fNIR Study of Cognitive Decline and Reading in Parkinson's Disease: Preliminary Data

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Abstract: As yet, there has been little research applying functional near-infrared spectroscopy (fNIR) neuroimaging studies to aspects of brain activation such as cognitive decline or working memory deficits with reading difficulties in Parkinson's disease (PD). The purpose of this study is to investigate cerebral hemoglobin concentration changes related to reading and cognitive load tasks in an individual with PD. An individual with PD and a healthy normal person of the same age with no history of neurogenic disorders participated in this study. Functional near-infrared spectroscopy (fNIR) measurements were recorded while the participants carried out a reading task (grandfather passage) and four cognitive load tasks. The fNIR results for the reading task revealed significant differences in the changes in the oxygen concentration levels experienced by the two participants and this was also manifested in both the left and right hemispheres. There were also significant differences between the two participants across all of the cognitive tasks. Unlike the non-PD participant, the PD participant did not exhibit any significant differences among the four cognitive tasks and no significant oxygenation change between the left and right hemispheres when performing cognitive tasks 1 and 4 was observed. These results suggest that PD patients either lack sufficient brain activation to complete linguistic or cognitive tasks or are unable to use oxygenation effectively in a specific brain area when seeking to accomplish these types of tasks.

Keywords: fNIR, Parkinson's disease, cerebral hemoglobin concentration changes, cognitive deficits, reading, hemisphere differences, brain activation.

INTRODUCTION

Cognitive deficits, motor impairment, and altered precision and intelligibility have been reported to be major clinical and linguistic characteristics of Parkinson's diseases (PD) [1-3]. Since PD is a degenerative disease, cognitive processes deteriorate depending on the severity. A common cognitive deficit in PD is information processing; patients with PD show deficits in working memory referred to as the memory process of temporarily storing information and then using it a short time later, which involves mainly the frontal and parietal lobes in the brain [4-5]. The links between working memory and language, anatomical structures and the attentional control of working memory have been studied extensively [4, 6-8]. Research into the relationship between cognitive functions and reading has shown that vocabulary learning difficulties, working memory deficits, and reading impairments are interrelated, with young adults suffering from reading difficulties also exhibiting an impaired verbal working memory [9]. Studies of language processing in PD have also revealed that basal ganglia dysfunction affecting frontal lobe function, including attention, working memory, reasoning, executive functioning and other cognitive abilities, is associated with linguistic processing impairments [10-13].

Brain imaging studies utilizing an fMRI imaging technique have been widely used to investigate the relationships between anatomical areas, cognitive and linguistic processing in PD. It was discovered that people with PD have different neural activation patterns for sentence comprehension tasks compared with healthy controls as well as reduced brain activity in the left anteromedial prefrontal area [11]. An fMIR study found that despite there being no significant difference in brain activity during object naming and action-verb generation, people with PD exhibit dysfunctional patterns in the left frontal operculum area compared with normal healthy subjects [14]. Although a number of studies utilizing fMRI have been reported, the relatively new technique of functional near-infrared spectroscopy (fNIR) neuroimaging has not yet been widely applied to examine brain activation related to cognitive declines or working memory deficits with reading difficulties in PD [15-16].

fNIR measures NIR light absorbance in blood hemoglobin with and without oxygen and provides information about ongoing brain activities in a similar way to fMRI [17]. Cognitive or linguistic processing deficits afflicting PD patients can be quantitatively measured and analyzed by fNIR, which provides information on oxygenated hemoglobin (Hbo), deoxy-

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genated hemoglobin (Hbr), oxygenation (Oxy; Hbo-Hbr), and total oxygenation (Hbt). This technique offers several advantages over fMRI as it is more portable, easy to use, and relatively insensitive to body or head movements and is thus especially useful when working with children, elderly, and Parkinson's or dementia patients, providing a non-invasive method for investigating brain function in real time [17].

Therefore, this study utilized fNIR to investigate changes in the cerebral hemoglobin concentration related to reading and cognitive load tasks in an individual with PD. We hypothesize that a patient with PD would demonstrate a different brain activation pattern than a normal healthy participant in reading and cognitive tasks. Furthermore, the fNIR results would be similar to those from other imaging technique studies (e.g., PET or fMRI).

METHODS AND PROCEDURES

Participants

An individual with PD and a healthy normal person with no history of neurogenic disorders participated in the study. The participants were comparable in terms of age (59 years), gender (female), handedness (right handed), and education (years of education: PD=20 and control=19) and were recruited at the Senior Center and the Conley Speech, Language and Hearing Center at the University of Maine. The PD participant's current medications were Stalevo, Requip, and Azilect. Neither participant had a history of drug or alcohol abuse. The Cognitive Linguistic Quick Test (CLQT) used to screen for cognitive functioning indicated that the PD participant's overall cognitive functioning fell within normal limits for all domains [18] (Table **1**).

