SCHOLARLY REVIEW

ADHD superior frontal gyrus is hypoactive during working memory tasks and experiences a smaller activation difference between tasks

By Yvonne Li Yiwen

Author Biography

Born in 2008, Yvonne Li Yiwen is a high school student at Singapore American School who is passionate about neuroscience and neuroimaging analysis. In this study, she investigated functional neural interactions during visuospatial working memory tasks. In the future, she wishes to continue delving into the field of neuroscience, hoping to contribute valuable findings through clinical research.

Abstract

Attention-deficit/hyperactivity disorder (ADHD) is a common neurobehavioral disorder that affects children's learning and daily activities. According to a survey in 2022, 11.4% of children in the U.S. have been diagnosed with ADHD (Centers for Disease Control and Prevention, 2024). To better understand the biological impact of ADHD on human brains, I tested for a functional difference in their brain activation by fMRI neuroimaging analysis on the superior frontal gyrus of ADHD and TD (Typically Developed) boys during working memory and fixation tasks. They were asked to perform visuospatial working memory tasks with 1-back and 2-back tracks, with a fixation task before each 2-back track task. They were shown a series of single letters being presented at one of the four corners of a square, and were asked to determine whether the new letter was in the same corner. The fixation task required minimal cognitive effort, in which participants were asked to press down a button as the color of the box changed, thus serving as a baseline condition. The brain area studied was the superior frontal gyrus, the part of the brain responsible for cognitive functioning especially in working memory. Results of average beta weight estimates suggested ADHD boys' superior frontal gyrus to be hypoactive during visuospatial memory tasks and hyperactive during fixation tasks compared to TD boys, suggesting potential difficulty in task engagement and managing disruptive thoughts; and a smaller difference in ADHD boys' brain activation between the two tasks, suggesting potential difficulty in brain specialization and task switching.

Keywords: Superior Frontal Gyrus, ADHD, Neuroimaging analysis, fMRI, Working Memory Tasks, Brain Activation, Brain Specialization, Functional Difference

Introduction

Attention deficit hyperactivity disorder (ADHD) is a neurobehavioral disorder characterized by symptoms including consistent patterns of inattention, hyperactivity, and impulsivity. ADHD can make daily casual activities challenging, especially for children, because they may find challenges in controlling impulsive activities (National Health Service, 2021). Studies have shown that ADHD brains differ from typically developed brains in both anatomical and functional ways.

ADHD patients often experience impaired working memory function. According to a study by Whitney D. Fosco et al. in 2020, 67% to 71% of ADHD youth reflected working memory impairments in at least one experiment tasks assessing reordering, updating, and dual-processing of information (Fosco et al, 2020).

The superior frontal gyrus (SFG) is a region in the frontal cortex of the cerebrum. Previous functional neuroimaging studies had revealed the activation of the frontal cortex during verbal working memory tasks (Petrides et al, 1993). The superior frontal gyrus can create a temporary buffer that allows voluntary behaviors to be generated, including maintaining short-term memory, manipulating and organizing information, and performing working memory tasks (Boisgueheneuc, 2006).

This paper investigates the connection between specific tasks and brain activation in the superior frontal gyrus in ADHD. A group of ADHD boys was compared to a typically developed (TD) control group during visuospatial working memory and fixation tasks through fMRI imaging analysis. Fixation tasks were tasks that minimized cognitive demands which required minimal but consistent cognitive effort, serving as baselines of brain conditions which can be compared to activation during the working memory tasks. Participants participated in visuospatial working memory tasks with 1-back and 2-back trials, with a fixation task before each 2-back trial. By examining fMRI data, I aimed to find patterns of deviating brain activation in the SFG for ADHD patients. This would allow us to better understand the biological impact of ADHD on patients' brains, assisting us to investigate potential physiological treatments of ADHD symptoms.

