MULTIVARIATE ANALYSIS OF BRAIN FUNCTION CONSISTENCY OF CHILDREN WITH ADHD ACROSS TASKS BASED ON FNIRS

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ABSTRACT

This study conducts a comprehensive multivariate analysis of brain function consistency across tasks among children with Attention Deficit Hyperactivity Disorder (ADHD) based on functional near-infrared spectroscopy (fNIRS). Brain activation patterns and functional connectivity were assessed in 33 children with ADHD and 40 healthy controls (HC) in rest (REST), and in 33 children with ADHD and 32 HC in a verbal fluency task (VFT). The results indicate that children with ADHD exhibit unexpected left hemisphere reversals and activation amplitudes that differ less from those of HC both in REST and VFT, reflecting similar characteristics of neural engagement. Additionally, a notable weakness in both channel and region of interest functional connectivity within the prefrontal cortex of ADHD children was observed, particularly emphasizing inter-hemispheric disparities. These findings underscore the importance of functional consistency across tasks in the neurophysiological mechanisms underlying ADHD, enhancing the understanding of the disorder's cognitive and behavioral characteristics.

Index Terms— child with ADHD, fNIRS, brain function consistency, multivariate analysis, across tasks.

1. INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is characterized by hyperactivity, impulsivity, and inattention [1]. The inattention observed in individuals with ADHD may stem from impaired interference control, which permits various external and internal stimuli to override the executive functions that facilitate self-regulation [2]. Such deficits can adversely impact a child's development as they transition into early adulthood. However, the pathological mechanisms for these changes remain unclear. The functional near-infrared spectroscopy (fNIRS) represents a high-ecological-value brain imaging technology that provides realtime observations of children's brain function (BF) states and hemodynamic responses, effectively identifying neural function, thus offering critical insights into the pathophysiological mechanisms underlying the disorder [3].

ADHD involves functional abnormalities in multiple brain regions, particularly those related to executive function, attention, and impulse control, such as the prefrontal cortex, basal ganglia, dorsolateral prefrontal cortex, cingulate gyrus, and cerebellum [3]. Research using rest-state (REST) fNIRS in children with ADHD highlights disruptions in spontaneous neural activity signals linked to brain connectivity [4]. In contrast, fNIRS studies using task paradigms focus on abnormal brain activation patterns [5]. However, both REST spontaneous neural activity and task-related connectivity patterns offer important insights into ADHD's neural mechanisms. Therefore, multitask analysis is needed to explore to better understand the complexity of BF abnormalities in children with ADHD.

Prior research on brain activation in ADHD has typically relied on univariate analyses to examine the differences between ADHD and healthy controls (HC). Notable features employed in fNIRS studies include integral values, z-scores, mean values, max values, tissue oxygenation indices, general linear models, wavelet coherence, and permutation entropy analyses. However, these univariate methods may overly simplify the complexities of ADHD-related BF, with the identified significant channels potentially being heavily influenced by the choice of specific features, leading to pronounced discrepancies in channel localization between different studies. Well, multivariate analysis methods are enabling a more nuanced exploration of the interrelationships among various neural features and their collective contributions to ADHD pathology [6]. Additionally, previous studies have primarily focused on statistical analyses comparing ADHD children with HC to explore brain regions potentially influencing the onset of ADHD. However, this approach often neglects the possibility that specific brain regions in

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children with ADHD may exhibit functional abnormalities across different tasks

We undertook comprehensive investigations that characterized functional activity across multiple tasks and employed multivariate analysis, thereby revealing the broader dysregulatory patterns associated with the underlying mechanisms of ADHD within affected brain regions. We proposed the following hypotheses: the functional abnormalities observed in brain regions of children with ADHD during different tasks may not be limited to a specific task, but rather demonstrate cross-task consistency, reflecting underlying neurophysiological mechanisms.

