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The effects of transcranial direct current stimulation on dual-task walking in Parkinson's disease

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THE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON DUAL-TASK WALKING IN PARKINSON’S DISEASE

by

VICTORIA NGUYEN

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Approved by

First Reader
Maryann MacNeil, M.A.
GMS Faculty – Anatomy & Neurobiology

Second Reader
Brad Manor, Ph.D.
Director of the Mobility and Brain Function Program
Institute for Aging Research
DEDICATION

I dedicate my efforts of completing this thesis and the master of medical science program to my loving parents who have endlessly supported me throughout my journey as an aspiring physician.
ACKNOWLEDGMENTS

I take this opportunity to express gratitude to all of my colleagues at the Institute for Aging Research for teaching me many valuable lessons in clinical research. I would especially like to acknowledge Rachel Harrison for transitioning me and staying by my side whenever I needed help, Tim Granger for taking the time out teach me about data collection and analysis, and lastly Dr. Brad Manor for his guidance and expertise in all aspects of research.
THE EFFECTS OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON DUAL-TASK WALKING IN PARKINSON’S DISEASE

VICTORIA NGUYEN

ABSTRACT

Background: Parkinson’s disease (PD) is a common debilitating disorder that largely effects the aging population. It is associated with a loss of dopamine-producing brain cells, which leads to abnormal brain activity and ultimately, a loss of locomotor control. Transcranial direct current stimulation (tDCS) is a technology that effectively modulates brain excitability by sending low electric current through the scalp. It has been demonstrated to improve working memory, intelligence, learning ability, as well as relieving symptoms of depression, Alzheimer’s and schizophrenia (Kekic, Boysen, Campbell, & Schmidt, 2015; Khedr et al., 2014; Manor et al., 2015). tDCS may thus serve as an effective therapeutic strategy for this vulnerable PD population.

Objective: The primary purpose of this study was to examine the acute effects of single sessions of tDCS targeting different brain networks on locomotor control metrics and other outcomes in patients with PD.

Design: A pilot, double-blinded, sham-controlled study.

Methods: A total of 15 older adults between the ages of 40-85 with a physician diagnosis of PD will be recruited. Participants are screened with questionnaires to determine
eligibility. If eligible, participants will undergo a dual task assessment and a freezing of gait (FOG) provoking protocol prior to, as well as immediately after, a 20-minute session of tDCS. The acute effects of each stimulation session will be observed. There will be three different stimulation conditions that each target different areas of the brain: the motor cortex (M1), the motor cortex and the dorsolateral prefrontal cortex (DLPFC), and a sham (i.e., control) condition. Multiple aspects of locomotion (i.e., FOG, gait speed, stride time variability, percent of each walking stride spent with both feet on the ground) and cognition are assessed.

**Results:** This study began enrolling participants on March 3rd, 2016. To date, one participant has been enrolled and completed baseline testing as well as all three tDCS visits. This 42-year-old participant was diagnosed with PD two years ago and symptoms are mild. No side effects were observed during tDCS and the participant was unable to decipher between the M1 and the sham stimulation, but was able to tell the difference between sessions when receiving multi-focal stimulation.

**Discussion:** In this case study, tDCS was well tolerated by the patient and double-blinding procedures were effective. Thus, while tDCS did not induce significant improvements in gait or cognition in this relatively high functioning patient, the developed study protocol and tDCS intervention are highly feasible in the PD population.
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LIST OF ABBREVIATIONS

BU ........................................................................................................ Boston University
C........................................................................................................... Color task
CT ........................................................................................................... Cognitive task
DLPFC .......................................................................................... Dorsolateral prefrontal cortex
FOG ............................................................................................... Freezing of Gait
NFOGQ .............................................................. New Freezing of Gait Questionnaire
M1 .............................................................................................. Primary motor cortex
MDS-UPDRS .............................................................. Movement Disorder Society Sponsored Revision of the United Parkinson’s disease Rating Scale
MMSE .................................................................................. Mini-mental state exam
MT ............................................................................................ Motor task
NW .............................................................................................. Normal walk
PD .............................................................................................. Parkinson’s disease
SB3 .................................................................................. Serial subtraction by 3’s
SB7 .................................................................................. Serial subtraction by 7’s
tDCS ........................................................................................ Transcranial Direct Current Stimulation
TMS ........................................................................................ Transcranial Magnetic Stimulation
V1, 2, 3, or 4 ................................................................. Visit 1, 2, 3, or 4
W .............................................................................................. Word task
WC .............................................................................................. Word color task
INTRODUCTION

Parkinson’s disease (PD) is the second most common dementing neurodegenerative conditions following Alzheimer’s disease (Mollenhauer et al., 2010). According to the National Institute of Neurology Disorders and Stroke, approximately 500,000 people suffer from PD in the United States alone. PD affects people worldwide and with the increasing average life expectancy rising in developed countries, this number is expected to grow. A resting tremor of a limb is typically the initial symptom and overtime it increases in severity with the addition of other debilitating symptoms such as bradykinesia, rigidity and freezing of gait (FOG) (Morris, 2000). These symptoms are attributable to the degeneration of dopaminergic neurons of the substantia nigra that feed into the motor striatum (Mendez et al., 2005). The presence of lewy bodies, an abnormal aggregation of proteins, and nerve cell loss in the substantia nigra are defining features present in those with Parkinson’s disease. An exact cause of PD has not yet been discovered; however, its pathogenesis likely stems from a plethora of factors including genetics, environmental stimuli, oxidative stress, and mitochondrial dysfunction (Mizuno et al., 1998).

Parkinson’s disease (PD) is a neurodegenerative disorder classically recognized as a constellation of motor symptoms including locomotor instability. Cognitive function is also affected; however, and together with motor symptoms, worsens with time (Breen & Drutyte, 2013). Executive dysfunction includes progressive difficulty with selective and sustained attention, planning, and inhibitory control and dual tasking (Dirnberger & Jahanshahi, 2013). Together, motor and cognitive impairments diminish quality of life.
and psychiatric comorbidities such as depression typically appear (Schrag, Hovris, Morley, Quinn, & Jahanshahi, 2006).