Methods

Dataset and experimental design

The dataset analyzed in this paper was acquired from Openneuro, available at https://openneuro.org/datasets/ds002424/versions/1.2.0. It consisted of anatomical and functional fMRI scans from two participant groups: clinically diagnosed ADHD boys (mean age 10.42 years) and TD boys (mean age 10.96 years). Anatomical scans provided detailed structure of the brain, while functional scans measured brain activity over time using BOLD (Blood Oxygen Level Dependent) signal. All participants were right-handed native English speakers and had normal/corrected vision, with their IQ being in the normal range.

In the experiment, the participants performed visuospatial working memory (VSWM) tasks with different conditions (large/small reward, delayed/immediate feedback). They were shown a series of single letters being presented at one of the four corners of a square, and were asked to determine whether the new letter was in the same corner as the previous letter for the 1-back trails and whether it's in the same corner as the letter two positions back for the 2-back trails. Participants were asked to perform a fixation task before and after each 2-back VSWM tasks. The fixation task was a simple motor action in response to a visual stimulus, unrelated to the cognitive demands in the visual spatial working memory task. They were required to press their fingers as they saw a black cross turn red. Therefore, it acted as a baseline which is isolated from the brain activations in the working memory task.

This study focused on the specific condition of large reward, delayed feedback. Participants made $0.25 for every correct response and were shown their overall accuracy at the end of each experimental block. 5 subjects from each population group were analyzed, which were sub-04, sub-06, sub-09, sub-14, sub-44 for the ADHD group and sub-16, sub-19, sub-20, sub-23 and sub-26 for the TD group.

Data processing

Data processing was done with SPM12 (Statistical Parametric Mapping), a voxel-based neuroimaging analysis tool, working with Matlab (version R2023a). The sequence of data processing on SPM12 was preprocessing of anatomical and functional fMRI scans, first-level analysis of each individual subject contrasting between working memory and fixation tasks, second-level group analysis contrasting between the ADHD and control groups, and ROI (Region of Interest) analysis on the superior frontal gyrus on each second-level contrast, which were group-level contrasts that investigated interactions between different sample groups. During ROI analysis, I extracted data of whitened and filtered y from the nearest super threshold voxel in the superior frontal gyrus of each second-level contrast map. In the analysis, y was a measurement of BOLD signal intensity across different time series in a voxel, and whitening and filtering removed autocorrelation and low-frequency noises. Using the y data extracted, I estimated the beta weights of each sample in each task, a signal of the overall brain activity during the chosen task. This allowed comparison of brain activity between ADHD and TD groups during the working memory and fixation tasks, and also the comparison of brain activity between the two tasks across the groups.

Preprocessing included several steps to prepare the fMRI data for analysis. The first step was realignment, which all functional images were estimated and resliced to correct for head motion. Slice timing was then applied to correct delays and align each slice with a temporal reference. Coregister was then performed to align functional images with anatomical scans, which were then segmented to separate different tissue classes. The functional images were then normalized, transforming them to fit into a standard template space. The last step was smoothing, which removed noises.

First-level analysis compared the differences in brain activation of each subject between visuospatial working memory and fixation task conditions. Each subject generated contrasts Working Memory task>Fixation task (WM>FIXATION), Fixation task>Working Memory task (FIXATION>WM), Working Memory task (WM), Fixation task (FIXATION) for each subject (Figure 2).

Second-level group analysis contrasted between the two subject groups which generated contrasts WM>FIXATION, FIXATION>WM, WM, FIXATION for ADHD>TD (Figure 3) and TD>ADHD. These contrast maps allowed comparison of overall brain activation across participant groups. Examples of ADHD>TD contrast maps are shown in Figure 3, where clusters represent voxels that were more activated in the ADHD group than the TD group.

During second-level region of interest (ROI) group analysis, data of estimated beta weight, a signal of the overall brain activity, was extracted from whitened and filtered y from the nearest super threshold voxel in the spherical ROI mask with center (-2, 58, 20)mm and radius 1mm (Figure 1). This allowed comparison of brain activity between ADHD and TD groups during the working memory and fixation tasks, and also the comparison of brain activity between the two tasks across the groups.

