Gray matter abnormalities in ADHD: A structural MRI study in medication-naive adolescents without learning disorders

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1. Background

•Attention deficit hyperactive disorder (ADHD) is a childhood-onset neuropsychiatric disease, afflicting 3-7% of the pediatric population worldwide.

•Neuroimaging studies reported abnormalities of brain regions involved in attention and executive functioning control, including frontal, striatal and parietal areas [1].

• However, as findings can vary significantly across studies, so far there are still no reliable biomarkers specific for ADHD. Several methodological confounds (type of measurement, sample size, etc.) and/or implication of demographic/cognitive variables (age, medication status, learning disabilities, etc.) may account for inconsistencies across findings.

• Here, we aimed at handling part of these concerns by investigating the neurobiological substrate of ADHD by comparing a group of drug-naïve ADHD adolescents with no learning disabilities against a group of healthy controls (HC).

2. Methods

Sixteen ADHD adolescents and sixteen HC underwent structural MRI at 3T to collect T1-weighted volumes. T1-weighted volume were processed according to a optimized method of voxel-based morphometry analysis [2] to obtain individual grey matter (GM) maps for cross-sectional group comparisons (Figure A) and correlations with clinical-neuropsychological measures (Figure B). Therefore, ADHD participants were also administered with Conners' Parents-Teacher Rating Scale, and a cognitive battery for the assessment of attention (TMT-A), short-term memory (Digit and Corsi's span), reasoning (Raven's Colored Progressive Matrices), and executive functions (TMT-B, Tower of London, ToL).

3. Results

A.ADHD participants compared to HC showed a significant increase of GM volumes in the right insular cortex and in the right inferior frontal gyrus (IFG).

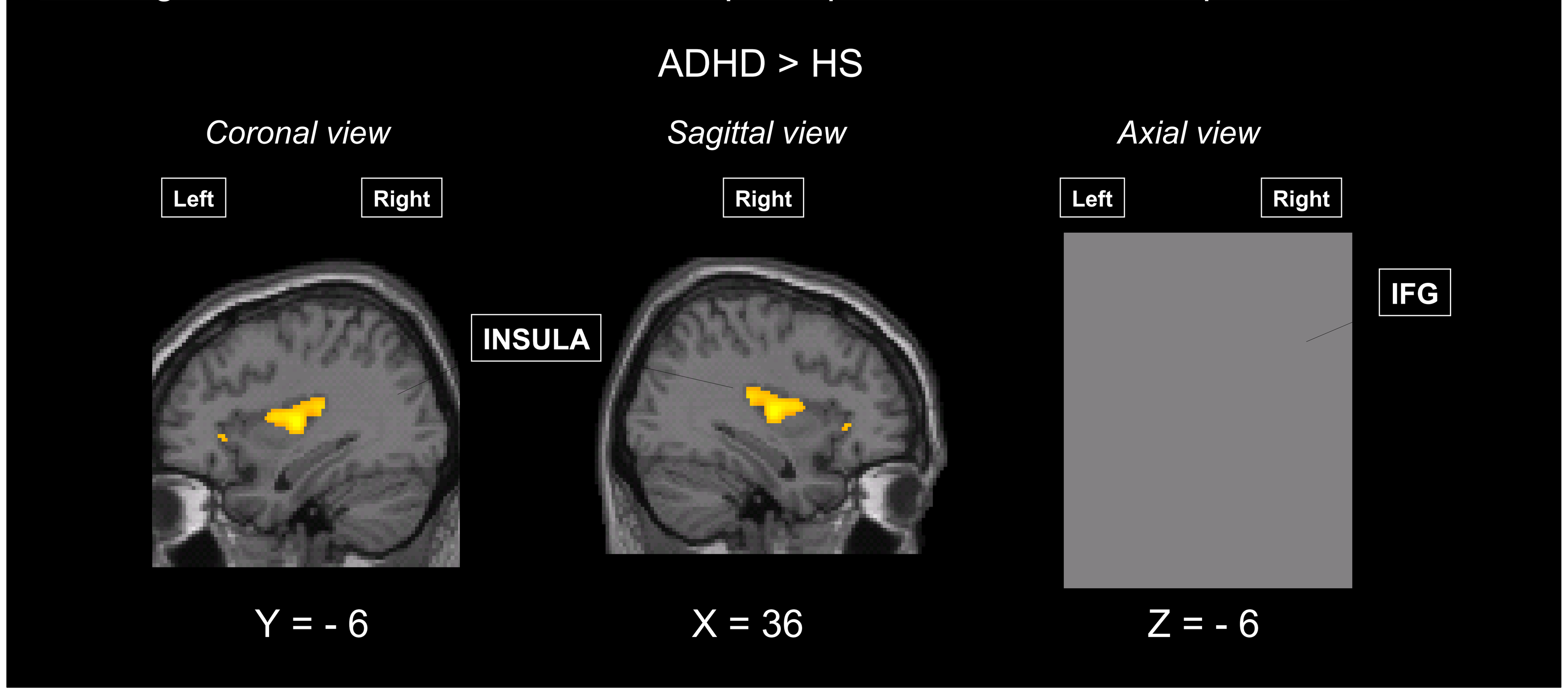
B.In ADHD participants, GM volumes of the prefrontal and parietal areas were negatively associated with their performance on the TMT-B. Moreover, GM volumes of prefrontal and premotor areas were negatively associated to patients' performance at ToL, and GM volumes in the orbitofrontal and anterior cingulate cortex (ACC) correlated positively with patients' reasoning performance. Finally, parent behavior rating of ADHD symptoms was associated with increased GM volume in the dorsolateral prefrontal cortex and ACC.