The increased prevalence of neurodegenerative diseases like Parkinson’s disease brings attention to the necessity of catering to our aging population (Wright Willis, Evanoff, Lian, Criswell, & Racette, 2010). Unfortunately, the wide range of PD-related symptoms and associated clinical manifestations has made it difficult to develop treatments that cater to the specific needs of each individual patient. Dopamine therapy is a common treatment; however, its efficacy diminishes with the progression of the disease as it spreads further past the dopaminergic neuronal systems (Gerlach et al., 2002). PD can be thought of as a syndrome of interacting dysfunctions from a variety of neural networks that influence a wide range of cognitive and motor functions (Gratwicke, Jahanshahi, & Foltynie, 2015). Surgical interventions such as deep brain stimulation have become an option of treatment but risk serious complications. Recently, non-invasive brain stimulation, including both transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), has shown early promise an effective therapy for multiple PD symptoms.

tDCS is safe, user-friendly and cost efficient. It has therefore recently gained popularity as a research and clinical tool (Nitsche & Paulus, 2000). tDCS works by sending weak (≤ 2.0 mA) electrical currents between two or more sponge or gel electrodes placed upon the scalp. This current alters brain polarization and thus, increases or decreases neuronal membrane excitability (Liebetanz, Nitsche, Tergau, & Paulus, 2002). A single 20-minute “dose” of tDCS does not directly induce neuronal firing, but
instead alters neuronal excitability (i.e., the likelihood of firing) for up to four hours following administration. Moreover, the brain networks influenced by tDCS are dependent upon electrode placement. As such, electrode configuration can be manipulated to target different brain networks and as such, may eventually enable researchers and clinicians to selectively target specific networks on a patient-to-patient basis (Brunoni et al., 2012).

PD is not only associated with altered function of the basal ganglia (located deep within the brain), but also with reduced excitability of numerous “higher-level” brain regions, including the motor cortex and the dorsolateral prefrontal cortex (Pascual-Leone et al., 1994). Previous studies have shown that a single stimulation session over the primary motor cortex (M1) significantly improved the execution of particular tests such as accuracy in arm tracing, shaping tasks like buttoning a shirt or pouring water, and knee-extension force in post-stroke patients (Matsuo et al., 2011; Tanaka, 2015; Williams, Pascual-Leone, & Fregni, 2010). A single stimulation session targeting the DLPFC has also demonstrated promising results in those affected by depression. Specifically, modulating the excitability of this brain region helped alleviate major depressive symptoms by averting attention away from emotional stimuli and improving accuracy on a working memory test and a Go-NoGo inhibition task testing simple reaction time (Boggio et al., 2007; Wolkenstein & Plewnia, 2013).

**Dual Tasking**

Dual task walking refers to the ability to walk while concurrently talking, reading or thinking, and is thus of critical importance to the safe completion of most activities of
daily living. Without the ability to properly attend to both tasks, the elderly may put themselves at risk of falling (Beauchet, Dubost, Gonthier, & Kressig, 2005; Lundin-Olsson, Nyberg, & Gustafson, 1997). The ability to maintain stable locomotor control, especially when dual tasking, is dependent upon one’s ability to activate the appropriate motor and cognitive networks within the brain (Salo, Rinne, Salonen, & Alho, 2015). These regions include both the M1 and DLPFC regions, which are both functionally and anatomically linked to the basal ganglia (Galvan, Devergnas, & Wichmann, 2015). As such, dual task capacity is often significantly reduced in patients with PD as compared to their age-matched counterparts (Fernandes et al., 2015).

There are various mechanisms that may serve as an explanation as to why performance suffers in dual-tasking. Specifically, dual task deficits may arise due to a lack in the ability to switch one’s attention between each task or a generally limited attentional capacity. A motor deficit may be due to an increased demand over postural control for limited attentional resources (Hall, Echt, Wolf, & Rogers, 2011). There are 3 common theories:

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<td>The capacity-sharing theory</td>
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<tr>
<td>The bottleneck theory</td>
<td>Processing of multiple tasks will cause a delay as the one task gets processed at a time.</td>
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The multiple resource models theory states that multiple tasks share common resources and cause an uneven distribution.

As such, strategies designed to enhance excitability of the M1 and DLPFC regions, such as tDCS, may be particularly well suited for the improvement of dual task walking and other motor and cognitive outcomes in PD.

**Freezing-of-gait (FOG)**

Balance impairment is a key symptom in the progression of PD. Bradykinesia, rigidity, impaired proprioception, and freezing of gait (FOG) contribute to the increased risk of falls in those with PD (Park, Kang, & Horak, 2015). In particular, approximately 70% of those suffering with PD will specifically develop FOG (Heremans, Nieuwboer, & Vercruysse, 2013; Maidan et al., 2015). Giladi and Nieuwboer define FOG as “an episodic inability (lasting seconds) to generate effective stepping in the absence of any known cause other than Parkinsonism. It is most commonly experienced during turning and or step initiation, but may also occur when the patient is faced with spatial constraints, stress, or distractions. Patients have described this sensation as having their feet “glued to the floor” and can often be observed as a shuffling motion as they attempt to initiate movement.

The pathophysiology of FOG is poorly understood and finding a treatment that best suits a particular patient’s case is challenging. Dopamine treatments such as the long-term use of Levodopa may control certain PD symptoms, but may actually worsen FOG symptoms (Ambani & Woert, 1973; Vorovenci, Biundo, & Antonini, 2015).

Focused attention and/or external stimuli (cues), including the use of devices such as the
modified inverted stick and a visual laser beam stick, may assist in overcoming an episode (Giladi & Nieuwboer, 2008).” These devices, however, have not shown to be consistently beneficial and FOG is still considered an untreatable clinical symptom (Kompoliti, Goetz, Leurgans, Morrissey, & Siegel, 2000). Although new methods are being researched and some have demonstrated promise (e.g., deep brain stimulation or intrajejunal infusion of levodopa-carbidopa intestinal gel through the insertion of a gastrojejunostomy tube), research has been largely limited to case studies and may involve invasive procedures (Cossu et al., 2015; Niu et al., 2012).

Figure 1. Progression of PD on postural instability – Overtime symptoms such as bradykinesia and rigidity worsen as new debilitating symptoms like freezing begin. Figure taken from (Park et al., 2015).
**Rationale and Objectives**

The control over one’s balance is dependent on various brain processes that communicate with the peripheral neuromuscular system to integrate and utilize sensory feedback during both dynamic and static balance conditions (Takakusaki, Habaguchi, Ohtnata-Sugimoto, Saitoh, & Sakamoto, 2003). The coordination of locomotion is particularly reliant upon the involvement of the basal ganglia to regulate muscle tone and adapt postural response patterns to ever-changing environmental and task conditions (Horak, Dimitrova, & Nutt, 2005).

In 2006, Fregni and colleagues examined the effects of tDCS targeting the primary motor cortex (M1) on motor function in PD participants. In comparison to sham stimulation (i.e., placebo), 20 minutes of real tDCS induced acute enhancement of simple reaction time and the motor sub-score of the Unified Parkinson’s Disease rating scale (UPDRS) (Fregni et al., 2006). Benninger and colleagues (2010) also reported motor improvements in terms of walking speed in PD patients receiving real tDCS, as compared to receiving sham stimulation. In this particular study, eight sessions of tDCS were given over multiple days, and the target for stimulation was alternated between M1 and the dorsolateral prefrontal cortex (DLPFC). This intervention was associated with both immediate and longer-term improvements in locomotor control (Benninger et al., 2010).

