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Brain structure in adhd across the life span: the enigma adhd working group

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*Abstract:*
Introduction
Neuroimaging studies in ADHD show structural alterations of various brain regions in affected children and adults (Frodl and Skokauskas, 2012; Nakao et al., 2011; Valera et al., 2007). It is unclear, however, how these differences develop across the lifespan, and whether they are global effects or area-specific. To clarify brain changes across the lifespan, an ADHD Working Group was formed within the ENIGMA consortium (http://enigma.ini.usc.edu/). Within the working group, we are sharing brain imaging data from children and adults with ADHD and healthy comparison subject. Our first aim is to study subcortical brain differences in ADHD across the lifespan, and the potential effects of medication and co-morbidity. A second aim is to investigate effects of gender.

Methods
The ENIGMA-ADHD Working Group has adopted a rolling mega-analysis design: new groups can join at any time, and fixed data "freezes" allow analysis at different time points. Images are analyzed using fully automated and validated neuroimaging segmentation algorithms (FSL FIRST or FreeSurfer), for which protocols are available on the ENIGMA website. For all subjects, we collect volumetric data for hippocampus and the following subcortical structures: nucleus accumbens, amygdala, caudate nucleus, putamen, pallidum, and thalamus. We also share information on co-morbidity, ADHD symptoms, IQ, and medication use. The database currently includes 1640 cases and 1503 controls.

Results

So far, 22 international sites have joined the working group (see the ENIGMA website for a full list). Data from 452 ADHD cases and 405 controls have been analyzed to date. This sample has an age range of 6-63 years and includes 60% males. Our first analysis showed subtly but significantly smaller volumes for the left and right nucleus accumbens ($d$: 0.16 and 0.26), left amygdala ($d$: 0.16), right caudate nucleus ($d$: 0.16), and left putamen ($d$: 0.15) for cases compared to controls. These differences were independent of age.

Conclusions

The developmental trajectory of alterations in brain structure of individuals with ADHD remains largely unknown. This is due to the scarcity of large, well-powered longitudinal studies. Through data sharing, the ENIGMA-ADHD Working Group, with a sample of over 3000 cases and controls across the lifespan, will begin to address this gap. With sample sizes already similar to those of previous neuroimaging meta-analyses upon first data-freeze and analysis of the enlarged sample currently ongoing, our mega-analysis will help to clarify outstanding questions regarding age, medication and gender effects on brain-developmental trajectories.

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