The frontal aslant tract (FAT) is an early frontal lobe white matter biosignature differentiating young children with ADHD from typical controls.

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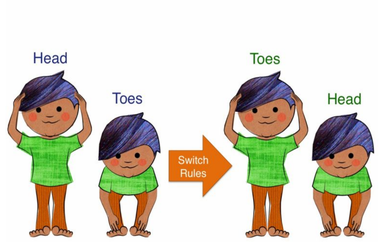
Introduction

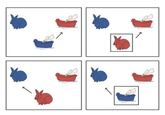
Attention-deficit/hyperactivity disorder (ADHD) is typically diagnosed in early childhood, and is characterized by deficits in executive function (EF) and in motor coordination. The neurobiology of ADHD with respect to EF in young children is not well understood, though identifying biosignatures of EF deficits in ADHD could serve as indicators of treatment response. To explore potential biosignatures, we mapped a recently-defined fiber pathway known as the frontal aslant tract (FAT). Given its connectivity profile connecting the right inferior frontal gyrus with the pre-SMA/SMA, and its previous association with EF in children (Garic et al., 2019), Dick and colleagues (2019) proposed that the right FAT might be involved in the planning, sequencing, and inhibitory control of potentially conflicting motor plans for manual movements.

Method and Analysis

Participants: 196 children (137 males; age range = 4-7 years; *M* age = 5.6 years). There were 96 children in the control sample and 100 within the ADHD sample.

Assessments: Language was assessed using NEPSY-II semantics and phonetics measures, which require a child to list as many objects as they can think of starting with a certain letter or in a category within 60 seconds. Three EF measures were used: Head-Toes-Knees-Shoulders (HTKS) task (Ponitz et al, 2008), and NIH Toolbox Flanker and Dimensional Change Card Sort (DCCS) tasks. The HTKS task (pictured on the right) requires children to first touch their toes and head, but then switch to do the opposite, taxing working memory and inhibition over three task blocks.





The Toolbox DCCS (pictured on the left) requires children to match objects based on one dimension (e.g., color), and then switch to match the same objects on the other dimension (e.g., shape; taxing inhibitory control/working memory). The Toolbox Flanker task requires children to choose which way the middle fish/arrow is pointing when surrounded by "flankers" pointing in the opposite direction (taxing inhibitory control/attention).

General Design and Parameters: DSIStudio was used to reconstruct DTI and HARDI images from a 3T scanner, b=500, 1000, 2000, 3000, 1.7 x 1.7 x 1.7 mm voxel size with 102 directions.

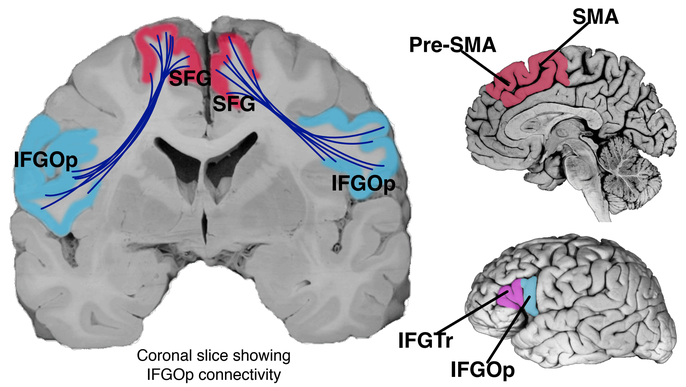
Approach and Reconstruction: Four regions of interest (ROI) were identified on each individual participants anatomy: inferior frontal gyrus (*pars opercularis* and *pars triangularis*), pre-supplementary motor area (pre-SMA) and supplementary motor area (SMA). Tracking was terminated when the relative QA for the incoming direction dropped below a preset threshold or the track exceeded a 40° turning angle.

Analyses: We related the fractional anisotropy (FA) of the bilateral FAT to the behavioral outcome measures using multiple regression. We controlled for age, sex, wholebrain FA, parental income, and movement in the scanner. Group (ADHD vs. Control) was entered as a moderator.

Results

- The Control Group outperformed the ADHD Group on all language and EF tasks
- Greater FA in the right hemisphere FAT predicted better performance on NIH toolbox tasks for children with and without ADHD
- However, for right FAT there was a significant interaction between the Group factor and FA for the HTKS task, with FA predicting better performance on HTKS for the Control Group, but not the ADHD Group.

Results Cont.



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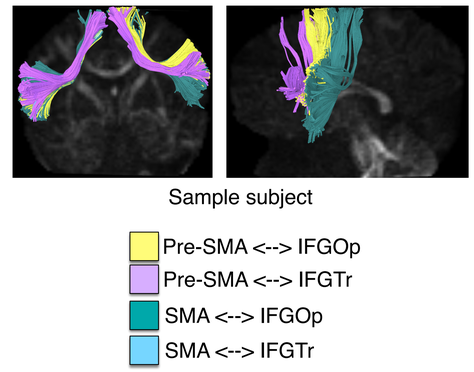

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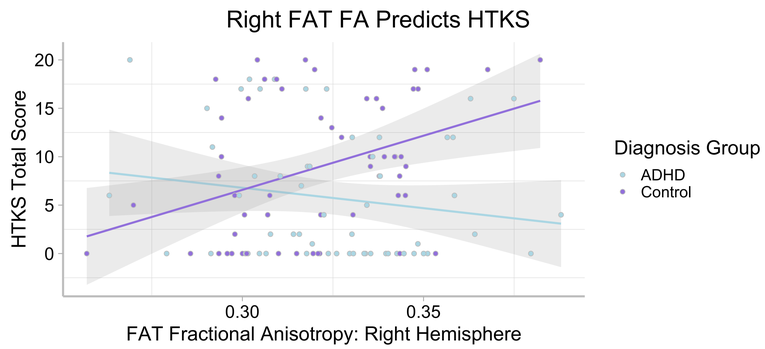

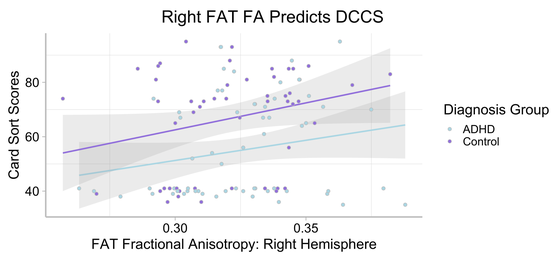

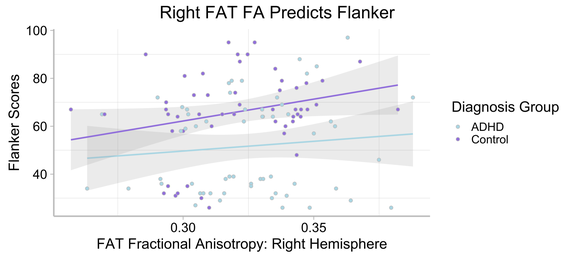

Summary

Results of the DWI study were in line with the prediction that right FAT is involved in the planning, sequencing, and inhibitory control of potentially conflicting motor plans for manual movements (Dick et al., 2019). We found that group status (ADHD vs Control) moderated the significant association between right FAT microstructure and performance on a motor sequencing task requiring inhibitory control (i.e., the Head-Toes-Knees-Shoulders task; $p < .05$). Group status did not moderate the significant association between microstructure and performance on typical EF tasks (Flanker and Dimensional Change Card Sort). Thus, 1) the right FAT is a potential biosignature of early ADHD diagnosis, but 2) only for tasks that require inhibitory control over sequenced movements.

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