THE EFFECTS OF DANCE ON MOTOR AND NON-MOTOR FUNCTIONS, AND RESTING STATE ELECTROENCEPHALOGRAPHY IN INDIVIDUALS WITH PARKINSON'S DISEASE AND AGE-MATCHED CONTROLS

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ABSTRACT

We investigated the effects of a single Dancing with Parkinson's (DwP) class on behavior (balance, walking speed, depression) and electroencephalography (resting state - rsEEG) in individuals with Parkinson's disease (PD) and age-matched controls (C_{ONs}). Following a single 75-minute DwP class, individuals with PD demonstrated significant improvements in balance and depression, and C_{ONs} showed improvements in walking speed. The rsEEG also showed significant changes in both individual alpha peak frequency (iAPF) and individual alpha peak power (iAPP). C_{ONs} showed a global increase in iAPF during eyes open (EO) rsEEG and in iAPP during both eyes closed (EC) and EO conditions. Individuals with PD showed an increase in iAPP lateralized to right frontal areas, while this increase was lateralized to the left in C_{ONs}. We provide novel evidence for change in motor and non-motor functions with modulation of rsEEG alpha activity following dance class in individuals with PD and C_{ONs}.

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LIST OF ABBREVIATIONS

BBS – Berg Balance Scale

BG – Basal Ganglia

BOLD – Blood Oxygen Level Dependent

CNS – Central Nervous System

C_{ONs} – Controls

D1 – Dopamine 1

D2 – Dopamine 2

DBS – Deep Brain Stimulation

DwP@NBS: Dancing With Parkinson's at Canada's National Ballet School

EC – Eyes Closed

EEG – Electroencephalography

EO – Eyes Open

ERP – Event-Related Potential

FFT – Fast Fourier Transformation

GABA – Gamma-AminoButyric Acid

GDS: Geriatric Depression Scale

GPe – Globus Pallidus Externa

GPi – Globus Pallidus Interna

ICA: Independent Component Analysis

iAPF – Individual Alpha Peak Frequency

iAPP – Individual Alpha Peak Power

PD – Parkinson's Disease

PDD: Parkinson’s Disease with Dementia

QoL: Quality of Life

rCBF: Relative Cerebral Blood Flow

rsEEG – Resting State Electroencephalography

SNc – Substantia nigra pars compacta

SNr – Substantia nigra pars reticulate

STN – Subthalamic nucleus

TUG – Timed Up and Go

UPDRS-III – Unified Parkinson’s Disease Rating Scale III

1. INTRODUCTION

1.1 PARKINSON'S DISEASE

1.1.1 OVERVIEW

Parkinson's disease (PD) is a common hypokinetic movement disorder of the central nervous system (CNS) primarily associated with dysfunction of the basal ganglia (BG) and frontostriatal circuits (Tröster & Fields, 2008). This neurodegenerative disease affects about 1% of the worldwide population over 55 years of age (Han et al. 2013), and is believed to be present in the brain for many years before the development of motor symptoms (Gershanik, 2012). It is estimated that by the time overt motor symptoms develop, 70-80% of dopamine-producing striatal cells have been lost (Graybiel, 2000; Brown, 2003; Obeso et al. 2008; Tröster & Fields, 2008).

Individuals with PD face a plethora of motor impairments, including difficulties with transfers (i.e. sitting to standing), walking, and balance (Earhart, 2009; de Dreu et al. 2012), postural instability, rest tremor, muscle rigidity, freezing of gait, and asymmetric bradykinesia (slowness of movement) (Keus et al. 2007; Earhart, 2009; Heiberger et al. 2011; Gershanik, 2012, George et al. 2013), all of which rarely occur in individuals with PD before the age of 50 (Tröster & Fields, 2008). Resulting immobility may give rise to many non-motor symptoms as well, including osteoporosis, muscle weakness and/or cardiovascular disease, and may ultimately lead to social isolation, low self-esteem, and decreased quality of life (QofL) (Keus et al. 2007; Earhart, 2009; Heiberger et al. 2011). Patients can also experience non-motor symptoms such as cognitive impairments (Graybiel, 2000; Gershanik, 2012; Hashimoto et al. 2015; Sandoval-Rincón et al. 2015) within executive functions including working memory and

attention (Tröster & Fields, 2008) early in the course of their illness (Bassett, 2005), in addition to major depressive disorder (Hashimoto et al. 2015), which affects anywhere from 7 to 76% of individuals with PD (Sandoval-Rincón et al. 2015).

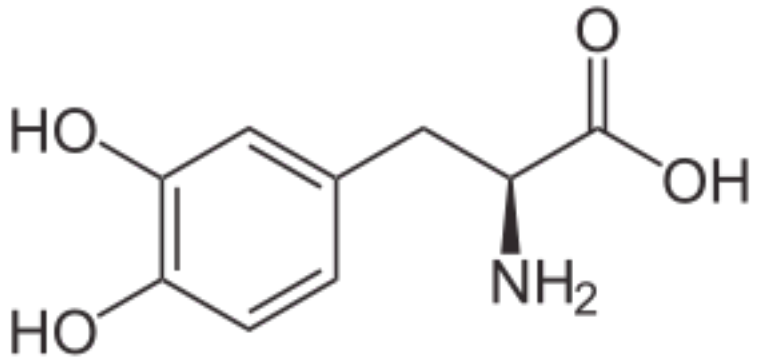
1.1.2 BRIEF HISTORY

In 1817 James Parkinson wrote 'An Essay on the Shaking Palsy', which included the description of six individual cases of what he termed 'Shaking Palsy' or *Paralysis Agitans* (Parkinson, 1817). These subjects suffered a range of slowly progressing symptoms including muscle weakness, unilateral trembling of the extremities, problems with voluntary movement initiation and gait (such as shuffling of the feet), stooped posture, and problems with speech and swallowing. Parkinson's essay was notably the first well-detailed description of what would later be coined *maladie de Parkinson*, or Parkinson's disease by the father of neurology Jean Martin-Charcot (Lees, 2007). Parkinson had hoped that through his description of these symptoms, physicians of the day would begin to search for its causes within the brain, having thought himself that it was potentially caused by trauma to the top of the cervical cord (Lees, 2007).

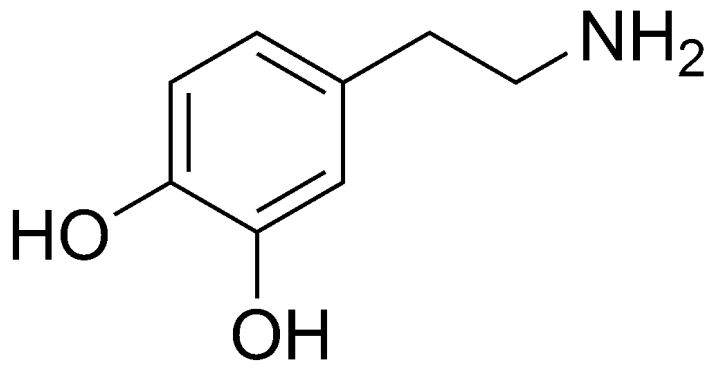
> *" … it has not yet obtained a place in the classification of nosologists; some have regarded its characteristic symptoms as distinct and different diseases, and others have given its name to diseases differing essentially from it;"* – James Parkinson, 1817.

