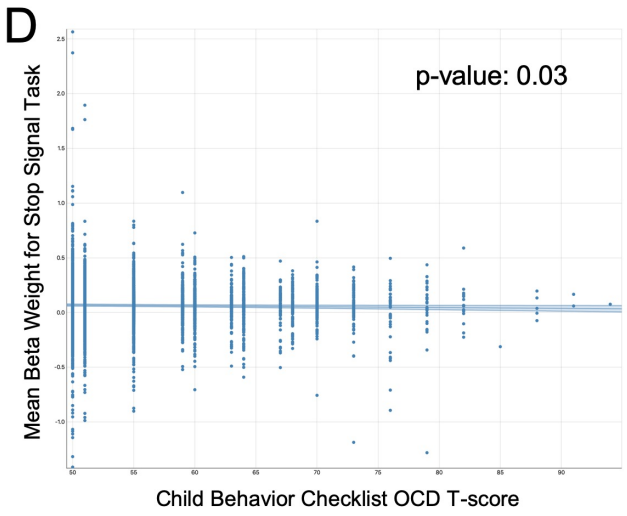
Compared to matched controls, subjects with OCD demonstrated significant decreases in both dACC cortical volume (*p=0.03*; **Figure A**) and dACC relative task activation during correctly executed 'stop' versus 'go' trials of the SST (*p=0.03*; **Figure B**). Furthermore, both dACC cortical volume (*p=0.03*) and relative task activation (*p=0.03*) showed significant negative correlations with OCD severity (**Figures C & D**). Finally, in OCD subjects, rsfMRI correlations demonstrated significantly altered network connectivity both within and between the dorsal attention (task-positive) and default mode (task-negative) networks. Specifically, OCD subjects demonstrated decreased connectivity within the dorsal attention network (*p=0.04*) and within the default mode network (*p=0.001*) but increased connectivity between these networks (*p=0.04*). Furthermore, these altered network connectivities also significantly correlated with OCD severity.

CONCLUSIONS

We found systematic differences in dACC structure and function between subjects with OCD and matched controls. Specifically, in OCD subjects, the dACC showed decreased cortical volume and selectively decreased activity during SST trials that demand cognitive control. In addition, in OCD subjects, rsfMRI correlations demonstrated altered connectivity within and between normally opposing task-positive and task-negative networks. Furthermore, we found that these effects varied with increased OCD symptom severity. These results support the hypothesis that dysfunction in cognitive control mediated by structural and functional aberrations in the dACC plays a central role in the neurobiology of OCD. As we follow these adolescents in the ABCD study, we can determine how these findings evolve and are impacted by medical and behavior interventions. Moreover, we hope that these findings may lead to the development of reliable imaging biomarkers to improve the diagnosis and treatment of OCD.


A
Effect of OCD on Cortical Volume
0.0300
0.0100
-0.0100
-0.0300
beta
n = 725
p-value = 0.025
B
Effect of OCD on Activity During
Correct 'Stop' vs. 'Go' Trials of SST
0.0300
0.0100
-0.0100
-0.0300
beta
n = 524
p-value = 0.026


C
p-value: 0.03
Cortical Volume (mm³)
Child Behavior Checklist OCD T-score


D
p-value: 0.03
Mean Beta Weight for Stop Signal Task
Child Behavior Checklist OCD T-score