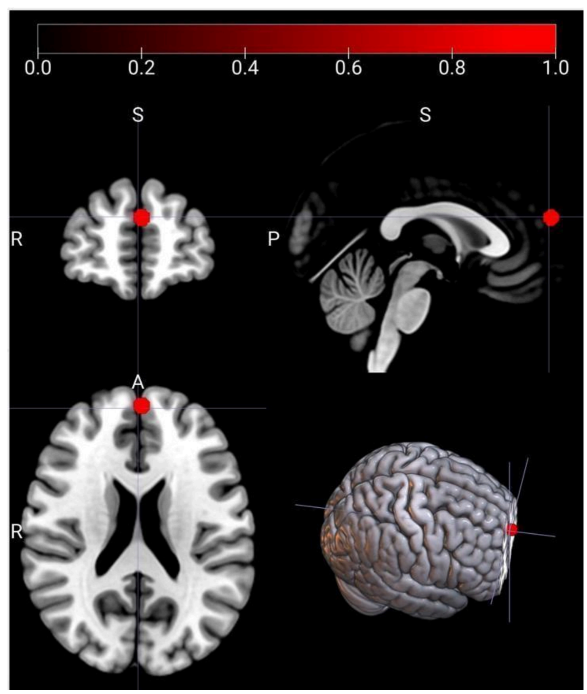
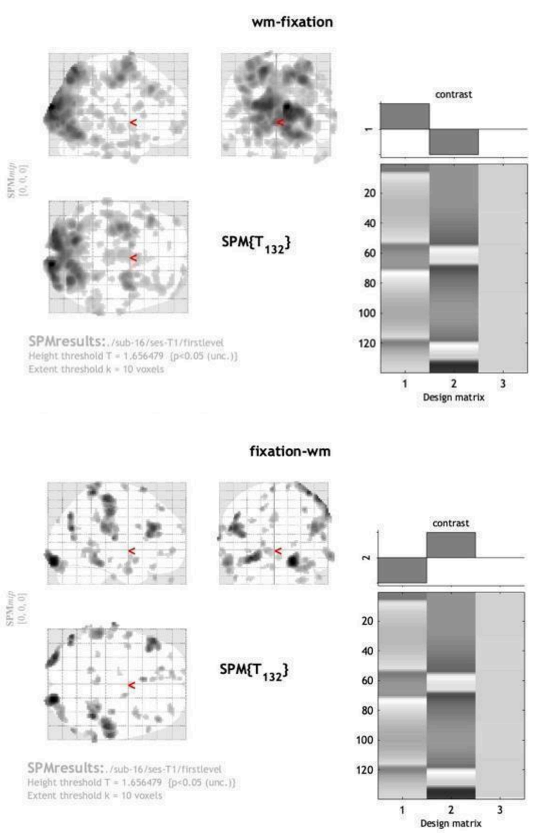


Figure 1: Illustration of the superior frontal gyrus from MRIcroGL. Using standard map mni152

overlaid with a spherical ROI mask created by mars bar with center (-2, 58, 20)mm and radius 1mm.

Results

First-level contrast maps showed brain activation of individual groups during individual tasks, and allowed comparison of brain activation across tasks. More clusters in the wm-fixation contrast map compared to the fixation-wm map of sub-08 shown in Figure1 suggested higher brain activation during the working memory task compared to the fixation task.