Most recently, Manor, Zhou and colleagues (2014, 2015) demonstrated that a single 20-minute session of real tDCS targeting the DLPFC, as compared to sham, significantly reduced the dual task cost to walking speed and stability in both younger and older healthy adults (Manor et al., 2015; Zhou et al., 2014). Studies
have also shown that dual-tasking can trigger short-term movement cessations in those who suffer from FOG (Giladi & Nieuwboer, 2008; Spildooren et al., 2010). Thus, by targeting cortical networks that are involved in the control of dual-tasking, tDCS may additionally alleviate FOG symptoms.

Together, these recent studies provide preliminary evidence that tDCS targeting the M1 or DLPFC may improve locomotor control in PD. Moreover, recent advancements in the modeling of tDCS current flow have enabled researchers with the ability to simultaneously target multiple regions of the brain (Ruffini, Fox, Ripolles, Miranda, & Pascual-Leone, 2014). We contend, therefore, that simultaneous stimulation of cognitive and motor networks will improve locomotor control, especially when dual tasking, and reduce FOG, in patients with PD. The effects of such "multi-focal" tDCS on these outcomes in patients with PD, however, have not been established.

The aim of this study is to examine the acute effects of single sessions of tDCS targeting different brain networks on locomotor control metrics and other outcomes in patients with PD. We hypothesize that tDCS simultaneously targeting the DLPFC and M1 cortex will reduce the dual task cost to gait speed, the number of FOG episodes, more so than tDCS targeting the M1 region alone or sham stimulation.

**Application and importance**

PD is associated with often debilitating motor and cognitive impairments, locomotor disturbances such as FOG, and falls. The pathophysiology of FOG is still not fully understood but has been associated with gait pattern generation disturbances in those with...
PD (Heremans et al., 2013). This study will provide valuable preliminary data on the potential for tDCS to be used as a therapy for PD and its various debilitating symptoms. Specifically, this research will demonstrate the effects of noninvasive brain stimulation on the ability of patients with PD to walk with and without performance of additional cognitive tasks. It will therefore serve as grounds for further investigation into the use of tDCS to provide symptomatic relief within the vulnerable population.
METHODS

Study cohort

This study will be achieved with the participation of senior citizens recruited from the Boston area through newspaper ads (The Metro and The Herald) as well as through recruitment at Hebrew Senior Life affiliated senior-living facilities (Orchard Cove and NewBridge). Study inclusion criteria are ages 40-85 years, a physician-diagnosis of idiopathic PD, a stable medication regimen (i.e., no change in medications within 1 month of the study, with no plans of changes medications during the study), and mild-to-moderate severity of PD-related symptoms as determined by:

A) a Hoehn and Yahr (H&Y) score of 1-3.5, and

B) freezing of gait (FOG) identified by the validated "New FOG" questionnaire with a score of 9 or above.

Exclusion criteria includes any self-reported cardiovascular, neurological, or musculoskeletal disorder not related to PD, current use of any centrally acting medication, recent hospitalization, an inability to read, write, or communicate in English, an Mini Mental State Examination (MMSE) score less than 22, and any other condition resulting in abnormal physical function.

Study Protocol

Phone screen

Study personnel screen subjects over the phone in order to determine if they qualify for an in-person screening. Questions are asked regarding overall health, PD
diagnosis, and FOG episodes (if applicable). The FOG symptom is assessed using a 10 question “freezing-of-gait” questionnaire (NFOGQ) to determine frequency and severity.

Visit 1 (V1): Screening and baseline assessment of physical and cognitive function

During this initial in-person visit, subjects read and sign an informed consent form approved by the IRB as well as answer questions pertaining to demographics and timing/dosage of medications. Potential subjects are required to describe in their own words the purpose and risks of the study in order to be eligible. Subjects will complete the MMSE to ensure sufficient mental capacity to understand the study procedures and follow instructions. (Mungas, 1991). A score of less than 22 will exclude a subject from continuing with the study. Blood pressure, height, and body mass are measured.

Other baseline measures include PD assessments, mobility, and cognitive exams. Severity of PD is measured through the validated Movement Disorder Society revised United Parkinson’s Disease Rating Scale (MDS-UPDRS) (Goetz et al., 2007). Mobility is tested through the Timed Up-and-Go (TUG) test, which comprises standing from a chair, walking three meters, turning around a cone and returning to a seated position in the chair (Podsiadlo & Richardson, 1991). Cognition is assessed through a 30-minute computerized neuropsychological test battery (Mindstreams, NeuroTrax Corp., NJ) (Doniger, Simon, & Zivotofsky, 2006). The computerized cognitive assessment, NeuroTrax, assesses different cognitive domains including memory, attention, executive function, visual spatial processing and a global cognitive composite. The battery includes tests such as 1) “Go-NoGo” which tests response inhibition (Fig 2a), 2) Stroop which
tests a subject’s ability to switch his or her mindset to changing demands, 3) Catch Game to test motor related thinking, 4) finger-tapping to test motor skills (Fig 2b), 5) non-verbal memory (immediate and delayed) by asking the subject to remember a shapes particular orientation (Fig 2c), 6) information processing by asking different levels of arithmetic problems varying from one to three numbers, and 7) problem solving by completing a pattern from a set number of choices (Fig 2d). Scores are age- and education-adjusted composite indices of each cognitive domain on an IQ-like scale, with the score of 130 representing the estimated population mean normalized for age and education level. This battery has been validated in elderly adults with and without a history of falls, patients with mild cognitive impairment, and patients with PD, and has shown to be useful in predicting falls and is responsive to therapeutic intervention (Ben-Itzhak, Giladi, Gruendlinger, & Hausdorff, 2008, p. -; Doniger et al., 2005; Giladi et al., 2006; Hausdorff et al., 2006; Mamikonyan, Xie, Melvin, & Weintraub, 2015; Paleacu et al., 2007).
A dual task assessment and a FOG provoking protocol are also completed at visit 1 (and repeated at visits 2-4, see following section). Mobility data will be collected by instrumenting subjects with six small, wireless movement sensors (Mobility Lab®, APDM Inc., Seattle WA) that each contain a three-dimensional accelerometer and goniometer. These sensors are secured to the sternum, waist, wrists and ankles using

**Figure 2. Neurotrax Cognitive Assessment tests.** (a) Go-NoGo: tests simple reaction time and response inhibition. The participant must quickly press the mouse button if the square is any color but red. (b) Finger Tapping: tests motor dysfunction by asking the participant to tap the mouse button as many times as possible while the rectangle fills red. (c) Non-verbal memory: measures immediate and delayed recognition memory by asking participants to remember 8 geometric patterns. A screen is presented with 4 alternatives figures that the participant must identify as being on the previous page. (d) Problem solving: tests executive functioning and abstract reasoning as participants are asked to complete the pattern.
elastic straps. A dual-task paradigm was created to assess the ability to balance cognition and mobility. Subjects complete trials of walking back and forth along a 20m hallway in each of the following conditions:

1) A “single task” condition, during which subjects will walk quietly at their preferred normal walking speed.

