Prefrontal Cortex Activity during Dual Task Performance in Patients with Chronic Obstructive Pulmonary Disease

by

Syed Ahmed Hassan

A thesis submitted in conformity with the requirements for the degree of Master of Science
Rehabilitation Sciences Institute
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Abstract

The purpose of this study was to compare changes in dorsolateral prefrontal cortex (DLPFC) oxygenated hemoglobin ($\Delta$O$_2$Hb), accuracy of backwards spelling, and decrements in gait velocity during single and dual tasks in patients with COPD (n=8), and healthy younger (n=20) and older adults (n=20). Participants performed: (1) backwards spelling cognitive task (CT); (2) preferred paced walk (PPW); and (3) fast paced walk (FPW). The dual tasks then paired CT with PPW and FPW. In older adults, $\Delta$O$_2$Hb was significantly higher in left DLPFC compared to patients with COPD and bilaterally compared to younger adults during FPW+CT versus FPW. Furthermore, older and younger adults exhibited higher decrements of velocity during FPW+CT compared to PPW+CT. CT accuracy tended to be lower in older adults. Decrements in performance during dual tasking highlight the impact of increased cognitive load and need of cognitive-motor interventions to improve cognition and physical function.
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List of Abbreviations

COPD: Chronic Obstructive Pulmonary Disease

CT: Cognitive Task (backwards spelling)

DLPFC: Dorsolateral Prefrontal Cortex

DTE: Dual Task Effect

ETCO₂: End Tidal Carbon Dioxide

FEV₁: Forced Expiratory Volume in 1 Second

fNIRS: Functional Near-Infrared Spectroscopy

GOLD: Global Initiative for Chronic Obstructive Lung Disease

FPW: Fast Paced Walk

FVC: Forced Vital Capacity

IPAQ: International Physical Activity Questionnaire

MAP: Mean Arterial Pressure

MoCA: Montreal Cognitive Assessment

O₂Hb: Oxygenated Hemoglobin

PFC: Prefrontal Cortex

PPW: Preferred Paced Walk

SLS: Single Leg Stance
Chapter 1

1 Introduction

1.1 Statement of the Problem

The prevalence of seniors (≥ 65 years old) has increased from 8% in 1971 to 14% in 2010 and is expected to rise to 23-25% in 2036 (Statistics Canada, 2011). Aging has been linked to reduced gait speed (Hageman & Blanke, 1986; Liu, Chan, & Yan, 2014) and is predictive of risk of falls, future hospitalization and mortality in older adults (Middleton & Fritz, 2013; Salzman, 2010). James et al. (2016) reported that gait impairment is linked to mobility issues that lead to limitations in activities of daily living. In addition, age-related changes in brain structures are linked to gait and balance deficits (Seidler et al., 2010). Limitations in mobility represent a preclinical state to disability in older adults (Manini, 2013). Risk factors of mobility impairment have been identified including impairments in the central nervous system, muscles, joints and sensory physiological systems in older compared to younger adults (Bean et al., 2013; Ferrucci et al., 2016; Montero-Odasso, Verghese, Beauchet, & Hausdorff, 2012). Therefore, evaluation of gait and balance is important for identification of at-risk individuals and prevention of falls.

Patients with chronic obstructive pulmonary disease (COPD) exhibit motor impairment (mobility and balance issues), which may, in part, be a pathological outcome of narrowed airways causing airflow limitation to the lungs. Reduced oxygen transport across the alveolar membranes causes hypoxemia leading to muscle wasting, lower limb weakness and neural damage (Alosco, Spitznagel, Josephson, Hughes, & Gunstad, 2015; Anderson & Arciniegas, 2010; Andrianopoulos, Gloeckl, Vogiatzis, & Kenn, 2017; Dodd, Getov, & Jones, 2010; Etnier et al., 1999; Hauer et al., 2003; Karamanli, Ilik, Kayhan, & Pazarli, 2015; Zhang et al., 2016). Patients with COPD also report difficulties in their activities of daily living and feel restricted in their ability to socialize, and achieve life goals (Fletcher, Albrow, Jenkins, & Walker, 2011).

The prefrontal cortex (PFC) is involved in attentional control and executive functions including memory, planning and decision making (Rossi, Pessoa, Desimone, & Ungerleider, 2009). These cognitive functions are required during simple walking and to a greater extent during complex walking that have higher balance demands (e.g., when maneuvering around obstacles) (Chen et al., 2017). Structural changes in the PFC occur as a result of aging and are found to be greater in
patients with COPD compared to older adults (Dodd et al., 2012). Alterations in the neural structures (e.g., white matter atrophy) have been linked to changes in neural hemodynamics in the elderly and decline in cognitive functions (Dodd et al., 2012; Purkayastha et al., 2014). Hypoxemia and oxidative damage may, in part, explain the neural damage and the commonly reported motor deficits and cognitive impairment in patients with COPD. Lower cerebral perfusion has been reported in hypoxemic compared to non-hypoxemic patients with COPD (Incalzi et al., 2003; Ortapamuk & Naldoken, 2006). Ortapamuk and Naldoken (2006) documented reduced perfusion in frontal and parietal cortices in hypoxemic, but only in the frontal cortex in non-hypoxemic individuals. Reduced activity in the primary motor, premotor and prefrontal cortices have been reported in non-hypoxemic patients with COPD compared to healthy controls, which might also contribute to their muscle weakness and motor deficits (Alexandre, Heraud, Oliver, & Varray, 2014).

Pulmonary rehabilitation is one of the available treatment options for patients with COPD. It aims to improve their mobility with a primary focus on increasing endurance and strength of the peripheral musculature. Balance exercises, although recently recognized, are not always provided. Furthermore, cognitive impairment (prevalence: 27-61%) is usually overlooked in these therapies even though it is a common pathological feature of COPD (Grant et al., 1987; Torres-Sánchez et al., 2015) and may be associated with alterations in neural activity and structures that also play a role in gait and balance. Although, the focus of rehabilitation interventions is to improve motor deficits, the relationship between brain activity, PFC function and gait has not been widely studied in this patient population.

Activities of daily living usually involve doing more than one task simultaneously and may include a cognitive and a motor component. Thus, the dual tasking experimental paradigm has proven to be effective in determining the association between cognitive-motor control (Huang & Mercer, 2001; Karatekin, Couperus, & Marcus, 2004). Some examples of dual tasking involve texting, talking or thinking about chores while walking. Falls are common while walking (Oxley, O’Hern, Burtt, & Rossiter, 2018) and may indicate an inability to effectively meet the cognitive and physical demands of dual tasking (Shumway-Cook & Woollacott, 2000). Change in performance of one or both tasks during dual tasking, as compared to the performance of that task on its own, is known as the dual task effect (DTE) or dual task interference and may be attributed to limited attentional resources (Plummer & Eskes, 2015). Thus, the evaluation of
DTE has become part of rehabilitation of patients with neurological disorders (Brauer et al., 2011; Plummer-D’Amato et al., 2012); however, it is not commonly used in people with COPD. Measurement of brain activity (e.g., from the PFC) during the dual tasking experimental paradigm can provide a model of competing demands of our activities of daily living as well as insight into age and disease related differences in neural mechanisms associated with walking at different speeds and cognitive performance.

The PFC neural activity can be measured using functional near-infrared spectroscopy (fNIRS) during a dual tasking experimental paradigm. The fNIRS is a non-invasive optical neuroimaging technique that effectively provides a measure of neural activity by measuring changes in oxygenated hemoglobin (\(\Delta O_2\text{Hb}\)) (Piper et al., 2014). Although, functional magnetic resonance imaging (fMRI) is the conventional neuroimaging method that indirectly measures neuronal activity using blood-oxygen-level dependent imaging (BOLD), it is limited in its use during tasks that involve mobility, unlike fNIRS (Silva, See, Essayed, Golby, & Tie, 2017).

The overall objective of this study was to compare PFC \(\Delta O_2\text{Hb}\) and decrements in cognitive and motor performance during dual tasks between healthy younger adults (18-35 years), healthy older adults (\(\geq 45\) years) and patients with COPD (\(\geq 45\) years). It was hypothesized that dual tasks will cause a greater increase in PFC \(O_2\text{Hb}\) and decrements in both cognitive and gait performance compared to single tasks. Furthermore, it was postulated that the increase in PFC \(O_2\text{Hb}\) and decrements in performance will be greater in older adults compared to younger adults and patients with COPD compared to older adults.

1.2 Literature Review

1.2.1 Mobility in Older Adults

Aging is associated with impairment of mobility (Alfieri et al., 2010; Seidler et al., 2010). Optimal mobility is defined as the “relative ease and freedom of movement in all of its forms” including walking, exercising, driving, climbing stairs or moving from a bed to a chair (Satariano et al., 2012). Walking is one of the leading forms of mobility (Ko, Hausdorff, & Ferrucci, 2010) and requires balance and coordination. Reduction in walking speed is the most consistently reported consequence of aging (Cruz-Jimenez, 2017). Limitations in walking can, therefore, result in a loss of independence as it is involved in several activities of daily living (Manini,
Thus, evaluation of gait, balance and mobility in older adults is essential to reduce the risk of falls and prevent loss of independence. Middleton and Fritz (2013) summarize some of the evaluative tools for the assessment of gait (4-Meter Walk Test, 6-Minute Walk Test, Dynamic Gait Index, Walking While Talking and Modified Gait Efficacy Scale), balance (Berg Balance Scale, Mini Balance Evaluation Systems Test (BESTest), Performance-Oriented Mobility Assessment and Falls Efficacy Scale - International) and mobility (Timed Up and Go Test, 5 Times Sit to Stand Test, Backward Walking and Short Physical Performance Battery). Walking speed is a predictive variable for independent mobility and rehabilitation in older adults (Friedman, Richmond, & Baskett, 1988).

1.2.2 Overview of COPD – Definition, Etiology and Burden

COPD is defined as “a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities” (GOLD, 2018). It is highly prevalent in the aging population, especially in adults over the age of 45 years (Akinbami & Liu, 2011). COPD poses a significant financial and healthcare burden. It is the fourth leading cause of death in Canada (Dang-Tan, Ismaila, Zhang, Zarotsky, & Bernauer, 2015) with a prevalence of 11.7% in people aged ≥ 30 years. COPD affected 384 million individuals globally in 2010 (Adeloye et al., 2015) and causes 3 million deaths per year (Lozano et al., 2012). The death toll is expected to rise to 4.5 million in 2030 (World Health Organization, 2013). Moreover, the direct cost emanating from COPD in Canada is estimated to be CAD $1.5 billion (Mittmann et al., 2008).

Smoking has been identified as the primary causative risk factor for COPD development (Buist, Vollmer, & McBurnie, 2008; Forey, Thornton, & Lee, 2011). A large fraction of individuals with COPD are either past or current smokers. The majority of the COPD cases (75%) were found to be a result of long term smoking, while 25% of the patients had never smoked (American Thoracic Society, 2017). Furthermore, individuals with low socioeconomic status, and those living in low- and middle-income countries are at a greater risk of developing this disease (Grigsby et al., 2016); it has been estimated that 90% of the total deaths from COPD occur in these countries (May & Li, 2015). The higher risk of development and deaths is hypothesized to be due to a greater level of exposure to environmental pollution (Figure 1).
Biological factors such as genetics, hormones and sex increase the risk of developing COPD. Deficiency of alpha-1 anti-trypsin has been the only clearly identified genetic factor that makes an individual more susceptible to damage from smoke and environmental pollution that can subsequently lead to the development of COPD (American Thoracic Society, 2017).

Furthermore, estrogens are known to upregulate proteins such as cytochrome P450 and aldehyde oxidase. These enzymes lead to an increase in metabolism of cigarette smoke and production of oxidative agents without a balancing activation of detoxifying agents. Since the levels of estrogen are significantly higher in women compared to men, the production of the damaging oxidative agents is much greater in women; thus, women are more susceptible to lung tissue damage from smoking and developing COPD (Aryal, Diaz-Guzman, & Mannino, 2013; Chen, Horne, & Dosman, 1991; Sin et al., 2007; Sørheim et al., 2010).

Even with low exposure to smoking, reduced lung function was found in women as indicated by the results of spirometry that showed reduced forced expiratory volume in one second (FEV1) (Sørheim et al., 2010). The prevalence of COPD has been increasing in women, which may, in part, be attributable to the increasing rate of smoking. The rate of smoking in women is expected to rise to 20% by 2020 from the historical 9% in the early 2000s (Aryal et al., 2013). Moreover, a greater number of women now hold industrial jobs that were predominantly occupied by men in the past (Aryal et al., 2013), which increases their risk of being exposed to pollution and developing COPD. Out of the major risk factors identified, environmental agents can be the most readily managed (i.e., smoking cessation) to control the development, progression and severity of COPD.
Figure 1. Etiology and pathology of COPD. Smoking is the primary risk factor for developing COPD, and cognitive impairment and motor deficits are its commonly diagnosed pathological characteristics.
1.2.3 Symptoms and Diagnosis

Dyspnea or shortness of breath is the most characteristic symptom of COPD. Other common signs and symptoms include coughing, wheezing, chest tightness, recurring respiratory infections, energy loss and weight loss (American Thoracic Society, 2017). The symptoms are a result of emphysema (parenchymal destruction) and obstructive bronchitis (small airways disease). Emphysema is characterized by damaged and enlarged alveoli causing air to be trapped during the expiratory phase due to increased pleural pressure causing airway closure. On the other hand, in chronic bronchitis, the airways become inflamed that increases mucous production and bronchospasm of the smooth muscle surrounding the airway walls. In addition, cilia in the airways are damaged making it harder to clear mucous. Chronic bronchitis and emphysema changes contribute to narrowing of the airways leading to airflow limitation and altered gas exchange across the alveoli (Figure 2). The severity and occurrence of COPD symptoms varies from one day to another and are usually exacerbated during physical exertion or a viral infection (Ramsey & Hobbs, 2006).

![Figure 2. Phenotypic features of airways in a healthy lung compared to that with COPD.](https://emedprimarycare.com/wp-content/uploads/2018/02/Blog-image.jpg)

Evaluation of lung function using spirometry is the gold standard for diagnosing COPD (Johns, Walters, & Walters, 2014). The results of spirometry are affected by several factors including height, age, sex and ethnicity. Two results of this test are considered to make the diagnosis and evaluate the severity of the disease. The ratio of FEV$_1$ to forced vital capacity (FVC) is evaluated
to determine the presence of airflow limitation, while the results of FEV$_1$ are used to evaluate the severity of the illness. FEV$_1$ is the volume of air that a person can exhale in one second during a forced breath from total lung capacity, while FVC is the total volume of air that a person forcefully exhales during a similar maneuver. A post-bronchodilator spirometry test result of FEV$_1$/FVC < 0.70 provides the basis for diagnosis of COPD by a physician (GOLD, 2018). Upon confirmation of the presence of COPD, the severity can be determined using the FEV$_1$ results. Recommendations for the classification of COPD severity using the cut-off values of FEV$_1$ results have been outlined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) (Table 1).

Table 1. Classification of COPD severity based on the GOLD criteria (GOLD, 2017).

<table>
<thead>
<tr>
<th>GOLD Stage</th>
<th>COPD Severity Level</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>Mild</td>
<td>FEV$_1$ ≥ 80% predicted</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>Moderate</td>
<td>50% ≤ FEV$_1$ &lt; 80% predicted</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>Severe</td>
<td>30% ≤ FEV$_1$ &lt; 50% predicted</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>Very Severe</td>
<td>FEV$_1$ &lt; 30% predicted</td>
</tr>
</tbody>
</table>

Abbreviations: COPD, chronic obstructive pulmonary disease; FEV$_1$, forced expiratory volume in one second; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

1.2.4 Cognitive Impairment

Cognition is defined as “any and all processes by which a person becomes aware of his/her situation, needs, goals, and required actions, and uses this information to implement problem solving strategies for optimal living” (Borson, 2010). Some of the cognitive functions involve attention, memory, perception, language, decision making and planning (Andrianopoulos et al., 2017; Borson, 2010). Most activities of our daily living require at least one if not more of these cognitive functions to execute tasks successfully and independently. Some examples of these activities include driving to work, communicating with others, managing finances and cooking (Murman, 2015).
Mental functions decline as a function of age, especially attention and memory (Glisky, 2007; Hebert et al., 1995). The incidence of cognitive decline has also been reported to increase with hypoxemia and disease severity (Yohannes, 2014). Deficits in cognitive functions such as memory loss or confusion have been reported in one-eighth of the elderly over the age of 60 years (Adams, Deokar, Anderson, & Edwards, 2013). Decline in a person’s ability to maintain and effectively utilize cognitive functions is known as cognitive impairment (Vega & Newhouse, 2014).

Cognitive impairment is a well-documented manifestation of COPD (Andrianopoulos et al., 2017; Crişan et al., 2014; Roig, Eng, Road, & Reid, 2009; Torres-Sánchez et al., 2015) with several risk factors and associated pathophysiology. In the nocturnal oxygen therapy trial, the prevalence of moderate to severe cognitive impairment was found to be 42% in patients with COPD (Grant, Heaton, McSweeny, Adams, & Timms, 1982). The prevalence of mild cognitive impairment in patients with COPD has been reported to be 32-36% as estimated using the Mini-Mental State Examination and Montreal Cognitive Assessment (MoCA) (Dong et al., 2010; Villeneuve et al., 2012). Using the Halstead-Reitan Battery for neurological testing that includes components such as the Tapping Test, Trail Making Test, Sensory Perceptual Examination and Aphasia Screening Test, Grant et al. (1987) showed that cognitive impairment is associated with the level of hypoxemia as it was shown to increase from 27% in individuals with mild to 61% in those with severe hypoxemia.

In patients with COPD, factors including disease severity (Hung, Wisnivesky, Siu, & Ross, 2009), smoking (Cleutjens et al., 2017), hypoxemia (Grant et al., 1982), systemic inflammation, cigarette smoke (Dodd et al., 2010), comorbidities (e.g., depression) (Incalzi et al., 1998), cerebral hypoperfusion (Incalzi et al., 2003), hippocampal atrophy (Li & Fei, 2013) as well as atrophy, lesions and alterations in the integrity of white matter bundles’ in superior longitudinal fasciculus (Dodd et al., 2012; Um et al., 2017) are shown to be associated with cognitive impairment. Some factors that may contribute to cognitive impairment in younger and older adults include inflammation (Sartori, Vance, Slater, & Crowe, 2012), oxidative stress (Baierle et al., 2015), reduced physical activity (Guure, Ibrahim, Adam, & Said, 2017), intracranial hypertension (Zur, Naftaliev, & Kesler, 2015), genetics (Lin, Lin, & Lane, 2017) and tobacco smoking (Chamberlain, Odlaug, Schreiber, & Grant, 2012; Richards, Jarvis, Thompson, &
Wadsworth, 2003; Sabia et al., 2012). Cognitive impairment diminishes an individual’s ability to independently and efficiently perform everyday tasks.

1.2.5 Gait and Balance Issues

“Balance is a generic term describing the dynamics of body posture to prevent falling. It is related to the inertial forces acting on the body and the inertial characteristics of body segments” (Winter, 1995). The human body utilizes two strategies of postural adjustment to maintain balance and prevent falls: anticipatory postural adjustment and compensatory postural adjustment (de Azevedo, Claudino, Conceição, Swarowsky, & dos Santos, 2016). The anticipatory postural adjustment involves minimization of the anticipated disturbance through muscular response and is based on learning from past experience, while the compensatory postural adjustment involves muscle response after postural disturbance to minimize its impact (de Azevedo et al., 2016). Paillard and Noé (2015) have summarized several tests that are used to evaluate postural abilities that include Berg Balance Scale, Timed Up-and-Go, Tinetti test, Short Physical Performance Battery, Mini BESTest and Unified Balance Scale. Some of the instrumented tests include the use of force platforms and wobble boards. Moreover, single leg stance (SLS) has also been used to assess postural control in the elderly and individuals with Parkinson’s disease (Chomiak, Pereira, & Hu, 2015), which was also used in this study.

Patients with COPD exhibit impairments of gait and balance as measured by the BESTest, Community Balance and Mobility Scale, and Timed Up-and-Go test (Beauchamp et al., 2013, 2012; Butcher, Meshke, & Sheppard, 2004; Roig et al., 2011). Gait and balance impairments predispose an individual to a three times greater risk of falls compared to those with normal physical functioning (Rubenstein & Josephson, 2006). Maintenance of balance requires coordination of not only the musculoskeletal system but also the nervous system that is involved in motor, sensory and higher order cognitive functions (Horak, 2006). Impairment of balance has been shown to be greater in patients with COPD compared to age matched healthy controls (Beauchamp et al., 2012), which puts them at a higher risk of falls (Crişan, Oancea, Timar, Fira-Mladinescu, & Tudorache, 2015). In patients with COPD, several other factors contribute to this increased risk such as the number of medications they take, visual deficits as well as cognitive impairment (Roig et al., 2009). An estimated 30–50% of people over the age of 65 years fall at least once a year (Crişan et al., 2015) with an incidence of 1.17 falls/person-year (Oliveira et al.,
The rate of falls has been reported to be five times higher in individuals with COPD compared to healthy adults (Roig, Eng, MacIntyre, Road, FitzGerald, et al., 2011)

Balance deficits and motor impairments in the elderly and patients with COPD are linked to reduced physical activity. This limits an individual from adequately performing activities of daily living (Eggermont et al., 2014; Iwakura et al., 2016; Mlinac & Feng, 2016; van Nimwegen et al., 2011). Low physical activity is a predictor of all-cause mortality (Waschki et al., 2011) and has been linked to increased hospitalization (Hartman, Boezen, de Greef, Bossenbroek, & ten Hacken, 2010). On average, inactive individuals have approximately 38% longer stays in the hospitals and, consequently, use a greater proportion of healthcare services (e.g., physician visits) compared to active people (Sari, 2009). Deficits in gait rhythm have been documented in patients with COPD who were fallers compared to non-fallers (Lahousse et al., 2015). The reduced functional capabilities of patients with COPD, compared to age matched healthy adults, are evident by the reduced distance walked during the 6-Minute Walk Distance test, the most commonly used functional test of mobility in these patients (Spruit et al., 2010). Hypoxemia induced muscle wasting and lower limb muscle weakness may, in part, explain the motor impairments in patients with COPD (Wüst & Degens, 2007).

Gait and balance deficits in patients with COPD may also be partially attributable to PFC damage (Roig, Eng, MacIntyre, Road, & Reid, 2011; Takakusaki, 2017). The PFC is involved in several executive functions (e.g., working memory, attentional control), which are required for gait (Bruijn & van Dieën, 2018; Elliott, 2003; Miller & Cohen, 2001). Activation in the PFC has been reported prior to the onset of walking indicating its involvement in preparation for gait (Suzuki, Miyai, Ono, & Kubota, 2008). In addition to the PFC, an interplay between several other neural regions such as basal ganglia, motor cortex and cerebellum enables the achievement of stable gait (Takakusaki, 2017). Investigations of gait and posture impairment in patients with Parkinson’s disease have elucidated several mechanisms that could be potential contributors to motor impairments. Some of them include impaired cognitive information flow from temporoparietal to frontal cortex, impaired integration of sensory information in thalamus, reduced activity in the motor cortex, failure of motor programming in motor areas such as primary motor cortex, supplementary motor and premotor area and their connection to basal ganglia and cerebellum, and impairment of brain stem areas involved in posture and gait (Takakusaki, Habaguchi, Ohtinata-Sugimoto, Saitoh, & Sakamoto, 2003; Takakusaki, Saitoh,
Harada, & Kashiwayanagi, 2004; Takakusaki, Chiba, Nozu, & Okumura, 2016). Takakusaki (2017) has also postulated that activity in the supplementary and premotor area can be triggered by signals from the PFC. Thus, cognitive impairment and damage to PFC may impair gait and balance. Cognitive impairment is associated with an increased risk of falls in patients with COPD indicating motor control deficits (Roig et al., 2009). Depending on the disease severity, cognitive and motor deficits can significantly interfere with and impair performance of many activities of daily living such as bathing, cooking and doing groceries (Mlinac & Feng, 2016). This can lead to dependence on caregivers for physical, social and emotional support as well as increase the burden on the healthcare system (Mlinac & Feng, 2016).

