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High Correlation during Motor Tapping in Young Adults with Attention Deficit-Hyperactivity Disorder: A Controlled Functional MRI Study

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Abstract

The aim of this study was to check the correlation between brain areas in participants with attention deficit-hyperactivity- disorder (ADHD) during rhythmic motor activity. Children with ADHD have abnormal motor oscillatory activity. This maybe a result of synchronous activity and high connectivity between regions involved in motor tasks. We examined correlation between brain regions using functional-MRI in six individuals with ADHD and four controls during finger tapping (according to 1-4Hz cue). We found activation in the right cerebellum, left motor cortex, bilateral basal ganglia and left supplementary motor region. Right frontal cortex was selected as a control region. Correlation between motor regions was higher in participants with ADHD compared to controls (p=0.0046). Correlations between motor and non-motor regions were low in all participants. High correlations between motor regions but not between non- motor brain regions in participants with ADHD may reflect higher synchrony between motor regions and suggests increased, connectivity during rhythmic activity.

Keywords: Motor tapping; Attention deficit-hyperactivity disorder; MRI

Introduction

While clinical symptoms of "attention deficit-hyperactivity disorder (ADHD)" are well characterized and recognized the neurological underpinnings of this common neurodevelopment disorder remains unknown. Similar to neurodevelopment disorder it is thought that the cause for ADHD lies beyond localized neuroanatomical regions and is probably due to a general abnormality in brain function. Recently neuroimaging studies suggest that various disturbances in ADHD are associated with abnormal brain connectivity. Connectivity is the functional infrastructure connecting various brain regions. This system functions during activity and resting states in different ways. In children with ADHD connectivity was found to be different than age matched controls during different tasks. ADHD-related increased connectivity between cortical– subcortical areas was associated with greater impulsivity [1]. While tighter coupling was found during cognitive assignments [2], changes in connectivity during motor performance were not previously reported.

Individuals with ADHD have various motor oscillatory abnormalities that may reflect the increased connectivity during action. Children with ADHD tend to have excessive mirror overflow movements [3]. In our previous studies we found that more than half of the children with had an abnormal rhythmic response during tapping tasks; instead of tapping according to the frequency requested they tapped at a constant higher frequency [4]. This abnormal response remained constant on Methylphenidate treatment [5].

We hypothesized that individuals with ADHD will have increased synchrony between brain regions that may explain motor oscillatory abnormalities. To test this we examined individuals with ADHD and controls for correlation between brain regions during rhythmic motor tapping using functional-magnetic resonance imaging (fMRI).

Methods

Participants

Ten young adults participated in this fMRI controlled study: six with ADHD (mean 22, SD 1.3 years; 5 males) and four controls (mean 32, SD .8 years; 3 females). All participants were right handed and stated that they are able to lie still for an hour of testing. ADHD diagnosis was made by neurologists using the DSM-4 criteria. The study was approved by the Shaare Zedek Helsinki committee, and each participant signed an informed consent and was compensated for time loss and travel expenses.

Testing procedure

fMRI data was acquired using a block design paradigm. Participants tapped on an optical button immediately after the appearance of auditory stimuli with the right index finger. The auditory stimuli were presented in six frequencies (1, 2, 2.5, 3, 3.5 and 4 Hz) in blocks of 12 seconds with 6-12 seconds of rest in between. Each frequency appeared in a random order and was presented 3 times within the session. Finger tapping was tested in different frequencies in attempt to elicit an abnormal rhythmic response found in children with ADHD.

MRI data acquisition

MRI measurements were performed in a whole-body 3.0 Tesla MRI scanner (GE Signa EXCITE, Milwaukee, WI, USA). Functional protocol was based on Echo planar Gradient echo ($T2^*$)-weighted images (GE-EPI) (TR/TE/flip angle=3000/55/90) with FOV of 24 cm^2 and matrix size of 80 × 80). In addition, a 3D spoiled gradient echo (SPGR) sequence, with high resolution, was acquired for each subject to allow volume statistical analyses. Auditory stimuli were provided by shareware version of the GoldWave digital audio editor (http://www.goldwave.com) and generated by a program protocol written using Presentation 0.71 software.