Approximately 80 years later, Edouard Brissaud speculated that the localization of PD must stem from a subthalamic or peduncular region (Brissaud, 1895; Lees, 2007). His speculation was based on Parkinsonian symptoms being noted in a case report by Blocq and Marinesc (Blocq & Marinesc, 1894; Lees, 2007) in a patient suffering from a

tuberculomatous noisette [necrotic tissue caused by tuberculosis] in the midbrain. Another 50 years passed, during which time Tretiakoff reported nine damaged substantia nigras in Parkinsonian patients in his doctoral thesis (Lees, 2007, Tretiakoff, 1919), after which Hassler (1938) and Greenfield and Bosanquet (1953) solidified that Parkinson's related damage stemmed more specifically from the pars compacta region of the substantia nigra (Lees, 2007). With the realization that the pigmented cells of the substantia nigra were almost entirely depleted in individuals with PD, George C. Cotzias and colleagues began testing the hypothesis that Parkinsonian symptoms were a result of depleted neuromelanin (Fahn & Poewe, 2014). They attempted to replace the missing pigment and resultantly alleviate Parkinsonian symptoms by using three separate drugs in their 1967 study, namely, melanocyte stimulating hormone, D,L-phenylalanine (both of which were unsuccessful), and finally D,L-dopa, which provided some benefit to the patients. Having known that L-dopa (Figure 1a) was a precursor to dopamine (Figure 1b), and that earlier papers had reported a depletion of dopamine in the striatum of individuals with PD (Ehringer et al. 1960), Cotzias published a follow-up study in 1969, in which L-dopa was given to patients, rather than D,L-dopa (Cotzias et al. 1969), and the results were remarkable (Fahn & Poewe, 2014). It seemed that a larger dosage of L-dopa was necessary to alleviate symptoms, and after a follow up study by Yahr in 1969 confirming Cotzias' findings (Yahr et al. 1969), the use of this revolutionary drug for treating Parkinsonian symptoms gained acceptance (Fahn & Poewe, 2014), and research in to the neurodegenerative circuitry of PD burgeoned.



L-DOPA: (*S*)-2-Amino-3-(3,4-dihydroxyphenyl)propanoic acid



DOPAMINE: 4-(2-Aminoethyl) benzene-1,2-diol

Figure 1. L-Dopa is a precursor molecule to Dopamine. A. L-Dopa molecule. B. Dopamine Molecule.

1.1.3 SIMPLISTIC PATHWAY OF NEURODEGENERATION

A simplified schematic of the 'classical' proposed mechanism underlying the dopamine denervation-based pathway in PD has been suggested (Figure 2), resulting in the variety of motor and cognitive symptoms often observed. Pathological deviations found in PD stem from dopamine denervation along two neural pathways that compete with each other to functionally release movement (Graybiel 2000): the direct and indirect striato-pallidal pathways, both of which cause excessive inhibition of thalamo-cortical

nuclei (Obseo et al. 2008). Lack of dopamine in the substantia nigra affects the direct pathway via decreased gamma-aminobutyric acid (GABA) -ergic inhibition of the globus pallidus interna (GPi) in PD (Braak & Del Tredici, 2008; Obeso et al. 2008). Whereas, lack of dopamine in the indirect pathway results in excessive GABAergic inhibition of the globus pallidus externa (GPe), as well as decreased GABAergic inhibition of the subthalamic nucleus (STN), resulting in greater Glutamatergic excitation of the of the GPi (Braak & Del Tredici, 2008; Obeso et al. 2008). Combined, a much stronger GABAergic inhibition of the thalamus via an overstimulated GPi is observed in PD patients compared to non-diseased individuals. This results in decreased excitation of various brain regions such as the supplementary motor area, which is responsible for voluntary motion (Braak & Del Tredici, 2008; Tröster & Fields, 2008).

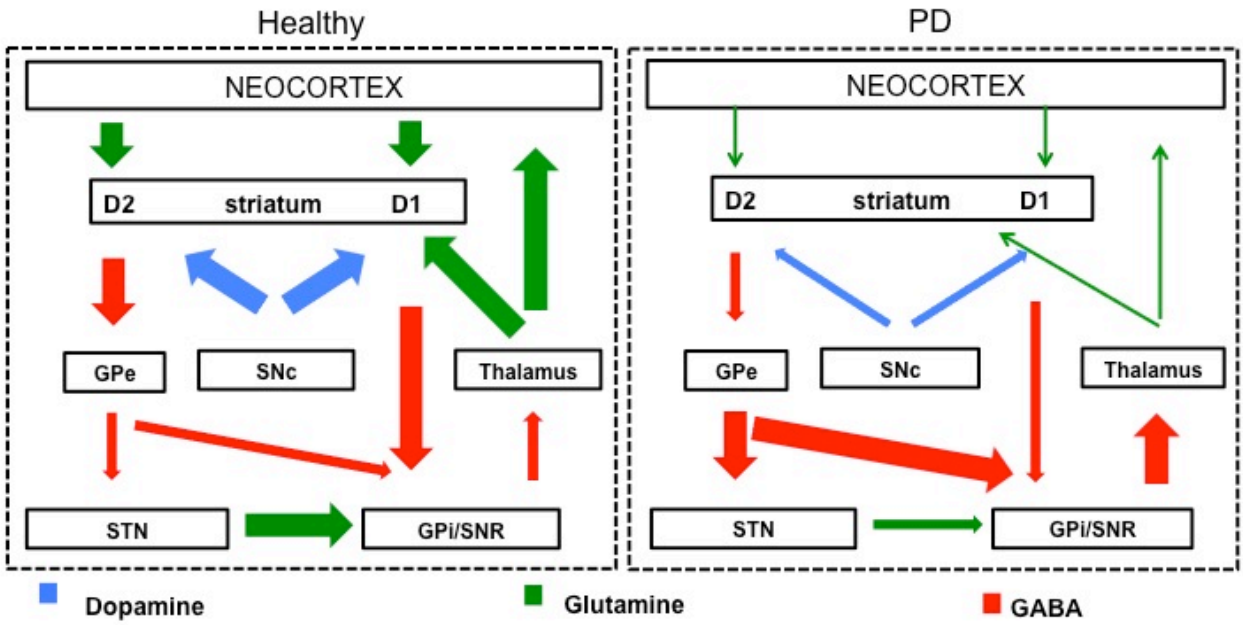


Figure 2. [1]Striato-Pallidal Pathway in healthy individuals and in individuals with PD. In the healthy brain (left), dopamine from the substantia nigra pars compacta (SNc) is released along two pathways, the direct and indirect. In the direct pathway, dopamine from SNc flows to Dopamine 1 (D1) receptors in the striatum, after which GABA neurotransmitters inhibit the Globus Pallidus Interna (GPi) and substantia nigra pars reticulata (SNr), allowing for a decreased inhibitory signal to be sent to the thalamus. In the indirect pathway, the SNc sends dopamine to Dopamine 2 (D2) receptors in the striatum, which send inhibitory GABA to the globus pallidus externa (GPe), which in turn decreases GABA inhibition of the subthalamic nucleus (STN), allowing for greater glutaminergic excitation of the GPi/SNr, and greater inhibitory GABA to the thalamus. In the Parkinsonian brain (right), decreased dopamine in both pathways results in a combined increase in inhibition of the thalamus.

1.1.4 TREATMENTS I – L-DOPA & DBS

Typical treatments for PD to date aim to restore equilibrium between the indirect and direct neural pathways implicated in PD (Braak & Del Tredici 2008). These include pharmacological and surgical interventions such as L-Dopa replacement and deep brain stimulation (DBS), respectively (Heiberger, 2011). Dopamine, taken in its precursor L-Dopa form, passes through the blood-brain-barrier in order to elevate the depleted dopamine levels in the striatum without significantly changing levels of noradrenaline or

[1] Figure 2 is an altered Figure 1a from Braak & Del Tredici (2008), with adjustments from Graybiel (2000) and Obeso et al. (2008).

serotonin (Brown, 2003). Unlike targeted DBS, dopamine replacements commonly prescribed for PD, such as levodopa and carbidopa, may have adverse side effects such as hallucinations, delusions, confusion, depression, anxiety, agitation, nightmares, and cognitive 'frontal' effects (Tröster & Fields, 2008), resulting from its widespread modulation of cortical and subcortical areas (George et al. 2013). Although chronic high-frequency DBS in pathologically overactive brain circuits of PD patients, such as the STN and GPi, has been found to produce profound clinical benefits (Graybiel, 2000; Mayberg et al., 2005), this procedure is highly invasive. It should also be noted that many of the balance, gait, and freezing problems are not alleviated by pharmacological and/or surgical treatments (de Dreu et al. 2012; Earhart, 2009). Between the adverse side effects of pharmacological interventions, the invasiveness and exclusivity of DBS, and the uncertainty that either of these treatments will significantly diminish symptoms, scientific research has turned to examining the motor and cognitive benefits of physiotherapy with particular emphasis on dance for individuals with PD.