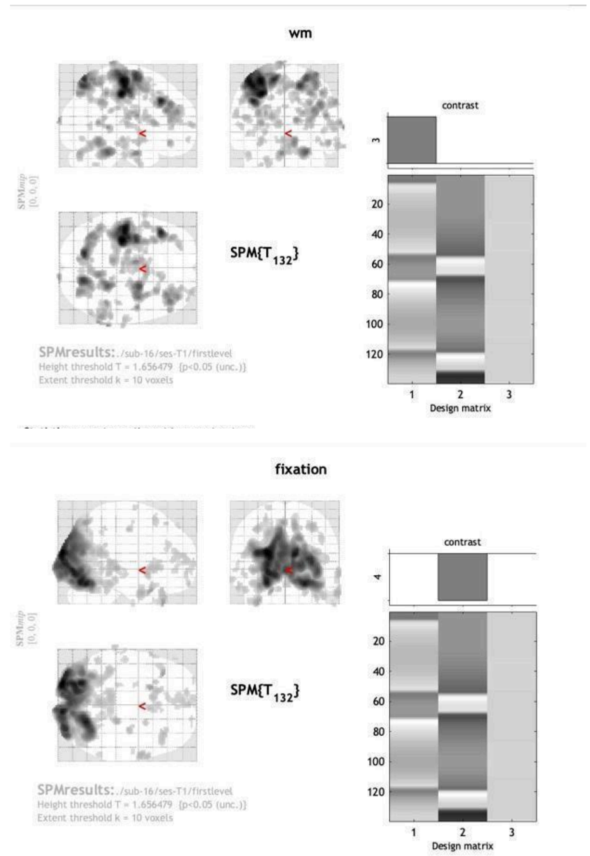


Figure 2: First-level contrast maps of sub-08. Contrast maps between fixation and working memory and individual condition maps showing brain activation during the two conditions. In sequence: WM>Fixation, Fixation>WM, WM, Fixation. Clusters in WM and Fixation represent activated brain areas during individual tasks. Clusters in WM>Fixation represent voxels that are more activated during the working memory task compared to the fixation task, and clusters in Fixation>WM represent voxels that are more activated during the fixation task compared to the working memory task. The columns of the design matrix represent the weight of different regressors at different time series.

Second-level contrast maps showed differences in brain activation across different participant groups. The large number of clusters in the contrast map of ADHD>TD_FIXATION showed that the ADHD group experienced overall higher activation of brain activity during the fixation task, which was a simple motor action that acted as a baseline of brain condition, isolated from the brain activations in the working memory task.