1.2.6 Alterations in Brain Structures

Aging and COPD related functional and structural changes have been documented in the PFC. Svennerholm, Boström, and Jungbjer (1997) reported that brain size shrinks by approximately 5% per decade after 40 years of age. Older adults (mean age: 64-89 years) were shown to have PFC atrophy (Jernigan et al., 2001; Raz et al., 1997; Salat, Kaye, & Janowsky, 2001) as well as reduction in synaptic density (Masliah, Mallory, Hansen, DeTeresa, & Terry, 1993) and gray matter (Dixon, Bäckman, Park, Backman, & Nilsson, 2004; Scahill et al., 2003). Similarly, patients with COPD showed greater reduction in gray matter in several regions of the frontal brain in contrast to healthy controls (Esser et al., 2016; Zhang et al., 2012; Zhang et al., 2013). However, the findings of structural changes are not consistent across studies as Ryu et al. (2013) reported a lack of significant volumetric differences. The documented neural changes in patients with COPD may be a result of hypoxemia, vascular or other comorbidities (Dodd et al., 2012), a consequence of COPD, disease severity or may have existed prior to the development of COPD. Nonetheless, the precise etiology or time of the structural changes in the brain of patients with COPD are not well known. Moreover, neural structural changes in older adults and patients with COPD have been linked to a decline in cognitive function, which can be delayed or minimized through protective interventions such as exercise, diet and intellectually stimulating activities (Peters, 2006).
1.2.7 Neural Activity during Cognitive and Motor Tasks

Neuronal metabolism, indicative of neural activity, is dictated by the cognitive and motor tasks being executed (Haier et al., 1992). The type and difficulty of the tasks affect the magnitude and regional specificity of the neuronal metabolism (Ayaz et al., 2012; Kameyama, Fukuda, Uehara, & Mikuni, 2004; Mandrick et al., 2013a). Various cognitive and motor tasks have been employed across studies. Some of the cognitive tasks used involve verbal fluency, working memory, Stroop, arithmetic, and visuomotor reaction time (e.g., driving) tests. However, the most common motor task used is walking. Some of the other upper and lower limb motor tasks include finger tapping, stepping, grasping and simulated driving (Leone et al., 2017).

Age-related differences have been reported in the cortical hemodynamic response during performance of cognitive and motor tasks. Some studies have analyzed the cortical hemodynamic response during either single or dual tasks in only younger adults (Meester, Al-Yahya, Dawes, Martin-Fagg, & Piñon, 2014; Mirelman et al., 2014; Suzuki et al., 2004), only older adults (Harada et al., 2009) or have compared data between younger and older adults (Beurskens, Helmich, Rein, & Bock, 2014; Eggenberger, Tomovic, Münzer, & de Bruin, 2017; Holtzer et al., 2011). Older adults tended to have higher Δ$O_2$Hb in the left and right PFC during color-word Stroop task and right PFC during tasks evaluating working memory and attention (Makizako et al., 2013; Reuter-Lorenz, 2002; Schroeter, Zysset, Kruggel, & von Cramon, 2003). Compared to older adults, greater increase in $O_2$Hb in the left or right lateral PFC during comparable cognitive tasks (i.e., calculation, verbal fluency) have been documented in younger adults (Hock et al., 1995; Milham et al., 2002). Similarly, fast compared to slower walking has shown to increase $O_2$Hb bilaterally or just left PFC in younger and older adults (Harada, Miyai, Suzuki, & Kubota, 2009; Suzuki et al., 2004). Moreover, dual compared to single tasks resulted in a greater increase in PFC $O_2$Hb in both the elderly and younger adults (Holtzer et al., 2011). On the contrary, a decrease in PFC $O_2$Hb has also been reported during dual compared to the single tasks in older adults during walking with a complex visual task (Beurskens et al., 2014). The higher level of activation in older compared to younger adults that is reported in some studies may, in part, be explained by the less efficient processing in neural networks and recruitment of cognitive resources from other brain regions (Reuter-Lorenz, 2002).
Factors such as age, sex, intelligence, learning and task difficulty influence the hemodynamic response during cognitive and/or motor tasks (Barch et al., 1997; Kameyama et al., 2004). The neural efficiency hypothesis may partially explain the variation in neural activation across individuals. The hypothesis states that individuals with more efficient neural activation network processing have lower activity during performance of a cognitive task with low to moderate difficulty compared to individuals with less efficient neural mechanisms (Neubauer, Grabner, Fink, & Neuper, 2005; Uemura et al., 2016; Yang et al., 2009). The lower activation in more intelligent individuals is also linked to a lower use of glucose metabolism (Dunst et al., 2014; Haier et al., 1992). Thus, greater recruitment and activation that is usually reported in the elderly may be attributed to reduced neural efficiency and cognitive impairment (Serrien, Ivry, & Swinnen, 2007).

1.2.8 Characteristics of Current Pulmonary Rehabilitations Programs

The European Respiratory Society and American Thoracic Society define pulmonary rehabilitation as “an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities” (Gibson, Loddenkemper, Sibille, & Lundbäck, 2013). These rehabilitation programs involve members from multidisciplinary teams and usually include a physiotherapist, dietician, pharmacist, general practitioner and a respiratory nurse. Working collectively, the healthcare team contributes to patient assessment, education, exercise training and psychosocial support (Corhay, Dang, Van Cauwenberge, & Louis, 2013).

The rehabilitation programs target some of the major symptoms of COPD. The chronic state of hypoxemia and dyspnea resulting from airflow limitation in patients with COPD lead to systemic inflammation and oxidative stress. One consequent pathophysiology includes impairment of the skeletal muscle. To address these symptoms and minimize the occurrence of exacerbations, the standard rehabilitation programs in the United States often involve 6-12 weeks of training consisting of 2-3 weekly sessions (Hopkinson, 2017; Nici, Lareau, & ZuWallack, 2010).

Dyspnea and skeletal muscle dysfunction have been linked to fatigue, impaired balance, and reduced physical activity that limit participation in activities of daily living. To enhance skeletal muscle strength and endurance, the programs involve aerobic exercise and strength training. Exercise is known to improve mental and physical health as well as reduce the risk of developing
several conditions such as cardiac disease, diabetes mellitus and cancer (Warburton, Nicol, & Bredin, 2006). In addition to physical training, patients benefit through assistance with smoking cessation and training in self-management of dyspnea symptoms. Pulmonary rehabilitation has shown benefits that include improvement in exercise performance, dyspnea relief, improved health-related quality of life, psychological benefits and reduced healthcare utilization (Nici et al., 2010). Thus, pulmonary rehabilitation has been recommended to be a part of patients’ therapy in GOLD guidelines as well as clinical practice guidelines from the American College of Physicians (Corhay et al., 2013).

1.2.9 Gap in the Rehabilitation Programs

Several rehabilitation programs are in place to assist the elderly and those with neurological disorders. The programs for individuals with acquired brain injury or stroke involve cognitive and motor training components; however, not in a combined fashion (Faria et al., 2018). Repetitive practice with feedback and task-oriented training are provided to promote relearning of motor skills (Faria et al., 2018; Holden, 2005; Levin, Weiss, & Keshner, 2015), while programs such as Gist reasoning training have been used in the elderly to improve cognition through tasks requiring integrated reasoning, innovative thinking and strategic attention (Chapman et al., 2015).

Patients with COPD exhibit pathological characteristics that involve skeletal muscle dysfunction and cognitive impairment. However, the association between cognitive impairment and motor dysfunction, and use of cognitive-motor rehabilitation interventions have not been widely considered in this patient population. The main focus has mainly been on enhancing endurance and exercise capacity as well as improving the peripheral musculature (Clark, Cochrane, & Mackay, 1996; Mador, Bozkanat, Aggarwal, Shaffer, & Kufel, 2004; Panton et al., 2004; Roig & Reid, 2009). Moreover, patients with COPD are not always administered balance exercises even though in a recent randomized control trial involving balance exercises performed thrice weekly participants showed a significant improvement in balance and scores of overall physical health status questionnaires (Beauchamp et al., 2013).

Recently, the connection between cognitive impairment and motor dysfunction in patients with COPD was brought to light. A publication by Andrianopoulos et al. (2017) posed a question
asking whether cognitive assessment should be a part of the respiratory assessment and noted that cognition has an impact on clinical outcomes of the respiratory treatment, but is being neglected. Heraud et al. (2018) also conducted a study on patients with COPD and found greater variability in stride time during performance of a dual task (involving walking and subtractions) compared to a control group of healthy older adults; this study highlighted greater age-independent decrements in performance of individuals with COPD. Therefore, therapies involving a cognitive and a motor component with simultaneous or subsequent measurement of neural activity in at-risk individuals may provide insight into the neural mechanisms associated with tasks’ performance. The information gained from such studies can be used to develop more effective rehabilitation interventions that target specific neural regions to strengthen the neural processing of motor control to enhance mobility, balance, muscular strength and endurance to ultimately reduce the risk of falls.

1.3 Rationale for Methodology

1.3.1 Functional Magnetic Resonance Imaging and Functional Near-Infrared Spectroscopy

Neuroimaging techniques such as functional magnetic resonance imaging (fMRI) have been widely used not only in research but also clinical settings. fMRI is a conventional neuroimaging technique and has been used since 1990s to evaluate neural activity (Bandettini, 2012). This non-invasive modality provides high resolution data to construct neural activity maps, which are based on energy demands and the associated blood flow during an activity (Logothetis, 2003). The underlying mechanism of fMRI is dependent on the BOLD contrast. The BOLD signal is based on the changes in the concentration of oxygenated and deoxygenated hemoglobin during neuronal activity. A decrease in deoxygenated hemoglobin and an increase in $O_2Hb$ associated with blood flow, caused by neural activity and associated vasodilation during performance of a task, causes an increase in image intensity (Buxton, 2013; Heeger & Ress, 2002). Measurement of the changing levels of the hemoglobin chromophores provides a measure of neuronal metabolic activity. However, fMRI is expensive and precludes measurement of neural activity during many real-life activities that require mobility.

The fNIRS is an emerging neuroimaging modality that has several advantages over fMRI. One of the critical values added by many fNIRS devices is that they permit proxy measurements of
neural activity during movement (Ferrari, Muthalib, & Quaresima, 2011). Moreover, fNIRS is less expensive and provides $\Delta O_2$Hb data consistent with fMRI (Strangman, Culver, Thompson, & Boas, 2002). However, fNIRS can only measure data from superficial structures, while fMRI can be used to visualize the whole brain. Nonetheless, the test-retest reliability of fNIRS measures has been established in several studies during performance of cognitive and motor tasks (Plichta et al., 2006; Schecklmann, Ehlis, Plichta, & Fallgatter, 2008; Strangman, Goldstein, Rauch, & Stein, 2006; Watanabe, Matsuo, Kato, & Kato, 2003), with greater reliability at the group level analyses (Schecklmann et al., 2008). It has been shown that $\Delta O_2$Hb is a reliable fNIRS measure and is sensitive to blood flow changes related to locomotion (Harada et al., 2009; Miyai et al., 2001). Moreover, fNIRS measures have been cross-validated with fMRI signals (Kato, Izumiyama, Koizumi, Takahashi, & Itoyama, 2002; Mehagnoul-Schipper et al., 2002; Murata, Sakatani, Katayama, & Fukaya, 2002; Toronov et al., 2001). The reliability, validity and portability of some fNIRS devices opens avenues to possibilities that include proxy neural activity measurements in research protocols that involve walking as well as in clinical settings for evaluation of claustrophobic individuals who are uncomfortable being tested in fMRI machines. In addition, the portability of some fNIRS devices has applications for use in remote locations during research on rehabilitation programs to monitor treatment progress. Indirect measurements of the neural activity during tasks that challenge motor and cognitive skills (Hauer et al., 2003) can provide insight into the association between performance and neural activity.

Since its development in 1977, fNIRS is being used increasingly to assess $\Delta O_2$Hb concentrations in various regions of the cerebral cortex including the PFC (Jöbsis, 1977). The ability of infrared light to penetrate bone, skin, and the underlying tissue makes it a feasible and effective tool to measure the changes in concentrations of various hemoglobin chromophores in mobile participants during real-life situations (Li, Li, Luo, & Gong, 2009; McKendrick, Parasuraman, & Ayaz, 2015). Transparency of most biological tissues to the wavelengths between 700-900nm, a range within that of infrared light, makes the measurement of hemoglobin chromophores’ concentrations possible. The light emitting optodes on the fNIRS devices have a depth penetration capability that is half the inter-optode distance. For example, an inter-optode distance of 25mm allows a light penetration depth of 12-13mm into the tissue underneath the probe. Detection of the reflected light back at the surface of the skin is used to quantify the concentration of $\Delta O_2$Hb using the modified Beer-Lambert law (Figure 3). The isosbestic point of
the hemoglobin chromophores, the wavelength at which their light absorbance is the same, is 800nm. The highest light absorbance of the oxygenated and deoxygenated hemoglobin occurs around the isosbestic point, where the light absorbance of other biological molecules is low. Thus, to measure the relative concentrations of the oxygenated and deoxygenated hemoglobin, the light intensities at 850nm and 730nm, respectively, are measured using fNIRS (Bakker, Smith, Ainslie, & Smith, 2012).

1.3.2 Dual Tasking

Mobility during most activities of daily living involves performing two tasks simultaneously (dual tasking) (Brustio, Magistro, Zecca, Rabaglietti, & Liubicich, 2017). One of the tasks is usually a motor task, while the other is a mental task requiring attention and/or other executive functions (e.g., walking and talking or being attentive to obstacles on the pavement to avoid trips and falls). The execution of multiple tasks requires focus and attention to avoid making errors either in gait performance or the mental task. As a result, the dual tasking experimental paradigm has been proven to be effective to measure the impact of divided attention and higher cognitive demands during dual tasking.

Attention is a limited resource and cannot be devoted indefinitely to all the tasks at hand. Consequently, divided attention among tasks can cause deterioration in performance of at least one task according to the capacity-sharing theory (Yogeiv-Seligmann, Hausdorff, & Giladi, 2008). The relative change in performance of one or both tasks during dual tasking is termed the

Figure 3. A sample time series graph of the PFC ΔO₂Hb during single and dual PPW tasks.
DTE or dual task interference (Plummer & Eskes, 2015). The already limited attentional resources are known to decline further with age, which increases the DTE on gait and lead to a greater risk of falls during dual tasking (Beauchet et al., 2009; Hsu, Nagamatsu, Davis, & Liu-Ambrose, 2012; Muir-Hunter & Wittwer, 2016). Cognitive impairment can further amplify the impact of limited attention resources by increasing the DTE and worsening physical performance (Montero-Odasso et al., 2009). The DTE can be quantified using the equation below. A positive value from this equation represents improved performance, while a negative value represents a decrement in performance during dual tasking.

$$DTE = \frac{(\text{dual task} - \text{single task})}{\text{single task}} \times 100\%$$ (Plummer & Eskes, 2015)

In previous studies, several researchers have used dual tasking in their protocols by combining various motor and cognitive tasks to evaluate the effects of limited attentional resources. One of the most common findings across dual tasking studies is decrements in cognitive task accuracy and gait performance: increased variability and reduced speed\(^1\) (Hausdorff, Rios, & Edelberg, 2001; Springer et al., 2006; van Iersel, Ribbers, Munneke, Borm, & Rikkert, 2007).

### 1.3.3 Cognitive Tasks and Rationale for Choosing Spelling Backwards

Various cognitive tasks have been used across studies to measure the cortical hemodynamic response ($\Delta O_2 Hb$) resulting from the associated neural activity. The performance of the cognitive task is either compared with a rest/baseline task or a paired dual task involving a motor component such as walking. However, choosing a cognitive task is a complex decision as considerable thought needs to be given to whether it would be an appropriate measure of the cognitive function of interest. Neural activation is task dependent and region specific as different cognitive tasks utilize different mental processes. A systematic review and meta-analysis classified cognitive tasks into categories based on the mental processes that are required to execute them: reaction time, discrimination and decision-making, mental tracking, working memory and verbal fluency tasks (Al-Yahya et al., 2011). Working memory tasks were defined as the tasks that require holding information in mind, while mental tracking tasks were

\(^1\) Velocity and speed are used interchangeably in this thesis.
characterized as those that require manipulating information in addition to holding them in mind (Al-Yahya et al., 2011).

Spelling words backwards was chosen as the cognitive task in this study because it is thought to be challenging. In their systematic review, Al-Yahya et al. (2011) documented that gait is disturbed more during performance of a cognitive task that involves internal interfering factors such as manipulation of information (mental tracking) compared to those that involve external interfering factors (e.g., auditory or visual distraction). Spelling backwards involves holding and manipulating information in mind (i.e., mental tracking); thus, it has an internal interfering factor. Utilizing such a task that requires greater cognitive resources (e.g., attention, working memory and information manipulation) compared to a simple task (e.g., counting forwards) enables one to measure how gait and cognitive performance would be affected due to increased cognitive demands and division of mental resources between tasks. The spelling backwards cognitive task has been used as a measure of attention for several decades as indicated by its inclusion in the Mini-Mental State Examination, which assesses cognitive functions to determine the presence of cognitive impairment. In addition, it has been used previously in studies involving younger adults, the elderly and individuals with concussion (Catena, van Donkelaar, & Chou, 2007; Hollman et al., 2010; Hollman, Kovash, Kubik, & Linbo, 2007).

1.3.4 Gait Velocity and Implications

Gait impairment is commonly observed in the elderly and those with neurological deficits (Pirker & Katzenschlager, 2017). Increase in swing and stride time variability during dual tasking is linked to an increased risk of falls (Hausdorff et al., 2001; Springer et al., 2006). Furthermore, reduction in velocity has been reported during dual tasking in older adults and other patient populations such as those with stroke, Alzheimer’s disease, concussion and Parkinson’s disease and is associated with cognitive impairment (Al-Yahya et al., 2011; Bowen et al., 2001; Catena et al., 2007; Hollman et al., 2007; Lindenberger, Marsiske, & Baltes, 2000; Maquet et al., 2010; Rochester et al., 2005; Sheridan, Solomont, Kowall, & Hausdorff, 2003; Springer et al., 2006; Toulon, Thevenon, Watelain, & Fabre, 2006). In these studies, walking was paired with a cognitive task that involved memorization, digit span (repeating digits forwards), serial subtraction, listening to text, spelling backwards and verbal fluency.
Gait speed has important clinical implications as it is associated with health-related outcomes and can be used to effectively assess functional mobility (Kim, Park, Lee, & Lee, 2016). Since walking involves the use of energy, cognitive and motor control as well as physical strength, it requires the coordination of several organ systems such as circulatory, nervous and musculoskeletal. Therefore, a reduction in gait speed may also indicate impairment of one of these organ systems (Studenski et al., 2011). In addition, gait speed is positively associated with survival (Cesari et al., 2005; Ostir, Kuo, Berges, Markides, & Ottenbacher, 2007). Thus, measurement of gait speed has been suggested as part of regular assessment of patients with COPD. Evaluation of the DTE on gait speed can provide insight into the function and safety of patients with COPD.

1.3.5 Neural Activity in the Dorsolateral Prefrontal Cortex

Dorsolateral PFC (DLPFC) is involved in attentional control and executive functions. Activation in the DLPFC is observed during working memory tasks, attentional control, memory, planning, and performance of dual compared to single tasks (MacDonald, Cohen, Stenger, & Carter, 2000). Studies using neuroimaging modalities such as fMRI and positron emission tomography have reported activation in the DLPFC during tasks that involve cognitive processes such as memory, problem solving and sustained attention; similar findings have been found in studies that used fNIRS (Izzetoglu, Bunce, Onaral, Pourrezaei, & Chance, 2004). The ∆O$_2$Hb and the change in cerebral blood flow observed during performance of tasks are directly proportional and indicate neural activity (Hoshi, Kobayashi, & Tamura, 2001; Leff et al., 2011; Quaresima et al., 2005). Therefore, fNIRS can be effectively used to study the impact of divided attention (Izzetoglu et al., 2005) during dual tasking to determine the neural correlates of cognitive and motor tasks.

1.4 Specific Objectives and Hypotheses

1.4.1 Chapter 2

Objective 1: To compare ∆O$_2$Hb from left and right DLPFC during dual versus single tasks and cognitive versus baseline task between healthy younger and older adults.

Hypothesis 1: DLPFC O$_2$Hb will increase more during dual tasks compared to single tasks and during cognitive versus baseline task. The increase in O$_2$Hb will be greater in older compared to younger adults.
Objective 2: To compare the DTE on cognitive task accuracy and gait velocity during preferred paced and fast paced walking dual tasks between healthy younger and older adults.

Hypothesis 2: Greater decrements in cognitive task accuracy and gait velocity will occur during fast paced walking dual task and in older adults compared to younger adults.

Objective 3: To determine the contribution of age to the DLPFC ΔO₂Hb, and DTE on velocity and on backwards spelling cognitive task accuracy in healthy adults while controlling for potential confounders: sex, cognitive impairment (evaluated using MoCA), number of comorbidities, level of physical activity and SLS duration.

Hypothesis 3: Factors including sex, cognitive impairment (evaluated using MoCA), number of comorbidities, level of physical activity and SLS duration may affect the association between age and outcome variables: DLPFC ΔO₂Hb, and DTE on velocity and on backwards spelling cognitive task accuracy.

1.4.2 Chapter 3

Objective 1: To determine the feasibility of the dual tasking experimental paradigm for patients with COPD using fNIRS.

Hypothesis 1: Patients with COPD will be able to complete the study protocol with minimal to no discomfort, breathlessness, fatigue or pain as the level of physical exertion is low.

Objective 2: To compare ΔO₂Hb from left and right DLPFC during dual versus single tasks and cognitive versus baseline task between healthy older adults and patients with COPD.

Hypothesis 2: DLPFC ΔO₂Hb will increase more during dual tasks compared to single tasks and during cognitive versus baseline task. The increase in O₂Hb will be greater in patients with COPD compared to older adults.

Objective 3: To compare the DTE on cognitive task accuracy and gait velocity during preferred paced and fast paced walking dual tasks between healthy older adults and patients with COPD.

Hypothesis 3: Greater decrements in cognitive task accuracy and gait velocity will occur during fast paced walking dual task and in patients with COPD compared to older adults.
Chapter 2

2 Prefrontal Cortex Activity in Younger and Older Healthy Adults during Dual Task Performance: A Functional Neuroimaging Study

2.1 Abstract

INTRODUCTION: Older age is associated with altered hemodynamics (e.g., changes in oxygenated hemoglobin, ΔO₂Hb) in the dorsolateral prefrontal cortex (DLPFC) that might contribute to motor deficits and an increased risk of falls.