1.1.5 TREATMENTS II - PHYSIOTHERAPY

While there is currently no widely accepted physiotherapy guideline for PD patients based on practical recommendations from scientific literature, researchers have outlined necessary components of physiotherapy for PD. Keus et al. (2007) believe that although physical therapy is unlikely to influence the disease process itself, it can improve daily functioning by teaching and training PD patients in the use of compensatory movement strategies. The necessary components of physical therapy for PD include *cueing strategies*, such as visual or auditory cues. Cues facilitate automatic and repetitive movements (de Dreu et al. 2012) and heighten awareness of all parts of

the body (Westheimer, 2008), which may allow for bypass of the dysfunctional loop from the BG while correcting for the improperly supplied internal rhythm (Earhart, 2009; Heiberger et al., 2011).

Other components of physiotherapy for PD are *cognitive movement strategies* (complex automated movements transformed into a series of sub-movements that must be executed in a fixed order in order to improve transfers), *balance training*, and improvements in *physical capacity* (through improving joint mobility and muscle power) (Keus et al. 2007; Earhart, 2009). In a review of dance therapy for PD, Earhart (2009) explains that dance incorporates all of the abovementioned requirements set forth by Keus et al. (2007), with its combined inclusion of both physical and cognitive stimulation (Dhami et al. 2015). Interest has shifted from standard physiotherapy practices to dance therapy due to the lack of compliance and regular participation from PD patients during physiotherapy. Additionally, dance is an enjoyable alternative to regular physiotherapy and has been found to improve adherence to a physical multifaceted exercise (Heiberger et al. 2011; Houston & McGill, 2013; Dhami et al. 2015), and to contribute to the mental, emotional, and physical well being of elderly (da Silva Borges et al. 2014).

1.1.6 TREATMENTS III - DANCE

Several studies have investigated the effects of dance in a PD population. In one study, the immediate benefits of a single dance class in PD patients who had been participating in said class for 8 months were investigated (Heiberger et al. 2011). This study examined motor control and QofL of PD patients before and after a single dance class. They found strongest improvements in rigidity scores of the limbs and not the neck, which may be a direct consequence of better proprioceptive-motor integration, as

well as improvements in hand movements, finger taps, and facial expression as measured by the Unified Parkinson's Disease Rating Scale (UPDRS-III). With regards to the QofL examination, PD patients noted improvements after 8-month participation in the dance class in categories such as active recreation, mobility, socializing, health, relationships, helping others, and expressing oneself creatively, as measured by the Oregon Health Science QofL Questionnaire. In a 17-month dance for PD study, Westheimer (2008) had participants fill out the QofL Questionnaire and they were also asked to indicate whether any items changed for the better as a result of attending the dance class. The two items that received the highest number of responses were Socializing and Health, both of which are problematic areas for individuals with PD.

Dance therapy can either be applied in the form of individual gait training or in a group setting. A meta-analysis of six studies that totaled 168 PD patients by de Dreu et al. (2012) looked at the benefits of dance therapy in PD patients, both individually and in groups, when compared to conventional physiotherapy therapy or no therapy. They examined standing balance, transfers, gait performance, severity of freezing, and QofL. The results showed relevant improvements in standing balance control due to partnered dance as measured by the Berg Balance Scale (BBS), improvements in activities of daily life as measured by the Time Up and Go (TUG), and finally, normalization and stabilization of walking pattern as measured by stride length. Additionally, a preliminary study in our lab examining the effects of dance in individuals with PD showed a reduction in TUG speed and improvement in the BBS (McDonald et al. 2014), and was the shortest reported dance intervention to date for PD (11 weeks between testing sessions) (Westheimer, 2008; Heiberger et al. 2011).

With the growing number of studies indicating positive benefits of recreational exercise for PD patients, such as improved gait speed, strength, balance, and QofL (Earhart, 2009), combined with the knowledge that dance therapy results in more significant improvements than other types of exercise and/or no exercise (Westbrook & McKibben, 1989; Hackney et al., 2007; de Dreu et al. 2012), our next step in this line of research is to examine brain-related plasticity as a function of dance for PD, as few studies have examined the neural correlates of dance class participation (Karpati et al. 2015; Li et al. 2015). To date, no studies investigating the effects of dance on rsEEG exist in the literature.

1.2 ELECTROENCEPHALOGRAPHY

1.2.1 WHAT DOES IT MEASURE?

Electroencephalography (EEG) is a non-invasive technique of recording natural oscillations of neural electrical potential activity in the brain, using electrodes placed on the human scalp (Buzsáki, 2006; Nunez & Srinivasan, 2006; Han et al. 2013). EEG is used in research for its excellent temporal resolution and high test-retest reliability (Han et al. 2013). However, it lacks spatial resolution (Buzsáki, 2006), making it difficult to allocate the underlying structural source of oscillatory activity (known as the 'inverse' problem, Lopes Da Silva & Storm Van Leeuwen, 1977; Goldman et al. 2002). There is however a fundamental assumption in EEG research that the location of sensors can be correlated to underlying cerebral structures, with increasing electrode number allowing for better spatial resolution (Koessler et al. 2009). The mean field activity measured by EEG is the average behavior of roughly 100 million to 1 billion neurons (Nunez & Srinivasan, 2006), with the superficial layers of the cortex generating most of the

synaptic electric potential activity measured on the scalp (Goldman et al. 2002; Buzsáki, 2006; Nunez & Srinivasan, 2006). From a cellular level, the field potentials recorded by EEG are a linear sum of numerous overlapping fields generated by current sources (i.e. ions moving from intracellular to extracellular space) and sinks (i.e. ions moving from extracellular to intracellular space). These mostly reflect post-synaptic potentials, both excitatory and inhibitory, stemming from cortical pyramidal cells arranged in parallel and space-averaged over cortex (Lopes Da Silva & Storm Van Leeuwen, 1977; Buzsáki, 2006; Han et al. 2013).

Spontaneous scalp EEG, or resting state EEG (rsEEG), is recorded in the absence of any external stimuli and has been an important tool for diagnosing, monitoring, and treating certain illnesses, such as brain tumors, strokes, epilepsies, severe head injury, sleep disorders, and brain death (Nunez & Srinivasan, 2006; Han et al. 2013). rsEEG reflects a state of highly organized processes within neuronal circuits and systems influenced by activation of voltage-gated channels, availability of neurotransmitters and neuromodulators, and distribution of synaptic weights (Buzsáki, 2006). EEG oscillations are typically labeled according to the frequency ranges of delta (1 – 4 Hz), theta (4 – 8 Hz), alpha (8 – 13 Hz), beta (13 – 20 Hz), and gamma (> 20 Hz) (Han et al. 2013); however, for our purposes, we will only be focusing on the alpha rhythm.

1.2.2 ALPHA RHYTHMS

Sometime in the late 1920s, German neurologist and inventor Hans Berger noticed a sinusoidal wave of roughly 10 cycles per second (Hz) while recording from scalp EEG (Berger 1920); he later named this the alpha rhythm (also known today as

the posterior dominant rhythm) (Goldman et al. 2002; Bazanova & Vernon, 2014). Alpha amplitude is highest when an individual is awake and relaxed with EC, and is attenuated when eyes are opened, when mental effort is applied, and/or when an individual feels drowsy or sleeps (Goldman et al. 2002; Han et al. 2013). No firm explanation exists regarding the origin of alpha rhythms (Lopes Da Silva & Storm Van Leeuwen, 1977; Goldman et al. 2002), however multiple hypotheses exist (Buzsáki 2006). The "Pacemaker" hypothesis suggests that alpha rhythms originate from a central source of cortical or thalamic neurons which entrain other thalamocortical neural populations, whereas an alternative hypothesis suggests that there is no single group responsible for the rhythm but rather that alpha oscillations come from synaptic coupling of neural sources widely distributed over the neocortical surface (Buzsáki, 2006; Han et al. 2013). In clinical settings, using EEG examination of the alpha rhythm is often a starting point (Han et al. 2013), as increased alpha activity is believed to correlate with decreased functional activity in underlying cortical areas (Goldman et al. 2002; Bazanova & Vernon, 2014). To test this hypothesis, researchers have begun using medical imaging techniques (i.e. Positron Emission Tomography and functional Magnetic Resonance Imaging) in combination with EEG in order to determine the cortical and subcortical sources of the alpha rhythm in humans (Goldman et al. 2002). Researchers have associated increases in resting alpha power with increased relative cerebral blood flow (rCBF) in areas including the thalamus, pons and midbrain, the basal frontal cortex (Sadato et al. 1998; Goldman et al. 2002; Bazanova & Vernon, 2014), and insula (Goldman et al. 2002). Additionally, decreased blood oxygen level dependent (BOLD) response has been associated with increased alpha power during rest in the parietal

