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Brain Activation in the Prefrontal Cortex during Motor and Cognitive Tasks in Adults

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Abstract

The prefrontal cortex (PFC) plays an important role in cognitive function, involved in Executive Functions (EFs) such as planning, working memory, and inhibition. Activation in the PFC also occurs during some motor activities. One commonly used tool to assess EF is the Tower of Hanoi, demonstrating sensitivity to PFC dysfunction. However, limited neuroimaging evidence is available to support the contribution of the PFC in the Tower of Hanoi task. In the current study, we use functional near infrared (fNIR) spectroscopy to examine hemodynamic responses associated with neural activity in the PFC in adults as they participate in the Tower of Hanoi task. We compared changes in cerebral oxygenation during resting, a motor task (tapping), and the Tower of Hanoi in 16 neurotypical adults, with measures of relative changes in concentration of oxygenated hemoglobin (Δoxy-Hb) and deoxygenated hemoglobin (Δdeoxy-Hb) taken throughout tasks, as well as total hemoglobin (ΔHbT) and oxygenation (Δoxy). Performance on the Tower of Hanoi was measured by the number of moves used to complete each level and the highest level of successful performance (3, 4, or 5 disks). We found a significant higher value of Δoxy-Hb and Δoxy in dorsolateral PFC (DLPFC) during the Tower of Hanoi as compared to tapping and resting. Significant changes in Δdeoxy-Hb and ΔHbT during the Tower of Hanoi were found in the right DLPFC only. These results support the notion that the Tower of Hanoi task requires higher levels of PFC activity than a similar motor task with low executive function demands.

Keywords

Prefrontal Cortex, Functional Near Infrared (fNIR), Cognitive Task, Tower of Hanoi

1. Introduction

The prefrontal cortex (PFC), often described as the center of cognitive function, is involved in Executive Functions (EFs) that include cognitive processes such as problem solving, decision making, working memory, planning, inhibition of responses, and cognitive flexibility. In addition, the PFC also contributes to motor functions. The activation in the PFC has been linked to motor timing, movement selection, and control of gait [1] [2] [3]. Motor timing involves determining the appropriate time for movement initiation [1]. Movement selection helps to suppress automatically triggered responses and prepare for a proper reaction to a task [3]. Examining the activity in the PFC can help us to better understand its role in the neural basis of motor control and this knowledge can be applied to populations with motor dysfunctions. In the current study, task-induced activity in the PFC was measured during a simple motor task and an EF task to examine the role of the PFC in each task.

Many tasks have been used to assess EFs of the PFC. The Tower of Hanoi is a commonly used tool to assess EFs [4]. The game consists of three vertical pegs and a number of disks graduated in size with the largest disk at the bottom. The object of the game is to move all the disks from a start state to a goal state while following two rules: 1) only one disk may be moved at a time, and 2) a disk may never be placed on top of a disk smaller than itself. The completion of the Tower of Hanoi requires complex EFs including inhibition, working memory, and planning [5] [6].

Due to the EF elements required in completion of the Tower of Hanoi, it has been used in patients with PFC lesions [4]. In the study, participants were asked to move disks to a goal state, in which all disks were stacked in descending order on a specific peg, from different start states. A performance score was calculated by a computer based on movement accuracy, movement speed, and problem difficulty. Patients with PFC lesions had lower score than the control group but the strategy they used to solve the puzzle was similar to the one used by the controls. The finding suggested that these patients had deficits in inhibition control rather than planning. Nonetheless, the contribution of the PFC during the Tower of Hanoi has been verified by studies using functional Magnetic Resonance Imaging (fMRI) [7] and electroencephalogram (EEG) [8] [9]. Increased prefrontal-parietal intrahemispheric correlation was observed during the Tower of Hanoi task in both left and right hemispheres [9]. Changes in absolute power of EEG activity in the PFC were also observed during the Tower of Hanoi [8]. However, limited resources can be found on using functional near-infrared (fNIR) spectroscopy to examine brain activity during the Tower of Hanoi.

fNIR measures the hemodynamics changes in cortical function based on the optical properties of hemoglobin. It provides a balance between spatial and temporal resolution for monitoring local and instance changes of oxygenation in the cerebral cortex [10] [11] [12] [13]. In addition, fNIR is more tolerant to motion artifacts than other non-invasive neuroimaging technologies making its feasibility enhanced for clinical studies, especially in motor tasks [14] [15].