PURPOSE: To compare DLPFC ΔO₂Hb and decrements in cognitive and gait performance between single and dual tasks in healthy younger and older adults. A second aim was to determine the contribution of age, while controlling for confounding factors, to the DLPFC ΔO₂Hb, and dual task effects (DTE) on velocity and backwards spelling (cognitive task [CT]).

METHODS: Participants performed three single tasks: (1) CT; (2) 30m preferred paced walk (PPW); and (3) 30m fast paced walk (FPW). The dual tasks then paired the CT with PPW and FPW. ΔO₂Hb from the left and right DLPFC, backwards spelling accuracy and gait velocity were analyzed.

RESULTS: Healthy younger (n=20) and older (n=20) adults participated. DLPFC O₂Hb increased during FPW+CT versus FPW bilaterally, but only in the right DLPFC during PPW+CT versus PPW in older adults. The ΔO₂Hb did not differ between the left and right DLPFC in either younger or older adults. Furthermore, the negative DTE on velocity was greater during FPW+CT compared to PPW+CT in both younger and older adults. Age was significantly associated with the DTE on velocity during PPW+CT after adjusting for confounders.

CONCLUSIONS: Decrements in CT performance and gait velocity were observed during dual tasks compared to single tasks. Utilization of dual tasking in rehabilitation programs may enhance cognitive-motor performance of the participants.

Keywords: Prefrontal Cortex; Near-Infrared Spectroscopy; Gait; Cognition
2.2 Introduction

Injuries from falls are the leading cause of hospitalization in Canada with an associated financial burden of $2 billion annually, a cost 3.7 times greater in seniors compared to younger adults (Stinchcombe, Kuran, & Powell, 2014). Mobility in the community is a complex task and involves execution of cognitive tasks concurrently (e.g., walking and texting on a cell phone), which usually coincides with the time of falls and injuries that subsequently lead to hospitalization and deaths (Montero-Odasso, Verghese, Beauchet, & Hausdorff, 2012; Oxley et al., 2018); decline in functional gait has been observed as an age-related change in the elderly (Alfieri et al., 2010; Montero-Odasso, Verghese, et al., 2012; Oxley et al., 2018; Seidler et al., 2010). It is estimated that nearly one-third of seniors aged 65 and over worldwide fall at least once a year (Dionyssiotis, 2012). Age associated cognitive decline, manifested as a decline in processing speed, memory, and/or executive functions (Deary et al., 2009; Harada, Natelson Love, & Triebel, 2013; O’Sullivan et al., 2001), is a known risk factor for falls (Camicioli & Majumdar, 2010; Muir, Gopaul, & Odasso, 2012). Determining age-related changes in cognitive functions and their impact on mobility may provide insight to reduce the risk of falls (Liu et al., 2014).

Dual tasking is defined as doing two things at once and the dual task effect (DTE) reflects the change (e.g., decrement) in performance of one or both tasks while dual tasking. It can be calculated by the equation: DTE = [(dual task–single task) ÷ single task] x 100% (Plummer & Eskes, 2015). The DTE commonly occurs when attentional demands of performing two tasks concurrently exceed an individual’s attentional capacity (Al-Yahya et al., 2011) and is more pronounced in individuals with cognitive impairment (Hollman et al., 2007; Montero-Odasso, Muir, & Speechley, 2012; Patel, Lamar, & Bhatt, 2014; Simoni et al., 2013). Since listening to music or talking while walking requires attention, planning and strategizing, deficits in executive functions can result in decrements in gait and subsequently increase the risk of falls (Herman, Mirelman, Giladi, Schweiger, & Hausdorff, 2010; Montero-Odasso, Muir, et al., 2012). Thus, the dual tasking experimental paradigm is effective in evaluating the association between a person’s attentional capacity, mobility and age (Al-Yahya et al., 2011; Huang & Mercer, 2001; Muir-Hunter & Wittwer, 2016; Snijders, Verstappen, Munneke, & Bloem, 2007; Woollacott & Shumway-Cook, 2002).
Cognition involves several domains including attention, memory, language, and executive functions (e.g., decision making, problem solving, planning, multitasking). Tasks that utilize cognitive functions elicit neural activation. Activation in the dorsolateral prefrontal cortex (DLPFC) has been linked to tasks that require attention and working memory, and is involved in motor planning and regulation (Izzetoglu et al., 2004; Kane & Engle, 2002; MacDonald et al., 2000; Ruocco et al., 2014). These cognitive functions are known to decline with age (Murman, 2015). The neurophysiological changes underlying cognitively demanding tasks can be measured using functional near-infrared spectroscopy (fNIRS).

The fNIRS is a non-invasive optical neuroimaging technique that measures relative changes in oxygenated hemoglobin ($\Delta O_2Hb$) concentration. The $\Delta O_2Hb$ data obtained using fNIRS infers changes in neuronal metabolic activity because neural activation increases oxygen utilization. A subsequent increase in blood flow to the active brain area increases $O_2Hb$ (León-Domínguez, 2012). The $\Delta O_2Hb$ during a dual tasking experimental paradigm with a cognitive and a motor component can provide insight into how age-related changes in neuronal activity are associated with cognitive and motor performance.

Therefore, the objectives of this study were (i) to compare $\Delta O_2Hb$ from left and right DLPFC during dual versus single tasks and cognitive versus baseline task between healthy younger and older adults; (ii) to compare the DTE on cognitive task accuracy and gait velocity during preferred paced and fast paced walking dual tasks between the two groups; and (iii) to determine the contribution of age to the DLPFC $\Delta O_2Hb$, and DTE on velocity and on backwards spelling cognitive task accuracy in healthy adults while controlling for potential confounders: sex, cognitive impairment (evaluated using MoCA), number of comorbidities, level of physical activity and SLS duration. It was hypothesized that: (i) DLPFC $O_2Hb$ will increase more during dual tasks compared to single tasks and during cognitive versus baseline task. The increase in $O_2Hb$ will be greater in older compared to younger adults; (ii) greater decrements in cognitive task accuracy and gait velocity will occur during fast paced walking dual task and in older adults compared to younger adults; (iii) factors including sex, cognitive impairment (evaluated using MoCA), number of comorbidities, level of physical activity and SLS duration may affect the association between age and outcome variables.
2.3 Materials and Methods

2.3.1 Participants

Healthy younger (n=20) and older participants (n=20) were recruited through word of mouth, emails and flyers from the University of Toronto, University Health Network associated hospitals and community centers in the downtown area of Toronto, Canada. Equal number of males and females were recruited within each group and these subgroups were matched for age. Inclusion criteria included healthy men and women aged between 18-35 (younger group) and ≥45 years (older group). Individuals with the following characteristics were excluded: smokers; experienced an acute illness during the last 3 months; unstable cardiovascular, neurological or musculoskeletal conditions that interfere with independent ambulation or ability to stand on one leg; consumed oral corticosteroids within the last 3 months and cognitive impairment or lack of English fluency that may interfere with providing informed consent or following study instructions. The study was approved by the University of Toronto’s Research Ethics Board (protocol ID: 33466).

2.3.2 Procedure

Participants were screened with the American College of Sports Medicine (ACSM) questionnaire to determine their eligibility to safely participate in the study (Thompson, Gordon, & Pescatello, 2010). Their height and weight were measured. The dominance of their hand and leg was determined by asking which hand they normally use to write or kick a ball, respectively. The following assessments were then administered: Digit Span, subtest from the Wechsler Adult Intelligence Scale (WAIS) III (Wechsler, 1997), Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), Medication and Comorbidities Questionnaire (Charlson, Pompei, Ales, & MacKenzie, 1987; Deyo, Cherkin, & Ciol, 1992; HajGhanbari, Yamabayashi, Garland, Road, & Reid, 2014) and International Physical Activity Questionnaire (IPAQ) (Craig et al., 2003).

After the assessments were completed, the fNIRS device (FNIR100W-1, wireless fNIR Imager System, BIOPAC) was secured over the participant’s forehead (McKendrick, Mehta, Ayaz, Scheldrup, & Parasuraman, 2017; McKendrick et al., 2016) before they performed the single and dual tasks. DLPFC ΔO₂Hb data were recorded during all subsequent measures. Before and after each single and dual task, the participants completed a baseline task that involved spelling words
forward by reading them from flashcards for 1 minute. The baseline task was chosen based on the data of a pilot study conducted to determine a task that elicited the least neural activity compared to other tasks (eyes closed or crosshair fixation on a computer screen). The following single tasks were performed: (1) preferred paced walk (PPW); (2) fast paced walk (FPW); and (3) spelling backwards cognitive task (CT). Subsequently, changes in $O_2$Hb were measured during dual tasks which involved pairing tasks 1 and 2 with the CT (i.e., PPW+CT, FPW+CT). All single tasks were randomly ordered; thereafter, all dual tasks were randomly ordered (Figure 4). Furthermore, blood pressure (BP), heart rate (HR) and oxygen saturation via pulse oximetry ($SpO_2$) were measured before the first single task, after the last single task, and after the last dual task.

![Figure 4](image)

**Figure 4.** Single and dual tasks administered. All the single tasks were randomly ordered. Then dual tasks were randomly ordered. Each task preceded by a one minute baseline period.

### 2.3.3 Neuropsychological and Physical Activity Assessment

The following assessments were used to characterize cognitive function and physical activity of the study groups.

1. **Digit Span** includes Digit Span Forward and Digit Span Backward. During the Digit Span Forward, an investigator recited shorter (2), then longer (up to 5 digits) sequences of digits, one by one, that the participant was instructed to recall in the same order. Sattler and Ryan (2009) have reported that Digit Span Forward test is an assessment of attention, auditory short-term memory, and auditory sequential processing. During the Digit Span
Backward, the participants were asked to recall a different set of recited sequences in the reverse order. This test is a measure of working memory and assesses an individual’s ability to hold and manipulate information before responding, in addition to the processes involved in Digit Span Forward (Sattler & Ryan, 2009). Each component was administered up to 5 digit long sequences or until the participant was unable to recall two sequences with the same number of digits. This was administered to obtain some insight into the participant’s attention and working memory abilities to complete the CT involving spelling 5 letter words backwards.

2. **Montreal Cognitive Assessment (MoCA)** is a valid and reliable tool to assess cognitive dysfunction in various populations (Gill, Freshman, Blender, & Ravina, 2008; Hoops et al., 2009). It evaluates attention and concentration, executive functions, memory, language, visuocstructional skills, conceptual thinking, calculations, and orientation (Mast & Gerstenecker, 2010; Nasreddine et al., 2005). A score below 26 out of 30 in MoCA suggests mild cognitive impairment.

3. **Medication and Comorbidities Questionnaire** was used to document participants’ current medications and health conditions related to mood, eyes, cancer and various body systems: cardiovascular, musculoskeletal, endocrine, nervous, digestive, immune, renal and respiratory. The number of comorbidities was included as a potential confounding factor in the linear regression model when determining the association between age and outcome variables: DLPFC ∆O$_2$Hb and DTE on CT accuracy and gait velocity.

4. **International Physical Activity Questionnaire (IPAQ)** long form utilized in this study contains 27 questions that pertain to physical activity during various tasks, intensities and settings in the past 7 days: at work, at home (inside and the yard), to get from place to place and during recreational activities. It has been validated in several languages, countries and various population subgroups (Craig et al., 2003; Hagströmer, Oja, & Sjöström, 2006; Wanner et al., 2016). Participants were assigned an overall physical activity level of low, moderate or high after converting their responses to Metabolic Equivalent Task minutes (MET-min) per week. The level of physical activity was also included as a potential confounder in the linear regression model when determining the association between age and outcome variables.
2.3.4 Experimental Tasks

1. **Cognitive Task:** The CT involved spelling 5 letter words backwards from a list of 100 unique words for 1 minute. The spelling accuracy and number of words attempted were recorded. Spelling words backwards is thought to be a challenging CT (Hollman et al., 2010, 2007).

2. **Walking Tasks:** The walking tasks consisted of walking at a preferred and fast pace, each individually and paired with the CT. During each of these four tasks, the participants walked a distance of approximately 30 meters (m) that comprised 6 passes over a 5x0.88m pressure sensitive Zeno mat containing a grid of 13,824 sensors. Participants were instructed to walk as fast as they could, while ensuring their safety during the fast paced walk tasks. During the dual walking tasks, an investigator continued to read aloud 5 letter words and recorded the accuracy of backwards spelling until the participant completed 6 passes on the mat. Gait velocity was calculated using the ProtoKinetics Movement Analysis Software.

2.3.5 Functional Near-Infrared Spectroscopy: Data Collection and Processing

The fNIRS device (FNIR100W-1, wireless fNIR Imager System, BIOPAC) with 4 optodes was secured over the forehead (McKendrick et al., 2017, 2016) and the center of each sensor pad was vertically aligned with the participants’ iris. The optodes over the left and right forehead approximately target the dorsal PFC (Figure 5). Light intensity data were obtained at two wavelengths (730nm and 850nm), at a sampling frequency of 4Hz, using the Cognitive Optical

![Figure 5. Visualization of the fNIRS probes and their position over the forehead. Each probe contains 2 channels (i.e., a total of 4 channels) with an inter-optode distance of 2.5cm.](image-url)
Brain Imaging (COBI) Studio (fNIR Devices, LLC). LED current and the detector gain settings were adjusted for each participant to prevent very low or saturated light signals. The light intensity data were processed in fnirSoft. A low-pass, finite impulse response, filter with a hamming order of 57 and a cutoff frequency of 0.05 was applied to attenuate the physiological artifacts of respiration and pulse (Ayaz et al., 2011; Izzetoglu, Bunce, Izzetoglu, Onaral, & Pourrezaei, 2007). The data were further inspected for motion artifacts through the Sliding Motion Artifact Rejection (SMAR) algorithm (Ayaz, Izzetoglu, Shewokis, & Onaral, 2010), while some artifacts were identified and manually removed in fnirSoft through visual observation.

Time markers placed at the onset and end of each task were used to extract data blocks of the processed light data. Subsequently, relative ΔO₂Hb were calculated using the modified Beer-Lambert law. The first 5 seconds of each task were used as a local baseline during processing. Data from the left and right DLPFC were analyzed.

### 2.3.6 Statistical Analysis of Neuroimaging and Gait Data

Neuroimaging data (DLPFC ΔO₂Hb) acquired via the fNIRS device and processed in fnirSoft were compared between tasks and groups as well as between left and right DLPFC using two-way repeated measures analysis of variance (ANOVA). To compare the differences in DLPFC ΔO₂Hb during the CT and the baseline task between the two groups, independent t-tests were performed. Furthermore, the DTEs were calculated using the following equation: DTE = [(dual task–single task) ÷ single task] x 100% (Plummer & Eskes, 2015). The DTE on the accuracy of cognitive and physical tasks was compared between younger and older adults and the PPW+CT and FPW+CT using two-way repeated measures ANOVA. Bonferroni correction was applied to adjust for multiple comparisons and effect sizes (ηp²) of the main findings were calculated.

Multiple linear regression analysis was performed to determine the contribution of age to the outcome variables - DLPFC ΔO₂Hb and DTE on CT accuracy and gait velocity - for the samples of younger and older adults while adjusting for confounding variables. Potential confounding variables adjusted in the analyses were sex, MoCA scores, number of comorbidities, IPAQ data as well as SLS duration. Adjusted regression coefficients, standard errors, and p-values of the significant associations were reported. Post hoc power analyses were performed with a sample size of 40 and α₂ < 0.05 to determine the effect size (f²) and power of each outcome variable.
2.4 Results

2.4.1 Participants’ Characteristics

Twenty healthy younger and twenty healthy older adults participated in the study (27±4 and 64±11 years, respectively [p<.0001]). All were able to recall at least one forward 5 digit sequence; however, only about half of the participants could recall the digit span backward task at the level of 5 digits. MoCA scores and the physical activity levels of the two groups did not differ (p>.05), but SLS duration of older adults was shorter compared to younger adults (p<.001) (Table 2). Older and younger adults did not differ in their number of comorbidities and medications (p>.05).

Table 2. Characteristics of younger and older adults. Mean (SD) reported unless stated otherwise.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Younger (n=20)</th>
<th>Healthy Older (n=20)</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n of M:F)</td>
<td>10M:10F</td>
<td>10M:10F</td>
<td>1.000</td>
</tr>
<tr>
<td>Age (years)</td>
<td>27.6 (3.5)</td>
<td>63.5 (11.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.7 (0.1)</td>
<td>1.7 (0.1)</td>
<td>.396</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.3 (15.8)</td>
<td>71.5 (16.2)</td>
<td>.665</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.1 (3.8)</td>
<td>25.8 (4.3)</td>
<td>.200</td>
</tr>
<tr>
<td>Handedness (n)</td>
<td>20R</td>
<td>19R, 1L</td>
<td>.311</td>
</tr>
<tr>
<td>Dominant Leg (n)</td>
<td>18R, 2L</td>
<td>14R, 6L</td>
<td>.114</td>
</tr>
<tr>
<td>Digit Span Forward‡</td>
<td>n (%)</td>
<td>20 (100)</td>
<td>-</td>
</tr>
<tr>
<td>Digit Span Backward‡</td>
<td>n (%)</td>
<td>11 (55)</td>
<td>1.000</td>
</tr>
<tr>
<td>MoCA</td>
<td>27.4 (2.4); 20-30</td>
<td>26.1 (2.8); 21-30</td>
<td>.126</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>0.6 (1.1); 0-4</td>
<td>1.6 (2.5); 0-10</td>
<td>.108</td>
</tr>
<tr>
<td>Medications</td>
<td>0.3 (0.8); 0-3</td>
<td>0.8 (1.2); 0-5</td>
<td>.173</td>
</tr>
<tr>
<td>IPAQ - Activity Level (n, MET-min/week)</td>
<td>High (n)</td>
<td>8,6969</td>
<td>11,8449</td>
</tr>
<tr>
<td></td>
<td>Moderate (n)</td>
<td>11,1639</td>
<td>8,1398</td>
</tr>
<tr>
<td></td>
<td>Low (n)</td>
<td>1,198</td>
<td>1,243</td>
</tr>
<tr>
<td>SLS Duration (s)</td>
<td>109.1 (89.9)</td>
<td>30.9 (32.4)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; F, female; FPW, fast paced walk; IPAQ, International Physical Activity Questionnaire; L, left; M, male; MET, metabolic equivalent task; MoCA, Montreal Cognitive Assessment; PPW, preferred paced walk; R, right; SLS, single leg stance; † p values for comparisons between groups; ‡ correctly recalled 5 digits sequence(s).
2.4.2 Hemodynamic Response in the Prefrontal Cortex

The $\Delta O_2$Hb in the left and right DLPFC during the baseline, single and dual tasks are shown in Figure 6. Between groups analysis of the left DLPFC $\Delta O_2$Hb during PPW, PPW+CT, FPW and FPW+CT in younger and older adults indicated a significant main effect of tasks (Table 3). Post hoc analysis showed that $\Delta O_2$Hb was significantly higher during FPW+CT compared to FPW in older adults ($p=.036$) in the left DLPFC. Similarly, significant main effect of tasks was found in the right DLPFC (Table 3), which showed that $\Delta O_2$Hb was significantly higher during FPW+CT compared to FPW ($p=.005$) and PPW+CT compared to PPW ($p=.020$) in older adults.

Comparison of the changes in $O_2$Hb from baseline to CT, PPW to PPW+CT and FPW to FPW+CT between the left and right DLPFC did not show significant main effects for PFC regions*tasks interaction, PFC regions or tasks in younger and older adults (Table 3).

![Figure 6](image.png)

**Figure 6.** DLPFC $\Delta O_2$Hb during the baseline, single and dual tasks in healthy younger and older adults. In older adults, $O_2$Hb significantly increased during FPW+CT and PPW+CT in the right DLPFC (A) compared to FPW and PPW, respectively, and during FPW+CT compared to FPW in the left DLPFC (B). * indicates statistical significance at $p<.05$. 
Table 3. Summary table of ANOVAs between groups (younger and older adults), tasks and PFC regions.

<table>
<thead>
<tr>
<th>Source</th>
<th>Type III SSE</th>
<th>Degrees of Freedom</th>
<th>Mean Square</th>
<th>F</th>
<th>p</th>
<th>ηp²</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left DLPFC ΔO₂Hb during single and dual walking tasks in younger and older adults</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†</td>
<td>7.98</td>
<td>2.66</td>
<td>2.99</td>
<td>7.84</td>
<td>&lt;.001</td>
<td>0.171</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>0.76</td>
<td>2.66</td>
<td>0.29</td>
<td>0.75</td>
<td>.511</td>
<td>0.019</td>
</tr>
<tr>
<td>Error</td>
<td>38.67</td>
<td>101.23</td>
<td>0.38</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>47.41</td>
<td>106.55</td>
<td>3.66</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Right DLPFC ΔO₂Hb during single and dual walking tasks in younger and older adults</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†</td>
<td>7.99</td>
<td>2.81</td>
<td>2.85</td>
<td>9.82</td>
<td>&lt;.001</td>
<td>0.205</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>0.25</td>
<td>2.81</td>
<td>0.09</td>
<td>0.31</td>
<td>.803</td>
<td>0.008</td>
</tr>
<tr>
<td>Error</td>
<td>30.90</td>
<td>106.62</td>
<td>0.29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>39.14</td>
<td>112.24</td>
<td>3.23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>In younger adults: left versus right DLPFC ΔO₂Hb from baseline to CT, PPW to PPW+CT and FPW to FPW+CT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions</td>
<td>0.34</td>
<td>1</td>
<td>0.34</td>
<td>1.62</td>
<td>.219</td>
<td>0.078</td>
</tr>
<tr>
<td>Error</td>
<td>3.96</td>
<td>19</td>
<td>0.21</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks††</td>
<td>2.31</td>
<td>2</td>
<td>1.16</td>
<td>0.68</td>
<td>.514</td>
<td>0.034</td>
</tr>
<tr>
<td>Residual</td>
<td>64.79</td>
<td>38</td>
<td>1.71</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions × Tasks</td>
<td>0.26</td>
<td>2</td>
<td>0.13</td>
<td>0.56</td>
<td>.577</td>
<td>0.029</td>
</tr>
<tr>
<td>Error</td>
<td>8.86</td>
<td>38</td>
<td>0.23</td>
<td></td>
<td></td>
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<tr>
<td>Total</td>
<td>80.52</td>
<td>100</td>
<td>3.78</td>
<td></td>
<td></td>
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<tr>
<td><strong>In older adults: left versus right DLPFC ΔO₂Hb from baseline to CT, PPW to PPW+CT and FPW to FPW+CT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions</td>
<td>0.03</td>
<td>1</td>
<td>0.03</td>
<td>0.08</td>
<td>.786</td>
<td>0.004</td>
</tr>
<tr>
<td>Error</td>
<td>8.51</td>
<td>19</td>
<td>0.45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks††</td>
<td>2.33</td>
<td>2</td>
<td>1.17</td>
<td>2.26</td>
<td>.118</td>
<td>0.106</td>
</tr>
<tr>
<td>Residual</td>
<td>19.61</td>
<td>38</td>
<td>0.52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions × Tasks</td>
<td>0.95</td>
<td>1.27</td>
<td>0.75</td>
<td>2.21</td>
<td>.146</td>
<td>0.104</td>
</tr>
<tr>
<td>Error</td>
<td>8.16</td>
<td>24.04</td>
<td>0.34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>39.59</td>
<td>85.31</td>
<td>3.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DTE on CT accuracy between younger and older adults</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†††</td>
<td>1297.98</td>
<td>1</td>
<td>1297.98</td>
<td>3.55</td>
<td>.067</td>
<td>0.085</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>55.28</td>
<td>1</td>
<td>55.28</td>
<td>0.15</td>
<td>.700</td>
<td>0.004</td>
</tr>
<tr>
<td>Error</td>
<td>13893.59</td>
<td>38</td>
<td>365.62</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15246.85</td>
<td>40</td>
<td>1718.88</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DTE on gait velocity between younger and older adults</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†††</td>
<td>1887.99</td>
<td>1</td>
<td>1887.99</td>
<td>11.76</td>
<td>.001</td>
<td>0.236</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>13.56</td>
<td>1</td>
<td>13.56</td>
<td>0.08</td>
<td>.773</td>
<td>0.002</td>
</tr>
<tr>
<td>Error</td>
<td>6099.20</td>
<td>38</td>
<td>160.51</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>8000.75</td>
<td>40</td>
<td>2062.06</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ηp², Partial Eta Squared; CT, cognitive task; DLPFC, dorsolateral prefrontal cortex; DTE, dual task effect; FPW, fast paced walk; PPW, preferred paced walk; SSE, sum of squares.
†Tasks include PPW, PPW+CT, FPW and FPW+CT
††Tasks include baseline to CT, PPW to PPW+CT and FPW to FPW+CT
††† Tasks include: PPW+CT and FPW+CT
Time series traces depicting an increase in $O_2$Hb in the left and right DLPFC during the baseline and CT are shown in Figure 7. The mean $\Delta O_2$Hb during the baseline and CT were similar in both younger and older adults (Figure 6). Thus, the difference in the $\Delta O_2$Hb from baseline to CT was not significant between the two groups in both the left ($p=.207$) and the right ($p=.351$) DLPFC.