and occipital lobes (Singh et al. 1998; Goldman et al. 2002), and in superior temporal, inferior frontal, and anterior cingulate regions (Goldman et al, 2002). Decreases in resting alpha power have been associated with decreased rCBF in bilateral occipital cortex and left dorsomedial prefrontal cortex (Sadato et al. 1998; Goldman et al. 2002). Unfortunately, as the mode of oscillatory generation is not entirely understood, correlations between alpha power and changes in rCBF and BOLD signal should be interpreted with caution. Correlations may stem from generator regions (as in the "Pacemaker" hypothesis), regions that are part of the generating regions but do not themselves generate the oscillations (alternate hypothesis), and/or regions where activity is correlated but not causally linked to rhythm generation (Goldman et al. 2002; Bazanova & Vernon, 2014).

1.3 RESTING STATE EEG

1.3.1 … AND PARKINSON'S DISEASE

According to the "Pacemaker" hypothesis, one would expect abnormal alpha activity in the rsEEG of individuals with PD, as their thalamocortical network is working inefficiently due to the over inhibition of the thalamus via the striato-pallidal pathway. Consequently, several studies have examined differences in rsEEG between people with PD and C_{ONs}, and the results are inconsistent (Stoffers et al. 2007). Some studies show decreased resting alpha (8-13Hz) (Soikkeli et al. 1991) and beta (13-30Hz) power in PD (Soikkeli et al. 1991; Bosboom et al. 2006; Stoffers et al. 2007) when compared to C_{ONS}, whereas others show increased alpha (Bosboom et al. 2006; Stoffers et al. 2007) and beta power in PD (Moazami-Goudarzi et al. 2008). These inconsistencies likely stem from methodological differences (Moazami-Goudarzi et al. 2008) such as cortical

area/electrodes examined (i.e. frontal electrodes vs. occipital electrodes) (Bazanova & Vernon, 2014), calculations used to derive power (i.e. peak power vs. averaged power), and even eye state during rsEEG (EO vs. EC). One rsEEG difference between individuals with PD and C_{ONS} that remains consistent throughout the literature, even with methodological differences, is found in the examination of resting iAPF. Namely, individuals with PD are consistently found to have a lower iAPF when compared to C_{ONs} (Soikkeli et al. 1991; Moazami-Goudarzi et al. 2008). Lower frequencies are suggested to correlate to longer windows of phasic suppression (Haegens et al. 2014), a probable consequence of over inhibition of the thalamus reflected in rsEEG.

1.3.2 … AND DOPAMINE

Differences in oscillatory activity between individuals with PD and C_{ONS} may be a result of two mechanisms stemming from dopamine degeneration in the striatum, namely abnormal basal ganglia outflow to the frontal cortex and/or a loss of dopamine terminals in the frontal cortex itself (Stoffers et al. 2007). This being said, one might predict that dopamine replacement would return oscillatory activity to more normal levels, or change the oscillatory nature of the rsEEG. This however, is not necessarily the case; dopamine replacement does not normalize the firing pattern of the basal ganglia (Obeso et al. 2008), and several studies have demonstrated a lack of dopamine-induced alpha oscillatory modulation when specifically comparing rsEEG oscillatory power in PD patients ON and OFF levodopa (Stoffers et al. 2007; George et al. 2013). It should be noted, however, that local field potential studies during DBS surgery examining oscillatory activity in STN or GPi have revealed changes in neural synchronization and discharge patterns resulting from dopamine replacement, however

this was in beta and gamma bands only (Obeso et al. 2008). Thus, dopamine replacements will have no effect on alpha rhythm in our study.

1.3.3 … AND EXERCISE

Since dance is considered an exercise (Dhami et al. 2015), or physical activity (da Silva Borges et al. 2014) one can turn to studies examining exercise-induced changes in rsEEG to hypothesize the expected changes in the present study. Typically these studies report an exercise-induced increase in alpha power (Lardon & Polich, 1996, Kubitz & Pothakos, 1997, Schneider et al. 2009) and iAPF (Gutmann et al. 2015) while the underlying causes for the influence of physical exercise on the EEG remain unclear. In a study by Lardon and Polich (1996), rsEEG was compared between young adults who engaged in high levels of physical exercise and C_{ONS} subjects that performed comparatively little exercise. They found increased low alpha, high alpha, and high beta power in avid exercisers when compared to C_{ONS}. They also found higher mean frequency values in low, and high beta in avid exercisers compared to C_{ONS}. The researchers postulate that this may be due to the promotion of rCBF but its relation to increasing or decreasing rhythms is uncertain. A comprehensive review by Dustman et al. (1994) notes that there is evidence for a positive relationship between physical exercise and CNS health in animals, which occurs at least in part because of improved neurotransmitter functioning and preservation of dopaminergic cells (Lardon & Polich, 1996; Ermutlu et al. 2015).

Researchers have also examined changes in rsEEG, affect, and cognition in a cycling versus no exercise group, with results showing increased alpha and decreased beta power in exercisers versus C_{ONS} (Kubitz & Pothakos, 1997). Using activation

theory, the authors suggest that the meaning of shifts in alpha power can be understood by examining shifts in other EEG frequencies. For example, activation theory stipulates that increases in alpha power accompanied by increased theta or decreased beta, or both, would indicate decreased brain activation, whereas alpha increases accompanied by decreased theta or increased beta activity, or both, would indicate increased brain activation (Kubitz & Pothakos, 1997). Their findings imply that there is a period of decreased brain activation after exercise (i.e. within the first 15 minutes), contrary to previous research (Lardon & Polich, 1996). Interestingly, their participants felt more energetic and activated after exercise, while showing a temporary decline in cognitive function (Kubitz & Pothakos, 1997). These findings suggest that there is a negative correlation between physical energy and brain function immediately post-exercise. However, teasing apart the meaning of exercise-induced increases in overall cortical activation is very difficult, especially because emotional processes are tightly connected to changes in frontal alpha activity.

Further investigations on changes in rsEEG after intensive exercise have been conducted with respect to treadmill use (Schneider et al. 2009). Pre-exercise, immediately post-exercise, and 15 minutes post-exercise rsEEG measurements were obtained, and exercise-induced changes were anatomically localized. Researchers found increases in low alpha power in the left middle frontal gyrus immediately after exercising (unlike Kubitz & Pathakos, 1997). In the 15 minutes post-exercise condition, decreases in high alpha in one voxel of the left inferior temporal gyrus were found, and decreases in low beta power in the left inferior middle and superior temporal gyri were found when compared to the pre-exercise condition. Observed increases in frontal low

alpha power were associated with emotional effects of exercise, as the frontal cortex is strongly connected to emotional processing. Specifically, the authors postulate that greater left frontal lobe activity may serve as a marker of positive emotions. This is a key component of the well-documented model of frontal asymmetry (Wheeler et al. 1993). Schneider et al. (2009) also found decreased low beta power in the temporal cortex and similar decrease of gamma 15 minutes after exercise, which might reflect transformation of slow EEG rhythms into faster oscillations characteristic of aroused and alert states.