2) A “dual task” trial, during which subjects are asked to walk at their preferred speed, while at the same time performing a cognitive task. The cognitive task consisted of verbalized, serial subtractions of 3 from a random, 3-digit number between 200-999. The starting number for each trial will be randomized to minimize practice-induced learning.

The FOG provoking protocol is conducted, as proposed by Ziegler et al (2010). This protocol has been previously used in numerous studies (Herman, Rosenberg-Katz, Jacob, Giladi, & Hausdorff, 2014; Vandenbossche et al., 2012; Weiss, Herman, Giladi, & Hausdorff, 2015). This protocol takes less than five minutes to complete and includes situations that have been shown to provoke FOG. Patients are asked to sit, to stand up and to walk to a mark on the floor. They then perform two 360° turns, clockwise and counterclockwise. Then, the patients are asked to open a door and walk through it, turn outside, and come back to their chair. The subject does this under three different conditions: normal walk (NW) quietly, a motor task (MT) where the subject completes the course while holding a clear tray with a clear bottle of liquid, as well as a combined MT plus cognitive task (CT) where the subject is asked to continuously serial subtract 7s from a randomized number while also walking and carrying the tray.
Visits 2-4 (V2-V4): The effects of tDCS on walking

The effects of tDCS are tested by having subjects complete multiple tests both immediately before and after a 20-minute session of real or sham tDCS. Each of these visits last about 90 minutes and consists of the FOG protocol, the dual task paradigm (both described above), and a paper Stroop test. The Neurotrax computer assessment of V1 uses the same task and both forms of the Stroop test are meant to test executive function. This paper test takes 3-4 minutes to complete and includes three different tasks where the participant must read out loud from a list of words, as rapidly as possible, for 45 seconds. During the word task (W), the participant reads words printed in black ink. In the color task (C), he/she reads the words printed in colored ink (red, green, and blue) which are mixed in with grey words. In the word-color task (WC), he/she is asked to read the colors of the printed words. These assessments are administered immediately before and after a single, 20-minute session of stimulation. For this test, higher scores indicate more words completed correctly in 45 seconds and thus, better performance.

Each subject completes three tDCS visits in order to test the effects of the two different “real” tDCS conditions, as well as a sham condition (i.e. control or placebo). The study is double-blinded, such that the subjects are unaware of the specific condition, which are completed in random order. The following two “real” tDCS conditions will be tested:

1. Unilateral motor stimulation: tDCS was delivered to facilitate neuronal excitability within the primary motor cortex (M1) of the hemisphere contralateral to the more affected side of the body, as determined by the motor subcomponent
of the UPDRS scale. This target region has been selected based on previous research demonstrating that tDCS targeting this brain region significantly reduces the frequency and severity of FOG episodes (Valentino et al., 2014).

2. Unilateral motor and cognitive stimulation: tDCS will be delivered to simultaneously facilitate excitability within 1) the M1 region, and 2) the dorsolateral prefrontal cortex (DLPFC), of the contralateral hemisphere to the more affected side of the body, as determined by the motor subcomponent of the UPDRS scale. Simultaneous stimulation of these regions was chosen based on the aforementioned study by Benninger et al (2010), as well as studies by Manor et al (2014,2015), which demonstrated that facilitation of the DLPFC significant improves locomotor control in healthy younger and older adults. If both sides of the body are similarly affected, the left hemisphere will be targeted.
Study personnel certified by the Berenson-Allen Center for Noninvasive Brain Stimulation (BIDMC) in the administration of tDCS oversee the stimulation. Current is delivered with the Neuroelectrics Starstim device (Barcelona, Spain). A blinding scheme

**Figure 3. Electric field (V/m).** The above images depict the electric fields in each set up of the 2 real montages. The red indicates a more positive charge (V/m) and the blue a more negative charge (V/m). The circles indicate electrode placement. The left is motor stimulation condition and the right the multifocal condition.
was developed so that neither the participant nor study personnel knows which tDCS condition is delivered.

The Starstim device is connected to six gel electrodes positioned on the scalp and held in place with a Neoprene cap. Prior to stimulation, subjects undergo a short session to determine the max level of intensity they are able to receive comfortably. To ensure subject safety, the total amount of injected current was limited to 4mA, while the maximum current intensity delivered by any single electrode was limited to 2mA (Brunoni et al., 2012). For each of the two “real” tDCS conditions, 20 minutes of continuous anodal stimulation is delivered. At the beginning of each session, stimulation automatically “ramps-up” in 0.1 mA increments over a 60sec period. Current automatically ramped down over the final minute of the session. For sham tDCS, the same electrode montage and session duration is used and current targeted both the DLPFC and M1 region simultaneously. However, current automatically ramps down to zero after the first minute of stimulation. This is a reliable control as sensations arising from tDCS diminish considerably after the first minute of stimulation (Gandiga, Hummel, & Cohen, 2006). At the end of each visit, subjects complete a short questionnaire (Brunoni et al., 2012) to assess potential side-effects. They are also asked to state if, in their opinion, they received real or sham stimulation on that day. They are then asked to rate on a 10 point scale how confident they are that they received that type of stimulation, with “1” being not confident and “10” being extremely confident.
Data Analysis

As data collection is ongoing and the study is blinded, the final study analysis has yet to be completed. For the purpose of this thesis, we have focused on the results of the first subject as a case study. When the project is complete, the following measures will be analyzed:

The primary outcome will be the dual task cost to walking speed. The dual task cost will be quantified by the percent change in walking speed between single- and dual-task conditions. Secondary outcomes will include Stroop test performance as well as number and average duration of FOG episodes invoked by the FOG protocol. Additional temporospatial characteristics of single- and dual task-walking will also be computed from data collected by the Mobility Lab motion sensors. These measures will include stride time variability and the percent of each walking stride spent in double support (i.e., with both feet on the ground). “Adjuster” variables will include age, baseline severity of PD as indicated by the MDS-UPDRS score, baseline mobility (i.e., TUG time), baseline cognitive performance as indicated by the computer-based testing battery, and serial subtraction performance during the dual task walking condition.