![Figure 7](image)

2.4.3 Dual Task Effect on Gait Velocity and Cognitive Task Accuracy

Participants in both younger and older groups exhibited decrements in gait velocity during dual tasks. Older adults tended to have greater decrements in velocity compared to younger adults (Table 4). Between groups and tasks analysis showed a significant main effect of tasks (Table 3) indicating greater negative DTE on velocity during FPW+CT compared to PPW+CT in both the younger (-1 versus -11%; $p=.022$) and older (-12 versus -21%; $p=.029$) adults.

Participants in both groups attempted spelling similar number of words during each of the three tasks: CT, PPW+CT and FPW+CT (Table 4). A tendency towards lower CT accuracy was observed during dual tasks compared to single tasks in both younger and older adults (Table 4). Between the dual tasks, the DTE on spelling accuracy showed a tendency towards greater decrease during FPW+CT compared to PPW+CT in the younger (-16.9±21.4% vs. -10.5±18.4%) and older (-20.1±22.2% vs. -10.4±30.2%) adults. However, no significant main effect was found for DTE on CT accuracy (Table 3).
Table 4. Backwards spelling accuracy and gait velocity of healthy younger and older adults. Mean (SD) are reported.

<table>
<thead>
<tr>
<th>Velocity (m/min)</th>
<th>Healthy Younger (n=20)</th>
<th>Healthy Older (n=20)</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPW</td>
<td>72.8 (9.3)</td>
<td>77.5 (7.9)</td>
<td>.089</td>
</tr>
<tr>
<td>PPW+CT</td>
<td>71.9 (10.4)</td>
<td>68.4 (11.2)</td>
<td>.312</td>
</tr>
<tr>
<td>FPW</td>
<td>109.2 (14.4)</td>
<td>102.4 (15.8)</td>
<td>.165</td>
</tr>
<tr>
<td>FPW+CT</td>
<td>96.6 (17.7)</td>
<td>80.6 (12.8)</td>
<td>.002</td>
</tr>
<tr>
<td>DTE on Velocity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPW+CT</td>
<td>-0.8 (10.6)</td>
<td>-11.3 (14.5)</td>
<td>.012</td>
</tr>
<tr>
<td>FPW+CT</td>
<td>-11.7 (9.4)*</td>
<td>-20.6 (12.6)*</td>
<td>.016</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Accuracy (%)</th>
<th>Words Attempted (n)</th>
<th>CT</th>
<th>PPW+CT</th>
<th>94.1 (8.5)</th>
<th>87.2 (18.3)</th>
<th>.139</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>11 (3)</td>
<td>10 (2)</td>
<td>.074</td>
</tr>
<tr>
<td>CT Accuracy</td>
<td></td>
<td>PPW+CT</td>
<td>85.0 (20.3)</td>
<td>79.4 (25.1)</td>
<td>.437</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>7 (2)</td>
<td>7 (1)</td>
<td>.535</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>FPW+CT</td>
<td>79.1 (23.4)</td>
<td>69.1 (24.4)</td>
<td>.191</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6 (2)</td>
<td>6 (1)</td>
<td>.339</td>
<td></td>
</tr>
<tr>
<td>DTE on CT Accuracy</td>
<td></td>
<td>PPW+CT</td>
<td>-10.5 (18.4)</td>
<td>-10.4 (30.2)</td>
<td>.990</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>FPW+CT</td>
<td>-16.9 (21.4)</td>
<td>-20.1 (22.2)</td>
<td>.643</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CT, cognitive task; DTE, dual task effect; FPW, fast paced walk; PPW, preferred paced walk; † p values for comparisons between groups.

2.4.4 Effect of Age on Outcome Variables

Simple linear regression was performed to determine the association of age with DLPFC ∆O2Hb, DTE on CT accuracy and gait velocity. Results indicated that age (F(1,38)=9.92, p=.003) and number of comorbidities (F(1,38)=4.85, p=.034) were significantly associated with DTE on velocity during PPW+CT. Moreover, age (F(1,38)=9.57, p=.004), MoCA scores (F(1,38)=8.86, p=.005) and number of comorbidities (F(1,38)=5.52, p=.024) were associated with FPW+CT. After adjusting for confounding variables, age was still significantly associated with DTE on velocity during PPW+CT (F(2,37)=6.05, p=.005). Table 5 outlines the regression coefficient of
each independent variable included in the model for which the overall regression model was statistically significant.

**Table 5.** Adjusted regression coefficients for each of the independent variables significantly associated with the dependent variables in healthy adults.

<table>
<thead>
<tr>
<th>Outcome variables</th>
<th>Independent variables</th>
<th>Adjusted regression coefficient</th>
<th>Standard error</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTE on Velocity during PPW+CT*</td>
<td>Age</td>
<td>-0.263</td>
<td>0.103</td>
<td>.015</td>
</tr>
<tr>
<td></td>
<td>Comorbidities</td>
<td>-1.461</td>
<td>1.049</td>
<td>.172</td>
</tr>
<tr>
<td>DTE on Velocity during FPW+CT*</td>
<td>Age</td>
<td>-0.156</td>
<td>0.094</td>
<td>.104</td>
</tr>
<tr>
<td></td>
<td>MoCA</td>
<td>1.245</td>
<td>0.677</td>
<td>.074</td>
</tr>
<tr>
<td></td>
<td>Comorbidities</td>
<td>-1.276</td>
<td>0.887</td>
<td>.159</td>
</tr>
</tbody>
</table>

Abbreviations: CT, cognitive task; DTE, dual task effect; FPW, fast paced walk; PPW, preferred paced walk. * indicates that the regression model is statistically significant at p<.05.

The adjusted regression coefficients from the multiple regression model used in the calculation of the post hoc power analysis have been stated in Table 6 along with the calculated power. Age was not significantly associated with the right or left DLPFC ΔO₂Hb or DTE on CT accuracy during PPW+CT or FPW+CT; thus, their values are not included in the tables.

**Table 6.** Post hoc power analyses for the outcome variables in healthy adults.

<table>
<thead>
<tr>
<th>Outcome variables</th>
<th>No. of Predictors</th>
<th>Effect Size</th>
<th>Power</th>
<th>Adjusted R²</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTE on Velocity during PPW+CT</td>
<td>2††</td>
<td>0.33</td>
<td>0.88</td>
<td>0.246</td>
</tr>
<tr>
<td>DTE on Velocity during FPW+CT</td>
<td>3†</td>
<td>0.46</td>
<td>0.94</td>
<td>0.315</td>
</tr>
</tbody>
</table>

Abbreviations: CT, cognitive task; DTE, dual task effect; FPW, fast paced walk; PPW, preferred paced walk. † Age, MoCA and number of comorbidities; †† Age and number of comorbidities.

The mean arterial BP (MAP), HR and SpO₂ (Table 7) increased during dual tasks when compared to the baseline measures (before single tasks) in healthy younger adults: MAP
(p<.001), HR (p<.001) and SpO₂ (p=.003). Similarly, HR was higher (p=.004) during dual tasks compared to baseline values in healthy older adults. Although participants in both groups had similar HR at baseline, younger adults had significantly higher HR compared to the older adults during dual tasks.

Table 7. Vital signs of younger and older adults during the protocol. Mean (SD) are reported.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Younger</th>
<th>Healthy Older</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAP (mm Hg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>82.5 (10.5)</td>
<td>96.6 (12.3)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>After single tasks</td>
<td>86.6 (11.9)†</td>
<td>100.1 (14.1)</td>
<td>.001</td>
</tr>
<tr>
<td>After dual tasks</td>
<td>88.8 (10.6)†</td>
<td>99.3 (14.5)</td>
<td>.008</td>
</tr>
<tr>
<td><strong>HR (bpm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>68.9 (10.5)</td>
<td>67.8 (9.0)</td>
<td>.724</td>
</tr>
<tr>
<td>After single tasks</td>
<td>76.1 (7.7)†</td>
<td>71.9 (8.0)†</td>
<td>.104</td>
</tr>
<tr>
<td>After dual tasks</td>
<td>78.7 (7.6)†</td>
<td>71.9 (8.4)†</td>
<td>.010</td>
</tr>
<tr>
<td><strong>SpO₂ (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>97.0 (1.2)</td>
<td>95.2 (3.2)</td>
<td>.026</td>
</tr>
<tr>
<td>After single tasks</td>
<td>96.5 (4.2)</td>
<td>96.2 (1.6)</td>
<td>.769</td>
</tr>
<tr>
<td>After dual tasks</td>
<td>97.7 (1.1)†</td>
<td>96.1 (1.6)</td>
<td>.001</td>
</tr>
</tbody>
</table>

Abbreviations: bpm, beats per minute; HR, heart rate; MAP, mean arterial pressure; SD, standard deviation; SpO₂, peripheral capillary oxygen saturation measured by pulse oximetry; * indicates differences between groups; † indicates within group differences from baseline at p<.005.

2.5 Discussion

2.5.1 Summary of Findings

The unique findings of this study were that the O₂Hb increased in the left and right DLPFC during FPW+CT compared to FPW and increased in the right DLPFC during PPW+CT compared to PPW in older adults. These data imply that neural activity increased in left and right DLPFC during the FPW dual task and in the right DLPFC during PPW dual task in older adults. In contrast, neural activity did not change in single versus dual tasks in younger adults. Furthermore, regression analysis showed that older age was associated with DTE on velocity during PPW+CT after adjusting for the potential confounder: number of comorbidities. The DTE on the accuracy of backwards spelling demonstrated negative non-significant trends (p=.067), which were larger (more inaccuracies) during FPW+CT than PPW+CT. Of relevance, HR and MAP did not differ between single and dual tasks in older adults, which provides corroborating
support that the increased O$_2$Hb was due to an increase in neural activity and not due to a greater systemic cardiovascular response during the dual versus single tasks.

2.5.2 Prefrontal Cortex $\Delta$O$_2$Hb in Younger and Older Adults

Cerebral flow is altered in the elderly compared to younger adults (Schroeter et al., 2003) and is associated with gait speed (Harada et al., 2009). The increase in PFC O$_2$Hb during a cognitively demanding task is linked to an increase in cerebral blood flow (Fox & Raichle, 1986; Fox, Raichle, Mintun, & Dence, 1988; Heeger & Ress, 2002). In this study, O$_2$Hb increased in the left and right DLPFC during FPW+CT compared to FPW and in the right DLPFC during PPW+CT compared to PPW in older adults. This data may suggest that performance of dual tasks requires greater cognitive resources compared to single tasks in older adults. The increased DLPFC activity during dual tasks especially fast walking might be a result of greater intentional movement control and preparation for the upcoming sequential gait steps (Lau, Rogers, Haggard, & Passingham, 2004; Malouin, Richards, Jackson, Dumas, & Doyon, 2003; Pochon et al., 2001). Higher $\Delta$O$_2$Hb during FPW+CT compared to FPW may also suggest that older adults require more cognitive resources for goal directed actions (e.g., to walk at a high speed) (Frith, 2000; Harada et al., 2009). Malouin et al. (2003) reported that locomotor tasks with increasing cognitive load result in progressive activation of higher brain centers (e.g., DLPFC), which may have led to higher activation during the complex fast walking dual task.

In a review, Cabeza and Nyberg (2000) reported that neural activity in the left PFC increases in tasks that involve divided attention (e.g., dual tasking), semantic memory retrieval and language (e.g., generation of words) (Gabrieli, Poldrack, & Desmond, 1998; Sandrini, Cappa, Rossi, Rossini, & Miniussi, 2003), while tasks that involve sustained attention activate the right PFC. In addition, tasks that involve manipulating the information in the working memory (Petrides, 1995) are linked to bilateral PFC activation. The changes in O$_2$Hb in the present study corroborate the findings reported by Cabeza and Nyberg (2000) and may indicate utilization of working memory, language and attention during walking and spelling backwards.

Furthermore, in this study, the $\Delta$O$_2$Hb from baseline to CT was not significant between groups in either the left or right DLPFC. In contrast to this finding, Schroeter et al. (2003) found that older adults had a significantly higher PFC $\Delta$O$_2$Hb during a calculation CT. Furthermore, Kwee and Nakada (2003) reported an age-related decrease in blood flow response in the DLPFC in
response to CT. A high mean ∆O₂Hb during the baseline task may explain the lack of significant
difference from baseline to CT between the two groups in this study.

2.5.3 Motor and Cognitive Tasks' Performance

In this study, greater decrements in velocity were observed during FPW+CT compared to
PPW+CT in older adults. Furthermore, decline in velocity during PPW+CT was also found to be
positively correlated with age. The results of a meta-analysis conducted by Al-Yahya et al.
(2011) attribute the decline in gait speed to age and, thus, corroborate the finding of this study.
The greater decline in velocity and a trend towards greater decrements in CT performance during
FPW+CT might be due to the fact that greater cognitive demands are required to maintain
one of the largest age-related changes in the brain is observed in the PFC including a reduction in
the gray matter, in addition to reduced attentional control. Diversion of these cognitive resources
from the more demanding task of maintaining balance during FPW+CT may explain the greater
sacrifice in gait compared to CT performance. This reduced walking speed has been linked to an
increased risk of falls especially in older adults (Hong et al., 2016; Nemanich et al., 2013).

The DTE on spelling backwards accuracy during PPW+CT and FPW+CT was not different
between the tasks or groups. On the contrary, negative DTE on CT accuracy has been reported in
older compared to younger adults during performance of digit backwards test, serial subtraction
by 3 and 7, and number selecting task on smart phone (Brustio et al., 2017; Moraes et al., 2011;
Papegaaij et al., 2017; Takeuchi, Mori, Suzukamo, Tanaka, & Izumi, 2016). However, the higher
mean age of the older participants (low 70s) in these studies, compared to the present study
(mean age: 63.5 years), may help explain the differences. In this study, the lack of significant
DTE on backwards spelling accuracy may be attributed to the fact that the participants met the
challenge of this demanding task. Furthermore, the posture first strategy, which states that
individuals prioritize gait and balance, while sacrificing performance on the CT might also
explain our findings of a trend towards more errors in backwards spelling CT during dual tasks
(Bloem, Grimbergen, van Dijk, & Munneke, 2006).

Between group differences were not observed in this study. Lack of significant impact of the
groups on DLPFC ∆O₂Hb, and DTE on gait velocity and CT accuracy might be attributed to the
similar level of physical fitness and MoCA scores, and inclusion of adults with a mean age of
63.5 years rather than an older age group. Similar MoCA scores indicate a lack of difference in the level of cognitive impairment between the two groups. A sample of older, more cognitively impaired individuals might lead to significant differences between groups.

2.5.4 Limitations

The methodology of this study includes some limitations. The fNIRS device provides data on relative, rather than absolute ∆O\textsubscript{2}Hb. Therefore, absolute concentrations of hemoglobin chromophores could be quantified and compared between healthy younger and older adults. In addition, DLPFC ∆O\textsubscript{2}Hb measurements are dependent on the path length of infrared light from the fNIRS probe to the cortex. This distance is impacted by anatomical differences such as age-related cortical atrophy and skull thickness, which were not measured in this study.

2.5.5 Future Directions

Future studies may utilize fNIRS devices with measurement capabilities that span a greater surface area of the head. This will provide a more in-depth understanding of the neural regions involved during execution of certain cognitive and motor tasks. In addition, a greater coverage of the brain areas might also provide insight into the neural region recruitment strategies in the cognitively impaired (e.g., patients with COPD or Alzheimer’s disease). Moreover, a more challenging CT might produce a significant DTE on its accuracy.

2.5.6 Conclusions

The ∆O\textsubscript{2}Hb was higher during FPW+CT compared to FPW in the left and right DLPFC as well as during PPW+CT compared to PPW in the right DLPFC of healthy older adults. In addition, greater decrements in gait velocity were found during FPW+CT compared to PPW+CT in both younger and older adults. The reduced performance and higher ∆O\textsubscript{2}Hb may point to the limited attentional resources and impact of aging. Understanding the neural correlates of gait and cognitive performance may guide the development of rehabilitation interventions with a cognitive-motor component for improving mobility and reducing risk of falls in the elderly and other patient populations with gait and cognitive deficits.

**Declarations of interest:** none
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Chapter 3

3 Influence of Cognitive-Motor Single and Dual Tasks on Prefrontal Cortex Activity in Patients with Chronic Obstructive Pulmonary Disease: A Pilot Study

3.1 Abstract

INTRODUCTION: Cognitive impairment and motor deficits are commonly reported in patients with chronic obstructive pulmonary disease (COPD), but the link between them has not been studied. Proxy measurement of neural activity using functional near-infrared spectroscopy (fNIRS) during dual tasking can provide insight into this link.

PURPOSE: The first aim was to determine the feasibility of dual tasking for patients with COPD. A second aim was to compare changes in dorsolateral prefrontal cortex (DLPFC) oxygenated hemoglobin (ΔO$_2$Hb) and decrements in cognitive and motor performance between healthy older adults and patients with COPD.

METHODS: All participants performed the following single tasks: (1) backwards spelling as the cognitive task (CT); (2) 30m preferred paced walk (PPW); and (3) 30m fast paced walk (FPW). The dual tasks then paired CT with each of PPW and FPW. The DLPFC ΔO$_2$Hb data, as a marker of neural activation, were collected using fNIRS and processed in fnirSoft to attenuate physiological artifacts (respirations and heart rate) and motion artifacts. The ΔO$_2$Hb from the left and right DLPFC were calculated using the modified Beer-Lambert law. Gait velocity was measured using a 5*0.88m pressure sensitive mat (contains 13,824 pressure sensors) and processed using the ProtoKinetics Movement Analysis Software.

RESULTS: Twenty healthy older adults (10M:10F) with a mean age of 63.5±11.3 years and eight patients with COPD (4M:4F) with a mean age of 71.0±9.2 participated. All participants completed the 1.5-hour long study with ease demonstrating feasibility of the protocol. The ΔO$_2$Hb was found to be higher during FPW+CT compared to FPW in the left DLPFC in older adults. However, no significant differences were found in DLPFC ΔO$_2$Hb between the baseline and CT in either group. Velocity decreased more during FPW+CT compared to PPW+CT in older adults and a trend in the same direction was observed in patients with COPD.
CONCLUSIONS: The dual tasking protocol is feasible for patients with COPD. Reduction in velocity and increased DLPFC $O_2$Hb during dual tasking indicated dual task interference pointing to greater mental processing demands compared to single tasks.

Keywords: Chronic Obstructive Pulmonary Disease; Prefrontal Cortex; Near-Infrared Spectroscopy; Gait; Cognition
3.2 Introduction

Chronic Obstructive Pulmonary Disease (COPD) is the fourth leading cause of death in Canada (Dang-Tan et al., 2015) and is expected to be the third, globally, in 2030 (World Health Organization, 2004). Although, smoking is the main risk factor, several other factors also contribute to the development of COPD. Some contributing factors include indoor and outdoor pollution, an individual’s sex and genetic factors. Women are more susceptible to developing COPD from smoking compared to men. Moreover, the deficiency of alpha-1 antitrypsin, a protein known to provide protection against the damage from anti-inflammatory enzymes (e.g., neutrophil-elastase), increases susceptibility to developing COPD (American Thoracic Society, 2017). Ultimately, inflamed, narrowed airways and alveolar damage lead to airflow limitation and impaired gas exchange causing hypoxemia and dyspnea, the most characteristic symptom of COPD (GOLD, 2018).

Cognitive impairment and motor dysfunction are commonly reported in people living with COPD and may, in part, be attributed to hypoxemia and structural changes in the brain (Anderson & Arciniegas, 2010; Dodd et al., 2010; Grant et al., 1987; Villeneuve et al., 2012; Wüst & Degens, 2007). Neural tissue is highly sensitive to changes in oxygen concentrations. Therefore, reduction in oxygen can cause neural damage through an increase in oxidative stress leading to cognitive deficits manifested as a decline in memory and attention (Borson, 2010; Torres-Sánchez et al., 2015). In addition, anaerobic metabolism due to hypoxemia can cause muscle wasting and lower limb weakness (Butcher et al., 2004; Wüst & Degens, 2007) that can lead to reduced mobility, slower walking speed (Nantsupawat, Lane, Siangpraipunt, Gadwala, & Nugent, 2015) and an increased risk of falls (Roig, Eng, MacIntyre, Road, FitzGerald, et al., 2011; Roig, Eng, Road, & Reid, 2009b). Structural changes in the prefrontal cortex (PFC) have been found in older adults and patients with COPD using functional magnetic resonance imaging and position emission tomography (Esser et al., 2016; Ryu et al., 2013; Zhang et al., 2013; Zhang et al., 2012). One of the commonly reported findings is the reduction in gray matter in several regions of the frontal brain in contrast to healthy controls (Esser et al., 2016; Zhang et al., 2012; Zhang et al., 2013). The structural differences in the brain between healthy adults and individuals with COPD may affect the hemodynamic response during performance of cognitive and motor tasks.
Several physical activities of daily living require performing a cognitive task simultaneously (dual tasking) (e.g., walking on an uneven path and paying attention to the pavement to avoid trips and falls or walking and talking on a cell phone). Due to limited cognitive resources, changes in performance in one or both tasks occur during dual tasking, which is termed the dual task effect (DTE) (Plummer & Eskes, 2015). It has been demonstrated that individuals with impaired cognitive functions (e.g., the elderly and those with a neurological illness) are more susceptible to errors in cognitive performance and gait as cognitive functions including attention, planning, pacing and strategizing are required during walking (Herman et al., 2010; Montero-Odasso, Muir, et al., 2012). Although, patients with COPD are known to have both cognitive and motor dysfunction, the DTE has not been widely considered; thus rehabilitation protocols are not focused on assessing or strengthening the cognitive-motor connection. One approach to examine the association between neural activity and motor performance is using a non-invasive neuroimaging technique, functional near-infrared spectroscopy (fNIRS). Comparison of data between healthy older adults and patients with COPD may enable us to identify age-independent neural correlates of cognitive and motor performance in this patient population.