2. MATERIALS AND METHOD

2.1. Participants and Experimental Paradigm

In the clinical data from the Department of Children's Health Care at Xi'an People's Hospital, 33 children with ADHD (8.7±1.8 years, 28 male, 5 female) performed a verbal fluency task (VFT), and 32 HC children (8.7±1.6 years, 25 male, 7 female) were recruited. Moreover, 33 children with ADHD (8.7±1.7 years, 29 male, 4 female) and 40 HC (8.7±1.6 years, 31 male, 9 female) performed REST. This study was approved by the Ethics Committee of Xi'an People's Hospital (Xi'an Fourth Hospital) (No. KJLL-Z-H-2023005). All procedures adhered to the principles of the Declaration of Helsinki.

In VFT, the experimental protocol included three phases: a 30-second pre-task baseline, a 60-second task, and a 60-second post-task baseline. Participants sat upright, facing a white wall, and listened to auditory instructions. During the baselines, they counted from 1 to 5, while in the task, they generated phrases using three Chinese characters—小(small), 天(sky), and 红(red)—which changed every 20 seconds to reduce silent periods. In REST, participants sat upright with their right hand on the table, fixing their gaze on a black cross at the center of a white screen, positioned about half a meter away. The REST phase lasted 5 minutes.

2.2. Materials

This study employed the standard brain structural atlas for Chinese children aged 6 to 12 years (CHN-PD), developed by He Yong et al [7]. Based on distinct BF, the regions in CHN-PD collected through fNIRS were categorized into 6 ROIs: right Dorsolateral Prefrontal Cortex (rDLPFC), right Frontal Pole Cortex (rFPC), Brodmann Area 8 (BA 8), medial Frontal Pole Cortex (mFPC), left Dorsolateral Prefrontal Cortex (lDLPFC), and left Frontal Pole Cortex (lFPC). The ETG-ONE NIRS device (Hitachi Medical Corp., Tokyo, Japan) was used to continuously measure and record the concentration changes of brain oxygenated hemoglobin (HbO2) and deoxy hemoglobin during the task, with wavelengths of 695 nm and 830 nm, respectively, and a sampling rate of 10 Hz. The experiment uses 8 light sources and 7 detectors to form 22 effective channels, the average distance between the source and the detector is 3 cm. Moreover, The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) is diagnosised and assessed the intellectual functioning of children by two experienced child psychiatrists.

2.3. Data Preprocessing

A polynomial regression model was applied to remove linear trends from the raw data, followed by temporal derivative distribution repair to eliminate artifacts and baseline shifts. A band-pass filter (0.01-0.1 Hz) reduced baseline drift and physiological interferences. Finally, the modified Beer-Lambert Law with a differential pathlength factor of 6 converted the filtered signals into relative changes in HbO2 [5].

2.4. Multivariate Feature Analysis

Quantifying BF responses: Integral Value (i): a higher i suggests greater activity associated with the cognitive task; Centroid Value (c): a smaller c indicates a more rapid cortical response and relaxation following task completion. Slope Coefficient (s): a higher (and positive) s for HbO2 signifies larger and faster cortical activation. Slope Variance (sv): a larger sv indicates an unstable activation state. Pearson Correlation Coefficient (Z-value): employed to evaluate functional connectivity between ROIs and across channels, results with greater than 1/2 of the maximum channel correlation were retained. Meanwhile, a two-sample t-test was employed to compare differences in brain activation states and functional network connectivity patterns between the ADHD and HC children.

3. RESULT

3.1. Demographic variables

Comparative analyses of demographic characteristics of children with ADHD and HC revealed no significant differences in age and sex distribution between the two groups.

3.2. Multivariate Feature of BF Activity Analysis

As shown in Fig.1 and the table, multiple brain activation features showed significant differences in VFT, while brain function only showed significant differences in the feature c and sv in REST. significant differences in brain function are observed only in channels corresponding to features c and sv. Compared to HC, ADHD group show lower brain activation intensity ($i_{ADHD}<i_{HC}$) and slower

response (c_{ADHD}>c_{HC}) in both REST and VFT. In multivariate statistical analyses, channel 13, located in the left hemisphere, demonstrates significant differences across both REST and VFT. Furthermore, unexpected reversals were observed in channel 21 during VFT and in channels 4 and 9 during REST, all of which are located in the left hemisphere. In summary, the consistency of brain activation across tasks in ADHD group is limited, with significant trends and unexpected reversals predominantly occurring in the left hemisphere.