The overall goal of our research is to understand brain/behavior relationships in motor tasks requiring executive function. In this study, we wanted to examine PFC activation in a computerized Tower of Hanoi task and in a simple tapping task with similar motor and spatial requirements but no problem-solving component. By controlling for movement type and amplitude, we could compare activation patterns which may inform us on the relative contributions of the PFC to each task. We had two purposes: first, we wanted to compare levels of activation among TOH, tapping and a resting condition. We hypothesized that TOH would have significantly higher activation levels than the other two conditions. Second, we wanted to compare the sensitivity of four biomarkers in detecting differences among conditions. We made no a priori prediction about sensitivity.

2. Methods

2.1. Participants

Prior to initiation of this study, the protocol was approved by the Institutional Review Board of the institution. A total of 18 participants participated in this study. All participants were students at the University of Delaware recruited through flyers posted around the campus and through word of mouth. Prior to participation, they were screened for suitability for this research and all were healthy and without family history of cognitive or mental disorders. Data of two participants was removed because one fell asleep during the study and high motion artifacts in another participant's data, leaving a total of 16 adult participants (7 females and 9 males, 22.3 ± 3.2 years old) in the study. There was no a priori power analysis conducted for this work as the dependent measures would provide sufficient information on variability to calculate effect sizes for follow-up studies. Data were collected between April and September, 2014.

2.2. Procedures

Upon entering the laboratory, participants received a description of the research and were asked to provide written informed consent. The principal investigator instructed participants how to perform the tasks and participants practiced the Tower of Hanoi on an iPad until they understood the rules and were able to complete the 3-disk task once. Next, the fNIR sensor pad was applied on the forehead of participants. During the resting period, the participants were instructed to "Try to relax and do nothing" and "Do not fall asleep" and participants stared at a "+" sign (1 cm * 1 cm) in the middle of a monitor on a "15.6" laptop (Satellite L755-S5351, Toshiba). This was followed by performance of the tasks in a randomly assigned order (**Figure 1**). An auditory sound was provided to notify participants of the start and end of each condition. Participants were instructed to keep quiet and minimize their movements during data collection. Data collection was completed within 40 minutes for all participants.

2.3. Tasks

2.3.1. Tower of Hanoi

The Tower of Hanoi is a disk-transfer task. The goal of the task is to move disks from a

<table>
<tr><th>Baseline</th><th></th><th colspan="3">iPad tasks</th></tr>
<tr><td>3 mins</td><td>1 min</td><td>2 mins</td><td>1 min</td><td>2 mins</td></tr>
<tr><td rowspan="3">Resting with eyes open</td><td rowspan="3">Break</td><td>Tapping</td><td>Break</td><td>Tower of Hanoi</td></tr>
<tr><td colspan="3">or</td></tr>
<tr><td>Tower of Hanoi</td><td>Break</td><td>Tapping</td></tr>
</table>

Figure 1. Data collection procedure.

start state to a goal state using the fewest number of moves possible while following two rules: 1) only one disk may be moved at a time, and 2) a disk may never be placed on top of a disk smaller than itself. Tower Hanoi task in our study required participants to move disks from the leftmost peg to the rightmost peg. Participants performed the task on an iPad using Tap Towers (Madcap Studios, Inc.), starting from 3 disks (**Figure 2**) then progressed to 4 disks, 5 disks, and 6 disks if time allowed. The level participants reached and the number of moves to achieve goal states of each level were recorded.

2.3.2. Tapping

The tapping task was designed to be a simple motor task with minimal EF demands. Participants tapped two sides of iPad (about 5 cm in width and 13 cm apart, index of difficulty = 2.4 [16]) back and forth on an iPad at a self-selected pace for two minutes. The number of taps was recorded.