Sample Size Determination

In 37 healthy older adults, the pre-tDCS dual task cost to gait speed was approximately 0.1 m/s (Manor et al., 2015), a highly clinically-significant decrement, equivalent to an approximate 17% cost on average. Assuming a type-I error probability of 0.05 and a standard deviation of within-subject change in cost as high as 5%, a sample of
10 will provide 90% power to detect a true cost reduction attributable to real tDCS, as compared to sham, as small as 6%. To account for the potential for greater heterogeneity of tDCS effects in PD patients as compared to healthy older adults, and to enable analyses of secondary outcomes, we propose to complete all study procedures in 15 subjects.
RESULTS

Case-study

Participant 1 (initials JM) scored a 29 on the MMSE and was deemed cognitively able to understand the study and therefore eligible to participate. Overall JM scored a global cognitive score of 88.7 out of 130 on the Neurotrax cognitive assessment. The participant was below average (in comparison to age and education level) for the global cognitive score. In individual domains, JM was below average in attention, information processing speed, and more than 1 standard deviation below average in the memory domain. Scores were above average in executive function and motor skills. JM’s scores are shown in figure 4.

Figure 4. Neurotrax cognitive exam scores for case-study participant. JM scored a 40.4 in the tasks that tested memory (below average), 103.5 in the executive function tasks (above average), 97 on the attention tasks (below average), 96.5 on the information processing tasks (below average), and 106.2 on the motor skill tasks (above average).

Early onset PD was diagnosed about a year ago at the age of 42 with symptoms initially appearing on the left side. Symptoms have since progressed bilaterally. Although
JM indicated having FOG through the NFOGQ during the phone screen, no FOG was observed in person and reported difficulties were primarily limited to rigidity. The participant initially earned a NFOGQ score of 15 out of a possible 33 during the phone screen; however, once shown a video for FOG at the visit 1 the participant indicated that this was not the symptom he experiences. No festination, FOG, or shuffling was observed during the Ziegler protocol across all visits. No PD medications have been prescribed and this person earned a score of 32.5 on the motor portion (part III) of the MDS-UPDRS and a Hoehn and Yahr scale score of 1.5, which signifies symptom severity in between unilateral (1) and bilateral involvement (2) without impairment of balance.

**tDCS efficacy and blinding**

One primary purpose for this case study was to gauge the practicality and feasibility of tDCS as a therapeutic option within the PD population. The participants’ well-being was carefully monitored and their tolerance level of the stimulation was noted. Moreover, from a research standpoint, it is vitally important that the sham condition feels similar in comparison to the real tDCS conditions (i.e., motor and motor/DLPFC) to enable blinding, so that participants do not act based on pre-conception (i.e., the placebo effect). To observe side effects and blinding efficacy the participant answered if they experienced any side effects at each stimulation visit (Table 2). JM received the maximum allowable level of tDCS current during all visits. They did not experience any significant side effects, except after receiving the M1 stimulation, where they experienced mild redness of the skin and sleepiness. The participant claimed that the sleepiness was due to sitting
quietly for 20 minutes and not because of the stimulation itself. JM believed with high confidence that the first two sessions of stimulation were placebo and that the last session was the only real stimulation session.

**Table 2: tDCS side effects.** The following questions were asked posted stimulation during visits 2-4 to observe any adverse effects due to the stimulation.

<table>
<thead>
<tr>
<th>Questions</th>
<th>V2 (Real)</th>
<th>V3 (Sham)</th>
<th>V4 (Multi-focal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Neck pain</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Scalp pain</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td><strong>Sensations under the electrode</strong> (tingling, itching, burning, pain)</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Skin redness</td>
<td>Mild</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Sleepiness</td>
<td>Mild</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Trouble Concentrating</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Acute mood change</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Others</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>
The effects of tDCS on cognitive and motor outcomes

For the purpose of reporting this participant as a case study, investigators were unblinded to tDCS condition and the participant’s dataset will not be included in the overall pilot study. During the first stimulation visit, JM received tDCS targeting the M1 region. They received sham stimulation on their second visit, and multifocal tDCS targeting the both the M1 and DLPFC on the third visit.

As compared to pre-tDCS assessments, JM’s performance did not exhibit definitive improvement across any of the particular Stroop tasks of cognitive function. Specifically, JM scored slightly lower (less words correct) across all three tasks of the Stroop test following motor stimulation (Fig 5a). Following sham stimulation, JM decreased his score in the W task, increase his score in the C task, and matched his pre-

Table 3: Blinding efficacy. The following questions were asked posted stimulation as well as at the end of the entire visit/post-performance to determine how predictable which stimulation montage the participant received that day.

<table>
<thead>
<tr>
<th>Questions</th>
<th>V2 (Real) PS</th>
<th>V2 (Real) PP</th>
<th>V3 (Sham) PS</th>
<th>V3 (sham) PP</th>
<th>V4 (Real) PS</th>
<th>V4 (Real) PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received real tDCS or the placebo today? Post-stimulation (PS) Post-performance (PP)</td>
<td>Placebo</td>
<td>Placebo</td>
<td>Placebo</td>
<td>Placebo</td>
<td>Real</td>
<td>Real</td>
</tr>
<tr>
<td>Confidence: 1 being not and 10 being extremely confident?</td>
<td>8</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>
stimulation score on the WC task (Fig 5b). JM reported with full confidence that the last stimulation was the real condition. Their scores in both the W and C tasks increased, but their score on the WC task decreased (Fig 5c).

Figure 5. The effects of tDCS on Stroop test performance– The following scores are for the Stroop test, which assesses executive function. The blue (W) line was for the word task, the red (C) line for color task, and the green (WC) line for the word color-task. (a) Following M1 stimulation, the participant decreased performance across all three tasks. (b) Following sham stimulation, the participant increased performance in W, decreased in C, and remained the same for WC. (c) Following multifocal stimulation, the participant increased the score in W and C but decreased in WC.
The effects of tDCS on FOG were unable to be examined, as the participant did not exhibit any freezing episodes in the FOG-provoking task (i.e., the Ziegler protocol) or any of the gait assessments.

Unfortunately, the MobilityLab® sensors lost synchronization while tracking mobility and stride length and mean speed were not captured post-stimulation for visit 2. Sensors were in the process of being repaired when this participant completed visits 3 and 4 so no MobilityLab data was collected during V3-4. In the case that mobility lab sensors were not working, the participant was timed with a stopwatch when completing the tasks.