Therefore, the objectives of this study were (i) to determine the feasibility of the dual tasking experimental paradigm for patients with COPD using fNIRS; (ii) to compare relative changes in oxygenated hemoglobin (ΔO$_2$Hb) from left and right dorsolateral PFC (DLPFC) during dual versus single tasks and cognitive versus baseline task between healthy older adults and patients with COPD; and (iii) to compare the DTE on cognitive task accuracy and gait velocity during preferred paced and fast paced walking dual tasks between healthy older adults and patients with COPD. It was hypothesized that (i) patients with COPD will be able to complete the study with minimal to no discomfort, breathlessness, fatigue or pain as the level of physical exertion is low; (ii) DLPFC O$_2$Hb will increase more during dual tasks compared to single tasks and during cognitive versus baseline task. The increase in O$_2$Hb will be greater in patients with COPD compared to older adults; and (iii) greater decrements in cognitive task accuracy and gait velocity will occur during fast paced walking dual task and in patients with COPD compared to older adults.
3.3 Materials and Methods

3.3.1 Participants

Healthy older adults (n=20) were recruited through word of mouth, emails and flyers from the University of Toronto, University Health Network associated hospitals (Toronto General Hospital, Toronto Western Hospital, Princess Margaret Cancer Centre and Toronto Rehabilitation Institute) and community centers in the downtown area of Toronto, Ontario, Canada. Furthermore, patients with COPD (n=8) were recruited from West Park Healthcare Centre and the Abilities Centre in Whitby, Ontario. Equal number of men and women were recruited within each group. Inclusion criteria included: men and women aged ≥45 years. Individuals in the healthy adult group were excluded if they: were smokers; experienced an acute illness during the last 3 months; had unstable cardiovascular, neurological or musculoskeletal conditions that interfered with independent ambulation or ability to stand on a single leg; consumed oral corticosteroids within the last 3 months; had cognitive impairment or a lack of English fluency that interfered with providing informed consent or following study instructions. In addition, patients with COPD requiring supplemental oxygen were also excluded. The study was approved by the University of Toronto’s Research Ethics Board (protocol ID: 33466).

3.3.2 Procedure

Participants were screened with the American College of Sports Medicine (ACSM) questionnaire to determine their eligibility to safely participate in the study. Their height and weight were measured. Resting end-tidal carbon dioxide (ETCO₂) was measured using PowerLab/LabChart (ADInstruments, Sydney, Australia). In addition, standardized procedures (Miller et al., 2005) were used to measure the forced expiratory volume in 1 second (FEV₁), the forced vital capacity (FVC) and FEV₁/FVC ratio with a handheld spirometer (copd-6™, model 4000, Vitalograph Ltd., Ennis, Ireland). The following questionnaires were then administered: Digit Span test, subtest of the Wechsler Adult Intelligence Scale (WAIS) III (Wechsler, 1997), Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005), Medication and Comorbidities Questionnaire (Charlson et al., 1987; Deyo et al., 1992; HajGhanbari et al., 2014) and International Physical Activity Questionnaire (IPAQ) (Craig et al., 2003).
After questionnaires and assessments were completed, the fNIRS device (FNIR100W-1, wireless fNIR Imager System, BIOPAC) was secured over the participants’ forehead (McKendrick et al., 2017, 2016) before they performed the single and dual tasks. DLPFC ΔO$_2$Hb data were recorded during all subsequent measures. Before and after each single and dual task, the participants completed a baseline task that involved spelling words forward by reading them from flashcards for 1 minute. This task was chosen based on the data of a pilot study conducted to determine a baseline task that elicited the least neural activity compared to other potential baseline tasks (eyes closed or crosshair fixation on a computer screen). The following single tasks were performed: (1) preferred paced walk (PPW); (2) fast paced walk (FPW); and (3) spelling backwards cognitive task (CT). Subsequently, changes in O$_2$Hb were measured during dual tasks which involved pairing tasks 1 and 2 with the CT (i.e., PPW+CT, FPW+CT). Single tasks were randomly ordered; thereafter, dual tasks were randomly ordered. Furthermore, blood pressure (BP), heart rate (HR) and oxygen saturation via pulse oximetry (SpO$_2$) were measured before the first single task, after the last single task, and after the last dual task.

To determine if the dual tasking protocol is feasible for patients with COPD, two main parameters were considered by observation: the duration of the experimental protocol and the ease with which the participants completed the tasks.

3.3.3 Neuropsychological and Physical Activity Assessment

The following assessments were used to characterize cognitive function and physical activity of the study groups.

1. **Digit Span** includes Digit Span Forward and Digit Span Backward. During the Digit Span Forward, an investigator recited a few sequences of digits, one by one, that the participant was instructed to recall in the same order. Sattler and Ryan (2009) have reported that Digit Span Forward test is an assessment of attention, auditory short-term memory, and auditory sequential processing. During the Digit Span Backward, the participants were asked to recall a different set of recited sequences in the reverse order. This test is a measure of working memory and assesses an individual’s ability to hold and manipulate information before responding, in addition to the processes involved in Digit Span Forward (Sattler & Ryan, 2009). Each component was administered up to 5 digit long sequences or until the participant was unable to recall two sequences with the same
number of digits. This was administered to obtain some insight into the participants’ attention and working memory abilities to complete the CT involving spelling 5 letter words backwards.

2. **Montreal Cognitive Assessment (MoCA)** is a valid and reliable tool to assess cognitive dysfunction in various populations (Gill et al., 2008; Hoops et al., 2009). It evaluates attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation (Mast & Gerstenecker, 2010; Nasreddine et al., 2005). It provides a score out of 30, where a score less than 26 suggests mild cognitive impairment.

3. **Medication and Comorbidities Questionnaire** was used to document participants’ current medications and health conditions related to mood, eyes, cancer and various body systems: cardiovascular, musculoskeletal, endocrine, nervous, digestive, immune, renal and respiratory (Charlson et al., 1987; Deyo et al., 1992; HajGhanbari et al., 2014; Jerez-Roig, Santos, Souza, Amaral, & Lima, 2016). This information was obtained to gain a sense of the participants’ overall health status as it might affect their cognitive and motor tasks’ performance in this study.

4. **International Physical Activity Questionnaire (IPAQ)** long form utilized in this study contains 27 questions that pertain to physical activity during various tasks, intensities and settings in the past 7 days: at work, at home (inside and the yard), to get from place to place and during recreational activities. It has been validated in several languages, countries and various population subgroups (Craig et al., 2003; Hagströmer et al., 2006; Wanner et al., 2016). Participants were assigned an overall physical activity level of low, moderate or high after converting their responses to Metabolic Equivalent Task minutes per week (MET-min/week). A sense of the participants’ level of physical activity might help explain their cognitive and motor performance during dual tasking.

### 3.3.4 Experimental Tasks

1. **Cognitive Task:** The CT involved spelling 5 letter words backwards from a list of 100 unique words for 1 minute. The spelling accuracy and number of words attempted were recorded. Spelling words backwards is thought to be a challenging CT (Hollman et al., 2010, 2007).
2. **Walking Tasks:** The walking tasks consisted of walking at a preferred and fast pace, each individually and paired with the CT. During each of these four tasks, the participants walked a distance of approximately 30 meters (m) that comprised 6 passes over a 5x0.88m pressure sensitive mat containing a grid of 13,824 sensors. Participants were instructed to walk as fast as they could, while ensuring their safety during the fast paced walk tasks. During the dual walking tasks, an investigator continued to read aloud 5 letter words and recorded the accuracy of backwards spelling until the participant completed 6 passes on the mat. Gait velocity was calculated using the ProtoKinetics Movement Analysis Software.

3.3.5 **Functional Near-Infrared Spectroscopy: Data Collection and Processing**

The fNIRS device (FNIR100W-1, wireless fNIR Imager System, BIOPAC) with 4 optodes was secured over participants’ forehead (McKendrick et al., 2017, 2016) and the center of each sensor pad was vertically aligned with the participants’ iris. The optodes over the left and right forehead approximately target the dorsal PFC. Light intensity raw data at two wavelengths (730nm and 850nm) was obtained using the Cognitive Optical Brain Imaging (COBI) Studio (fNIR Devices, LLC) at a sampling frequency of 4Hz. LED current and the detector gain settings were adjusted for each participant to prevent signal saturation or very low light signals. The light intensity data was processed in fnirSoft. A low-pass, finite impulse response, filter with a hamming order of 57 and a cutoff frequency of 0.05 was applied to attenuate physiological artifacts such as respiration and pulse (Ayaz et al., 2011; Izzetoglu et al., 2007). The data were further inspected for motion artifacts through the Sliding Motion Artifact Rejection (SMAR) (Ayaz et al., 2010), while some artifacts were also identified and manually removed in fnirSoft through visual observation.

Time markers placed at the onset and end of each task in COBI Studio were used to extract data blocks of the processed light data. Subsequently, relative changes in O$_2$Hb were calculated using the modified Beer-Lambert law. The first 5 seconds of each task were used as a local baseline during processing. Data from the left and right DLPFC were analyzed.
3.3.6 Statistical Analysis of Neural Activity and Gait Data

The PFC ΔO₂Hb acquired via the fNIRS device and processed in fnirSoft were compared between tasks and groups as well as between left and right DLPFC using two-way repeated measures analysis of variance (ANOVA). To compare the differences in PFC ΔO₂Hb during the baseline and CT between the two groups, independent t-tests were performed. Furthermore, the DTEs on the accuracy of cognitive task and gait velocity during PPW and FPW dual tasks were compared between older adults and patients with COPD using two-way repeated measures ANOVA. DTEs were calculated using the following equation: DTE = [(dual task–single task) ÷ single task] x 100%. Bonferroni correction was applied to adjust for multiple comparisons. Effect sizes (ηp²) of the main findings were also calculated.

3.4 Results

3.4.1 Participants’ Characteristics

Twenty older healthy adults with a mean age of 63.5±11.3 and eight patients with COPD with a mean age of 71.0±9.2 participated in the study. All were able to recall at least one forward 5 digit sequence; however, only about half of the participants could recall the digit span backward task at the level of 5 digits. Spirometry was normal in all healthy older adults and was diagnostic of COPD in the patient group. Patients with COPD also had a greater number of comorbidities and were taking more medications compared to healthy older adults, but reported a similar level of physical activity (p<.05). However, older adults tended to stand longer during the single leg stance (SLS) task suggesting better balance compared to patients with COPD (Table 8). In addition, using a cut-off threshold of <26 (Nasreddine et al., 2005), performance on MoCA indicated 6 of the 8 patients with COPD and 7 of the 20 healthy older adults had mild cognitive impairment. However, the mean scores of older adults and patients with COPD were similar on MoCA (p=.073).

3.4.2 Protocol Feasibility

The protocol was completed by all participants in approximately 1.5 hours suggesting feasibility of the dual tasking experimental protocol. All of the participants were able to complete the questionnaires/assessments as well as the single and dual tasks with ease. Participants did not report fatigue or pain at the end of the experiment. During the study protocol, the participants
remained in a seated position in the first hour during which they completed the questionnaires. In the next 30 minutes, they completed the walking tasks, each of which lasted less than 1 minute; thus, the participants did not experience much fatigue. All tasks were separated by 1 minute baseline task during which participants also remained in a seated position and were able to rest.

Table 8. Characteristics of healthy older adults and patients with COPD. Mean (SD) are reported unless stated otherwise.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Older</th>
<th>Patients with COPD</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n of M:F)</td>
<td>10M:10F</td>
<td>4M:4F</td>
<td>1.000</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63.5 (11.3)</td>
<td>71.0 (9.2)</td>
<td>.109</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.7 (0.1)</td>
<td>1.7 (0.1)</td>
<td>.966</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.5 (16.2)</td>
<td>77.6 (17.3)</td>
<td>.386</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.8 (4.3)</td>
<td>28.0 (4.1)</td>
<td>.231</td>
</tr>
<tr>
<td>Handedness (n)</td>
<td>19R, 1L</td>
<td>8R, 0L</td>
<td>.520</td>
</tr>
<tr>
<td>Dominant Leg (n)</td>
<td>14R, 6L</td>
<td>8R, 0L</td>
<td>.081</td>
</tr>
<tr>
<td>FEV₁ (% Predicted)</td>
<td>94.4 (10.7)</td>
<td>57.8 (13.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>FEV₁/FVC (% predicted)</td>
<td>104.4 (6.0)</td>
<td>83.4 (16.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ETCO₂ (mm Hg)</td>
<td>35.0 (4.5)</td>
<td>30.2 (2.8)</td>
<td>.012</td>
</tr>
<tr>
<td>Digit Span Forward‡</td>
<td>20 (100)</td>
<td>8 (100)</td>
<td>-</td>
</tr>
<tr>
<td>Digit Span Backward‡</td>
<td>11 (55)</td>
<td>4 (50)</td>
<td>.811</td>
</tr>
<tr>
<td>MoCA</td>
<td>26.1 (2.8); 21-30</td>
<td>24.0 (1.9); 21-27</td>
<td>.073</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>1.6 (2.5); 0-10</td>
<td>6.4 (3.2); 3-12</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Medications</td>
<td>0.8 (1.2); 0-5</td>
<td>6.0 (4.0); 2-14</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>IPAQ - Activity Level (n, MET-min/week)</td>
<td>High (n)</td>
<td>11,8449</td>
<td>4,4861</td>
</tr>
<tr>
<td></td>
<td>Moderate (n)</td>
<td>8,1398</td>
<td>3,1423</td>
</tr>
<tr>
<td></td>
<td>Low (n)</td>
<td>1,243</td>
<td>1,515</td>
</tr>
<tr>
<td>SLS Duration (s)</td>
<td>30.9 (32.4)</td>
<td>11.6 (18.0)</td>
<td>.127</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; ETCO₂, end-tidal carbon dioxide; F, female; FEV₁, forced expiratory volume in one second; FPW, fast paced walk; FVC, forced vital capacity; IPAQ, International Physical Activity Questionnaire; L, left; M, male; MoCA, Montreal Cognitive Assessment; PPW, preferred paced walk; R, right; SD, standard deviation; SLS, single leg stance; ‡ correctly recalled 5 digits sequence(s); † p values for comparisons between groups.
3.4.3 Hemodynamic Response in the Prefrontal Cortex

Neural activation ($\Delta O_2$Hb) during performance of single and dual tasks was evaluated from the left and right DLPFC. The $\Delta O_2$Hb during baseline, CT and single and dual walking tasks are shown in Table 9. Comparison of DLPFC $\Delta O_2$Hb during single and dual tasks between the two groups indicated a significant main effect of tasks in the left DLPFC (Table 10). Post hoc analysis indicated that DLPFC $\Delta O_2$Hb was significantly higher during FPW+CT compared to FPW in older adults ($p=.044$) (Figure 8). However, no significant main effects were found for groups*tasks interaction or for tasks in the right DLPFC when $\Delta O_2$Hb during PPW, PPW+CT, FPW and FPW+CT was compared between older adults and patients with COPD. Furthermore, comparison of the changes in $O_2$Hb from baseline to CT, PPW to PPW+CT and FPW to FPW+CT between the left and right DLPFC did not show significant main effects for PFC regions*tasks interaction, PFC regions or tasks in older adults and patients with COPD.

Table 9. Left and right DLPFC $\Delta O_2$Hb ($\mu$M) in healthy older adults and patients with COPD during the baseline, cognitive and walking tasks. Mean±SD are shown.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Older Adults (n=20)</th>
<th>Patients with COPD (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left DLPFC</td>
<td>Right DLPFC</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
<td>0.758±1.103</td>
<td>0.402±1.092</td>
</tr>
<tr>
<td><strong>CT</strong></td>
<td>0.833±0.864</td>
<td>0.748±0.739</td>
</tr>
<tr>
<td><strong>PPW</strong></td>
<td>-0.355±0.843</td>
<td>-0.383±0.728</td>
</tr>
<tr>
<td><strong>PPW+CT</strong></td>
<td>0.199±0.766</td>
<td>0.116±0.696</td>
</tr>
<tr>
<td><strong>FPW</strong></td>
<td>-0.490±1.013</td>
<td>-0.387±0.722</td>
</tr>
<tr>
<td><strong>FPW+CT</strong></td>
<td>0.268±0.947*</td>
<td>0.185±0.825</td>
</tr>
</tbody>
</table>

Abbreviations: $\mu$M, micromolars; $\Delta O_2$Hb, change in oxygenated hemoglobin; COPD, chronic obstructive pulmonary disease; CT, cognitive task; DLPFC, dorsolateral prefrontal cortex; FPW, fast paced walk; PPW, preferred paced walk; SD, standard deviation; * indicates significant increase from FPW to FPW+CT at $p<.05$.  

Figure 8. Activation in left (L) and right (R) DLPFC during FPW+CT in healthy older adults as visualized in fnirSoft.
Table 10. Summary table of ANOVAs between groups (older adults versus patients with COPD), tasks and PFC regions.

<table>
<thead>
<tr>
<th>Source</th>
<th>Type III SSE</th>
<th>Degrees of Freedom</th>
<th>Mean Square</th>
<th>F</th>
<th>p</th>
<th>η²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Left DLPFC ΔO₂Hb during single versus dual walking tasks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†</td>
<td>4.68</td>
<td>1.73</td>
<td>2.71</td>
<td>4.08</td>
<td>.029</td>
<td>0.136</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>0.41</td>
<td>1.73</td>
<td>0.24</td>
<td>0.36</td>
<td>.671</td>
<td>0.014</td>
</tr>
<tr>
<td>Error</td>
<td>29.78</td>
<td>44.92</td>
<td>0.66</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>34.87</td>
<td>48.38</td>
<td>3.61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Right DLPFC ΔO₂Hb during single versus dual walking tasks</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†</td>
<td>2.44</td>
<td>1.66</td>
<td>1.47</td>
<td>1.78</td>
<td>.185</td>
<td>0.064</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>0.86</td>
<td>1.66</td>
<td>0.52</td>
<td>0.63</td>
<td>.511</td>
<td>0.023</td>
</tr>
<tr>
<td>Error</td>
<td>35.60</td>
<td>43.14</td>
<td>0.83</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>38.90</td>
<td>46.46</td>
<td>2.81</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>In older adults: left versus right DLPFC for ΔO₂Hb from baseline to CT, PPW to PPW+CT and FPW to FPW+CT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions</td>
<td>0.03</td>
<td>1</td>
<td>0.03</td>
<td>0.08</td>
<td>.786</td>
<td>0.004</td>
</tr>
<tr>
<td>Error</td>
<td>8.51</td>
<td>19</td>
<td>0.45</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks††</td>
<td>2.33</td>
<td>2</td>
<td>1.17</td>
<td>2.26</td>
<td>.118</td>
<td>0.106</td>
</tr>
<tr>
<td>Residual</td>
<td>19.61</td>
<td>38</td>
<td>0.52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions × Tasks</td>
<td>0.95</td>
<td>1.27</td>
<td>0.75</td>
<td>2.21</td>
<td>.146</td>
<td>0.104</td>
</tr>
<tr>
<td>Error</td>
<td>8.16</td>
<td>24.04</td>
<td>0.34</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>39.60</td>
<td>85.30</td>
<td>3.26</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>In patients with COPD: left versus right DLPFC for ΔO₂Hb from baseline to CT, PPW to PPW+CT and FPW to FPW+CT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions</td>
<td>0.68</td>
<td>1</td>
<td>0.68</td>
<td>0.52</td>
<td>.495</td>
<td>0.069</td>
</tr>
<tr>
<td>Error</td>
<td>9.14</td>
<td>7</td>
<td>1.31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks††</td>
<td>2.92</td>
<td>2</td>
<td>1.46</td>
<td>0.70</td>
<td>.514</td>
<td>0.091</td>
</tr>
<tr>
<td>Residual</td>
<td>29.30</td>
<td>14</td>
<td>2.09</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PFC regions × Tasks</td>
<td>0.09</td>
<td>2</td>
<td>0.04</td>
<td>0.10</td>
<td>.908</td>
<td>0.014</td>
</tr>
<tr>
<td>Error</td>
<td>6.11</td>
<td>14</td>
<td>0.44</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>48.22</td>
<td>40</td>
<td>6.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DTE on CT accuracy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†††</td>
<td>987.50</td>
<td>1</td>
<td>987.50</td>
<td>1.86</td>
<td>.185</td>
<td>0.067</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>2.05</td>
<td>1</td>
<td>2.05</td>
<td>&lt;0.01</td>
<td>.951</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Error</td>
<td>13829.95</td>
<td>26</td>
<td>531.92</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>14819.50</td>
<td>28</td>
<td>1521.47</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>DTE on gait velocity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tasks†††</td>
<td>1108.11</td>
<td>1</td>
<td>1108.11</td>
<td>8.36</td>
<td>.008</td>
<td>0.243</td>
</tr>
<tr>
<td>Tasks × groups</td>
<td>10.41</td>
<td>1</td>
<td>10.41</td>
<td>0.08</td>
<td>.782</td>
<td>0.003</td>
</tr>
<tr>
<td>Error</td>
<td>3447.98</td>
<td>26</td>
<td>132.61</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>4566.50</td>
<td>28</td>
<td>1251.14</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: η², Partial Eta Squared; COPD; chronic obstructive pulmonary disease; CT, cognitive task; DLPFC, dorsolateral prefrontal cortex; DTE, dual task effect; FPW, fast paced walk; PPW, preferred paced walk; SSE, sum of squares.
†Tasks include PPW, PPW+CT, FPW and FPW+CT
††Tasks include baseline to CT, PPW to PPW+CT and FPW to FPW+CT
†††Tasks include: PPW+CT and FPW+CT
The mean arterial BP (MAP), HR and SpO\textsubscript{2} are presented in Table 11. In older adults, HR increased significantly after single tasks ($p=0.011$) and dual tasks ($p=0.004$) compared to the baseline measures (before single tasks). Important to note that, patients with COPD had a higher HR at the onset of the study compared to older adults; thus, at the end of the study, HR within these patients did not change relative to the baseline measurement ($p>0.05$). MAP did not differ between and within the two groups, but SpO\textsubscript{2} was higher during single and dual tasks in older adults compared to patients with COPD (Table 11).

### Table 11. Vital signs of older adults and patients with COPD during the experiment. Mean (SD) are reported.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Older</th>
<th>Patients with COPD</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MAP (mm Hg)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>96.6 (12.3)</td>
<td>98.0 (12.3)</td>
<td>0.761</td>
</tr>
<tr>
<td>After single tasks</td>
<td>100.1 (14.1)</td>
<td>98.8 (16.1)</td>
<td>0.833</td>
</tr>
<tr>
<td>After dual tasks</td>
<td>99.3 (14.5)</td>
<td>100.3 (14.2)</td>
<td>0.843</td>
</tr>
<tr>
<td><strong>HR (bpm)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>67.8 (9.0)</td>
<td>77.1 (14.2)</td>
<td>0.046</td>
</tr>
<tr>
<td>After single tasks</td>
<td>71.9 (8.0)†</td>
<td>75.0 (12.5)</td>
<td>0.439</td>
</tr>
<tr>
<td>After dual tasks</td>
<td>71.9 (8.4)†</td>
<td>79.4 (12.3)</td>
<td>0.072</td>
</tr>
<tr>
<td><strong>SpO\textsubscript{2} (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>95.2 (3.2)</td>
<td>93.3 (2.2)</td>
<td>0.142</td>
</tr>
<tr>
<td>After single tasks</td>
<td>96.2 (1.6)</td>
<td>93.6 (2.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>After dual tasks</td>
<td>96.1 (1.6)</td>
<td>93.4 (3.0)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Abbreviations: bpm, beats per minute; COPD, chronic obstructive pulmonary disease; HR, heart rate; MAP, mean arterial pressure; SD, standard deviation; SpO\textsubscript{2}, peripheral capillary oxygen saturation measured by pulse oximetry; $p$ values of data comparison between groups; † indicates within group differences from baseline at $p<0.005$.