1.4 OBJECTIVES AND HYPOTHESES

1.4.1 OBJECTIVES

In our lab, we have begun to address the neural mechanisms of learning a dance in expert individuals through the use of functional magnetic resonance imaging (Bar & DeSouza, 2012; Olshansky et al. 2014), and now we plan to apply this line of research to individuals with PD, specifically through the use of behavioural measures and EEG. Our study will examine changes in balance, walking speed, depression, and rsEEG associated with dance in those with PD as well as in healthy age matched C_{ONS}, by examining these measures immediately before and after participation in one 75-minute dance class. We will examine changes in iAPP and iAPF rather than averaging alpha power over a pre-determined range (i.e. 8 – 12 Hz), as these values give a more accurate estimate of alpha modulated activity (Bazanova & Vernon, 2014; Haegens et al. 2014)

1.4.2 HYPOTHESES

A high degree of variability exists in the aforementioned studies examining exercise-induced changes in rsEEG. Extrapolating a directional hypothesis from the abovementioned studies should be done with caution as these studies examined healthy young adults exercising without music, whereas the present study will examine changes in rsEEG in an elderly and clinical sample before and after dance accompanied by music. An important property of dance is its inherent synchronization of movements to a rhythmic timekeeper (Brown et al. 2005), made possible with the help of the basal ganglia (more specifically the putamen) which aids in the selection and organization of predictable, and regularly timed movements (Brown et al. 2005) such as walking. Indeed, research has shown strong activity in the putamen resulting from dance movements made to metric rhythms (Brown et al. 2005; Hashimoto et al. 2015)

We hypothesize that dance will produce improvements in balance, walking speed, and depression scores, and that dance will induce changes in resting alpha, both in frequency peak (Hz) and it's associated power (μV^2), as both are hypothesized to be involved in changes in arousal, attention, and information processing (Gutmann et al. 2015). Specifically we expect to find changes in resting iAPP and iAPF; however the directionality of these changes remains elusive. We also expect to replicate lower iAPF in PD when compared to C_{ONS}, consistent with that which is shown in the literature. Additionally, we will investigate the influence of electrode position, and eye state on the rsEEG analysis while exploring effects of dance.

By examining these changes, we can begin to understand the neural mechanisms underlying the dance-induced behavioral improvements demonstrated in

the literature, and in our own evaluations of dance-induced changes in motor and non-motor symptoms. Observed dance-induced EEG changes will be related to the existing literature, and we will propose a neural model and hypothesize whether these changes reflect modulation of affect (through presence of lateralized differences), are associated with exercise more generally (no presence of lateralized differences), or perhaps reflect a return to more normal oscillatory activity as seen in the baseline rsEEG of our C_{ONs} (i.e. lower iAPP and higher iAPF).

2. METHODS

2.1 PARTICIPANTS

A total of 47 people participating in a Dancing with Parkinson's Program at Canada's National Ballet School (DwP@NBS) volunteered to participate in our study. Of these, 24 were individuals with PD (mean age = 68 ± 8.1 years), and 23 were C_{ONS} (mean age 62 ± 10.8 years) that comprised of spouses, caregivers, relatives, and volunteers at DwP@NBS. All participants were compensated $25/hour for their time and involvement in the study. In addition to the rsEEG component of our study, participants completed the TUG, the BBS, and the Geriatric Depression Scale (GDS), and were asked to fill out demographic and medical questionnaires (See Table 1, Appendix A, and, Appendix B). The behavioral and rsEEG measures were collected on different dates, and some participants did not complete all four measures (See Table 2).

Table 1. Medication information for individuals with PD participating in rsEEG. All participants were taking some form of L-Dopa replacement, while eight of 20 participants were taking antidepressants and/or antianxiety medication.

Sex	Age	Disease Duration (Years)	PD Medication	Antidepressant/Antianxiety Medication
F	67	0	APO-LEVOCARB SELEGILINE	
F	76	3	APO-LEVOCARB	ATIVAN
F	74	14	AMANTADINE APO-LEVOCARB NEUPRO PATCH	PAXIN
M	69	2	L-DOPA	
M	72	6	APO-LEVOCARB PRAMIPEXOLE	
M	69	5	L-DOPA PRAMIPEXOLE	
M	63	4	PRAMIPEXOLE APO-LEVOCARB	
F	68	4	DOMPERIDONE PRAMIPEXOLE	
M	69	3	APO-LEVOCARB	
M	67	0	L-DOPA	PRISTIQ
F	88	6	APO-LEVOCARB	
F	65	0	APO-LEVOCARB	
F	64	40	AMANTADINE APO-LEVOCARB PRAMIPEXOLE	
M	58	18	AMANTADINE L-DOPA PRAMIPEXOLE	APO-TRIHEX
M	69	9	APO-LEVOCARB	TRAZODONE
F	60	10	AMANTADINE STALEVO PRAMIPEXOLE	EFFEXOR CIPRALEX
F	67	2	L-DOPA	
F	53	2	L-DOPA	AMITRYPTILIN
M	82	0	APO-LEVOCARB	
M	52	15	APO-LEVOCARB	PAXIL/PAROXETINE WELLBUTRIN/BUPROPION CO QUETIAPINE

Table 2. Sample size for each motor, non-motor, and rsEEG measure.

Group	BBS	TUG	GDS	rsEEG
PD	n = 16	n = 16	n = 18	n = 20
C_{ONS}	n = 6	n = 6	n = 8	n = 21

2.2 BEHAVIORAL PROTOCOL

2.2.1 DATA COLLECTION

The TUG and BBS were performed before and after a single dance class on three separate dates, one in January 2014, one in April 2014, and one in June 2014. Nineteen out of 24 participants with PD, and 6 C_{ONS} out of the 23 completed the BBS and TUG scales during 1, 2 or 3 of the time points. Three participants with PD were excluded from this analysis, as they did not complete both a pre- and post- dance class evaluation during any of the time points, leaving 16 individuals with PD (mean age = 69.7 ± 7.1 years), and 6 C_{ONS} (mean age = 68.5 ± 5.02 years).

The GDS was completed before and after a single dance class on three separate dates, one in March 2014, one in April 2014, and one in June 2014. Nineteen out of 24 participants with PD (mean age = 68.6 ± 8.2 years), and 8 C_{ONS} (mean age = 64.6 ± 6.7 years) out of the 23 completed the GDS during 1, 2 or 3 of the time points.

2.2.2 DATA ANALYSIS

For those participants that completed more than 1 pre-/post-dance class evaluation (i.e. participated in April 2014 and June 2014), scores were averaged across time points in order to create a single score for each participant for each of the TUG_{avg}, BBS_{avg}, and GDS_{avg} measures, pre- and post-dance class. Statistical analyses were conducted with SPSS (Version 20, IBM Corp, 2011, Armonk, NY).

2.3 RESTING STATE EEG PROTOCOL

2.3.1 DATA COLLECTION

To obtain rsEEG data, subjects were asked to remain as still as possible and let their mind wander for two three-minute recording epochs: once with their EO, and once with their EC. The presented order of these conditions was randomized within and between subjects. Subjects performed the rsEEG paradigm before and after a single 75-minute dance class in a quiet, closed-door study room at NBS. Earphones with ear buds were provided to minimize any external noise and to ensure that participants heard the auditory prompts to open and close their eyes during the paradigm. All rsEEG recordings were acquired in the morning between 9:00am and 10:00am for the pre-dance class condition and between 11:30am and 12:30pm for the post-dance class condition. This recording schedule controlled for potential confounds of circadian factors on EEG activity (Moazami-Goudarzi et al. 2008). Subjects were also asked to refrain from consuming caffeinated beverages on the day of recording to avoid caffeine-induced alpha and theta decreases in EEG (Newman et al. 1992; Dimpfel et al. 1993; Moazami-Goudarzi et al. 2008). Researchers made note of what the subjects thought about during each session, and noted whether the participants felt drowsiness. This information is important as it may account for any unusual observations in the recorded waveform profiles. Data was collected once a week, from 1 to 2 participants, from January 2014 to December 2014.

EEG data was acquired using a wireless 14-channel Emotiv EPOC® EEG Neuroheadset and recorded with TestBench software (Emotiv Systems, 2012, San Fransisco, CA). The Emotiv EPOC® is an EEG system used both for gaming and

research purposes, and has been validated against a purely research based EEG system (Neuroscan system) for collection of auditory event-related potentials (ERPs) (Badcock et al. 2013)[2]. Emotiv EPOC® electrode sites are in accordance to the International 10-20 System and include AF3, F7, F3, FC5, T7, P7, O1, O2, P8, T8, FC6, F4, F8, and AF4 electrode sites. The headset has two reference electrodes (CMS and DRL) at P3 and P4 and samples at a rate of 128Hz with 16-bit ADC resolution and 0.02 to 45 Hz resolution, with digital notch filters at 50 and 60 Hz. All stimuli were created in and presented by MediaLab (v2012.4.119, Blair Jarvis for Empirisoft Co., New York, NY). Data markers were sent from MediaLab to TestBench via Virtual Serial Port Driver (Version 7.1, Eltima Software, 2013, Bellevue, WA).

