Voxel-based morphometry analysis reveals frontal brain differences in participants with ADHD and their unaffected siblings.


Abstract

BACKGROUND:
Data on structural brain alterations in patients with attention-deficit/hyperactivity disorder (ADHD) have been inconsistent. Both ADHD and brain volumes have a strong genetic loading, but whether brain alterations in patients with ADHD are familial has been underexplored. We aimed to detect structural brain alterations in adolescents and young adults with ADHD compared with healthy controls. We examined whether these alterations were also found in their unaffected siblings, using a uniquely large sample.

METHODS:
We performed voxel-based morphometry analyses on MRI scans of patients with ADHD, their unaffected siblings and typically developing controls. We identified brain areas that differed between participants with ADHD and controls and investigated whether these areas were different in unaffected siblings. Influences of medication use, age, sex and IQ were considered.

RESULTS:
Our sample included 307 patients with ADHD, 169 unaffected siblings and 196 typically developing controls (mean age 17.2 [range 8-30] yr). Compared with controls, participants with ADHD had significantly smaller grey matter volume in 5 clusters located in the precentral gyrus, medial and orbitofrontal cortex, and (para)cingulate cortices. Unaffected siblings showed intermediate volumes significantly different from controls in 4 of these clusters (all except the precentral gyrus). Medication use, age, sex and IQ did not have an undue influence on the results.

LIMITATIONS:
Our sample was heterogeneous, most participants with ADHD were taking medication, and the comparison was cross-sectional.

CONCLUSION:
Brain areas involved in decision making, motivation, cognitive control and motor functioning were smaller in participants with ADHD than in controls. Investigation of unaffected siblings indicated familiality of 4 of the structural brain differences, supporting their potential in molecular genetic analyses in ADHD research.