2.4. Functional Near Infrared (fNIR) Spectroscopy

The activity in the prefrontal cortex was measured by an fNIR system (fNIR100A, Biopac System Inc.). fNIR detects hemodynamic changes resulted from brain activation based on the general transparency of biological tissues to infrared light as well as optical properties of oxygenated-hemoglobin (oxy-Hb) and deoxygenated-hemoglobin (deoxy-Hb) [17]. The fNIR system has a sensor pad, a control box, and a computer installed with Cognitive Optical Brain Imaging (COBI) Studio software and fnirSoft [14] for data collection and analysis. The sensor pad contains 4 light sources (LED) and 10 light detectors creating an array of 16 channels (**Figure 3**). The source-detector distance is 2.5 cm and the depth of penetration is approximately 1.5 cm beneath the scalp [18] [19]. The light sources and detectors are embedded in a flexible pad made with medical grade silicone. The pad can be worn as a headband and match the contour of the foreheads. The light sources emit infrared light at 730 nm and 850 nm which penetrates the scalp. Part of light is absorbed by hemoglobin and the rest of light reaches detectors in a banana-shaped path. Oxygenated-hemoglobin and deoxygenated-hemoglobin has different absorption coefficients. Concentrations of hemoglobin can then be calculated by the ratio of light absorbed at different wavelengths. LED current and detector gain were adjusted before prior to the study to prevent signal saturation Base-

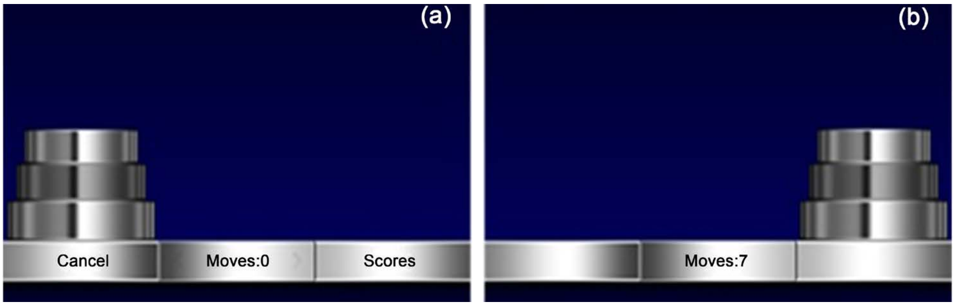

Figure 2. The Tower of Hanoi task using three disks: (a) starting position (b) ending position.

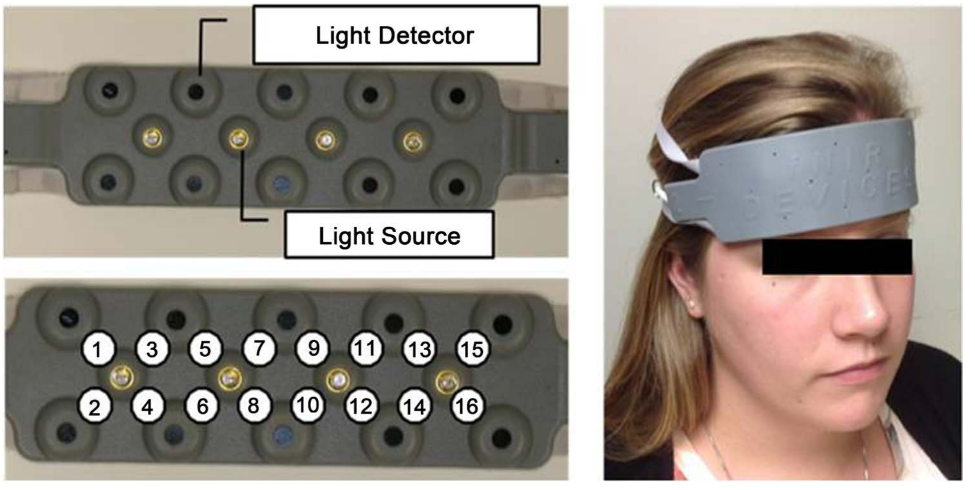

Figure 3. The sensor pad with 8 light detectors and 4 light sources (left, top) creates 16 channels (left, bottom). The sensor pad positioned on a participant (right).

line measurements were obtained with the fNIR signal recorded at 2 Hz.