2.3.2 DATA PREPROCESSING

Preprocessing of EEG data was conducted offline in Matlab (Version 7.10.0.99 R2010a, The Mathworks, Inc., Natick, MA) using the Fieldtrip toolbox (Oostenveld et al. 2011). Steps taken for data pre-processing are as follows:

Step 1: The .edf files from TestBench were converted to .mat files.

The data was converted from a 3D matrix (Channel, Samples, Epochs) to a 2D matrix (Channel, Samples) because a single Epoch was recorded for each participant and thus this dimension could be dropped. This was done in order to utilize Matlab software.

Step 2: Data markers were identified.

The Eltima software allowed numerical markers to be sent to the EMOTIV software

[2] Badcock et al. (2013) recorded EEG from participants listening to standard and deviant auditory tones in active and passive listening conditions whilst participants simultaneously wore the Emotiv EPOC® (gaming and research EEG) and the Neuroscan system (research EEG). Late ERP waveforms were created for each EEG system, for each combination of conditions (i.e. standard passive tones, standard active tones, deviant passive tones, and deviant active tones), and similarity of waveform peaks were compared. The study concluded that the waveforms derived from the Emotiv EPOC® EEG system compared well with the Neuroscan EEG system for the procurement of reliable auditory ERPs measuring P1, N2, P2, N2, and P3 peaks at frontal electrode sites (Badcock et al. 2013).

during recording. At the start of the EO rsEEG segment, the number 98 appears in the data. At the start of the EC rsEEG segment, the number 100 appears in the data. The code identified the start of each segment (via numbered marker), and the point 180 seconds after each segment began.

Step 3: Epoching segmentation: redefining in to EO and EC segments.

The data was then epoched in to a 3-minute EO segment and a 3-minute EC segment.

[3]Step 4: Epoching segmentation: redefining in to 2-second bins.

Each 180-second rsEEG segment was redefined in to 2 second bins, creating 90, 2 second bins for each rsEEG segment (EO and EC).

Step 5: Preprocessing for visualization

A twopass Butterworth filter was applied from 1 - 50 Hz. Demean (baseline correction) and detrend (removal of mean value or linear trend) corrections were applied.

Step 6: Visual inspection and data checking

Each 2-second epoch of data was visually inspected using variance, amplitude maximums and max z values. Obvious outliers in the data were rejected. In the PD group, in the pre-dance condition, an average of 14.5 ± 7.7 two-second epochs were rejected in the EO condition, and 13.7 ± 6.9 two-second epochs were rejected in the EC condition. This resulted in 151 ± 15.4 seconds (2.52 mins) of useable rsEEG data in the pre-dance EO condition, and 152.6 ± 13.7 seconds (2.54 mins) of useable rsEEG data in the pre-dance EC condition. In the C_{ONS} group, in the pre-dance condition, an average of 12.4 ± 4.3 two-second epochs were rejected in the EO condition, and 13.4 ± 6.2 two-second epochs were rejected in the EC condition. This resulted in 155.2 ± 8.6

[3] Steps 4 – 10 are completed for each participant, one at a time, for each pre- and post-dance class .mat files.

seconds (2.59 mins) of useable rsEEG data in the pre-dance EO condition, and 153.2 ± 12.3 seconds (2.55 mins) of useable rsEEG data in the pre-dance EC condition. In the PD group, in the post-dance condition, an average of 12.9 ± 7 two-second epochs were rejected in the EO condition, and 11.8 ± 8.2 two-second epochs were rejected in the EC condition. This resulted in 154.2 ± 14 seconds (2.57 mins) of useable rsEEG data in the post-dance EO condition, and 156.4 ± 16.5 (2.61 mins) seconds of useable rsEEG data in the post-dance EC condition. In the C_{ONS} group, in the post-dance condition, an average of 12.6 ± 7.1 two-second epochs were rejected in the EO condition, and 14.2 ± 7.1 two-second epochs were rejected in the EC condition. This resulted in 154.9 ± 14.2 seconds (2.58 mins) of useable rsEEG data in the post-dance EO condition, and 151.6 ± 18.9 seconds (2.53 mins) of useable rsEEG data in the post-dance EC condition.

Step 7: Independent Component Analysis (ICA)

To further clean the data, the raw signal was mathematically divided in to 14 independent components depending on naturally recurring variances in the data. The first few components house the largest variances, and are typically where artifacts such as eyes blinks, eyes movements, and/or noise are found.

Step 8: Visual inspection of the topographical disposition of the components

Topographic dispositions of each component were inspected for possible artifact profiles (Figure 3) such as eye blinks, eye movements, or noise (Figure 4).

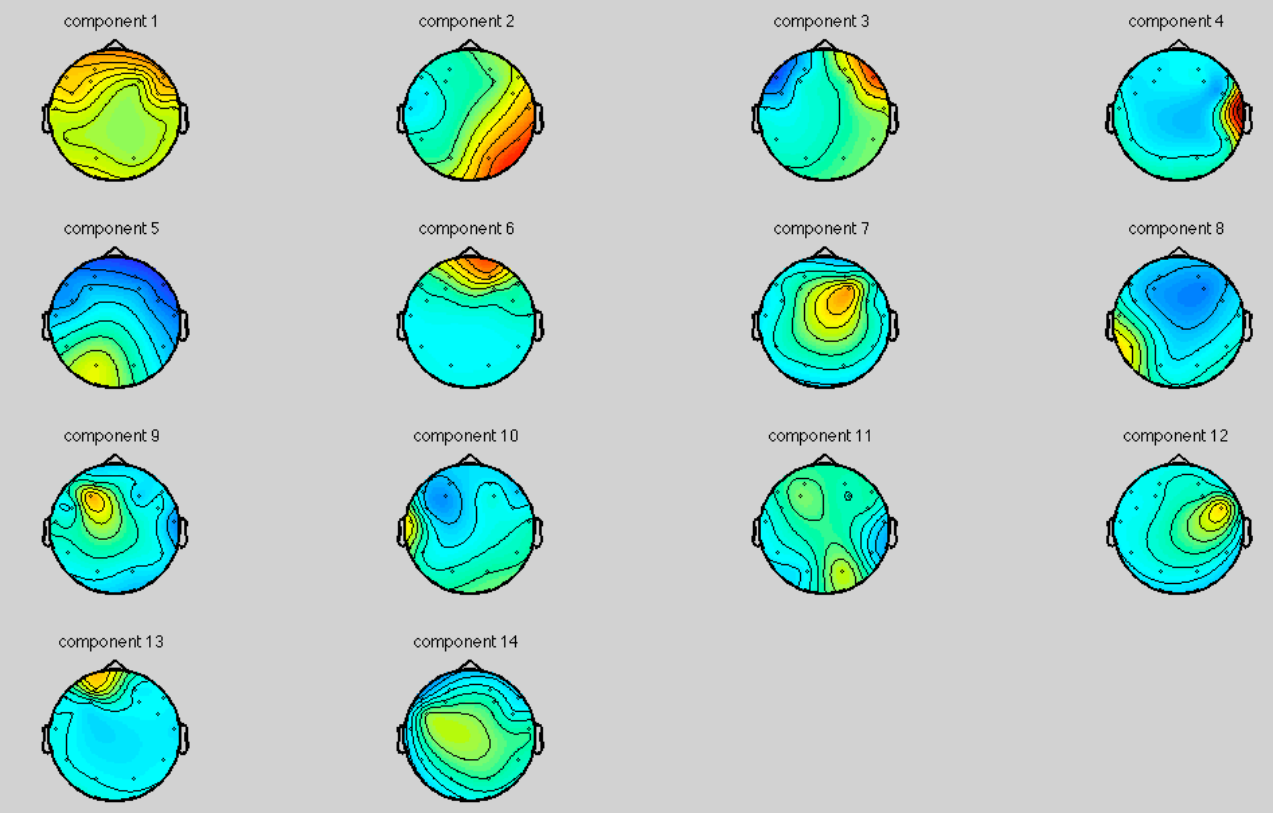
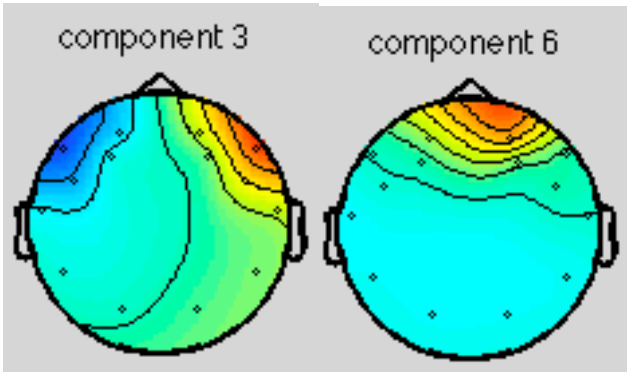


Figure 3: Sample topographic disposition of components. Components 1 to 14 created by ICA. All components are inspected for potential eye movements, eye blinks, or noise profiles.