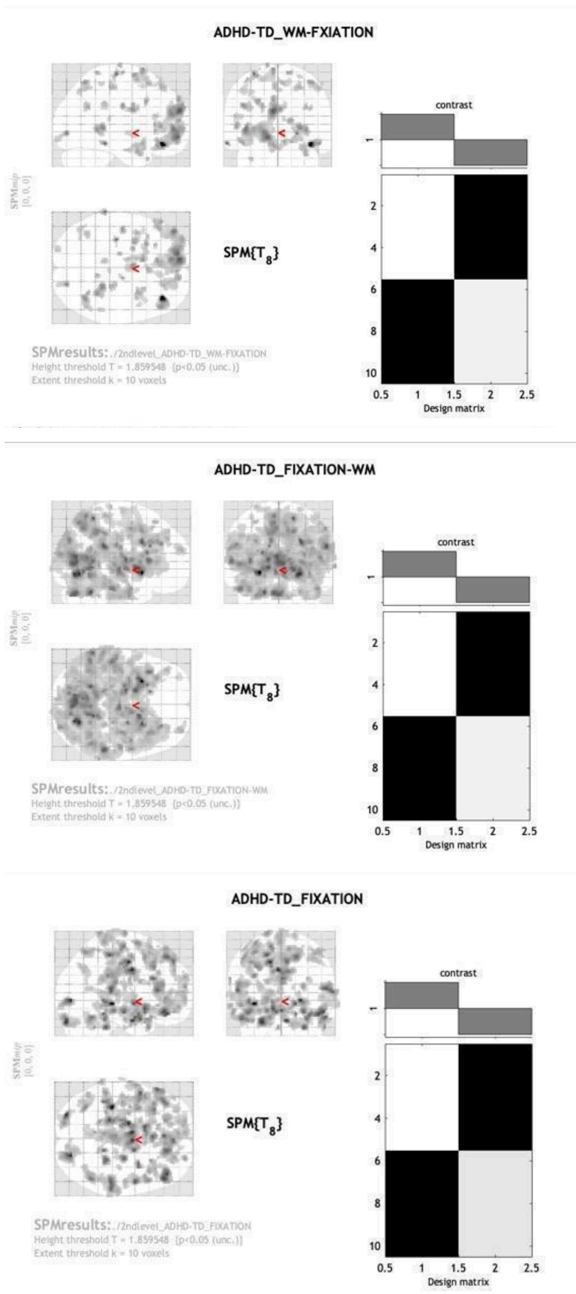


Figure 3: ADHD>TD second-level group contrast maps. Group-level ADHD>TD contrast maps showing brain voxels that were more activated in the ADHD group than the TD group during tasks. Clusters in ADHD-TD_WM and ADHD-TD_Fixation represent voxels that were more activated in the ADHD group than the TD group during the working memory task and fixation task respectively. Clusters in ADHD-TD_WM-FIXATION and ADHD-TD_FIXATION-WM represent voxels that had a greater difference in activation between the two tasks in ADHD than TD.

After applying a spherical ROI mask on the superior frontal gyrus (Figure 1), average beta weight from each sample group during each condition was calculated and graphed in comparison (Figure 4).

Beta weights were used in this study as a measurement of brain activation. They were the relative distribution of weights to each regressor in the General Linear Model (GLM).

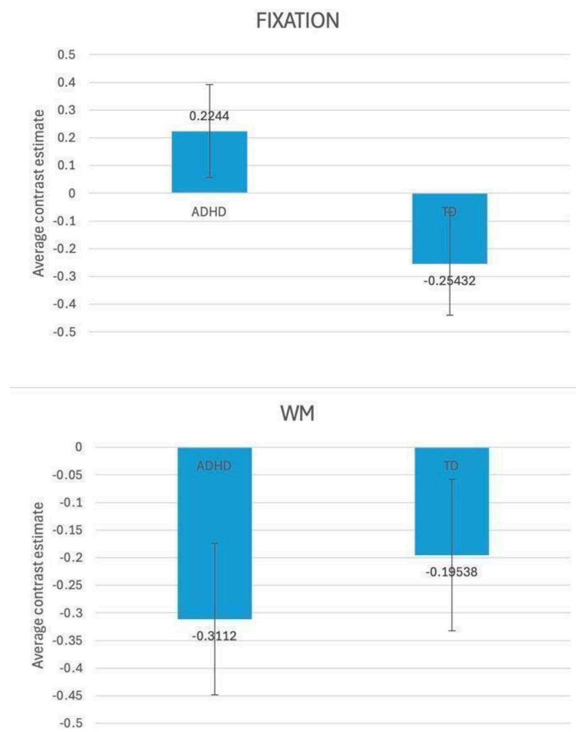


Figure 4: ADHD’s prefrontal gyrus experienced higher brain activation during the fixation task and lower brain activation during the working memory task. FIXATION (T.test p-value = 0.0458) and WM (T.test p-value = 0.283) showed the average level of brain activation of the two groups during fixation and working memory tasks respectively.

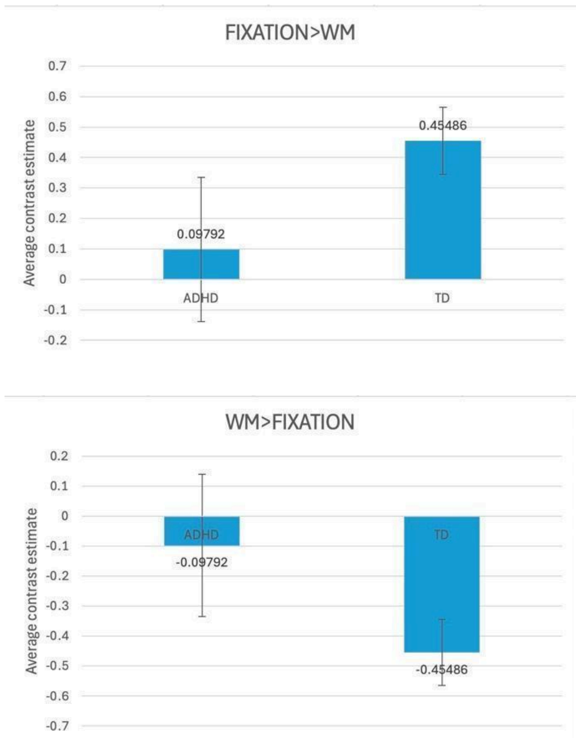


Figure 5: ADHD's prefrontal gyrus responds differently between working memory and fixation tasks compared to TD. FIXATION>WM (T.test p-value = 0.105) and WM>FIXATION (T.test p-value = 0.105) respectively showed the average difference in level of brain activation of the two groups between fixation and working memory tasks.