Conner's Continuous Performance Test (CPT) was administered to measure the cognitive characteristics of the PD patient [19]. The results of an attention task (CPT-II) showed that the PD participant's confidence index, which provides the degree of fit to the profile of clinical or non-clinical respondents, was borderline. Several CPT-II measures indicated that her attentional ability fell within normal limits (Omission and Commission). However, other measures showed mildly atypical inattention problems; her reaction times were substantially more variable than the normative group average (Variability, Perseverations, and Hit RT ISI change). Based on the overall results from the CPT-II test, at the time the test was conducted she was suffering from a potential attention problem (Table **2**).

Functional Near-Infrared System and Data Measures

The participants were monitored using functional near-infrared spectroscopy (fNIR) while accomplishing a reading task (the Grandfather Passage) and four cognitive load tasks. We used a 16-channel fNIR optical brain imaging system (fNIR 300A, Biopac company) linked to an fNIR sensor (18 cm x 6 cm x 0.8 cm) consisting of 4 LED light sources and 10 detectors to detect oxygen levels in the prefrontal cortices using 16 voxels with the source detector. The sensor, which emits light at two wavelengths (730nm and 850nm),

Table 1: The Results of the Cognitive Linguistic Quick Test (CLQT) for the PD Participant

Task	Raw score	Cognitive Domain Score				
		A	M	EF	L	VS
Personal facts	8		56		8	
Symbol cancellation	12	108				24
Confrontational naming	10				10	
Story retelling	9	18	54		9	
Symbol trails	10	30		10		20
Generative naming	9		9	9	9	
Design memory	6	12	60			24
Mazes	8	32		8		24
Design generation	9	9		9		9
Totals		*209*	*179*	*36*	*36*	*101*

*Attention (A), memory (M), executive functioning (EF), language (L), &visuospatial skills (VS).

Table 2: Conner's Continuous Performance Test II (CPT) Results for the PD Participant

	Confidence Index (%)	Omission	Commission	Hit RT	Variability	Perseverations	Hit RT ISI change
T-Score	50 %	47.93	48.52	53.75	69.22	63.07	66.30

*Hit RT: the mean response time in milliseconds for the all targets over the task; Hit RT.
ISI: the reaction time changes over the three inter-stimulus intervals (1, 2 and 4 seconds).

was placed on the participant's forehead over the international (10-20) electrode EEG placement F7, Fp1, Fp2, and F8 (left and right hemispheres) positions and secured using a flexible headband. Cognitive optical brain imaging (COBI) studio software was used to collect data and the fNIR device calibrated and a baseline established by asking the subjects to close their eyes for about 1 minute before the reading task began. The Grandfather Passage (Font: Times New Roman, 26) was presented on a computer screen and the subjects were asked to read the passage aloud, during which time the fNIR data was collected. The emerging light intensity from cortical areas in each voxel was obtained with the sampling rate of 2Hz (2 samples per second). fNIRSOFT (Biopac Systems, Inc.) visual spectroscopy signal analysis software [20] was used to process and analyze the data. Manual marker, which is recorded timestamps for each event during data acquisition from the COBI software allows to collect each fNIR data set for targeted tasks continuously. Therefore, the relative concentrations of average oxygenation values (Oxy; Hbo-Hbr) for each task in the prefrontal cortex, including Brodmann's areas 9, 10, 45, and 46, were collected and used as the dependent variable in this study. After a short break (5 minutes), the changes in brain activation for each of the following four cognitive tasks were measured: Task 1, name the 12 months in order (January, February, March……December); Task 2, name the 12 months in reverse order (December, November, October….. January); Task 3, match the first and last two months (January –December, February- November……June-July); and Task 4, a month and number count (January 12, February 24, March-36…..December-144). Four cognitive different tasks in the current study were selected since the tasks were at four levels of increasing complexity (cognitive loading), task1, 2, 3, and 4 respectively.

RESULTS

The average changes in relative concentrations of oxygenation comparing to the initial eye close phase were calculated using modified Beer-Lambert Law. The raw light intensity measures were filtered using first low pass filter with cut off 0.1 HZ and motion artifact induced by head or body movement was removed by using a sliding window motion artifact rejection (SMAR) system with fNIRSOFT.

Reading the Grandfather Passage

Both the PD and control participants completed the reading task, but the PD participant needed 20 seconds more than the control to do so. The independent sample t-tests revealed that there was a significant difference in the changes in the participants' oxygen concentration (Oxy) ($t(30) = -4.325$, $p < .05$) and this was visible in both the left hemisphere ($t(14) = -4.101$, $p < .05$) and the right hemisphere ($t(14) = -2.364$, $p < .05$) (Figure **1**).