E.g. Eye Movement E.g. Eye Blink

Figure 4: Identified components of interest. Component 3 is a typical profile of an eye movement, with a hot spot polarized by a cold spot in the frontal area. Component 6 is a typical eye blink profile, with a centralized hotspot in the frontal region.

Step 9: Component Inspection

Using channels AF3 and AF4 (black and blue), each 2-second epoch within identified components of interest (Step 8) is inspected for eye-blinks and/or eye-movements (Figure 5).

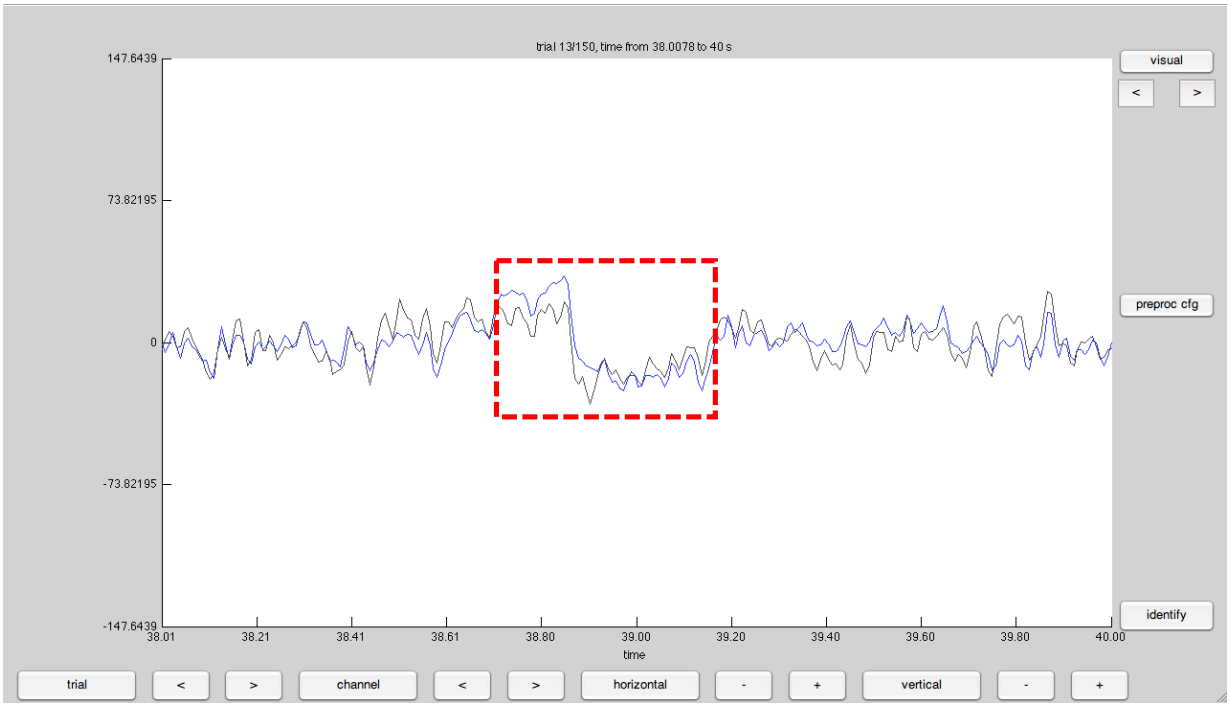


Figure 5. A two-second epoch within channels AF3 and AF4 containing a potential eye movement. This sample epoch shows a potential eye movement in the two-second bin of raw data from 38-40 seconds of recording. Resultantly, this epoch will be further investigated within component 3 (Figure 4) in Step 9.

When a two-second epoch containing one or all of these artifacts is identified, this specific epoch is examined within each identified components of interest (i.e. component 3 in our example, as this appears to be an eye movement) (Figure 6). This is done in order to ensure that the previously identified components of interest do in fact contain artifacts, before their removal in step 10. For each potential artifact identified in Step 8, a minimum of three, two-second epochs containing this artifact must be identified before a component is removed.

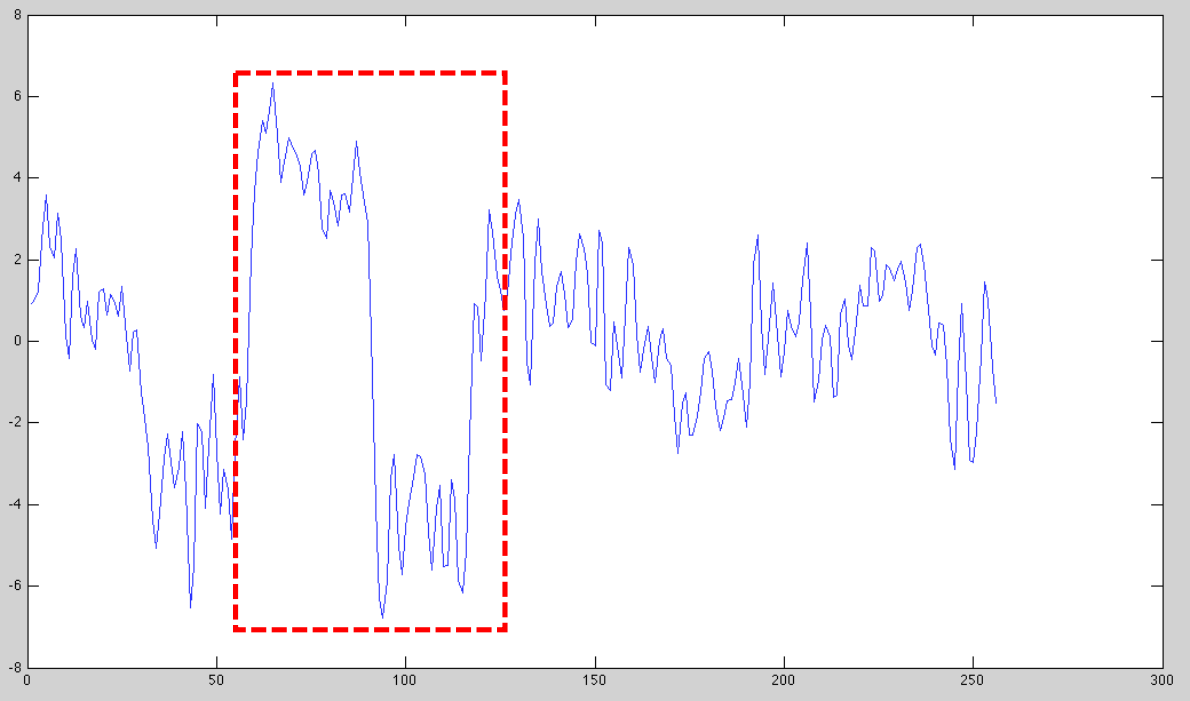


Figure 6. Component 3 houses noise created by eye movements. After identifying a two-second epoch in Step 8 that potentially contained an eye movement, this notion was confirmed through an examination of that specific 2-second epoch of raw data in only component 3. Here we see that noise caused by eye movements is housed in component 3, and thus, component 3 should be removed.

Step 10: Component removal

Components containing confirmed artifacts are removed from the data, and a component rejected .mat file is created.