A. Voxel-Based Morphometric differences between 16 participants with ADHD and 16 healthy control subjects (HS)

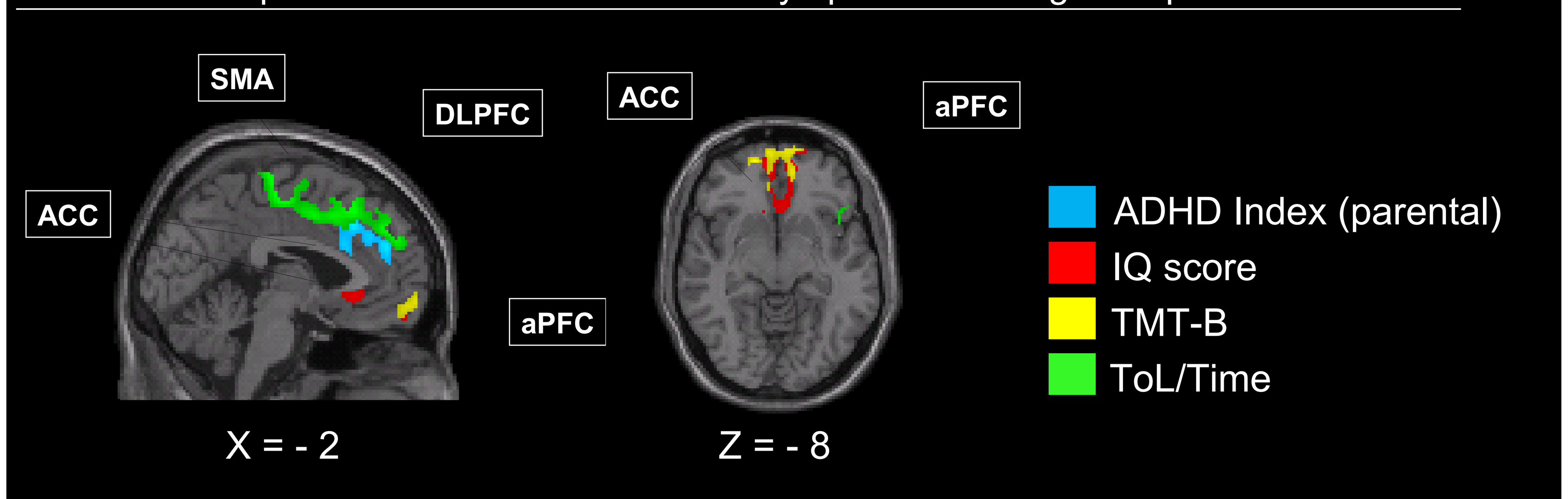
ADHD > HS				
Regions of increased GM volume in ADHD	p-corr*	size	Coord	equivZ
Right Insula/BA13	0.043	474	34 -12 8	3.84
Right IFG/BA47			46 26 -6	3.39

*= p-values FWE-corrected < 0.05 (cluster level, whole brain). Cluster sizes are in number of voxels. Coordinates are in Montreal Neurological Institute Space. Results are in the direction of larger volumes in the ADHD group than HS
BA = Brodmann's area; IFG = Inferior frontal gyrus;

A. Regions of increased GM volume in participants with ADHD compared to controls



B. Relationships of volume to ADHD-related symptoms and cognitive performance in ADHD



B. Relationship between GM volumes, cognitive performance and parental behavior rating in ADHD group

Brain correlates of parental rating of ADHD symptoms[a]				
Anatomical region	p-corr*	size	Coord	equivZ
Right dACC/BA32	0.003	700	4 18 34	3.71
Right DLPFC/BA9			12 26 28	3.33
Brain correlates of intelligence quotient in ADHD[b]				
Left OFC/BA11	<0.001	982	-10 56 -6	4.53
Left vACC/BA24			-8 38 -2	3.40
Brain correlates of visual divided attention in ADHD[c]				
Left postcentral gyrus/BA1-2	0.023	456	-42 -30 58	4.33
Right OFC/BA11	0.001	754	18 58 -8	3.86
Left aPFC/BA10			-10 68 0	3.62
Brain correlates of executive functioning in ADHD[d]				
Left aPFC	0.001	894	-26 58 20	4.64
Left IFG/BA45			-52 26 16	4.03
Left IFG/BA44			-52 10 4	3.97
Right SMA/BA6	<0.001	1606	4 -22 58	4.44
Left SMA/BA6			-4 -18 56	4.33
Right DLPFC/BA9	0.031	444	36 42 34	4.10

[a]Areas of significant positive correlation between gray matter volumes and Conners' ADHD index-parent in ADHD group
[b]Areas of significant positive correlation between gray matter volumes and IQ score in ADHD group
[c]Areas of significant negative correlation between gray matter volumes and Trial Making Test (Part B) score in ADHD group
[d]Areas of significant negative correlation between gray matter volumes and Tower of London score in ADHD group
*= p-values FWE-corrected < 0.05 (cluster level, whole brain). Cluster sizes are in number of voxels. Coordinates are in Montreal Neurological Institute Space.
BA = Brodmann's area; ACC = Anterior cingulate cortex; DLPFC = dorsolateral prefrontal cortex; OFC = Orbitofrontal cortex; aPFC = anterior prefrontal cortex; SMA = Supplementary motor area

4. Conclusion

We showed that drug-naive adolescents with ADHD show a peculiar pattern of cortical GM changes, mainly in the orbitofrontal cortex, even in the absence of learning disabilities. This regional increase of GM volumes is consistent with previous literature and might represent a putative neuroanatomical marker of ADHD in adolescence. Additionally, we found strict associations between some critical neuropsychological features of ADHD and regional GM volumetrics. Overall this study supports the hypothesis that ADHD is associated with deficits of the circuitry subserving decision making and emotional processing [3].

5. References

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