Locomotor measures were collected prior to and post M1 stimulation. The data collected were used to create charts such as the one below (Fig 6) to calculate measures including mean stride length in meters (m) which is defined as the distance between two successive placements of one foot while walking, mean speed defined as meters/second (m/s), cadence (steps/minute), and mean cycle time defined in seconds (s) which is the time it takes for one foot to make two successive placements. Double support time was also recorded. As a participant completes each task, they move through multiple gait cycles where their feet alternate between being both on the ground (double support) versus one foot as they take a step (single support). Double support occurs twice in one gait cycle, while single support occurs once. Data recorded using MobilityLab at visit 2 (Table 4) allowed the calculation of dual task costs and demonstrates the percent change from single to dual task (Table 5).
**Figure 6. Accelerometer and gyroscope measurements.** By recording the time it takes for the participant to complete the task as well as when each foot strikes the ground, values such as mean cycle time can be calculated. These are the values from the sensor placed on the left foot, so each blue peak of the accelerometer is an indication of when the left foot strikes the ground. The long green vertical bars indicate when the participant reached the 20m mark and turned around (3 turns). Data presented were recorded during the normal walk task post M1 stimulation.
On each stimulation visit, the participant completed two walking conditions prior to and post tDCS. As expected, prior to stimulation, performing serial subtractions (SB3) while walking caused a decrease in mean stride length (m), mean speed (m/s), and cadence (steps/minute), along with an increase in mean cycle time (s) and time spent in double support (% of gait cycle time). This indicates that given a dual task, JM took fewer, shorter steps and slowed down his speed. Following tDCS, performing SB3 also decreased cadence and double support time and increased gait cycle time (data was not collected for mean stride length or mean speed). By comparing pre-stimulation and post-stimulation it can be observed that for the SB3 task, JM had lower cadence post stimulation and required less steps per minute to complete the task in comparison to pre-stimulation. Post-stimulation, mean cycle time (s) and double support time increased in comparison to pre-stimulation and JM spent a longer time in double support as well as for an entire gait cycle.

Table 4: MobilityLab measurements. Mobility Lab sensors captured information on the movement of a participant’s legs as well as the lumbar region of their back. The following variables were calculated from these measurements.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-stimulation</th>
<th>Post-stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NW</td>
<td>SB3</td>
</tr>
<tr>
<td>Mean stride length (m)</td>
<td>1.63</td>
<td>1.58</td>
</tr>
<tr>
<td>Mean speed (m/s)</td>
<td>1.46</td>
<td>1.25</td>
</tr>
<tr>
<td>Mean cycle time (s)</td>
<td>1.11</td>
<td>1.27</td>
</tr>
<tr>
<td>Cadence (steps/minute)</td>
<td>107.94</td>
<td>94.62</td>
</tr>
</tbody>
</table>
The dual task cost to each walking metric was calculated as the percent change from the NW condition to the SB3 condition. This calculation was performed separately on pre- and post-tDCS trials. The dual task costs to mean cycle time significantly increased from -14.12% at baseline to -31.17% post tDCS. The dual-task cost also increased for cadence, which was 12.34% at baseline but 23.48% post tDCS (Table 5).

<table>
<thead>
<tr>
<th>Double support (% mean cycle time)</th>
<th>Pre-Stimulation</th>
<th>Post-Stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>21.46</td>
<td>26.00</td>
<td>24.59</td>
</tr>
</tbody>
</table>

**Table 5: Dual task cost.** Dual task cost, or the percent change in each walking metric from single to dual task conditions, was calculated for each variable (mean stride length, mean speed, mean cycle time, cadence, and double support). A positive percentage shows an increase, where as a negative shows a decrease.
DISCUSSION

Case-study findings

The results of this case-study indicate that tDCS did not have a significant effect on locomotion or cognitive function. However, the results do suggest that tDCS is feasible within the PD population, and that the sham stimulation condition is a largely valid control. The participant strongly believed that two of the three stimulation sessions were placebo, even though one of the supposed sham conditions was in fact real tDCS targeting the M1 region. When first asked whether they believed they received real or sham stimulation in this tDCS condition, the participant was less confident (8/10, refer to Table 2) in comparison to when asked post performance as well as the following visit (10/10). This indicates that the sham condition has a comparable sensation to the M1 stimulation, in that the participant was unable to distinguish the two from each other. In other words, blinding was largely successful. Moreover, the participant did not report any discomfort and tolerated all tDCS conditions.

When healthy older adults walk, their speed, cadence, and stride length all significantly decrease when asked to perform a dual task. Moreover, as compared to walking normally, walking while pronouncing alternate letters of the alphabet from a randomly selected letter resulted in increased time spent in double support (Pilgram, Earhart, & Pickett, 2016; Simoni et al., 2013). In the present study, JM exhibited a similar pattern when assigned the serial subtractions dual task when walking. In studies investigating stance and swing times, PD participants were found to have an increased percentage of time spent in double support in comparison to healthy controls and that
freezers spent more time in this phase than non-freezers during dual-tasks (Vervoort et al., 2016). It is thus possible that as JM’s PD progresses, these measures will be more severely impacted by the disease, especially if this participant begins to experience FOG.

As expected, data collected from the current case study did not provide enough evidence to either support or refute the hypothesis of the study. As this study continues, more data will be collected to statistically examine the effects of tDCS on primary and secondary outcomes and thus evaluate the efficacy of this therapeutic strategy within the PD. With the one participant who has completed the study, the protocol was feasible and presented data will assist in the construction of a larger randomized control trial.

Possibilities of ineffectiveness of tDCS in case study

There are multiple potential reasons as to why the results collected did not show an increase in the ability to dual-task or alleviate freezing of gait. tDCS is a new technology still undergoing research as a form of therapy for a variety of disorders. As such, the most effective protocol (i.e., electrode placement, current intensity, stimulation duration, etc.) may not have yet been established. Moreover, several studies have tested the effects of tDCS over two-week periods as compared to a single session. In a previously mentioned study, Benninger and colleagues gave eight stimulation sessions that alternated between the M1 cortex and the DLPFC and demonstrated both an acute change in walking time (decrease post stimulation when on medication) as well as a long-lasting improvement of bradykinesia (Benninger et al., 2010). A separate study examined the effects of tDCS stimulation targeting the DLPFC with current intensities of both 1mA
and 2mA and reported that the greater intensity improved working memory to a greater extent in PD patients (Boggio et al., 2006). It is thus possible that the data did not show conclusive results because a single session of stimulation to these specific areas was not enough stimuli to induce change in investigated study outcomes.