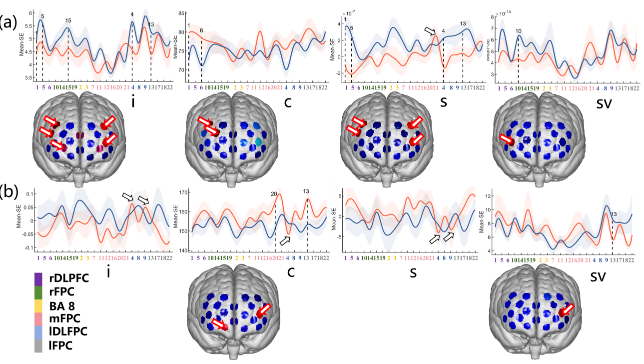

Fig. 1. Quantification of multivariate features of brain activation and visualization of significant difference channels in CHN-PD regions. White arrows indicate deviations from the overall trend, while red arrows mark the locations of significant difference channels. (a) VFT, (b) REST.

Table 1. The t-test results of BF activation features.

Task	Feature	Channel	ADHD		HC		T	p
			Mean	SD	Mean	SD		
VFT	i	1	0.028	0.234	-0.171	0.230	3.815	.0003**
		4	0.033	0.342	-0.100	0.235	2.0471	.044
		5	0.091	0.286	-0.120	0.337	2.981	.0038**
		13	-0.026	0.222	-0.142	0.253	2.157	.034
		15	0.051	0.268	-0.079	0.306	1.996	.049
	c	1	79.772	14.347	72.504	15.560	2.141	.035
		6	78.422	16.362	71.065	15.383	2.056	.043
	s	1	-1.056e-07	5.630e-07	3.621e-07	5.666e-07	-3.664	.0005**
		4	-1.193e-07	7.997e-07	2.193e-07	5.586e-07	-2.208	.030
		5	-2.131e-07	6.453e-07	2.526e-07	7.794e-07	-2.857	.0055**
		13	3.970e-08	5.385e-07	3.115e-07	5.984e-07	-2.104	.038
	sv	10	4.333e-14	3.712e-14	6.306e-14	4.511e-14	-2.095	.039
REST	c	13	166.471	20.328	153.280	19.742	2.754	.0075**
		20	165.082	25.405	151.340	21.116	2.461	.016
	sv	13	5.651e-15	4.070e-15	8.649e-15	6.739e-15	-2.252	.027

3.3. Correlation analysis

Channel correlations were shown in Fig.2, ADHD group exhibited weaker inter-channel correlations compared to HC in both REST and VFT. Task t-test indicated that the differences in inter-channel correlations between REST and VFT in ADHD were minimal, primarily involving channels 10, 14, and 16, and were smaller than the group differences between ADHD and HC within the same task, indicating cross-task consistency. Furthermore, the Group t-test results revealed that the distribution of significantly different channel correlations between REST and VFT was similar, further emphasizing the cross-task consistency of channel correlation features in ADHD group.

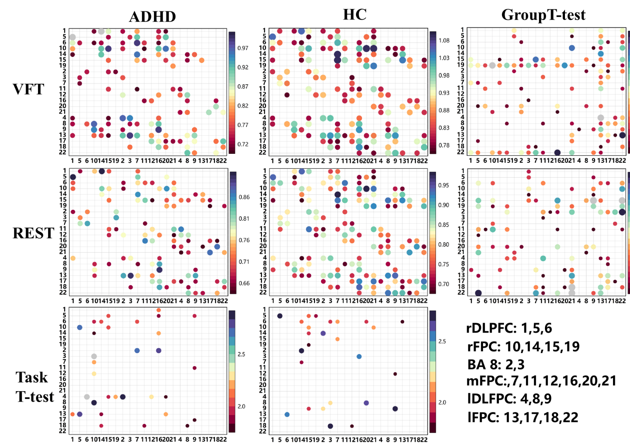

Fig. 2. Results of channel correlations and t-test for VFT and REST. In top left plots, bubbles show correlations between X and Y axis channels; larger bubbles indicate stronger correlations. In t-test plots, bubbles represent significant group differences in correlations (p<.05), larger bubbles indicating greater significance.