#### 3.4.4 Dual Task Effect on Cognitive Task Accuracy and Gait Velocity

Participants’ in both groups showed trends towards negative DTE on velocity and CT accuracy (Table 12). Velocity was found to be lower in patients with COPD compared to older adults when comparing each task (PPW, FPW, PPW+CT) between the two groups. Furthermore, a significant main effect of tasks (Table 10) was found for DTE on velocity. Post hoc analysis indicated that the negative DTE on velocity was significantly greater during FPW+CT compared to PPW+CT in older adults and showed a trend towards significance in patients with COPD ($p=0.073$, $\eta^2_p=0.388$).
Participants in both groups attempted spelling similar number of words during CT, PPW+CT and FPW+CT and tended to have the highest accuracy during CT (Table 12). Furthermore, a trend towards lower backwards spelling accuracy was observed during dual tasking. However, no significant main effects were found for groups*tasks interaction and tasks for the DTE on accuracy.

**Table 12.** Backwards spelling accuracy and gait velocity of older adults and patients with COPD. Mean (SD) are reported.

<table>
<thead>
<tr>
<th></th>
<th>Healthy Older Adults (n=20)</th>
<th>Patients with COPD (n=8)</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Velocity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(m/min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPW</td>
<td>77.5 (7.9)</td>
<td>64.1 (15.7)</td>
<td>.005</td>
</tr>
<tr>
<td>PPW+CT</td>
<td>68.4 (11.2)</td>
<td>57.2 (8.4)</td>
<td>.017</td>
</tr>
<tr>
<td>FPW</td>
<td>102.4 (15.8)</td>
<td>87.1 (11.1)</td>
<td>.019</td>
</tr>
<tr>
<td>FPW+CT</td>
<td>80.6 (12.8)</td>
<td>70.9 (11.3)</td>
<td>.074</td>
</tr>
<tr>
<td><strong>DTE on Velocity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPW+CT</td>
<td>-11.3 (14.5)</td>
<td>-8.1 (14.4)</td>
<td>.598</td>
</tr>
<tr>
<td>FPW+CT</td>
<td>-20.6 (12.6)*</td>
<td>-18.9 (4.5)</td>
<td>.720</td>
</tr>
<tr>
<td><strong>CT Accuracy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPW+CT</td>
<td>79.4 (25.1)</td>
<td>66.0 (33.9)</td>
<td>.260</td>
</tr>
<tr>
<td></td>
<td>7 (1)</td>
<td>7 (2)</td>
<td>.880</td>
</tr>
<tr>
<td>FPW+CT</td>
<td>69.1 (24.4)</td>
<td>56.0 (33.5)</td>
<td>.258</td>
</tr>
<tr>
<td></td>
<td>6 (1)</td>
<td>6 (2)</td>
<td>.464</td>
</tr>
<tr>
<td><strong>DTE on CT Accuracy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPW+CT</td>
<td>-10.4 (30.2)</td>
<td>-25.6 (33.1)</td>
<td>.252</td>
</tr>
<tr>
<td>FPW+CT</td>
<td>-20.1 (22.2)</td>
<td>-34.4 (40.2)</td>
<td>.234</td>
</tr>
</tbody>
</table>

Abbreviations: COPD, chronic obstructive pulmonary disease; CT, cognitive task; DTE, dual task effect; FPW, fast paced walk; PPW, preferred paced walk; SD, standard deviation; † p values for comparisons between groups. * indicates significant within group differences between PPW+CT and FPW+CT at p<.05.

### 3.5 Discussion

#### 3.5.1 Summary of Findings

In this study, the feasibility of the dual tasking experimental paradigm was demonstrated for patients with COPD. While completing the walking tasks, O$_2$Hb increased significantly in the left DLPFC during FPW+CT compared to FPW in older healthy adults; however, the ΔO$_2$Hb
was not significant in patients with COPD or between the two groups. Moreover, negative DTE on velocity was also found in older adults, who exhibited a significantly lower velocity during FPW+CT compared to PPW+CT; a similar trend was observed in patients with COPD. The small sample size of patients with COPD (n=8) in this study limited detection of significant differences in ΔO₂Hb and DTE on velocity and CT accuracy between groups, if they existed.

3.5.2 Protocol Feasibility

All patients as well as healthy older adults completed the approximately 1.5-hour long study session containing questionnaires, backwards spelling CT and walking tasks with ease. Participants did not complain of pain, discomfort, shortness of breath or difficulty in walking tasks indicating feasibility of the protocol. The total distance walked during the four walking tasks in this study was approximately 120 meters, which on average is less than the distance walked by most patients with COPD during the 6-minute walk test (6WMT). The mean distance walked during 6WMT in a group of patients with COPD was reported to be between 256 and 451 meters (Spruit et al., 2010).

3.5.3 Prefrontal Cortex ΔO₂Hb

In a review of neuroimaging studies using fMRI and PET scans during tasks involving cognitive functions, Cabeza and Nyberg (2000) reported that neural activity in the left PFC increases in tasks that involve divided attention (e.g., dual tasking), semantic memory retrieval and language (e.g., generation of words) (Gabrieli et al., 1998; Sandrini et al., 2003), while tasks that involve sustained attention activate the right PFC. In addition, tasks that involve manipulating the information in the working memory (Petrides, 1995) are linked to bilateral PFC activation. The findings from this review corroborate the significantly higher ΔO₂Hb in the left DLPFC during the FPW+CT compared to FPW in healthy older adults. However, unlike the study by Holtzer et al. (2011), O₂Hb during PPW+CT compared to PPW did not increase in the left and right DLPFC.

3.5.4 Motor and Cognitive Tasks’ Performance

Significantly greater decrements in gait velocity were observed during FPW+CT compared to PPW+CT in healthy older adults, but not in patients with COPD. The greater decrements during the FPW+CT may be a result of limited attentional resources that are insufficient to meet the
greater demands required to maintain a higher gait speed and balance while simultaneously being engaged in a cognitively challenging task. Alternatively, the interference exhibited as reduced speed may be due to an overlap of cognitive resources required to carry out both tasks (Bürki et al., 2017). Fast walking speed has been used in dual tasking experimental paradigms in previous studies (De Cock et al., 2017; Dennis et al., 2009; Eggenberger et al., 2017). Similar to the current study, Plummer-D’Amato, Altmann, and Reilly (2011) reported significant cognitive-motor interference and reduction in gait speed during dual tasking. In contrast, no significant differences in velocity were reported during fast walking and serial subtraction CT in older adults compared to stroke patients by Dennis et al. (2009). The differences in the results might be explained by the heterogeneity in the studies’ methodology (e.g., sample size, task difficulty).

3.5.5 Limitations

The results of this study might be impacted by some limitations. Firstly, the sample size of patients with COPD was small (n=8) compared to healthy older adults (n=20). This would have influenced the statistical analysis and prevented some variables from reaching significance, if a difference truly exists. Secondly, the fNIRS device used includes only 4 channels, two on the left and two on the right PFC, which limits one’s ability to capture the hemodynamic response from other brain regions that are associated with the execution of tasks. Thirdly, the PFC ∆O₂Hb measurements are dependent on the path length of infrared light from the fNIRS probe to the cortex, which has an impact on the measured intensity of the light signal. The path length is impacted by anatomical differences such as age-related cortical atrophy and skull thickness, which were not evaluated in this study. Lastly, the fNIRS device only provides data of relative, rather than absolute, changes in the concentration of O₂Hb. Baseline absolute levels of O₂Hb may impact the cortical hemodynamic response associated with the execution of tasks.

3.5.6 Future Directions

Future studies should aim to address some of these limitations. A greater sample size of patients with COPD will strengthen comparisons across groups to determine the impact of age and disease on brain activity and the associated DTE on gait and CT performance. Furthermore, fNIRS devices with a greater number of channels will provide a greater depth of information and more insight into the neural correlates of cognitive-motor tasks and the DTE. Lastly, fNIRS
should be used in conjunction with other imaging techniques to determine the path length of infrared light and appropriately adjust for the anatomical differences in the analysis.

### 3.5.7 Conclusions

Dual tasking experimental paradigm was found to be feasible for patients with COPD. Determination of neural correlates of cognitive and motor tasks during a feasible dual tasking protocol may help develop appropriate rehabilitation interventions to improve mobility and reduce risk of falls in the affected populations (e.g., individuals with cognitive deficits). The ∆O$_2$Hb was found to be significantly greater during FPW+CT compared to FPW in the left DLPFC in older adults. Moreover, older adults exhibited a greater negative DTE on velocity during FPW+CT compared to PPW+CT. The higher DLPFC ∆O$_2$Hb and significantly greater decrease in velocity during FPW+CT compared to other dual tasks in healthy older adults highlight the impact of higher cognitive demands during this complex dual task.

**Declarations of interest:** none

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Chapter 4

4 Discussion and Conclusions

4.1 Overview of Findings

4.1.1 Neural Activity Comparison between Tasks and Groups

In this study, neural activity was measured from the left and right DLPFC in healthy younger adults, healthy older adults and patients with COPD during preferred and fast paced walking as single tasks and combined with backwards spelling for dual tasks. Some studies have analyzed ∆O$_2$Hb from left and right PFC in younger and older adults while the participants walked on treadmill (Eggenberger et al., 2017), only in younger adults (Meester et al., 2014; Mirelman et al., 2014; Suzuki et al., 2004) or only in older adults (Harada et al., 2009). Unlike the present study, no study has compared data from left and right DLPFC between younger and older adults or older adults and patients with COPD during dual tasking involving walking on ground while performing a CT. Comparison of data between younger and older adults will provide insight into age-related changes, while data comparison between older adults and patients with COPD will elucidate the age-independent impact of COPD on cortical hemodynamic changes, and gait and cognitive performance.

The O$_2$Hb increased and was found to be higher in older adults compared to younger adults during FPW+CT compared to FPW in the left DLPFC. Similarly, ∆O$_2$Hb was significantly higher in older adults during FPW+CT and PPW+CT in the right DLPFC compared to their respective single tasks. However, these differences did not exist between groups (younger and older adults), which may have been due to the high fitness level, limited cognitive impairment and large age range (45-79 years) of individuals in the older group.

Dual tasking experimental paradigm involving measurement of DLPFC ∆O$_2$Hb was determined to be feasible for patients with COPD. Participants did not complain of any pain, discomfort, breathlessness or fatigue while performing the walking and cognitive tasks that were completed after administration of a few questionnaires in the first hour of the approximately 1.5-hour testing session. Within group comparison between single and dual tasks indicated a significantly higher ∆O$_2$Hb in left DLPFC during FPW+CT compared to FPW in older adults. However, no between groups differences (older adults and patients with COPD) were found.
4.1.2 Dual Task Effect on Gait and Cognitive Task Performance

Participants in the healthy younger and older groups exhibited reduction in gait velocity during dual tasks. The reduction was significantly greater during FPW+CT compared to PPW+CT in younger and older adults, but only showed a trend in patients with COPD. Multiple linear regression analysis indicated that the DTE on gait velocity during PPW+CT was positively associated with age in healthy adults after adjusting for the confounding influence of number of comorbidities. The DTE on spelling backwards accuracy did not differ between younger and older adults as well as older adults and patients with COPD during PPW+CT or FPW+CT.

4.2 Explanation of Findings and Comparison to the Literature

An increase in O$_2$Hb during tasks that involve cognitive/affective or motor stimuli indicates neural activation (neurovascular coupling), while a decrease occurs upon stimulus deactivation (Huettel, Singerman, & McCarthy, 2001; León-Domínguez, 2012). Several activities of daily living require walking and simultaneously performing another cognitively demanding task (e.g., talking on the phone or thinking about errands). To effectively achieve stable gait, several cognitive abilities are utilized such as attention, planning, decision making, reasoning and working memory, which are the functions of the PFC (Izzetoglu et al., 2004; Kane & Engle, 2002; MacDonald et al., 2000; Ruocco et al., 2014). However, cognitive functions such as attention and working memory decline as a function of aging and are associated with altered neural activity that might negatively affect cognitive and/or motor performance. Thus, variation and levels of neural activity between younger and older adults or those with COPD during performance of cognitive-motor tasks might reflect different activation mechanisms, inefficient cognitive processing and/or compensation strategies to minimize errors in performance.

In this study, neural activity was higher in the left and right DLPFC in older adults during FPW+CT compared to FPW, which might be a result of increased complexity of the tasks being performed (Hamacher, Herold, Wiegel, Hamacher, & Schega, 2015; Maidan et al., 2016). The well-documented reduction in brain mass in the frontal lobule in older adults aged 41-89 years (Coffey et al., 1992; Cowell et al., 1994; Meguro et al., 2001; Svennerholm et al., 1997) may be a contributing factor to the observed higher brain activity in contrast to younger adults. Furthermore, DLPFC ΔO$_2$Hb was higher during PPW+CT compared to PPW only in the right DLPFC in older adults. Bilateral increase in PFC O$_2$Hb have been reported during normal paced
walking dual tasks in healthy adults and patients with Parkinson’s disease (Holtzer et al., 2011; Maidan et al., 2016; Nieuwhof et al., 2016). The increased activity in the right DLPFC in older adults during PPW+CT suggests that regular speed walking may not be an automatic task and still requires cognitive resources.

In a review, Cabeza and Nyberg (2000) reported that the left DLPFC is activated during linguistic tasks and working memory, while the right DLPFC during tasks that require sustained attention. Furthermore, activation is observed in the left and right DLPFC during working memory tasks as well as those that require manipulating information regardless of whether the task requires sustained attention. The bilateral increase in DLPFC O₂Hb in older adults observed during the FPW+CT (walking combined with a task that requires holding words in working memory while manipulating them to spell backwards) supports the aforementioned functional characteristics of the PFC and suggests that the cognitive-motor tasks employed in this study utilize neural regions involved in attention, language and working memory. Asymmetry of activation in the left and right DLPFC has also been reported in younger adults during working memory tasks indicating specialized functions of PFC regions. However, no significant changes in O₂Hb were found in left or right DLPFC in younger adults in the present study. In contrast to younger adults, the phenomenon of hemispheric asymmetry reduction in older adults (HAROLD) has been reported in neuroimaging studies. It has been suggested that symmetrical PFC activation in older adults may be a consequence of declining unilateral neural efficiency and an inability to specifically recruit the required neural regions (Cabeza et al., 2004; Li, Moore, Tyner, & Hu, 2009; Rosen et al., 2002). This may explain the bilateral increase in DLPFC O₂Hb in older adults during FPW+CT compared to FPW.

A trend towards higher PFC ΔO₂Hb bilaterally was observed in patients with COPD during the performance of the challenging FPW+CT compared to FPW. In contrast to patients with COPD, an increased PFC neural activity has been documented during acceleration in stroke patients during walking (Mihara, Miyai, Hatakenaka, Kubota, & Sakoda, 2007). Patients with COPD live in a chronic state of hypoxemia that can lead to neural damage, and cognitive and motor deficits. Brain damage may alter neural activity and lead to less efficient neural processing during performance of a cognitive or motor task (Neubauer et al., 2005; Reuter-Lorenz, 2002; Uemura et al., 2016; Yang et al., 2009). Some compensatory strategies for the inefficient neural processing have been proposed that include augmented activation or recruitment of additional
brain regions (Crémers, D’Ostilio, Stamatakis, Delvaux, & Garraux, 2012; Jahn et al., 2009; Peterson, Pickett, Duncan, Perlmutter, & Earhart, 2014a, 2014b; Snijders et al., 2011; Wai et al., 2012). Such compensatory mechanisms may explain the ΔO₂Hb trends observed during performance of single and dual tasks.

A greater reduction in gait velocity was observed during FPW+CT compared to PPW+CT in older adults, but not in patients with COPD. Reducing gait speed is a potential compensatory strategy to reduce the complexity of the task being performed in order to maintain postural stability and balance (Bloem et al., 2006). However, reduced gait speed is associated with diminished functional capacity (Busch et al., 2015) and an increased risk of falls (Quach et al., 2011).

Several theories have been proposed to elucidate the potential mechanisms of the DTE on gait and CT performance. One of the well-known theories revolves around the central bottleneck model (Bratzke, Rolke, & Ulrich, 2009; Johnston & McCann, 2006; Ruthruff, Pashler, & Hazeltine, 2003). The central bottleneck model posits that some stages of central “thought-like processing” can only occur one by one. Therefore, information is filtered and attentional resources are directed towards the most important information to the individual. A second theory suggests that there are pools of processing resources such that if more resources are allocated to one task, it leaves less resources for the second task. Depending on the task that is prioritized, decrements in the other task’s performance will occur. Moreover, since not all resources are allocated to one task, errors in the performance of both tasks might occur. A third theory argues the notion of crosstalk among the cognitive resources suggesting that if two or more tasks being carried out require similar mental resources, the level of interference would be greater compared to tasks that are dissimilar and require different cognitive resources (Pashler & Johnston, 1998). The significantly negative DTE on gait velocity and a trend towards reduced CT accuracy in older adults might be explained by these theories.

4.3 Factors affecting Neural Activity and Cognitive-Motor Performance

Age and task related differences in the cortical hemodynamic response have been documented during performance of single tasks that challenge cognition. Some studies report that PFC O₂Hb in older adults increases a greater amount compared to younger adults during talking and
working memory tasks (Holtzer et al., 2011; Oboshi et al., 2014), while some studies report greater increase in younger adults during similar cognitive tasks including event-related Stroop task or calculation tasks (Hock et al., 1995; Schroeter et al., 2003). An increase in PFC O$_2$Hb during verbal fluency task in patients with schizophrenia and eating disorders have also been reported (Chou et al., 2015; Suda et al., 2010). However, in the current study, a significant increase in DLPFC O$_2$Hb was not found compared to the baseline task in either younger adults, older adults or patients with COPD.

Motor tasks also require several cognitive functions such as planning, strategizing and pacing, while paying attention to obstacles to maintain stability. Studies have shown that the PFC O$_2$Hb increases during walking (Metzger et al., 2017; Mihara et al., 2007; Suzuki et al., 2008, 2004) and walking dual tasks (Atsumori et al., 2010; Holtzer et al., 2015, 2017; Meester et al., 2014; Nieuwhof et al., 2016; Osofundiya, Benden, Dowdy, & Mehta, 2016; Verghese, Wang, Lipton, Holtzer, & Xue, 2007; Vitorio, Stuart, Rochester, Alcock, & Pantall, 2017). The results of the current study that DLPFC O$_2$Hb increased during FPW+CT compared to FPW in the left and right DLPFC in older adults corroborate the previously reported findings. However, a decrease in PFC O$_2$Hb has also been reported during dual task walking in older adults (Beurskens et al., 2014).

The differences across studies may potentially be explained by the heterogeneity in the methodology (e.g., task difficulty) and participants’ characteristics. Cognitive impairment (Serrien et al., 2007) resulting from aging, stroke, traumatic brain injury, Alzheimer’s, COPD or other conditions may be a contributing factor for the observed differences. Moreover, a person’s sex and neuroanatomical differences may also affect the PFC ∆O$_2$Hb during performance of a task. Females are reported to have nearly 23% larger DLPFC size compared to men (Schlaepfer et al., 1995) and men are reported to have a greater age-related decline in PFC size compared to women (Coffey et al., 1998). In a study on functional connectivity and cortical lateralization of the PFC using functional optical tomography, Chuang and Sun (2014) reported stronger neural networks connectivity in men compared to women. In addition, men were reported to have dominant activity in the left DLPFC, while women had bilateral dominance (Vikingstad, George, Johnson, & Cao, 2000). Furthermore, difficult tasks lead to a greater neural PFC ∆O$_2$Hb compared to easier tasks (Ayaz et al., 2012; Barch et al., 1997; Kameyama et al., 2004; Mandrick et al., 2013a, 2013b). However, through practicing and learning, the difficulty experienced
during performance of a task can be reduced, which may subsequently affect the associated cortical hemodynamic response.

4.4 Utility of Cognitive-Motor Experimental Paradigm

A cognitive-motor experimental paradigm is effective in determining the top down processing of specific neural regions during performance of dual tasks. Proxy measurement of neural activation during mobility has become possible with the emergence of non-invasive optical neuroimaging modalities such as fNIRS, some of which are portable. It can be used in natural settings to elucidate the impact of tasks and real life situations on cognitive and motor performance (Ayaz et al., 2012, 2011; Gentili, Shewokis, Ayaz, & Contreras-Vidal, 2013; Hatakenaka, Miyai, Mihara, Sakoda, & Kubota, 2007; Ikegami & Taga, 2008; Leff et al., 2008). Insight into the impact of certain tasks and situations on performance and neural activity in healthy participants may allow to devise similar protocols for rehabilitation interventions for patients with cognitive-motor deficits (e.g., elderly and those with COPD or neurological disorders) to enhance their functional status through improved cognition, balance and postural control. Improved motor and mental functions are linked to better functional capabilities, reduced risk of falls and better quality of life (Milanović et al., 2013; Riebe et al., 2009; Shah, Lin, Yu, & McMahon, 2017; Tuna, Edeer, Malkoc, & Aksakoglu, 2009).

The dual tasking experimental paradigm can be used to understand the role of cognition during motor tasks. The most common motor task used in both research and clinical settings is walking, which can be coupled with one of several CTs that require attention, use of memory and/or decision making. The complexity of walking (e.g., via introducing obstacles) and/or the CT can be modified to determine the impact of increased mental and physical demands on performance. Moreover, different types of distractions (e.g., cognitive, visual or auditory) can also be utilized to target particular cognitive functions.

4.5 Implications for Rehabilitation Science

4.5.1 Aging Population, Reduced Mobility and Cognitive Impairment

The prevalence of seniors living in the society is increasing due to increased life expectancy and is expected to continue rising along with the associated healthcare burden. The prevalence is estimated to rise from 524 million in 2010 to 1.5 billion in 2050 (World Health Organization,
Aging is linked to cognitive decline, gait changes and multimorbidities. The most common deficits in cognitive functions’ are of memory (Peters, 2006) and attention (Murman, 2015). Furthermore, a decline in physical functional capacity is commonly reported in the elderly as evidenced by a reduction in gait speed, a variable positively associated with survival and high risk of falls (Al-Aama, 2011; Berg, Alessio, Mills, & Tong, 1997; Chang, Lynm, & Glass, 2010; Maki, 1997; Studenski et al., 2011). In this study, it was found that increasing age is positively associated with the negative DTE on velocity during PPW+CT after adjusting for the confounding influence of number of comorbidities in healthy adults. Reduced functional capabilities lead to difficulties with independently performing activities of daily living (Tuna et al., 2009) and greater utilization of healthcare resources.