The observed inconclusive results may have also resulted from targeting sub-optimal regions of the brain. Indeed, the complexity of the brain makes it difficult to pinpoint the exact location for the most beneficial stimulation target. Distributed parts of the brain work together as networks to perform a given function and exciting each individual section would be nearly impossible. In the case of dual tasking, multiple brain areas are at play. The bottleneck effect (refer to table 1) can occur in different areas: perception involves areas such as the bilateral intraparietal sulcus and in response selection, the bilateral premotor area, left inferior frontal gyrus, and pre-SMA (Marois, Larson, Chun, & Shima, 2006). This study chose to stimulate the DLPFC and the motor cortex, but there is potential that anodal or cathodal stimulation would induce greater benefit in different regions such as those mentioned above. In addition to the vast number of options of regions to stimulate, restricting the current from reaching undesirable locations is also difficult to control. Hair acts as an insulator, so in this particular study the use of gel was used to reduce resistivity and allow the current more easily access the scalp. Bridging can occur, however, when excess gel leads to the possibility of the gel reaching other areas that were not initially planned to target (Horvath, Carter, & Forte, 2014).
The stimulation of a given brain region may affect many different functions either directly or indirectly. In addition to the changes in dual tasking, executive function, and FOG, there is a possibility that each participant improved in a task not tested. By targeting the DLPFC and the motor cortex, the benefits may be seen in different aspects of the participants’ abilities. A flaw that comes with brain stimulation studies is the inability to investigate each and every function that ties to a particular brain region. For example, the DLPFC is also known for its role in executive functioning and each task requiring this type of brain activity may be affected to a different extent. For example, studies stimulating the DLPFC with tDCS in PD patients reported increased performance in working memory, in terms of both task accuracy and phonemic fluency task (Boggio et al., 2006; Pereira et al., 2013). Stimulating the DLPFC has also shown benefits in dual-tasking and through the relationship between dual-tasking and FOG, it was proposed in this study that tDCS would then better freezing symptoms. As such, the chosen dual-task paradigm may not have been sensitive to the potential behavioral benefits induced by the tDCS intervention.

Another potential explanation as to why a significant difference was not seen pre- and post stimulation may be that the DLPFC is involved with an indirect route of processing that triggers FOG. Vandenbossche et. al proposed that the activation of the indirect route, which involves the prefrontal cortex, leads to a freezing episode as a result of increased cognitive demands (Vandenbossche et al., 2012). Measurements using functional infrared spectroscopy (fNIRS) supported this notion through a study measuring the blood perfusion of Brodmann 10, an area associated with executive
function. The results showed increased perfusion right before and also during a FOG episode (Fig 7) (Maidan et al., 2015). The DLPFC is located in Brodmann 46, which is located right behind Brodmann 10. In the future, studies should investigate the role of the anterior brain region more closely in FOG and determine if the stimulation of the DLPFC is beneficial to lessening FOG episodes.

![Figure 7: Blood Perfusion through Brodmann 10 during FOG.](image)

**Figure 7: Blood Perfusion through Brodmann 10 during FOG.** The red line indicates an increased activation of Brodmann area 10, reflecting an increase in oxygenated hemoglobin concentration, immediately prior to and during freezing of gait episodes in PD patients. The green line and blue line represent the level of perfusion when freezing did not occur during trials of normal walking and turning, respectively. Figure taken from (Maidan et al., 2015).

Inter-subject variability may also be at play. Parkinson’s disease symptoms vary at different stages and some participants have more progressed symptoms versus the others. This may be subject to either a decreased chance or even more room for improvement. Freezing of gait is typically a symptom that appears much later in disease progression along with more severe symptoms and may not be seen in early age diagnoses (Spildooren et al., 2010). The subject who completed the protocol at the
Hebrew Senior Life location was diagnosed relatively young at 40 years old, about two years ago. JM is relatively high functioning— a score of 29 on the MMSE places JM in the “normal” range and detects little to no cognitive impairment. The motor portion of the Neurotrax computer assessment scored JM as above average. As such, beneficial effects of tDCS may still be observed in the larger pilot study, as the average subject is expected to have a longer duration of PD progression and more severe symptoms.

A significant placebo-effect has been commonly observed in the PD population. In a literature review, a statistically significant difference was found in the efficacy of the placebo and that of the active drug in 61% of participants. In a literature search investigating the PD response to anti-oxidative treatment, out of the 198 placebo participants, 140 of them reported having a response to the medication (Shetty, Friedman, Kieburtz, Marshall, & Oakes, 1999). It has been hypothesized that this placebo effect is likely due to an activation of the damaged dopamine pathway. In PD, the degeneration of nerve cells that produce dopamine causes a reduced ability to begin or coordinate movements. In fact, one study reported that placebo-induced improvements in PD symptoms were correlated with reduced binding of the dopamine competitor, $[^{11}\text{C}]$raclopride (RAC) (Fuente-Fernández et al., 2001). Neuroimaging studies have also found that placebos stimulate the release of dopamine in the striatum of PD patients and therefore, can affect their performance and related symptoms (Lidstone, 2014). This has led researchers to conclude that there is a higher placebo effect in Parkinson’s disease, since an expectation-induced neurochemical change may lead to the improvement of performance within particular tasks. It is thus crucial that a controlled sham condition is
monitored in order to determine what the potential cause of change in behavior is in result of.

A final mechanism that may have influenced results of the presented case study is the learning effect. In particular, the Stroop test was completed pre and post stimulation and a learning effect may have influenced performance. To minimize this effect, future research should include multiple versions of the Stroop test that each present the words in shuffled order. Since the same tests are repeated multiple times in visit 2-4, this change is likely to reduce the learning effect and yield better results.

**The potential of tDCS as a form of treatment**

Although this one participant did not show significant improvement on any task, there is strong likelihood that others will receive greater benefit. The reasoning behind the effectiveness of brain stimulation is still in question (fig 8); however, there are multiple theories as to how tDCS works to improve mobility and cognition. Orban De Xivry and Shadmehr proposed three explanations of tDCS’s effect on motor control and learning: 1) the anodal stimulation increased neuronal firing rates while cathodal decreased them, 2) anodal stimulations strengthen newly formed associations, 3) the polarization caused by anodal stimulation modulates the memory of new or preferred firing patterns. By increasing firing rates and strengthening connections, the brain is better able to process and accomplish particular tasks (Orban de Xivry & Shadmehr, 2014). This notion was also supported by a study that found tDCS modulates functional
connectivity of the cortico-striatal and thalamo-cortical circuits as well between each hemisphere in the human brain (Polania, Nitsche, & Paulus, 2011).

Particularly in PD, it has been suggested that tDCS may play a role on protecting dopaminergic neurons and increasing dopamine levels. Due to the invasive procedures required to measure changes of dopamine in the brain, most of these studies are completed on animal models and have not yet been demonstrated in humans. In mice, anodal tDCS stimulation played a role reducing oxidative damage to dopaminergic neurons while cathodal stimulation to the frontal cortex found a significant increase of dopamine extracellularly (Lu et al., 2015; Tanaka, 2015).

By finding techniques in improving dual tasking, the overall lives of the elderly may be improved. With increased ability to dual task, executive function and attention may benefit and decrease the risk of falling. It has been found that those who have fallen
at least twice have scored less on cognitive exams in comparison to non-fallers (Hausdorff et al., 2006). The slower gait speed, shorter stride length, and increased double support time with dual tasking seen in JM as well as other studies in the elderly and PD, has been associated with an increased fear of falling (Verghese, Holtzer, Lipton, & Wang, 2009). The use of physical or cognitive training or technology such as tDCS can help improve the overall quality of life in the aging population.