ROI correlations were shown in Fig.3, the strongest ROI connectivity of children with ADHD occurs between the rDLPFC and rFPC in both REST and VFT (Z=0.92 and Z=0.98), suggesting robust intra-hemispheric connections. However, ADHD children exhibit lower ROI correlations compared to HC (Z_{ADHD}<Z_{HC}), and VFT shows higher ROI correlations than REST (Z(VFT)>Z(REST)). Furthermore, the number of significantly different ROI correlations between groups is greater in REST (3 pairs) and VFT (6 pairs) than across tasks (1 pair for ADHD). Group t-test reveal that the significant differences in ROI correlations between ADHD and HC during REST and VFT stem from interactions between the left and right DLPFC and between the mFPC and BA 8, highlighting discrepancies in both ipsilateral and interhemispheric connectivity. Additionally, task t-test show that only the correlation between BA8 and lDLPFC exhibits significant differences across tasks (T=2.25, p=.027), while other ROI consistency remains high. Overall, the ROI correlations in ADHD are not confined to a single task but demonstrate cross-task consistency.

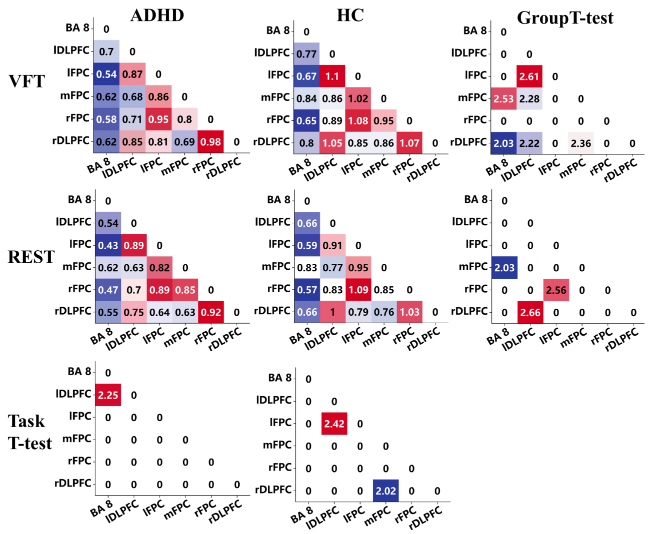

Fig. 3. Quantification of ROI correlations and t-test for VFT and REST. In the four plots in the top left, the values represent Z-value. The t-test plots display only those correlations that show significant differences (p<.05), with the values representing the absolute T-value.

4. DISCUSSION AND CONCLUSION

This study employed fNIRS for an in-depth multivariate analysis of brain function characteristics in children with ADHD, revealing consistent features in activation patterns and functional connectivity across REST and VFT. While cross-task consistency in functional activation was limited, significant trends and unexpected reversals were observed primarily in the left hemisphere. The functional connectivity analysis indicated a notable reduction in connectivity within the prefrontal cortex of ADHD children during both conditions, highlighting diminished inter-regional cooperation between the right and left prefrontal areas, which suggests impaired collaborative function in these regions. The strongest connectivity was observed between rDLPFC and rFPC. Additionally, the study identified features of homotopic and intrahemispheric connectivity while emphasizing the weakness of heterotopic connectivity in ADHD children. These findings not only underscore the cross-task consistency of brain function characteristics in children with ADHD but also provide new insights into the underlying neural mechanisms, paving the way for the development of targeted intervention strategies.

5. COMPLIANCE WITH ETHICAL STANDARDS

The authors have no relevant financial or non-financial interests to disclose.

6. ACKNOWLEDGMENTS

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