Performing the Cognitive Tasks

The control participant successfully completed four cognitive tasks. However, the PD participant was unable to complete cognitive tasks 3 and 4. The MANOVA test revealed significant differences in the oxygen concentration changes between the two participants across all of the cognitive tasks (Task 1-$F(1, 30)=39.27$, $p<.001$; Task 2-$F(1, 30)=85.402$, $p<.001$; Task 3-$F(1, 30)=112.724$, $p<.001$; Task 4-$F(1, 30)=187.229$, $p <.001$). The oxygen concentration changes in task 1 and task 4 were only analyzed to identify a clearer picture of brain activation pattern since these tasks are the easiest and the most difficult respectively. The PD participant showed no significant differences among the four cognitive tasks and no significant oxygenation change between the left and right hemispheres on cognitive tasks 1 and 4 ($F(1, 7)=1.553$, $p = .253$). However, a one way repeated ANOVA test revealed a significant oxygenation change among the cognitive tasks ($F(3, 45)=124.45$, $p< .001$) in the control participant. Pairwise comparisons showed that all the cognitive tasks showed a significant difference with each other. A repeated 2x2 ANOVA revealed no significant oxygenation changes between the left and right hemispheres on both the task 1 and task 4 ($F(1, 7)=.025$, $p =.878$) in the control participant (Figure **2**).

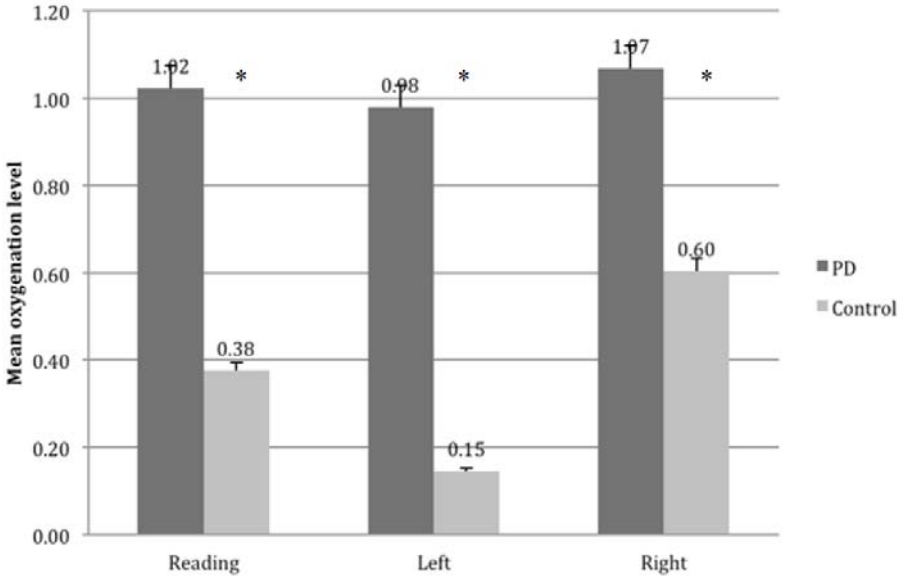

Figure 1: Comparison of the oxygenation levels for the reading task between the PD and control participants (reading oxygenation; and left and right hemispheres). *denotes *p*<.05.

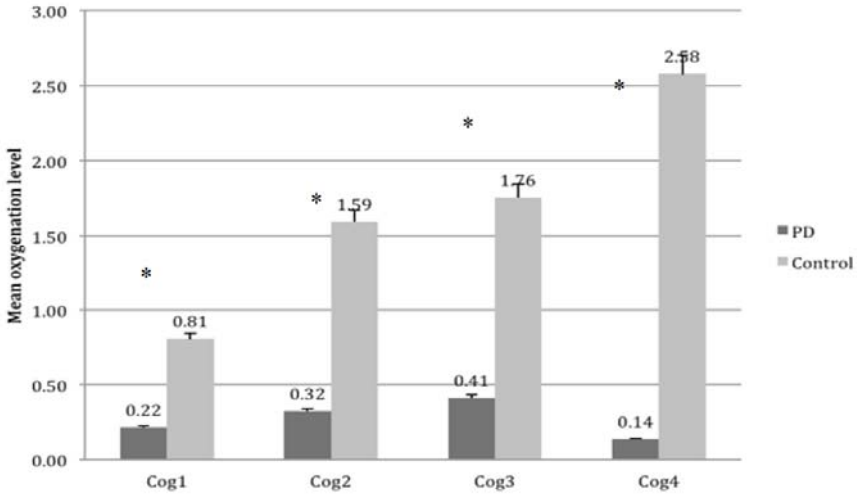

Figure 2: Comparison of the oxygenation levels for each of the four cognitive tasks between the PD and control participants. *denotes *p*<.05.