Research involving the dual tasking methodology has been widely published in various populations such as those with mild cognitive impairment, traumatic brain injury, multiple sclerosis, neuropathy and stroke (Azulay, Mesure, & Blin, 2006; Chaparro et al., 2017; Galletly & Brauer, 2005; Kelly, Eusterbrock, & Shumway-Cook, 2012; Malcay, Grinberg, Berkowitz, Hershkovitz, & Kalron, 2017; Muir, Speechley, et al., 2012; Rucker, Jernigan, McDowd, & Kluding, 2014; Strouwen et al., 2016; Yogev et al., 2005). One advantage of using the dual tasking model in a rehabilitation setting is that it can improve individuals’ tolerance to distractions and enhance performance when multitasking. Thus, cognitive-motor rehabilitation protocols have been used in various patient populations such as those with stroke (Faria et al., 2018; Liu, Yang, Tsai, & Wang, 2017), neurological injuries (e.g., traumatic brain injury) (Evans, Greenfield, Wilson, & Bateman, 2009; Silsupadol et al., 2009; Silsupadol, Siu, Shumway-Cook, & Woollacott, 2006) and Alzheimer’s disease (Olazarán et al., 2004). These therapies have either shown improvement or maintenance of one or both cognitive and motor abilities. However, their use has been limited in patients with COPD. Incorporating dual tasking in rehabilitation of patients with COPD might be beneficial to collectively improve their commonly reported deficits in cognition and gait.

The results of this study demonstrate feasibility of the dual tasking experimental paradigm for patients with COPD. Recently, more attention has been paid to protocols that involve both a cognitive and a motor component to determine their impact on improving dual tasking capabilities. Several studies have elucidated the notion that cognitive efforts help individuals maintain, if not improve, cognition in addition to being beneficial for improving motor control.
(Mullick, Subramanian, & Levin, 2015; Pichierri, Wolf, Murer, & de Bruin, 2011; Verstraeten, Mark, & Sitskoorn, 2016). One way that the dual tasking experimental paradigm can be incorporated into rehabilitation settings is through virtual reality (Faria et al., 2018). In the past, virtual reality has been used to mainly improve motor function in patients with stroke (e.g., via a protocol involving arm reaching); for dual tasking, a physical task like arm reaching can be coupled with a cognitive component requiring attention (e.g., selection of a target from distractors) (Faria et al., 2018). Recently, in a study involving the Stroop test coupled with virtual reality maze navigation, Killane et al. (2015) demonstrated the positive impact of dual tasking on improving cognitive and motor performance (i.e., stepping time and rhythmicity). Strengthening the cognitive-motor association through more interactive rehabilitation interventions may increase adherence and subsequently task performance.

Evaluation of the DTE and proxy measurement of neural activity in at risk populations using fNIRS, in possible combination with other neuroimaging modalities, may provide greater insight into cognitive and motor deficits. Insight into a person’s cognitive and motor capabilities can be used to implement preventative measures to reduce the risk of falls, mortality and subsequent utilization of healthcare resources. With the advent of portable fNIRS devices, changes in cortical hemodynamics can be monitored in individuals with neurological deficits even in remote locations without the need to transport heavy medical equipment.

4.6 Limitations and Future Directions

4.6.1 Limitations

The results and interpretations of this study might be influenced by a few limitations. First, the sample size of patients with COPD was small (n=8) compared to healthy younger (n=20) and older (n=20) adults. Due to the small sample size, the interpretation of the analyzed data might not be an accurate representation of the population characteristics. Secondly, the fNIRS device employed in this study was limited by the number of channels (n=4) that only provided coverage of the forehead. Thus, information on other neural regions involved in the execution of the cognitive and motor tasks could not be obtained. Lack of data from other cortical and subcortical regions that might be activated differentially in younger adults, older adults and patients with COPD limits one’s ability to make inferences regarding the compensation strategies (e.g., recruitment of neural regions) in different population subgroups. Thirdly, the fNIRS device
provided relative, rather than absolute, concentrations of $O_2$Hb; the cortical hemodynamic response elicited by a cognitive or motor task may be influenced by the absolute levels of $O_2$Hb. Lastly, the measurement of PFC $\Delta O_2$Hb from the fNIRS device is also influenced by the path length of the emitted light from the probe to the hemoglobin chromophores in the blood. The path length is impacted by the skull and cortical thickness, which was not measured in this study.

### 4.6.2 Future Directions

Future studies should aim to address some of the aforementioned limitations. First, the sample size of the healthy adults and patients with COPD should be increased to strengthen comparisons across groups. Secondly, the effects of sex on the outcome variables should be analyzed provided the neuroanatomical and functional differences between males and females. Elucidating the differences in sex might provide insight into more personalized rehabilitation interventions for the two sexes. Thirdly, studies should aim to have testing environments as realistic as possible. Conducting studies in realistic settings using everyday common tasks where the participants are able to freely move around, rather than being confined to a room, would be useful in providing more accurate insight into the neural correlates of cognitive and motor tasks. Provided the portability of some fNIRS devices, one can understand the impact of the natural environments’ complexity on performance to make more appropriate interpretations of the data collected.

The limitation of the small number of channels in the fNIRS device could be addressed by utilizing devices that cover a greater region of the skull so activation of other neural regions can be monitored, analyzed and interpreted in the context of the tasks being performed. Integrating fNIRS and electroencephalography (EEG) during data collection may provide a more in-depth understanding of the neural mechanisms during dual tasking. EEG is one of the most commonly used techniques in neuroscience for investigating the underlying mechanisms of brain activity and provides electrical current data associated with neuronal activity (Ahn & Jun, 2017). In addition, magnetic resonance imaging may allow to estimate the path length of the infrared light by providing insight into the neuroanatomical variations, which can then be taken into account during data processing. Lastly, future studies should aim to incorporate virtual reality during dual task experimental paradigms. Utilizing virtual reality in a research setting and demonstrating the benefits of interactive participation will ease the transition of research protocols and findings into
clinical settings. As a result, patients will be able to take advantage of the effective rehabilitation protocols as early as possible.

4.7 Conclusions

The results discussed in this thesis suggest distinct patterns of neural activity during single and dual tasks and the DTE across the three groups: healthy younger adults, healthy older adults and patients with COPD. Neural DLPFC O$_2$Hb increased during FPW+CT and PPW+CT compared to FPW and PPW, respectively, in the right DLPFC and only during the FPW+CT compared to FPW in the left DLPFC in healthy older adults. No significant differences were found between any tasks for DLPFC ΔO$_2$Hb in healthy younger adults and patients with COPD when compared to healthy older adults in either left or right DLPFC. Nonetheless, there was a trend towards higher PFC ΔO$_2$Hb bilaterally during dual compared to single tasks in all three groups. Furthermore, the DTE on velocity was found to be higher during FPW+CT compared to the PPW+CT in healthy younger and older adults. The reduced performance in gait may be suggestive of cognitive decline due to aging as found by the multiple linear regression analysis indicating that the negative DTE on velocity during PPW+CT is associated with age. Moreover, the DTE on CT accuracy did not show any significant differences between tasks and groups. The increase in neural activity and the decrease in motor performance in older adults may suggest greater cognitive efforts, neural inefficiency and/or competition for limited cognitive resources to perform the tasks.

Dual tasking experimental paradigm is feasible for use in patients with COPD. Determining the neural correlates of dual tasking can provide insight into the cognitive demands associated with the tasks being performed. The DTE observed during dual tasking supports the idea that rehabilitation should involve cognitive-motor interventions to improve cognition, enhance physical function and subsequently reduce the risk of falls in the elderly and populations with cognitive impairment such as patients with COPD.
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https://doi.org/10.1016/j.apmr.2006.10.031


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Appendices

Appendix 1: Research Ethics Board Approval and Renewal Letters

November 4, 2016

DEPT OF PHYSICAL THERAPY
FACULTY OF MEDICINE

Re: Your research protocol entitled, "Prefrontal cortex activity during dual-task performance in patients with chronic obstructive pulmonary disease"

ETHICS APPROVAL

| Original Approval Date: November 4, 2016 |
| Expiry Date: November 3, 2017 |
| Continuing Review Level: 2 |

We are writing to advise you that the Health Sciences Research Ethics Board (REB) has granted approval to the above-named research protocol, for a period of one year. Ongoing research under this protocol must be renewed prior to the expiry date.

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events in the research should be reported to the Research Oversight and Compliance Office - Human Research Ethics Program as soon as possible.

Please ensure that you submit an Ethics Renewal Form or a Study Completion/Closure Report 15 to 30 days prior to the expiry date of your current ethics approval. Note that ethics renewals for studies cannot be accepted more than 30 days prior to the date of expiry.

If your research is funded by a third party, please contact the assigned Research Funding Officer in Research Services to ensure that your funds are released.

Please note, all approved research studies are eligible for a routine Post-Approval Review (PAR) site visit. If chosen, you will receive a notification letter from our office. For information on PAR, please see http://www.research.utoronto.ca/wp-content/uploads/documents/2014/09/20140924-PAR-Program-Description-1.pdf.

Best wishes for the successful completion of your research.

Yours sincerely,

REB Chair
October 17, 2017

DEPT OF PHYSICAL THERAPY
FACULTY OF MEDICINE

Re: Your research protocol entitled, “Prefrontal cortex activity during dual-task performance in patients with chronic obstructive pulmonary disease”

ETHICS APPROVAL

Original Approval Date: November 4, 2016
Expiry Date: November 3, 2018
Continuing Review Level: 2
Renewal: 1 of 4

We are writing to advise you that you have been granted annual renewal of ethics approval to the above-referenced research protocol through the Research Ethics Board (REB) delegated process. Please note that all protocols involving ongoing data collection or interaction with human participants are subject to re-evaluation after 5 years. Ongoing research under this protocol must be renewed prior to the expiry date.

Any changes to the approved protocol or consent materials must be reviewed and approved through the amendment process prior to its implementation. Any adverse or unanticipated events should be reported to the Research Oversight and Compliance - Human Research Ethics Program as soon as possible. If your research is funded by a third party, please contact the assigned Research Funding Officer in Research Services to ensure that your funds are released.

Please ensure that you submit an Ethics Renewal Form or a Study Completion/Closure Report 15 to 30 days prior to the expiry date of your protocol. Note that ethics renewals for studies cannot be accepted more than 30 days prior to the date of expiry as per our guidelines.

Please note, all approved research studies are eligible for a routine Post-Approval Review (PAR) site visit. If chosen, you will receive a notification letter from our office. For information on PAR, please see http://www.research.utoronto.ca/wp-content/uploads/documents/2014/09/PAR-Program-Description-1.pdf.

Best wishes for the successful completion of your research.

Yours sincerely,

REB Chair
Notification of JREB Approval

January 13, 2017

Department of Physical Therapy
University of Toronto
500 University Avenue
Toronto, ON M5G 1V7

<table>
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Documents Approved

- Dual Task COPD Reid West Park Application 22 Nov 2016
  - JREB Application Form
  - Canada Foundation for Innovation document
  - University of Toronto Ethics review application form
  - Appendix A Recruitment email – Healthy Participants
  - Appendix B Recruitment Flyer – Healthy Participants
  - Appendix C Telephone Script – Healthy participants
  - Appendix D Follow-up Email – Healthy Participants
  - Appendix E Recruitment email for COPD
  - Appendix F Recruitment Flyer for COPD
  - Appendix G Follow-up email for COPD
  - Appendix H Telephone Script for COPD
  - Appendix I Consent Form
  - Appendix J MMSE
  - Appendix K MoCA
  - Appendix L Medication and Comorbidities Questionnaire
I am writing to confirm that your protocol entitled, *Prefrontal Cortex Activity during Dual-task Performance in Patients with Chronic Obstructive Pulmonary Disease* has received *full ethical approval* and you may proceed with data collection.

If, during the course of the research, there are any serious adverse events, any confidentiality concerns, changes in the approved protocol or consent form, or any new information that must be considered with respect to the project, these should be brought to the immediate attention of the JREB. In the event of a privacy breach, you are responsible for reporting the breach to the JREB (in accordance with Ontario health privacy legislation – Personal Health Information Protection Act, 2004). Additionally, the JREB requires reports of inappropriate/unauthorized use of the information.

The Joint West Park Healthcare Centre-Toronto Central Community Care Access Centre- Toronto Grace Health Centre Research Ethics Board (JREB) operates in compliance with the Tri-Council Policy Statement, ICH/GCP Guidelines, the Ontario Personal Health Information Protection Act, and Part C, Division 5 of the Food and Drug Regulations of Health Canada.

Should you wish to make any further changes or revisions to any aspect or portion of the approved project, they must be submitted for consideration to the board prior to amending the protocol. Address any proposed changes to: Joint Research Ethics Board, West Park Healthcare Centre, 82 Buttonwood Avenue, Toronto, ON, M6M 2J5.

Finally, all research conducted at West Park Healthcare Centre, Toronto Central Community Care Access Centre or Toronto Grace Health Centre is subject to ongoing monitoring that includes the submission, in writing, of an *annual* status report of project activities to the board. If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The JREB must be notified of the completion or termination of this study and a final report provided. As the Principal Investigator, you are responsible for the ethical conduct of this study.

Best wishes for the progress of this work.

Yours very truly,

[Signature]

[Name]

Chair, Joint West Park Healthcare Centre / Toronto Central CCAC/Toronto Grace Health Centre Research Ethics Board
Notification of JREB Continued Approval

January 27, 2018

Department of Physical Therapy
University of Toronto
5-500 University Avenue
Toronto, ON M5G 1V7

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<td>Documents Approved</td>
<td>• JREB Annual Review-Renewal signed</td>
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<td>Documents Acknowledged</td>
<td>• Consent Form</td>
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Dear Dr. Reid,

The above-named study has received continued approval from the Joint West Park-Toronto Central LHIN- Toronto Grace Research Ethics Board (JREB) until the expiry date noted above. If the study is expected to continue beyond the expiry date, you are responsible for ensuring the study receives re-approval. The JREB must also be notified of the completion or termination of this study and a final report provided.

If, during the course of the research, there are any serious adverse events, confidentiality concerns, changes in the approved project, or any new information that must be considered with respect to the project, these should be brought to the immediate attention of the JREB. In the event of a privacy breach, you are responsible for reporting the breach to the JREB. Additionally, the JREB requires reports of inappropriate/unauthorized use of the information. As the Principal Investigator, you are responsible for the ethical conduct of this study.

The Joint West Park-Toronto Central LHIN- Toronto Grace Research Ethics Board operates in compliance with the Tri-Council Policy Statement, ICH/GCP Guidelines, the Ontario Personal Health Information Protection Act (2004), and Part C, Division 5 of the Food and Drug Regulations of Health Canada.

Best wishes for the successful completion of your project.
Appendix 2: Consent Form

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Study Name: Prefrontal Cortex Activity during Dual-task Performance in Patients with Chronic Obstructive Pulmonary Disease

Researchers:
Dr. Darlene Reid, Professor, Department of Physical Therapy
Dr. Dina Brooks, Professor, Department of Physical Therapy
Dr. Kara Patterson, Professor, Department of Physical Therapy
Dr. Leandro Viques Bonetti, Visiting Scientist, RAMP Lab – University of Toronto
Dr. Luana Melo, Post-doctoral Fellow, RAMP Lab – University of Toronto
Dr. Karina Tam Kasawara, Post-doctoral Fellow, RAMP Lab – University of Toronto
Syed Ahmed Hassan, Masters Student, RAMP Lab – University of Toronto

Phone: 416-946-8548
Email: ramp.lab@utoronto.ca

Purpose of the Research:
The purpose of this study is to compare signals from the front of your brain while you perform one task or two tasks simultaneously. This study is being conducted with chronic obstructive pulmonary disease (COPD) patients and healthy people using a technique that monitors oxygen levels in your brain cells. This technique is called functional near infrared spectroscopy (fNIRS), a non-invasive technique, and you will not feel anything during the measurements.

What will you be asked to do:
Initially, you will be screened over the phone to ask questions to determine your eligibility. During the phone call, you will be asked a few health related questions as well as your weight and height. If you are eligible, you will be asked to attend an approximately 1.5 hour long testing session at the Rehabilitation Science Building, located at 500 University Ave, Toronto, Toronto Western Hospital (399 Bathurst St, Toronto, ON M5T 2S8), The Abilities Centre (55 Gordon Street, Whitby, ON) or West Park Healthcare Centre, located at 82 Buttonwood Ave, York, ON M6M 2J5. During this 1.5 hour session, more screening will be performed followed by walking (fast and at your usual pace), standing on a single-leg on a pressure sensitive mat and performing a cognitive task (spelling words backwards). You will then be asked to perform the cognitive task, while walking (fast and at usual pace) and standing on one leg.

For screening measurements during the test session –
We will measure your lungs function with a breathing test, heart rate, height and weight. Afterwards, you will complete short questionnaires that ask about your memory, attention, different health conditions and physical activity. You will then be set up with an fNIRS device on your forehead (see picture on this page). This device is non-invasive and small. It provides a measure of brain oxygen levels by transmitting and receiving light in the near infrared spectrum. In order to obtain an accurate measure, the area underneath the device must be cleaned with an alcohol swab. The device will be used for:

Page 1 of 3

Version 7 - Mar. 7, 2018
Measurement of brain activity during a spelling task: You will be asked to spell five-letter words backwards over a 1 minute time period.

Measurement of brain activity during walking task: You will be asked to walk back and forth 3 times on a 5m long walkway at your usual pace and then your fastest pace in a safe manner.

Measurement of brain activity while standing on one leg: You will be asked to stand on your dominant leg for as long as you can.

Measurement of brain activity during walking and spelling: You will be asked to walk back and forth 3 times on a 5m long walkway at your usual pace and then your fastest pace in a safe manner while you spell five-letter words backwards from a list of 100 unique words.

Measurement of brain activity while standing on one leg and spelling: You will be asked to stand on your dominant leg for as long as you can and spell the provided five-letter words backwards.

Potential Risks and Discomfort:
You will not be exposed to any major health risks during the study. Some possible risks include:
- Fatigue due to exertion from visiting the research lab and performing the walking tests. The walking test is short – 30 meters each. You will be asked to perform the 30 meters walking four times – once while walking at your usual pace, once while walking fast and then both the usual and fast walking while spelling words backwards. You will be able to sit between each walking test. Any fatigue should diminish within a few hours and should not affect your daily activities.

Benefits of the Research:
Although there are no direct benefits to you, the information collected in this study will provide insight into brain activity during walking and while standing on one leg, as well as during spelling while walking and standing on one leg. In addition, this study will provide insight into how impaired brain activity can alter walking and balance.

Reminders and Responsibilities:
It is required that you refrain from alcohol, caffeine and excessive physical activity 12 hours prior to the visit. Also, avoid big meals 1 hour prior and minimize fluid consumption 30 minutes prior the visit. Lastly, please make sure that you wear flat shoes - walking shoes or loafers and bring a list of your medications.

Voluntary Participation/ Withdrawal from the study:
Your participation in the study is completely voluntary and you may choose to stop participating at any time. Should you wish to terminate participation you will still be eligible to receive the agreed upon compensation. All data obtained prior to your withdrawal from the study will be retained, unless you request otherwise.

Compensation:
As a token of appreciation, you will be compensated with $30 for participation and travel costs.
Confidentiality:
All personal information collected during the research will be held in confidence; your name or any identifying features will not appear in any report or publication of research. Signed consent forms will be stored in a locked filing cabinet in the locked laboratory, of the primary investigator - Room B57, 500 University Avenue, University of Toronto. For the purpose of data collection, participants will be assigned an arbitrary subject ID number and all data collected from the experimental protocol will be associated with this ID number. All data collected throughout the study will be stored in a password-protected folder on a secured Rehabilitation Sciences, University of Toronto computer network.

Publication of Results and Commercialization:
Results of this study may be used in publications and/or presentations to benefit the academic and clinical community.

Questions about the Research?
If you have any questions about the research in general or about your role in this study please feel free to contact ramp.lab@utoronto.ca for further information. This research has been reviewed and approved by the University of Toronto Research Ethics Board and conforms to the standards of Canadian Tri-Council research ethics guidelines. You can contact the Office of Research Ethics at ethics.review@utoronto.ca or 416-946-3273, if you have questions about your rights as participants. Participants may take a copy of the information letter for their own reference.

Human Research Ethics Program
The research study you are participating in may be reviewed for quality assurance to make sure that the required laws and guidelines are followed. If chosen, a representative(s) of the Human Research Ethics Program (HREP) may access study-related data and/or consent materials as part of the review. All information accessed by the HREP will be upheld to the same level of confidentiality that has been stated by the research team.

Legal Rights and Signatures:

I, ________________________________, consent to participate in “Prefrontal Cortex Activity during Dual-task Performance in Patients with Chronic Obstructive Pulmonary Disease” study. I have understood the nature of this project and wish to participate. I am not waiving any of my legal rights by signing this form. My signature below indicates my consent.

Signature __________________________ Print Name __________________________ Date ________________
Participant

Signature __________________________ Print Name __________________________ Date ________________
Principal Investigator

Page 3 of 3
Appendix 3: Recruitment Posters

Version 5 - Jan. 16, 2018

PARTICIPANTS NEEDED
CAN YOU DO TWO THINGS AT ONCE? LET’S WALK AND TALK

We are looking for **men and women with COPD**, who do not need supplemental O₂, to take part in a study aimed to examine brain activity during backwards spelling and walking/standing on one leg.

Participants must **NOT** have joint problems that interfere with walking or standing on one leg.

Participants will be asked to complete the following:
- A quick breathing test
- Short questionnaires that ask about memory, attention, health conditions and physical activity
- Walk quickly: ~ 30 meters
- Walk at usual pace: ~ 30 meters
- Stand on one leg
- Spell words backwards

Participants will then do two things at once (e.g. walk and spell backwards)

**Testing session will be 1.5 hours** at the Rehabilitation Sciences Building (500 University Ave., Toronto, ON) and you will get **$30 as compensation.**
PARTICIPANTS NEEDED
CAN YOU DO TWO THINGS AT ONCE? LET'S WALK AND TALK

We are looking for men and women with COPD, who do not need supplemental O₂, to take part in a study aimed to examine brain activity during backwards spelling and walking/standing on one leg.

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- Walk quickly: ~ 30 meters
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- Stand on one leg
- Spell words backwards

Participants will then do two things at once (e.g. walk and spell backwards)

Testing session will be 1.5 hours at the Toronto Western Hospital (399 Bathurst St., Toronto, ON) and you will get $30 as compensation.
Appendix 4: Script of Instructions to Participants

Instructions Script
Prefrontal Cortex Activity during Dual-task Performance in Patients with Chronic Obstructive Pulmonary Disease

Hello Ms/Mr/Sir/Mrs __________________! Thank you for taking the time to come in. How are you doing today? Have you had a chance to go over the consent form? Do you have any questions or concerns?

Let me explain a little bit more about the screening procedures and protocol as I walk you down to our lab.

Today, I will measure your height and weight and administer two breathing tests.

Once that is done, we will go over the ACSM screening questionnaire that I administered over the phone that had questions regarding certain health conditions and symptoms. Then, you will complete the digit span test, where you will be asked to remember the numbers that I say to you and then recall them. Afterwards, I will administer a few short questionnaires that ask questions to assess memory, attention, different health issues and your physical activity.

We will then complete walking and standing on one leg tests with and without backwards spelling.

- “Please follow me, so I can measure your height and weight” *Record this and other demographics data on the data sheet*

“Now, you will complete a breathing test during which you will put a nose plug in one of your nostrils and breathe normally for about 2 minutes. This test measures the amount of carbon dioxide you exhale when breathing.

Could you please take a moment to verify and confirm your responses to this questionnaire that I administered over the phone?

If the subject had answered yes to any of the items on the checklist, ask the following questions to verify fitness to participate in the study:

- You indicated that you had xxxxxxxx. Can you tell me a little bit more about this?
- Does this limit your physical activity or bother you when walking fast or standing?
- If heart condition, ask if anyone in their immediate family has it.

- Next, is the second breathing test (spirometry). During this test, you will breathe out as hard as you can into a mouthpiece. This test will measure the strength of your lungs, which is based on how fast you are able to blow out air. So, please give it your best effort. We will repeat the test at least 3 times until we have a good measurements.