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Functional-MRI data analysis

MRI data was processed using Brain Voyager 4.4 software package (http://www.brainvoyager.com) [6,7]. Preprocessing steps included motion detection and correction of head motion, temporal linear trend removal and temporal high pass filter of 2 cycles per time course. 3D statistical parametric maps were calculated separately for each subject using a general linear model (GLM) [8]. Each condition (i.e. 1, 2, 2.5, 3, 3.5 and 4 Hz) was modeled separately as a boxcar regressor convolved with a canonical synthetic HRF and used in the model. Realignment parameters, reflecting head motions in six directions, were included in the model a nuisance regressors. Percent (%) signal was averaged to fit 0-1 in all regions –that did not affect correlation and Wilcoxon test. A cube was cropped (6859 pixels; 19 voxels) from each motor region of interest around the area of peak activation for regions of interest and in an area without activity for the control region. Anatomical and functional volumes were co registered and normalized to the Talairach space.

Statistical analysis

Pearson correlation coefficients were calculated between % signal values of pairs of all brain regions for the entire time course. Correlation coefficients are not expected to follow a normal distribution and several of the group comparisons have small sample sizes therefore groups were compared with a Wilcoxon two-sample test. Nominal p-values are presented.

Results

Brain activation

All participants successfully performed the task. When comparing all tapping conditions with resting state we found activation in all participants mainly in 5 regions: Right cerebellum (Rt Cb), Left motor cortex (Lt Cx), Right basal ganglia (Rt BG), Left basal ganglia (Lt BG), Left supplementary motor region (SMA). The Right frontal cortex (Rt Frt) was selected as a control region as it was not activated during motor tasks.

Group analysis

There was no statistically significant difference between the ADHD participants and controls with respect to the level of correlation between % activation of specific brain regions pairs (Table 1).

High correlation in motor areas in ADHD participants

Participants with ADHD (Figure 1) had a higher correlation level (mean 0.46 ± 0.26) between the 5 activated motor regions (% activation in pairs of: Rt Cb, Lt Cx, Rt BG, Lt BG, SMA) compared to controls (0.35 ± 0.29; Wilcoxon two-sample test, p=0.034). Both the groups, ADHD and controls, had higher correlation levels between % activation in pairs within motor regions (mean 0.54 ± 0.21) versus motor regions and non-motor regions (mean 0.16 ± 0.20; p<0.0001). However, the correlation between % activation in pairs of motor regions was significantly higher (mean 0.60 ± 0.16) in individuals with ADHD compared to controls (mean 0.46 ± 0.26; Wilcoxon two-sample test, p=0.013). Low correlations between % activation were found in pairs of motor regions and the non-motor region and were similar in both groups (mean 0.18 ± 0.19 in ADHD versus 0.13 ± 0.22 in controls; Wilcoxon two-sample test, p=0.73; Table 1).

Area analysis: high correlation within the basal ganglia

Correlation between % activation in the left and right basal ganglia was the highest (mean 0.79 ± 0.10) and correlation levels between the % activation in the right cerebellum and the right basal ganglia was the lowest (mean 0.37 ± 0.21) among the motor brain regions.

Correlation of	With		N	Mean	SD	Min	Median	Max	p-value
Right Cerebellum	Left Cortex	Control	4	0.43	0.33	-0.02	0.5	0.75	0.36
		ADHD	6	0.67	0.12	0.5	0.72	0.79	
	Right Basal Ganglia	Control	4	0.22	0.22	-0.08	0.28	0.41	0.14
		ADHD	6	0.47	0.14	0.28	0.52	0.59	
	Left Basal Ganglia	Control	4	0.32	0.32	-0.13	0.39	0.62	0.14
		ADHD	6	0.59	0.11	0.39	0.61	0.7	
	Sensory Motor Cortex	Control	4	0.48	0.22	0.2	0.51	0.71	0.61
		ADHD	6	0.6	0.14	0.41	0.64	0.77	
	Right Frontal Cortex	Control	4	-0.01	0.24	-0.25	-0.01	0.24	0.61
		ADHD	6	0.12	0.24	-0.17	0.13	0.53	
Left Cortex	Right Basal Ganglia	Control	4	0.42	0.14	0.22	0.47	0.51	0.76
		ADHD	6	0.41	0.07	0.33	0.41	0.51	
	Left Basal Ganglia	Control	4	0.55	0.09	0.47	0.53	0.68	0.92
		ADHD	6	0.53	0.12	0.32	0.53	0.66	
	Sensory Motor Cortex	Control	4	0.52	0.35	0	0.66	0.75	0.61
		ADHD	6	0.69	0.12	0.53	0.71	0.84	
	Right Frontal Cortex	Control	4	0.05	0.22	-0.26	0.1	0.24	1
		ADHD	6	0.1	0.22	-0.22	0.08	0.43	
Right Basal Ganglia	Left Basal Ganglia	Control	4	0.76	0.14	0.55	0.82	0.85	0.76
		ADHD	6	0.81	0.06	0.72	0.81	0.88	
	Sensory Motor Cortex	Control	4	0.4	0.23	0.18	0.37	0.66	0.2
		ADHD	6	0.54	0.15	0.27	0.56	0.69	
	Right Frontal Cortex	Control	4	0.34	0.16	0.14	0.35	0.51	0.61
		ADHD	6	0.32	0.06	0.27	0.29	0.4	
Left Basal Ganglia	Sensory Motor Cortex	Control	4	0.53	0.25	0.16	0.63	0.7	0.61
		ADHD	6	0.66	0.13	0.48	0.65	0.81	
	Right Frontal Cortex	Control	4	0.19	0.18	-0.05	0.22	0.36	0.92
		ADHD	6	0.18	0.14	0.1	0.13	0.48	