DISCUSSION

Reading

The PD participant appeared to experience greater changes in oxygenation levels during the reading task than the control participant. Changes in the oxygenation levels in both her left and right hemispheres were higher than those recorded for the control participant. According to previous fNIR studies focusing on the neural representation of reading (see, for example, [21-23]), healthy populations show bilateral Hbo increases and Hbr decreases in anterior prefrontal cortex areas and high oxygenation changes in Broca's and Wernicke's areas during reading tasks. The control participant in the current study, like the healthy normal participants in the previous studies, showed similar high oxygenation changes even under different control conditions (closed eyes/rest/blank screen etc.,). The higher oxygenation changes in the PD participant could be due to brain activation patterns similar to those observed in previous PET activation studies for prefrontal damage populations during language related tasks, where people with fluent and nonfluent aphasia showed higher oxygenation changes than normal elderly people [24-25]. This was ascribed to the brain activations in cortical areas not being utilized in normal control groups during language tasks, which is consistent with the current findings, where the PD participant completed the task with functioning in

cortical areas that are not usually activated during reading. This suggests that a language related task causes hemodynamic changes in the prefrontal cortices in the brain and that these brain activation changes are different between a normal older person and an individual with PD. Specifically, higher oxygenation changes in a simple passage reading may be linked to non-typical brain activation in PD.

Cognitive Tasks

In the cognitive tasks, the PD participant showed much lower levels of oxygenation changes than the control participant for all four of the cognitive tasks; the PD patient showed no significant oxygenation changes when performing cognitive tasks 1 to task 4, while the control showed significantly different oxygenation concentration changes across all four tasks, with the oxygenation concentration changes in task 4 (the most difficult) being much higher than task 1 (the easiest). These findings are consistent with earlier research demonstrating that harder cognitive tasks require greater prefrontal cortex activation [26]. However, unlike the control participant, the PD participant was unable to complete cognitive tasks 3 and 4, which may suggest markedly lower prefrontal cortex activation during the cognitive tasks in the PD patient. Oxygenation levels in the PD participant were not greatly affected by task difficulty which is consistent with previous studies in non-demented ALS and TBI people showing significantly reduced oxygenation levels during 1 back and 3 back working memory tasks, where no oxygenation changes were linked to task difficulty (ALS, [27]), and a visual discrimination task (TBI, [16]); in both these studies the controls showed higher oxygenation levels during the tasks and the changes in oxygenation levels varied based on the task difficulty. The current findings suggest that the decreased oxygenation levels are related to deficits in the cognitive ability of the PD participant when attempting cognitive tasks.

The considerably higher oxygenation changes in the PD participant when reading may indicate that PD patients use cortical areas less effectively than healthy subjects during language related tasks. Utilizing the areas adjacent to the language related areas to help with the language process may explain the non-typical higher oxygenation changes in PD [24-25]. A different mechanism may be involved when performing cognitive tasks, however. The low oxygenation changes during cognitively demanding tasks may suggest neurological deterioration or cortical structural changes due to the inefficient use of the neurotransmitter dopamine in PD [28]. Unlike in the control subject, there was no increase in the oxygenation changes during the four progressively more demanding cognitive tasks. A previous study on limited prefrontal cognitive capacity [29] suggested that cerebral activity decreases during excessive cognitive workloads. It is therefore possible that these cognitive tasks exceeded the possible cognitive processing abilities in the PD participant.

Overall, the reduced prefrontal brain activity in PD may be an indicator of cognitive deficits in working memory or executive functions, although the PD subject did not exhibit distinct cognitive deficit scores in the CPT and CLQT behavioral tests. The high prefrontal brain activity in PD during reading may explain why this subject required more time to finish reading the passage than the control.

However, the relationship between prefrontal cortex activation during the reading and cognitive tasks in the current study is not clear, although previous research has linked impaired working memory with reading difficulty in young adults [9]. The limited brain activation in language related prefrontal cortex areas may thus be related to an impaired verbal working memory, which may affect the PD participant's reading ability. Also, the involvement of non-language related areas during reading caused higher prefrontal brain activity, and hence a longer time to complete the passage. These findings suggest that PD patients may lack either sufficient brain activation to complete linguistic or cognitive tasks or the ability to use oxygenation effectively in the specific areas needed to complete these tasks.

LIMITATIONS

The current study suffers from several limitations. First, the results in the current study are preliminary, based on a single PD individual, and data from a larger sample is clearly necessary to produce generalizable results. Second, sensitive cognition tests (e.g., the digit span test, working memory token test etc.,) should be utilized to develop a broader picture of the cognitive capabilities of PD patients. Finally, the methodology utilized in the current study was not sufficient to thoroughly investigate the relationship between reading difficulty and cognitive deficits. Nonetheless, our findings suggest interesting differences in the brain activation patterns of our PD and normal participants for reading and cognitive tasks and that functional near-infrared imaging offers a useful and sensitive new

approach for investigating prefrontal brain activation in individuals with neurological disorders.

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