- “Please sit in an upright position with feet flat on the floor. Try not to lean forward during the test. Also, when you hold this device from the lower part and try not to cover the fan.”
- "You will take a deep breath in; place the mouthpiece in your mouth, seal your lips tightly around it to avoid any leaks and BLAST the air out, as quick and hard as possible. Continue to blow until you can no longer blow any more air out or until I ask to stop.
- "Do you have any questions?"

Maneuver: "When you're ready, put the nose clip on; take a deep breath in through your mouth; put the mouth piece in your mouth and BLAST OUT! Go, go, go, go, go. Keep going, keep going! Very good!

We will do the same at least two more times. *Repeat 2 more times*

"Now you will complete the digit span test, where I will say a few digits and you will recall them when I am done speaking."

"First, we will complete the digit span forward. I am going to say a sequence of numbers. Listen carefully and when I am finished, I want you to say them right after me. Just say what I say."

"Great, You are doing an excellent job" Now we will do the digit span backward: "Now I am going to say some more numbers. But this time when I stop, I want you to say them backwards. For example, if I say 7-1-9, what would you say?" If correct answers, say, "That is right!" If incorrect, say "No, you would say 9-1-7. I said 7-1-9, so to say it backwards, you would say, 9-1-7. Now try these numbers. Remember, you are to say them backwards: 3-4-8.

This task is quite difficult. Most people make mistakes, so don't worry about it.

We will now complete Montreal Cognitive Assessment (MoCA). Please let me know if you have any questions or require clarification at any point.

Hand over the MoCA assessment sheet and a pen

1. "Please draw a line, going from a number to a letter in ascending order. Begin here [point to (1)] and draw a line from 1 then to A then to 2 and so on. End here [point to (E)]."
2. "Copy this drawing as accurately as you can, in the space below".
3. "Draw a clock. Put in all the numbers and set the time to 10 past 11".
4. "Tell me the name of this animal".
5. "This is a memory test. I am going to read a list of words that you will have to remember now and later on. Listen carefully. When I am through, tell me as many words as you can remember. It doesn't matter in what order you say them". When the subject indicates that (s)he has finished (has recalled all words), or can recall no more words, read the list a second time with the following instructions
   - "I am going to read the same list for a second time. Try to remember and tell me as many words as you can, including words you said the first time." At the end of the second trial, inform the subject that (s)he will be asked to recall these words again by saying
   - "I will ask you to recall those words again at the end of the test."
6. "I am going to say some numbers and when I am through, repeat them to me exactly as I said them."
   - "Now I am going to say some more numbers, but when I am through you must repeat them to me in the backwards order."
   - "I am going to read a sequence of letters. Every time I say the letter A, tap your hand once. If I say a different letter, do not tap your hand."
   - "Now, I will ask you to count by subtracting seven from 100, and then, keep subtracting seven from your answer until I tell you to stop."
7. "I am going to read you a sentence. Repeat it after me, exactly as I say it [pause]: I only know that John is the one to help today." Following the response, say: "Now I am going to read you another sentence. Repeat it after me, exactly as I say it [pause]: The cat always hid under the couch when dogs were in the room."
8. Tell me as many words as you can think of that begin with a certain letter of the alphabet that I will tell you in a moment. You can say any kind of word you want, except for proper nouns (like Bob or Boston), numbers, or words that begin with the same sound but have a different suffix, for example, love, lover, loving. I will tell you to stop after one minute. Are you ready? [Pause] Now, tell me as many words as you can think of, that begin with the letter F. [time for 60 sec], Stop." Excellent
9. "Tell me how an orange and a banana are alike." If the subject answers in a concrete manner, then say only one additional time
   "Tell me another way in which those items are alike." If the subject does not give the appropriate response (fruit), say, "Yes, and they are also both fruit." Do not give any additional instructions or clarification. After the practice trial, say:
   "Now, tell me how a train and a bicycle are alike." Following the response, administer the second trial, saying; "Now tell me how a ruler and a watch are alike."
10. "I read some words to you earlier, which I asked you to remember. Tell me as many of those words as you can remember."
11. "Tell me the date today." If the subject does not give a complete answer, then prompt accordingly by saying: "Tell me the [year, month, exact date, and day of the week]." Then say: "Now, tell me the name of this place, and which city it is in."

"Now, we will do the Medication and Comorbidities Questionnaire. This questionnaire is designed to check all the previous or current medical conditions that you have been diagnosed with and the approximate date when you were diagnosed. Please let me know if need clarification with any part." Hand the questionnaire to the subject and allow some time to complete. "Do you have any questions or concerns that I can clarify?"

Now we will complete our last questionnaire called the International Physical Activity Questionnaire. Please complete this questionnaire. Hand over the questionnaire. Do you have any questions or concerns that I can clarify?
Now we will put this device over your forehead that measures blood oxygen. “Please, have a seat on this chair. I will clean your skin with an alcohol swab and attached the device.” Attach the device. “Is this okay for you? Let me know if it’s too tight or loose.”

“Now, you will complete 7 tests, each separated by a resting period during which you will spell words from flashcards. The tasks include: (1) backward spelling; (2) 30 meters walking at your usual pace; (3) 30 meters walking at fast speed; (4) standing on one leg.

Then you will do two things at once; (5) 30 meters walking at your usual speed while spelling words backwards; (6) 30 meters walking at fast speed while spelling backwards; and lately (7) standing on one leg and spelling backwards.”

I'll tell you the words while you are walking or standing during each task.

Now we will measure your blood pressure and blood oxygen by putting this small device (oximeter) on your finger. Please have a seat here (point to chair).

---

**Resting task**
Please remain seated in a comfortable position. Hand over deck of cards. When I say GO, start spelling the words on the flashcards and keep going until I tell you to stop. During spelling, you don’t have the say the words and the spelling speed is not important. GO. After 1 min. This is the end of this task. You did a great job.

---

All the single tasks and then the dual tasks are randomly ordered. Follow the instructions for the particular order of tasks being administered.

---

1. Now you will complete the **backwards spelling task**, where I will say 5 letter words and you will spell them backwards. For example, when I say the word “paint”, you will spell it backwards as “t”, “i”, “n”, “a”, “p”. The most important thing is that you try your best to spell the words backwards, so don’t worry if you make a mistake or don’t know how to spell a word, just say “SKIP” and I’ll give you another word.

   Are you ready? **Start saying the words and recording the responses**

   After 1 minute, “This is the end of this task.

---

**Resting task**
Please sit in a comfortable position. Hand over deck of cards. Just like before, when I say GO, start spelling the words GO. After 1 min. This is the end of this task.

---

2. "Now, you will complete the test, where you walk at your usual speed. Please stand here. Point to where the subject should stand"
When I say "go", please walk at your usual walking speed to the end of the mat; get off the mat; go around the marked position on the floor, orient yourself to the centre of the mat and walk back. You will then go around the marked position where you started and complete three rounds. When you are walking, try to maintain in the centre of the mat and look straight ahead at the mark on the wall/door. Once again, you will walk at your usual speed. Do you have any questions?

Please stand behind this marked position (point to the mark on the floor) "Go". After 3 rounds. This is the end of this task. Great job.

---

**Resting task**

Please sit in a comfortable position. Hand over deck of cards. Just like before, when I say GO, start spelling the words GO. After 1 min. This is the end of this task.

---

3. "Now, you will complete the test, where you **walk as fast and as safely as you can**". The rest of the protocol is the same as before. When I say "go", please walk to the end of the mat; get off the mat; go around the marked position on the floor, orient yourself to the centre of the mat and walk back. You will then go around the marked position where you started and complete three rounds. When you are walking, try to maintain in the centre of the mat and look straight ahead at the mark on the wall/door. Once again, you will walk as fast as you can but as safely as you can. Do you have any questions?

Please stand behind this marked position (point to the mark on the floor) "Go". After 3 rounds. This is the end of this task. Great job. How are you feeling?

---

**Resting task**

Please sit in a comfortable position. Hand over deck of cards. Just like before, when I say GO, start spelling the words GO. After 1 min. This is the end of this task.

---

4. Now, you will stand on your **(Left/Right) leg** for as long as you can. When I say "Go", bend your (Right/Left) leg at a 90 degrees angle, put your hands around your waist and stand for as long as you can. **Examiner will demonstrate**.

When standing, look straight ahead at the cross on the door and make sure that your legs don’t touch each other. If we notice your leg coming down, we will provide you a signal to lift it back up to 90 degrees. Throughout the test, if you experience too much discomfort or pain, you may put your leg down and the task will end at that time. Do you have any questions?

When I say GO, please bend your (Right/Left) leg. GO.

Great job!

Now, we will measure your blood pressure and oxygen again. Please sit in a comfortable position.

---
Resting task
Please remain seated in a comfortable position. *Hand over deck of cards.* Just like before, when I say *GO,* start spelling the words on the flashcards and keep going until I tell you to stop. As a reminder, you don’t have to say the words and the spelling speed is not important. *GO. After 1 min.* This is the end of this task.

-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Now you will do two things at once.

5. You will **walk at your usual speed and spell backwards** at the same time.
   The rest of the protocol is the same as before. When I say “go”, please walk to the end of the mat; get off the mat; go around the marked position on the floor, orient yourself to the centre of the mat and walk back. You will then go around the marked position where you started and complete three rounds. When you are walking, try to remain in the centre of the mat and look straight ahead at the mark on the wall/door. For spelling, the most important thing is that you try your best to spell the words backwards, so don’t worry if you make a mistake or don’t know how to spell the word, just say “SKIP” and I’ll give you another word. Do you have any questions?
   Please stand behind this marked position *(point to the mark on the floor).* When I say the first word, please start walking at your usual speed and spelling backwards.
   *Say the first word. After 3 rounds, say: This is the end of this task. How do you feel?*

-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Resting task
Please sit in a comfortable position. *Hand over deck of cards.* Just like before, when I say *GO,* start spelling the words *GO. After 1 min.* This is the end of this task.

-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

6. You will **walk as fast but as safely as you can and spell backwards**
   The rest of the protocol is the same as before. When I say “the first word”, please walk to the end of the mat; get off the mat; go around the marked position on the floor, orient yourself to the centre of the mat and walk back. You will then go around the marked position where you started and complete three rounds. When you are walking, try to remain in the centre of the mat and look straight ahead at the mark on the wall/door. As a reminder, for spelling, the most important thing is that you try your best to spell the words backwards, so don’t worry if you make a mistake or don’t know how to spell the word, just say “SKIP” and I’ll give you another word. Do you have any questions?
   Please stand behind this marked position *(point to the mark on the floor).* When I say the first word, start walking as fast as you can but as safely as you can.
   *Say the first word. After 3 rounds, say: This is the end of this task. How do you feel?*

-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------

Resting task
Please sit in a comfortable position. *Hand over deck of cards.* Just like before, when I say *GO,* start spelling the words *GO. After 1 min.* This is the end of this task.
7. Now, you will stand on your (Left/Right) leg for as long as you can just like before, but this time also spell backwards at the same time. Just like before, when I say “the first word”, bend your (Right/Left) leg at a 90 degrees angle, put your hands around your waist and stand for as long as you can. When standing, look straight ahead at the cross on the door and make sure that your legs don’t touch each other. If we notice your leg coming down, we will provide you a signal to lift it back up to 90 degrees. Throughout the test, if you experience too much discomfort or pain, you may put your leg down and the task will end at that time. When I say the first word, please bend your (Right/Left) leg and start spelling backwards. Say the first word and stop when both feet touch the ground.

Now, we will measure your blood pressure and oxygen one last time. Please sit in a comfortable position.

Resting task

Please sit in a comfortable position. Hand over deck of cards. Just like before, when I say GO, start spelling the words GO. After 1 min. This is the end of this task.

How do you feel?

We are finished with all the tasks and now will remove the device from your forehead.

*Take off the fNIRS device*

Thank you very much for participating and doing such a great job. Here is a token of appreciation for participating in this study. Can you please write your name and sign this form? Hand over money and get the form signed. Do you have any questions or concerns at this point? If you would like the results of this test, you may call us or send an email. If you don’t have any further questions, I can walk you out.
**Appendix 5: Data Collection Form**

<table>
<thead>
<tr>
<th>Subject ID</th>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
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<tr>
<td>Height</td>
<td></td>
<td></td>
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<tr>
<td>Weight</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handedness</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dominant Leg</td>
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### Spirometry

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<tr>
<th></th>
<th>Trial 1</th>
<th></th>
<th>Trial 2</th>
<th></th>
<th>Trial 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Volume (L)</td>
<td>% Predicted</td>
<td>Volume (L)</td>
<td>% Predicted</td>
<td>Volume (L)</td>
<td>% Predicted</td>
</tr>
<tr>
<td>FEV₁</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>FEF₅₀</td>
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<td></td>
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<tr>
<td>FEV₁/FEV₅₀</td>
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<tr>
<td>Lung age</td>
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</tr>
</tbody>
</table>

FEV₁: forced expiratory volume in 1 second; FEF₅₀: forced expiratory volume in 6 seconds

<table>
<thead>
<tr>
<th>Task</th>
<th>BP (mm Hg)</th>
<th>Pulse (beats/min)</th>
<th>SpO₂ (%)</th>
<th>ETCO₂</th>
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</tr>
</tbody>
</table>

PPW: preferred paced walk; FPW: fast paced walk; SLS: single leg stance; CT: cognitive task

**Comments:**

__________________________________________

Version 3 - Sept. 26, 2017
Appendix 6: Montreal Cognitive Assessment

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

VISUOSPATIAL / EXECUTIVE

Copy cube
Draw CLOK (Ten past eleven) (3 points)

CONTREUR Numbers Hands

NAME: Education: Date of birth:
Sex: DATE:

MEMORY
Read a list of words; subject must repeat them. Do 2 trials; even if 1st trial is successful, do 2 recall after 5 minutes.

FACE VELVET CHURCH DAISY RED Points
1st trial
2nd trial
No points

ATTENTION
Read a list of digits (1 digit/sec.). Subject has to repeat them in the forward order.
Subject has to repeat them in the backward order.

Read a list of letters. The subject must tap with his hand at each letter. No points if ≥ 2 errors.

MEMORY

LANGUAGE
Repeat: I only know that John is the one to help today. [ ]
The cat always hid under the couch when dogs were in the room. [ ]

Fluency: Name maximum number of words in one minute that begin with the letter F. [ ] ______ (N ≥ 11 words)

ABSTRACTION
Similarity between e.g. banana - orange = fruit [ ]
train - bicycle [ ]
watch - ruler [ ]

DELAYED RECALL
Has to recall words WITH NO CUE

FACE VELVET CHURCH DAISY RED
Category cue
Multiple choice cue

Optional

ORIENTATION
[ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

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Administered by: www.mocatest.org

TOTAL

Normal ≥ 26 / 30

Page 5 of 5
## Appendix 7: Medications and Comorbidities Questionnaire

### Record of Medication and Comorbidities

**Subject's code:**  
Date of birth (yyyy/mm/day): ........................................
Height: ..................  
Weight: ..................
Age: ..................

Please check all the medical conditions that you have been diagnosed with and the approximate date when you were diagnosed. See example provided in gray.

<table>
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<tr>
<th>Medical Condition</th>
<th>check</th>
<th>Date of diagnosis</th>
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<tbody>
<tr>
<td><strong>1. Heart disease</strong></td>
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<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina (pain in chest or heart)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic attack</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
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<td></td>
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<tr>
<td>Other (please specify):</td>
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<td></td>
</tr>
<tr>
<td><strong>2. Circulatory disease</strong></td>
<td></td>
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<tr>
<td>Hyperlipidemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td></td>
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<tr>
<td>Peripheral vascular disease</td>
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<tr>
<td>Faintness, lightheadedness, or dizziness by changing position</td>
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<tr>
<td>High blood pressure</td>
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<td></td>
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<tr>
<td>Low blood pressure</td>
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<tr>
<td>Other (please specify):</td>
<td></td>
<td></td>
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<tr>
<td><strong>3. Musculoskeletal disease</strong></td>
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<tr>
<td>Osteoarthritis</td>
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<tr>
<td>Rheumatoid arthritis</td>
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<tr>
<td>Broken bones (please specify):</td>
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<td></td>
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<tr>
<td>Other (please specify):</td>
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<td></td>
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<tr>
<td><strong>4. Endocrine disease</strong></td>
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<tr>
<td>Osteoporosis</td>
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<tr>
<td>Diabetes</td>
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<tr>
<td>Thyroid disease</td>
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<tr>
<td><strong>5. Cancer</strong></td>
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<tr>
<td>Please specify the type:</td>
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<tr>
<td>Other (please specify):</td>
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<tr>
<td><strong>6. Neurological disease</strong></td>
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<tr>
<td>Polyneuropathy</td>
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<tr>
<td>Parkinson</td>
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<tr>
<td>Stroke</td>
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<td>Other (please specify):</td>
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<td><strong>7. Mood</strong></td>
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<tr>
<td>Depression</td>
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<tr>
<td>Anxiety</td>
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<td>Other (please specify):</td>
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<tr>
<td><strong>8. Digestive disease</strong></td>
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<tr>
<td>Gastroesophageal reflux</td>
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<tr>
<td>Other (please specify):</td>
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<td><strong>9. Immune disease</strong></td>
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<td>HIV</td>
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<tr>
<td>Other (please specify):</td>
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<tr>
<td><strong>10. Eye disease</strong></td>
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<tr>
<td>Cataract</td>
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<tr>
<td>Glaucoma</td>
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<tr>
<td>Other (please specify):</td>
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<tr>
<td><strong>12. Renal disease</strong></td>
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<tr>
<td>Unintentional urine leakage</td>
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<tr>
<td>Other (please specify):</td>
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</tr>
</tbody>
</table>
14. Do you have asthma, emphysema, chronic bronchitis, shortness of breath? If yes, please specify:

15. If you have any other major health problems or conditions not listed above, please specify:

Please list all the medications that you are currently taking, including the dose, the frequency and why you are taking this medication. Please include also when you started to use it. See example provided. You may also attach a copy of your pharmacy or Shoppers list of medications. See example provided in gray.

<table>
<thead>
<tr>
<th>NAME</th>
<th>DOSE</th>
<th>FREQUENCY</th>
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Appendix 8: International Physical Activity Questionnaire

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the last 7 days. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the vigorous and moderate activities that you did in the last 7 days. Vigorous physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Moderate activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?
   [ ] Yes
   [ ] No  Skip to PART 2: TRANSPORTATION

   The next questions are about all the physical activity you did in the last 7 days as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, heavy construction, or climbing up stairs as part of your work? Think about only those physical activities that you did for at least 10 minutes at a time.
   _____ days per week
   [ ] No vigorous job-related physical activity  Skip to question 4

3. How much time did you usually spend on one of those days doing vigorous physical activities as part of your work?
   _____ hours per day
   _____ minutes per day

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like carrying light loads as part of your work? Please do not include walking.
   _____ days per week
   [ ] No moderate job-related physical activity  Skip to question 6

LONG LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised October 2002.
5. How much time did you usually spend on one of those days doing moderate physical activities as part of your work?

___ hours per day
___ minutes per day

6. During the last 7 days, on how many days did you walk for at least 10 minutes at a time as part of your work? Please do not count any walking you did to travel to or from work.

___ days per week
☐ No job-related walking ➔ Skip to PART 2: TRANSPORTATION

7. How much time did you usually spend on one of those days walking as part of your work?

___ hours per day
___ minutes per day

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the last 7 days, on how many days did you travel in a motor vehicle like a train, bus, car, or tram?

___ days per week
☐ No traveling in a motor vehicle ➔ Skip to question 10

9. How much time did you usually spend on one of those days traveling in a train, bus, car, tram, or other kind of motor vehicle?

___ hours per day
___ minutes per day

Now think only about the bicycling and walking you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the last 7 days, on how many days did you bicycle for at least 10 minutes at a time to go from place to place?

___ days per week
☐ No bicycling from place to place ➔ Skip to question 12
11. How much time did you usually spend on one of those days to bicycle from place to place?
   
   ________ hours per day
   ________ minutes per day

12. During the last 7 days, on how many days did you walk for at least 10 minutes at a time to go from place to place?
   
   ________ days per week
   □ No walking from place to place  →  Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

13. How much time did you usually spend on one of those days walking from place to place?
   
   ________ hours per day
   ________ minutes per day

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the last 7 days in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, chopping wood, shoveling snow, or digging in the garden or yard?
   
   ________ days per week
   □ No vigorous activity in garden or yard  →  Skip to question 16

15. How much time did you usually spend on one of those days doing vigorous physical activities in the garden or yard?
   
   ________ hours per day
   ________ minutes per day

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, sweeping, washing windows, and raking in the garden or yard?
   
   ________ days per week
   □ No moderate activity in garden or yard  →  Skip to question 18

LONG LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ, Revised October 2002.
17. How much time did you usually spend on one of those days doing moderate physical activities in the garden or yard?

____ hours per day
____ minutes per day

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate activities like carrying light loads, washing windows, scrubbing floors and sweeping inside your home?

____ days per week

☐ No moderate activity inside home → Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY

19. How much time did you usually spend on one of those days doing moderate physical activities inside your home?

____ hours per day
____ minutes per day

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the last 7 days solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the last 7 days, on how many days did you walk for at least 10 minutes at a time in your leisure time?

____ days per week

☐ No walking in leisure time → Skip to question 22

21. How much time did you usually spend on one of those days walking in your leisure time?

____ hours per day
____ minutes per day

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do vigorous physical activities like aerobics, running, fast bicycling, or fast swimming in your leisure time?

____ days per week

☐ No vigorous activity in leisure time → Skip to question 24
23. How much time did you usually spend on one of those days doing vigorous physical activities in your leisure time?

____ hours per day
____ minutes per day

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis in your leisure time?

____ days per week
☐ No moderate activity in leisure time

Skip to PART 5: TIME SPENT SITTING

25. How much time did you usually spend on one of those days doing moderate physical activities in your leisure time?

____ hours per day
____ minutes per day

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the last 7 days, how much time did you usually spend sitting on a weekday?

____ hours per day
____ minutes per day

27. During the last 7 days, how much time did you usually spend sitting on a weekend day?

____ hours per day
____ minutes per day

This is the end of the questionnaire, thank you for participating.
Appendix 9: Cognitive Task Assessment Sheet

**Study: Prefrontal Cortex Activity during Dual-task Performance in Patients with Chronic Obstructive Pulmonary Disease**

Participant Identification: ______________________ Date: ___/___/_____

### Set 1

<table>
<thead>
<tr>
<th>EARTH</th>
<th>CURVE</th>
<th>GUEST</th>
<th>ABOUT</th>
<th>PIZZA</th>
</tr>
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<td>E(l) Y(o) R(i) U(c) C(l)</td>
<td>T(ou) C(h) E(l) U(c) O(o) T(l)</td>
<td>T(ou) U(o) O(c) B(r) A(i)</td>
<td>A(c) L(e) Z(i) Z(0) P(0)</td>
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<td>MONTH</td>
<td>HOUSE</td>
<td>TOUCH</td>
<td>LEARN</td>
<td>DOZEN</td>
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<td>T(ou) C(h) E(l) U(c) O(o) T(l)</td>
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<td>STYLE</td>
<td>SOUND</td>
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<td>CABLE</td>
<td>SCALE</td>
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<td>Y(i) L(e) B(r) A(c) E(l)</td>
<td>C(1) T(c) U(c) O(o) C(c)</td>
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### Set 2

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