Table 1: Table of distribution of all pair wise correlation coefficients per region by group, with p-value comparing ADHD and controls

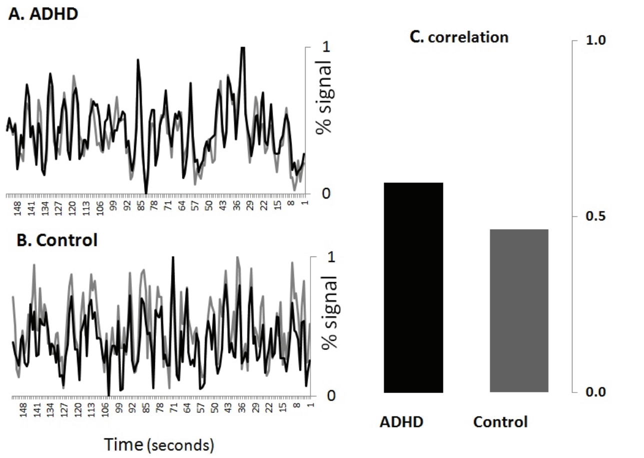

Figure 1: Correlation between motor regions during tapping task in participants with ADHD and controls. (A,B): BOLD brain activity (% signal) is presented over time (seconds) demonstrates high activation during tapping intervals and lower during rest. There is temporal correlation between the left (black) and right basal ganglia (grey) in both participants. However the participant with ADHD (A) hand higher correlation (=0.88) between left (grey) and right basal ganglia (black) than the control (B) participant (=0.54). (C): Group analysis demonstrates that participants with ADHD (n=6) have significantly higher correlations than controls (n=4) between motor regions (motor cortex, SMA, basal ganglia and cerebellum; Wilcoxon two-sample test, p=0.001).

Discussion

We found high correlations between motor regions but not between non- motor brain regions in participants with ADHD. The higher correlation during a rhythmic tapping detected in subjects with ADHD compared to controls reflects higher synchrony between motor regions during task engagement and may suggest increased functional connectivity during activity.

Connectivity studies in individuals with ADHD demonstrated varied results depending on task and brain region [9,10]. Resting-state fMRI studies have found connections characterized by both increased and decreased connectivity in ADHD. Decreased connectivity was found between cortical areas (e.g. posterior cingulate cortex and ventromedial prefrontal [11] and were normalized following stimulant medication [12]. Increased connectivity was found between the nucleus accumbens and the prefrontal cortex [1]. It is suggested that abnormal connectively is related with specific behavioral characteristics in ADHD. For example in ADHD children, the reward-motivation regions (striatum and anterior cingulate) had higher connectivity compared to controls [13]. Connectivity is related to the 'default-mode network' that may persist or intrude into periods of activity compromising attention. Increased connectivity during tasks may reflect the rest stage inadequate ability to shift from the rest stage to the attentional stage [14].

In our study the right and left basal ganglia were the area which demonstrated the highest connectivity during tapping. This increased coupling throughout motor tasks is similar to the reported coupling during non-motor assignments [2]. Thus we suggest that inability in ADHD to adjust brain connectivity levels to tasks may impact on performance. Namely while lower connectivity during rest leads to greater impulsivity [1] increased connectivity through activity may lead to lower performance of motor and non-motor tasks.

Limitations: Small sample size (n=10) and significant age difference between groups (p=0.005).

Future studies may study the role of motor training for treatment of attentional disorders. For example: biofeedback during motor activity may reflect changes in connectivity and thus enable training for gaining better control to shift from default mode to attentional mode.

Conclusions

This is first report, to the best of our knowledge, of increased synchrony in ADHD during a motor task. We believe that there is abnormal connectivity regulation in individuals with ADHD; maybe connectivity is abnormally low during the resting state causing inattention and increased during activities resulting in impulsivity and hyperactivity.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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