From single-task comparison results (Figure 4), the estimated beta weights reflected a greater level of brain activation during the fixation task (p-value = 0.0458) but a lower level of brain activation during the working memory tasks in the ADHD group than the TD group (p-value = 0.283). Double-task comparison (contrasts across visuospatial working memory and fixation task conditions) results reflected a smaller difference in the ADHD group between the two tasks than the TD group (p-value = 0.105).

The average beta estimate of the ADHD group during the fixation task was 0.2244, significantly greater than -0.25432, the average contrast estimate of the TD group during the fixation task. This showed that the ADHD group experienced a hyperactive superior frontal gyrus during the fixation task, which was cognitively isolated from the working memory tasks and was aimed to serve as a baseline condition of minimal but consistent attention.

The average contrast estimate of the ADHD group during the working memory tasks was -0.3112, lower than -0.19538, the average contrast estimate of the TD group. This showed that the ADHD group experienced a hypoactive superior frontal gyrus during the working memory tasks.

The absolute value of the ADHD group's average beta estimate across the fixation and working memory tasks was 0.09792, lower than 0.45486 for the TD group (Figure 5). This reflected a smaller difference of brain activation between the fixation and the working memory tasks in the ADHD group compared to the TD group.

Discussion

The difference of estimated beta weights between groups allowed investigation and inference on functional differences between the superior frontal gyrus of ADHD boys and TD boys.

The fixation task was aimed to serve as a baseline that requires minimal but consistent cognitive attention. The hyperactive superior frontal gyrus in ADHD boys during fixation tasks signalled abnormally higher brain activation compared to TD boys, suggesting potential difficulties in regulating brain activities and intrusive or disruptive thoughts. In contrast, the ADHD group's superior frontal gyrus was hypoactive during the visual spatial working memory task, suggesting potential difficulties in task engagement and consistent focus. The smaller difference of beta weights in the ADHD group between the two tasks signalled a smaller difference in brain activation across tasks, suggesting potentially lower levels of brain specialization and difficulties in switching between and focusing on tasks for ADHD boys compared to TD boys.

Future research can be carried out on ADHD's ability in task switching and brain specialization to verify the functional difference. Experiments with multiple task switching steps would be helpful for investigating potential functional differences in ADHD brains during task switching. ROI analysis on different brain structures, for example the hippocampus, the corpus callosum and the cingulate gyrus, could help to investigate potential differences in brain specialization between ADHD and TD groups. Examining fMRI data of ADHD and TD brains during resting state or tasks that require minimal cognitive effort can help to investigate ADHD patients' brain activity regulation and disruptive activations.

For this study, only 10 samples were analyzed. Future analysis using a larger set of data would be helpful in establishing claims regarding the functional difference in the superior frontal gyrus during visuospatial working memory and fixation tasks. This study only examined the interaction among ADHD boys. Future analysis using a dataset with a wider range of ages and genders would be helpful in establishing more generalizable patterns on the influence of ADHD on individuals' cognitive functioning and brain activation.

In conclusion, the ADHD group experienced a hyperactive superior frontal gyrus during the fixation task (Figure 4), suggesting potential difficulties in regulating brain activities and disruptive thoughts (Alegria et. al); and a hypoactive superior frontal gyrus during the working memory task (Figure 4), suggesting potential difficulties in consistent engagement with tasks. It is also observed that the ADHD group experienced a smaller difference in brain activation in the superior frontal gyrus between the two tasks (Figure 5), suggesting potential difficulty in activity management, task switching and brain specialization.

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