

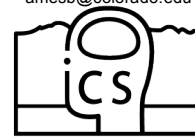


Gray and White matter differences in young adults with ADHD

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Introduction.

Numerous neuroimaging studies suggest anatomical differences between children and adolescents diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) and controls (see Bush et al., 2005 for review). These differences have been noted in a variety of regions including prefrontal, parietal & temporal cortex, as well as the basal ganglia (specifically the caudate) and the cerebellum. Although there is agreement of reduced grey matter in prefrontal regions, the basal ganglia and the cerebellum, there is much less agreement for other regions.

To our knowledge, only one study has examined brain morphology in adults with ADHD, and focused strictly on orbitofrontal cortex (Hesslinger et al., 2002). Given that changes in gray and white matter density continue into adulthood (Sowell et al., 2003), we utilized optimized voxel-based morphometry (VBM) to examine anatomical differences between young adults with and without ADHD.

Hypothesis. Based on our functional imaging studies (see posters 122 & 622), we hypothesized that adults with ADHD would show reductions in grey matter volume in prefrontal and parietal regions compared to controls.

Methods

Participants. 18 college-aged adults meeting DSM-IV criteria for ADHD (combined sub-type) as diagnosed via a structured interview assessing current and childhood symptoms as well as parent report. 18 control adults were of similar age and screened to not exhibit ADHD symptoms.

Table 1: Study Participants
Values indicate Mean and (s.d.)

	Patients (7 females)	Controls (11 females)
Age	19.94 (1.66)	19.00 (.84)
Hyper. scores	6.11 (2.19)	.17 (.38)
Inatt. scores	7 (1.84)	.28 (.46)

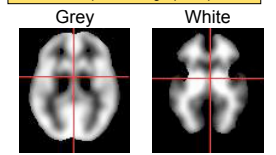
Image Acquisition & Analysis

Acquisition: T-1 weighted anatomical images were acquired on a 3 Tesla General Electric Magnetic Resonance scanner. **Preprocessing:** Using optimized VBM (Ashburner, 2000; Good et al., 2001), which is an unbiased whole brain voxel-wise analysis, we examined gray and white matter differences between individuals with ADHD and controls.

Image Acquisition & Analysis cont'd

Step 1: Spatial Normalization. Anatomical images were spatially normalized using a 12 parameter affine transformation in SPM2 to a custom template created from the 36 participants. **Step 2: Segmentation.** Images were segmented into partial volume estimate (PVE) maps of gray/white matter and cerebrospinal fluid (CSF) using FMRIB's Automated Segmentation Tool (FAST) and smoothed (FWHM=12 mm) **Step 3: Modulations** Data was modulated to correct for volume changes that may occur during spatial normalization.

Figure 1: Resulting smoothed and modulated maps for a single participant



Statistical Analysis: GLM as implemented in SPM2 for a voxel-wise comparison of gray and white matter for individuals with ADHD vs. controls while controlling for total brain volume.

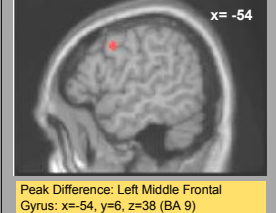
Statistical thresholds

1. $p < .001$ for grey matter in a priori ROIs (prefrontal, temporal, and parietal cortex)
2. $p < .0001$ for whole-brain analysis of grey and white matter
3. $p < .0001$ for the relationship of hyperactive/ inattentive symptoms with gray and white matter volume

Results

A. Anatomical Differences

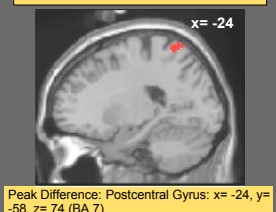
Figure 2: Controls > ADHD: Grey Matter



Peak Difference: Left Middle Frontal Gyrus: $x=-54, y=6, z=38$ (BA 9)

Reduced grey matter in ADHD individuals may interfere with the creation of an attentional set for task relevant information - a function we have hypothesized for this posterior region of DLPFC (Milham, et al. 2003).