2.5. Data Processing

Raw data was visually inspected and channels with saturated or very low signals were removed. Optodes on the sensor pad that may not contact completely with the skin resulted in saturated channels. Low signal values were due to interference with light transmission from the hair. Motion artifacts were excluded manually. Raw light intensity was filtered by a low-pass finite impulse response (FIR) filter with an order of 20 and cutoff frequency at 0.1 Hz to attenuate the high frequency noise, respiration, and cardiac cycle effects [20]. Relative changes of concentrations in oxygenated hemoglobin (Δoxy-Hb), deoxygenated hemoglobin (Δdeoxy-Hb), blood oxygenation (Δoxy; calculated from Δoxy-Hb-Δdeoxy-Hb) and blood volume changes (ΔHbT; calculated as Σ (Δoxy-Hb + Δdeoxy-Hb) were calculated using modified Beer-Lambert law, with a 10-second baseline recorded at the beginning of data collection [21]. Data was processed using fnir Soft [14]. The first and the last 15 seconds of each condition were removed to prevent an unstable state at the beginning of the test and the effect from previous activity [22]. The remaining data points were averaged in each channel for each task. Z scores were calculated using the mean and standard deviation of all 16 channels in each task of each participant using z = (x-mean)/SD. Channels with extreme values (z scores above 2 or less than-2) were removed as outliers [23]. Remaining channels were averaged for each condition. Four regions of interest (ROIs) were created for the prefrontal cortex which included averages of 4 channels for each biomarker: left dorsolateral prefrontal cortex (LDLPFC) which involved channels 1 - 4; left medial prefrontal cortex (LMPFC) channel 5 - 8 were used; right medial prefrontal cortex (RMPFC) used channels 9 - 12 and right dorsolateral prefrontal cortex (RDLPFC) involved channels 13 - 16.

2.6. Statistics

A one-way repeated measures ANOVA was used to examine the differences in the four biomarkers (*i.e.*, Δoxy-Hb, Δdeoxy-Hb, Δoxy, and ΔHbT) between the eyes open resting, tapping, and the Tower of Hanoi tasks. Tukey's post-hoc comparisons were calculated to determine specific differences. Effect sizes (Cohen's d) were calculated to aid in the interpretation of the results. We interpreted the values of d = 0.20 as considered small, d = 0.50 as medium, d = 0.80 as large and d = 1.3 as very large according to Cohen [24]. The level of significance was set at 0.05. Number Cruncher Statistical Systems (NCSS 9-www.ncss.com) was used for the analyses.

3. Results

3.1. Tower of Hanoi Behavioral Data

All participants completed 3-disk level in 2 minutes (9.9 ± 4.3 moves). Eleven participants finished at the 4-disk level (25.1 ± 9.3 moves) and 3 participants completed the 5-disk level (39.3 ± 4.9 moves) within the 2-minute time limit.

3.2. PFC Activation

The results of repeated measures ANOVA showed significant differences in all 4 biomarkers in RDLPFC among the three conditions. Tukey's post-hoc comparisons revealed significant increases in both Δoxy and Δoxy-Hb from eyes open resting condition and tapping condition to the Tower of Hanoi condition. A significant increase of ΔHbT was found from tapping to the Tower of Hanoi condition. These changes along with a significant decrease in Δdeoxy-Hb from eyes open resting to the Tower of Hanoi condition indicated that there was a higher activation in RDLPFC when participants were performing the Tower of Hanoi task. In addition, an increased activity in LDLPFC was observed with significant higher Δoxy and Δoxy-Hb during the Tower of Hanoi task. A significant change in Δoxy was also found in RMPFC among 3 conditions. **Figure 4** shows the average areas of activation for the three conditions. Note that in the TOH task, there are high levels of activity in the DLPFC on both the left and right sides. Detailed results were presented in **Table 1**.

4. Discussion

The aim of current study was to examine the differences in prefrontal cortex activity