In summary, additional data will need to be collected for conclusive analysis of the effects of multi-focal tDCS on locomotor control and cognitive function within the PD population. Results from this case study nevertheless give us confidence that tDCS is tolerable for PD patients and that blinding to tDCS condition is feasible. No side effects of pain or significant discomforted were reported. Moreover, in-depth review of this participant’s data provided valuable information that will be used to optimize the efficiency of data collection procedures in future studies. The chief complaint from JM was the time it took to set up sensors and prepare the stimulation. Technical difficulties with MobilityLab sensors extended the time of JM’s visits. In the future, the study team should thus implement additional ways to collect data such as an instrumented gait mat to more efficiently and effectively acquire mobility-related measures. Moreover, it is recommended that the study team expand the study inclusion criteria to also include those patients who received a PD diagnosis beyond ten years ago. FOG is typically a symptom that appears later with progression of the disease and as such, this change would allow study personnel to enroll participants who are more affected by Parkinsonian symptoms.
REFERENCES

http://doi.org/10.1056/NEJM197305242882108

http://doi.org/10.1159/000081435


http://doi.org/10.1016/j.jad.2006.10.026


http://doi.org/10.1016/j.gaitpost.2015.06.188

http://doi.org/10.1002/mds.21012

http://doi.org/10.1126/science.1060937


http://doi.org/10.1007/s00415-002-1307-y


Lu, C., Wei, Y., Hu, R., Wang, Y., Li, K., & Li, X. (2015). Transcranial Direct Current Stimulation Ameliorates Behavioral Deficits and Reduces Oxidative Stress in...
1-Methyl-4-Phenyl-1,2,3,6-Tetrahydropyridine-Induced Mouse Model of Parkinson’s Disease. *Neuromodulation: Journal of the International Neuromodulation Society, 18*(6), 442–446; discussion 447.
http://doi.org/10.1111/ner.12302


http://doi.org/10.1007/s00415-015-7650-6


http://doi.org/10.1016/j.neures.2015.10.012
Valentino, F., Cosentino, G., Brighina, F., Pozzi, N. G., Sandrini, G., Fierro, B., ...


http://doi.org/10.1002/mds.25897

Vandenbossche, J., Deroost, N., Soetens, E., Zeischka, P., Spildooren, J., Vercruysse, S., ...


http://doi.org/10.1093/gerona/glp033

Vervoort, G., Heremans, E., Bengevoord, A., Strouwen, C., Nackaerts, E.,


http://doi.org/10.1007/s00702-015-1463-8


http://doi.org/10.1007/s00702-014-1279-y


http://doi.org/10.1159/000275491

Curriculum Vitae
Victoria A. Nguyen
Year of birth: 1992
3 Buswell St. Apt 201
Boston, MA 02215
(781) 724-0599
vnguyen@bu.edu

PERSONAL PROFILE
Highly motivated second year master’s candidate and aspiring doctor. Enjoys engaging in clinical situations with diverse populations in hopes of developing an all-inclusive medical approach. Experience working with children, the elderly, and the homeless in a health related capacity.

EDUCATION

Boston University School of Medicine (2014-Present)
M.S., Medical Science (Expected Graduation May 2016)

Boston University (2010-2014)
B.S., Human Physiology with Minors in Psychology and Dance

Randolph High School (2007-2010)
President of National Honor Society, Vice President of Class, Vice President of Key Club and Captain of Cheerleading squad

RESEARCH

Research Assistant, Institute for Aging Research at Hebrew SeniorLife (September 2015-Current)
• Principal Investigator: Dr. Bradley Manor
• Currently working on a study investigating the benefits of transcranial direct current stimulation (tDCS) on older participants who suffer from slowed gait, cognition, and depression.
• Focusing master’s thesis on the effects of tDCS on Parkinson’s disease and dual-tasking.

Research Assistant, Boston University’s Vision & Cognition Laboratory (Summer 2013-Spring 2014)
• Advisors: Alice Cronin-Golomb Ph.D., Sandy Neargarder, Ph.D., & Daniel J Norton M.A.
• Norton D.J., Nguyen V.A., Lewis M.F., Reynolds G.O., Somers D.C., & Cronin-Golomb A. Visuospatial attention to single and multiple objects is
independently impaired in Parkinson’s disease. (in production-PLoS ONE, accepted March 2016)

• Worked in recruiting patients, data analysis (moderately proficient in excel, MATLAB, & SPSS), and neurophysiological testing.


• Advisor: Karen Louise Smith, Ph.D.
• Analysis of neurobiological mechanisms in relationship with exposure to rewards such as food and intracranial self-stimulation in rodents.
• Assisted in administering injections and caring for rats. Independently ran trials using operant conditioning chambers.

SHADOWING

Emergency Medicine, Boston Medical Center, Summer 2013 and 2014

• Supervisor: Dr. Mursal Tahouni M.D.
• I accompanied Dr. Tahouni as he made his visits with his patients in the emergency room as well as experienced the roles of emergency physicians when trauma patients were admitted. I learned about an immense range of illnesses from psychotic episodes to gunshot wounds.

Interventional Radiology, Tufts Medical Center, Spring 2014

• Supervisor: Dr. Neil Halin D.O.
• In the interventional radiology department I was able to shadow various doctors as they performed minimally invasive surgeries such as catheter insertions, IVC filter insertions, thoracenteses, etc. I was also given the opportunity to become familiar with different medical imaging techniques (MRI, CT scans, & ultrasound) and their use in the diagnosis of illnesses such as cancer.

Vascular Medicine, Massachusetts General Hospital, Dr. Michael Jaff, D.O.

VOLUNTEERING

Big Sister Association of Greater Boston (Spring 2015-Present)
Outreach Van Project (May 2014-Present)
Boston Children’s Hospital (Summer 2011 & 2012)
Sinai Hospital- Alzheimer’s Disease Center (Summer 2010)
OTHER WORK EXPERIENCE

**Office Assistant**, Office of Rental Property Management Maintenance (2011-Present)
**Stylist**, Club Monaco (2011-2012)
**Lab assistant**, Boston University Chemistry Department (2010-2011)

ACTIVITIES

**Resident Assistant**, Boston University (2012-Present)
**alpha Kappa Delta Phi Sorority Inc**, Boston University (2010-Present)
  - Alumnae Board position: Vice Chairperson
  - Active house executive-board positions: President, Vice President of Internal Affairs, Vice President of External Affairs, New-Member Educator
  - Volunteer work: Avon Breast Cancer Crusade, Half the Sky Foundation, Room to Grow, Sunday Bread, Rosie’s Place, Boston Marathon, etc.

**Dance Theatre Group**, Boston University (2011-2014)
**Boston University Cheerleading** (2010-2011)
**Vietnamese Student Association** (2010-2011)