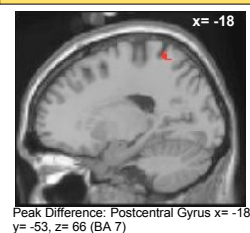
Figure 3: ADHD > Controls: Grey Matter



Peak Difference: Postcentral Gyrus: $x=-24, y=-58, z=74$ (BA 7)

Results (cont'd)

Figure 4: Controls > Patients: White Matter



Peak Difference: Postcentral Gyrus $x=-18, y=-53, z=66$ (BA 7)

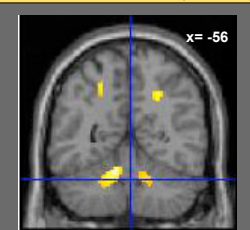
Decreased white matter and increased grey matter in individuals with ADHD in superior parietal regions may reflect decreased connectivity with prefrontal control regions. This could lead to poorer attentional control.

B Associations with symptoms

Here we examine how brain morphology is associated with symptoms in individuals with ADHD.

1. Hyperactivity

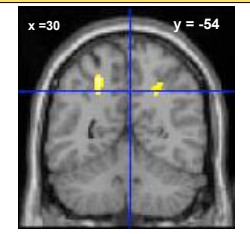
Figure 5: Decreased grey matter associated with increased hyperactivity



Peak Difference: Bilateral Precuneus (BA 7): (L) $x=-24, y=-56, z=42$; (R) $x=24, y=-56, z=36$

Peak Difference: Bilateral Cerebellum: (L) $x=-10, y=-54, z=-22$; (R) $x=14, y=-54, z=-28$

Figure 6: Increased white matter associated with increased hyperactivity



Peak Difference: Bilateral precuneus (BA 7): (L) $x=-22, y=-54, z=44$; (R) $x=28, y=-54, z=38$.

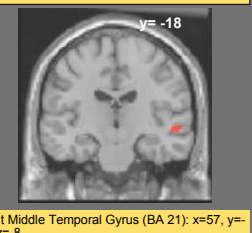
These findings suggest that more atypical morphology of the precuneus in individuals with ADHD is associated with greater hyperactivity. The reason for this association is unclear, but the precuneus has been implicated in a variety of memory and attentional functions (see Cavanna & Trimble (2006) for review).

Reduced volume in the cerebellum is consistent with prior research on children and adolescents with ADHD as well as the motor manifestation of ADHD symptoms that are reflected in hyperactivity.

Results (cont'd)

2. Inattentive Symptoms

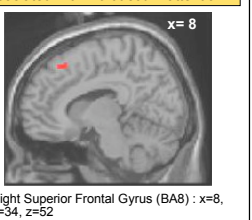
Figure 7: Increased grey matter associated with increased inattention



Right Middle Temporal Gyrus (BA 21): $x=57, y=-18, z=8$

Increased grey matter in temporal regions have been noted in children with ADHD (Sowell et al., 2003).

Figure 7: Increased white matter associated with increased inattention



Right Superior Frontal Gyrus (BA 8) : $x=8, y=34, z=52$

Discussion:

1a. Differences in both white and grey matter are observed between young adults with ADHD and controls.

1b. These differences are observed in prefrontal, parietal, temporal and cerebellar regions. 1c. Of note, no group differences were observed in the basal ganglia, an area of reduced volume in children with ADHD. However, that effect has been reported to decrease with age (Castellanos et al., 2002).

2a. Correlations between brain morphology and symptoms were noted in cerebellar, prefrontal, and parietal regions.

2b. These effects were noted in regions involved in attentional control (prefrontal and superior parietal regions), as well as the precuneus and temporal regions, which have been found to be atypical in other developmental disorders such as autism (McAlonan et al., 2004).

Conclusions:

Our results suggest that adults with ADHD exhibit atypical brain morphology. The regions noted are mainly related to a frontal-parietal attentional network that may be the cause of the behavioral deficiencies commonly found in the disorder.

See also:
Poster 122 (Mon P.M.) Dysfunction in maintaining tonic aspects of an attention set in adults with ADHD
Poster 622 (Wed P.M.) Prefrontal and parietal activity during Stroop task is correlated with hyperactive and inattentive symptoms in adults with ADHD

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