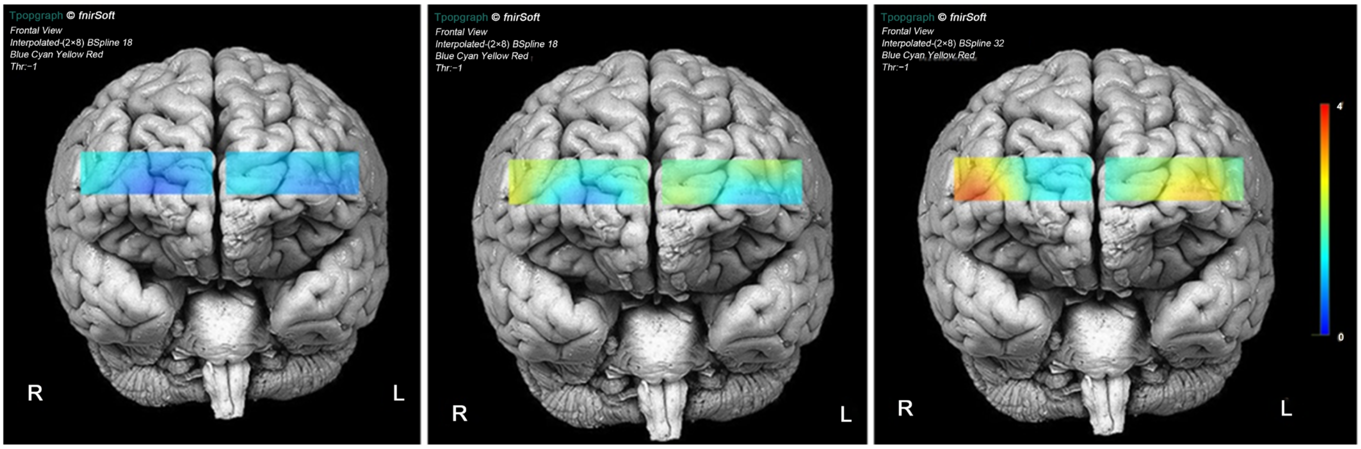

Figure 4. Comparison of areas of activation associated with a) resting, b) tapping and c) tower of hanoi condition. Areas of significant activation (t (15) = 1.756, one-tailed) are denoted in red and yellow, and areas with limited or no activation are denoted in cyan and blue.

Table 1. Four biomarkers descriptive and inferential statistics (N = 16).

	ΔOxygenation (Δoxy)						
	Eyes Open Resting Mean ± SD	Tapping Mean ± SD	Tower of Hanoi Mean ± SD	F (2, 30)	p-value	Tukey's	Cohen's d
LDLPFC	1.16 ± 1.09	1.32 ± 1.73	2.32 ± 1.86	10.04	<0.001	TOH > Tap, Rest	TOH/Tap: −0.56 TOH/Rest: −0.76
LMPFC	1.26 ± 1.38	1.44 ± 1.94	1.98 ± 2.15	2.57	0.093		
RMPFC	1.29 ± 1.49	1.32 ± 2.20	2.02 ± 2.40	3.36	0.048		
RDLPFC	1.51 ± 1.47	1.60 ± 2.08	2.63 ± 2.13	9.34	<0.001	TOH > Tap, Rest	TOH/Tap: −0.49 TOH/Rest: −0.61
			ΔOxygenated-hemoglobin (Δoxy-Hb)				
LDLPFC	0.79 ± 0.91	0.61 ± 1.56	1.50 ± 1.40	5.24	0.011	TOH > Tap	TOH/Tap: −0.60
LMPFC	0.83 ± 1.31	0.88 ± 1.74	1.22 ± 1.80	0.98	0.387		
RMPFC	1.07 ± 1.27	1.13 ± 2.02	1.62 ± 2.13	1.87	0.172		
RDLPFC	0.91 ± 1.43	0.80 ± 1.78	1.66 ± 1.95	7.66	0.002	TOH > Tap, Rest	TOH/Tap: −0.46 TOH/Rest: −0.44
			ΔDeoxygenated-hemoglobin (Δdeoxy-Hb)				
LDLPFC	−0.42 ± 0.56	−0.71 ± 1.00	−0.83 ± 1.02	3.09	0.060		
LMPFC	−0.43 ± 0.69	−0.56 ± 0.98	−0.78 ± 1.11	2.60	0.091		
RMPFC	−0.15 ± 0.53	−0.14 ± 0.70	−0.47 ± 1.10	1.96	0.159		
RDLPFC	−0.63 ± 1.31	−0.81 ± 1.24	−0.97 ± 1.31	3.51	0.043	TOH > Rest	TOH/Rest: 0.26
			ΔTotal Hemoglobin (ΔHbT)				
LDLPFC	0.32 ± 1.09	−0.11 ± 1.97	0.67 ± 1.59	2.02	0.150		
LMPFC	0.40 ± 1.57	0.31 ± 2.05	0.46 ± 2.08	0.09	0.918		
RMPFC	0.95 ± 1.37	0.97 ± 2.20	1.17 ± 2.44	0.21	0.809		
RDLPFC	0.26 ± 2.33	−0.00 ± 2.25	0.68 ± 2.55	3.61	0.039	TOH > Tap	TOH/Tap: −0.28

between an executive function task (Tower of Hanoi) and a tapping task with identical movement and spatial requirements using a fNIR system. Four fNIR biomarkers were measured during a simple motor task and Tower of Hanoi in adults. Our results found increased activities in bilateral DLPFC during Tower of Hanoi task. In contrast, there were no significant changes in brain activity during the tapping task as compared to the resting condition. The finding corresponded with previous studies exploring the involvement of the PFC in problem solving tasks using fMRI, in which activations of the DLPFC have been observed during Tower of London task [25] [26] [27] [28]. The involvement of the DLPFC in executive functions including working memory, inhibition, and planning has been long established [29] [30]. It is thought that the left DLPFC supports cognitive processes of recognizing specific features, reasoning, and problem solving, while the right DLPFC supports cognitive processes of planning and decision making [31] [32] [33]. Our results showing bilateral activation of DLPFC matched the signatures of Tower of Hanoi that require functions of DLPFC from both hemispheres.

In the current study, bilateral activation of DLPFC during Tower of Hanoi task was reflected by two biomarkers, Δoxy and Δoxy-Hb. This was not the case with Δdeoxy-Hb or ΔHbT which only had statistically significant changes in the right hemisphere. Furthermore, the associated effect sizes for Δoxy and Δoxy-Hb ranged from d = 0.44 - 0.76 which indicate a medium effect. In contrast, effect sizes for the measures of Δdeoxy were small. Our results suggested that Δoxy and Δoxy-Hb were more sensitive in event-related response than Δdeoxy-Hb or ΔHbT. To date, most commonly reported fNIR biomarkers are oxy-Hb, deoxy-Hb, and total-Hb. Limited studies exist comparing the sensitivity of Δoxy to other biomarkers. To our knowledge, the changes of Δoxy has not been compared to other neuroimaging methods (e.g., EEG, fMRI). Prior studies examined the correlation between fNIR biomarkers (oxy-Hb, deoxy-Hb, and HbT) and blood oxygen level dependent (BOLD) response measured by fMRI had provided conflicting results. Although significant correlations exist between the BOLD signal and all fNIR biomarkers, different biomarkers were reported to have the strongest correlation to BOLD signals [34] [35]. Strangman and colleagues correlated the event-related changes of BOLD signals to quantitative changes of oxy-Hb, deoxy-Hb, and total-Hb measured by fNIR during a motor task [35]. They found that oxy-Hb had the strongest correlation to BOLD signal and deoxy-Hb had the weakest correlation to BOLD signal. The result supported part of our finding that oxy-Hb was more sensitive than deoxy-Hb in response to an executive function task. Conversely, Huppert and colleagues examined the temporal correlation between the BOLDresponse measured by fMRI and fNIR biomarkers during a motor activity in healthy adults [34]. The result showed an improved correlation between deoxy-Hb and a BOLD signal than the correlation between oxy-Hb and a BOLD signal. Combining the results from both studies, it suggested that sensitivity of each fNIR biomarker varies in different dimensions of the hemodynamic response. Deoxy-Hb is more sensitive to temporal changes whereas oxy-Hb is more sensitive in quantitative measurements. Our results were closer to Strangman *et al.* [35] since quantitative changes were examined in our study.

A limitation of the current study was that we did not analyze temporal changes of fNIR data. We were not able to explore the time course of hemodynamic changes in response to the Tower of Hanoi task. In addition, cortical activity was not recorded during the orientation session nor was a control baseline session recorded. Assessing during an orientation and during a control session might have provided valuable information about cognitive processing and neural activation.

5. Conclusions and Future Directions

In the current study, we found a significant increase in bilateral DLPFC activation during the Tower of Hanoi, an EF task, over a simple tapping task and a rest condition in our sample of adults. The results confirmed the involvement of the PFC in the EF task. In addition, we found that Δoxy and Δoxy-Hb were more sensitive than Δdeoxy-Hb and ΔHbT. Further, Δoxy may be a more valuable measure when an event-related response is examined.

The fact that we could detect activation differences between TOH and tapping suggests that this methodology can be used in the future with clinical populations who have movement difficulties. In particular, we plan to replicate this study by using a population of children with Developmental Coordination Disorder (DCD), which is a neuromotor disability that affects motor coordination and the capacity to learn and acquire motor skills. While the etiology of DCD has yet to be fully understood, previous research has suggested associations between motor deficits and cognitive processing (e.g. [36]). The movement requirements in our existing protocol are relatively simple and have few motor planning requirements, thus enabling participants with poor motor coordination to successfully perform the task. Our proposed future work will allow us to look for EF differences in populations with and without DCD.

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