Step 11: Re-reference

To clean the signal further, the average signal across all electrodes is computed and subtracted from each electrode, for each time point.

Step 12: Frequency Analysis – Power Spectra Computed

A multitaper Fast Fourier Transformation (FFT) was applied, in which the entire spectrum for the entire data length was analyzed. Frequencies of interested were organized in to 0.5 Hz increments from 1 to 50 Hz, and a Hanning window was applied

in order to correct for leakage in the FFT.

Step 13: Alpha Peak Search

The alpha frequency peak (y-axis) and associated power (x-axis) are identified for each subject for EO and EC separately (see Appendix C for sample individual powerspectra), for each individual electrode in the pre-dance, and post-dance rsEEG. Data are exported to SPSS for statistical analyses.

2.3.3 DATA ANALYSIS

All iAPP values were log transformed before undergoing any statistical tests in order to be able to use *normal* statistical measures. Statistical analyses were conducted offline in SPSS (Version 20, IBM Corp, 2011, Armonk, NY).

3. RESULTS

3.1 BEHAVIORAL

3.1.1 Berg Balance Scale

A 2 (Time) x 2 (Group) repeated Measures ANOVA revealed that BBS_{avg} scores did not improve after a single dance class ($F(1,20) = 1.700$, $p = 0.207$, $\eta^2 = 0.078$). Additionally, there was only a trend approaching significance indicating that the C_{ONS} group had higher BBS scores than the PD group ($F(1,20) = 4.027$, $p = 0.058$, $\eta^2 = 0.168$). When groups were analyzed separately, the PD group demonstrated a significant increase in BBS_{avg} scores ($F(1,15) = 5.223$, $*p < 0.05$, $\eta^2 = 0.258$). BBS_{avg} scores did not improve significantly in the C_{ONS} group ($F(1,5) = 0$, $p = 1$, $\eta^2 = 0$) (Figure 7A).

3.1.2 Timed Up and Go

A 2 (Time) x 2 (Group) repeated Measures ANOVA revealed that TUG_{avg} scores improved significantly after a single dance class ($F(1,20) = 9.088$, $p < 0.01$, $\eta2 = 0.312$). There were no significant group differences ($F(1,20) = 2.489$, $p = 0.13$, $\eta^2 = 0.111$) When groups were analyzed separately, the C_{ONS} group demonstrated a significant increase in TUG_{avg} scores ($F(1,5) = 13.965$, $*p < 0.05$, $\eta^2 = 0.736$), whereas the PD group did not ($F(1,15) = 1.435$, $p = 0.249$, $\eta^2 = 0.087$) (Figure 7B).

3.1.3 Geriatric Depression Scale

A 2 (Time) x 2 (Group) repeated Measures ANOVA revealed that GDS_{avg} scores improved after a single dance class ($F(1,25) = 4.240$, $*p = 0.05$, $\eta2 = 0.145$). Additionally, there was only a trend approaching significance indicating that the PD group had higher GDS scores than the C_{ONS} group ($F(1,25) = 3.932$, $p = 0.058$, $\eta^2 =$

0.136). When groups were analyzed separately, the PD group demonstrated a significant decrease in GDS_{avg} scores ($F(1,18) = 9.617$, $^{**}p < 0.01$, $\eta^2 = 0.348$). GDS_{avg} scores did not improve significantly in the C_{ONS} group ($F(1,7) = 0.118$, $p = 0.741$, $\eta^2 = 0.017$) (Figure 7C).

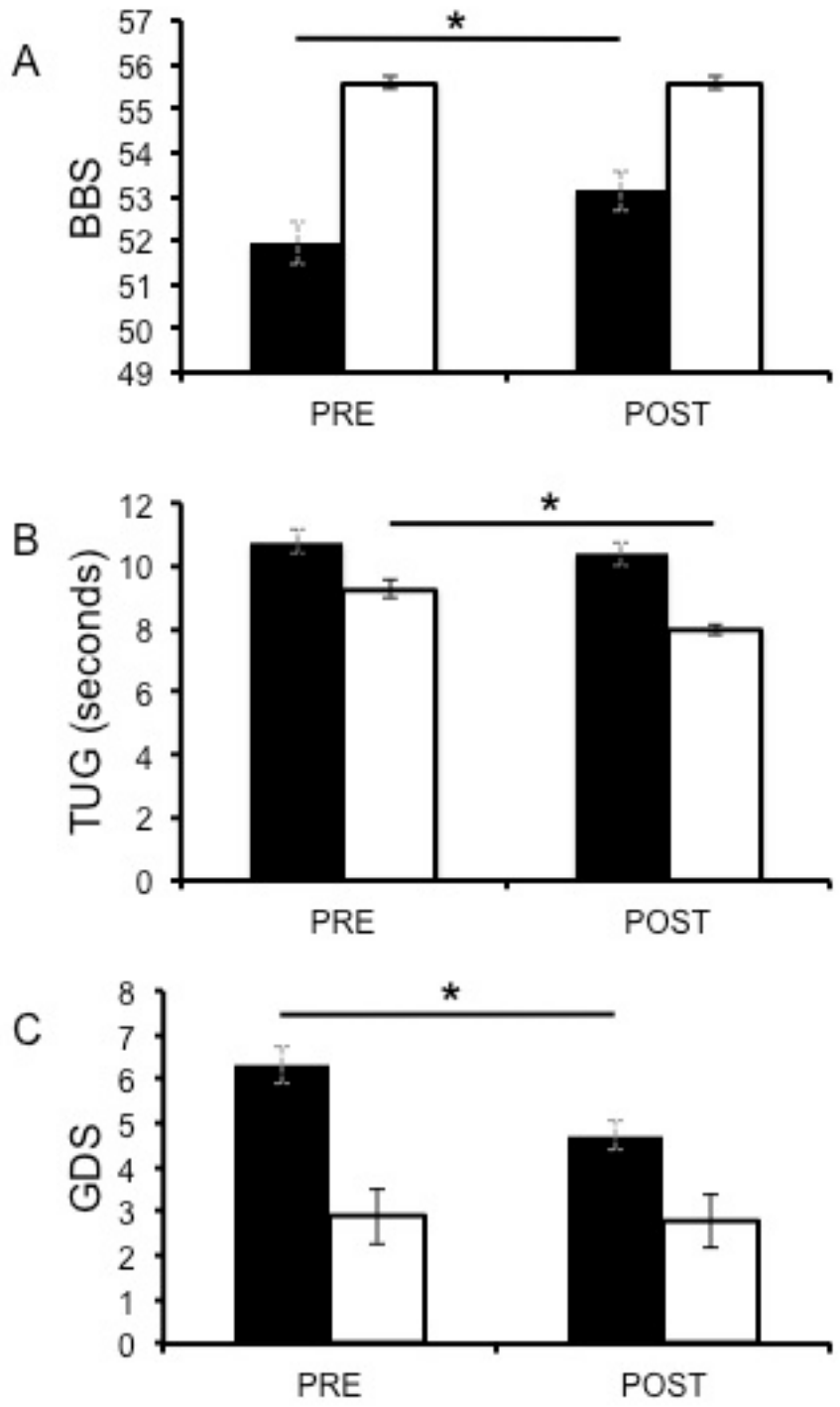


Figure 7. Behavioral Results. (A) BBS_{avg} scores improved after a single dance class in the PD group ($F(1,15) = 5.223$, $^*p < 0.05$, $\eta^2 = 0.258$). (B) TUG_{avg} scores decreased significantly after a single dance class in the C_{ONS} group ($F(1,5) = 13.965$, $^*p < 0.05$, $\eta^2 = 0.736$). (C) GDS_{avg} scores improved after a single dance class in the PD group ($F(1,18) = 9.617$, $^{**}p < 0.01$, $\eta^2 = 0.348$). Black = PD, White = C_{ONS}, Bars = SEM.

3.2 RESTING STATE EEG: ALPHA (5.5 – 12.5 Hz)

3.2.1 INDIVIDUAL ALPHA PEAK FREQUENCY

A 2 (Group) x 2 (Eye State) x 2 (Time) x 14 (Electrode) repeated measures ANOVA revealed a main effect of Group (F (1, 39) = 25.863, p < 0.01, η^2=0.399), in which C_{ONS} exhibited a higher iAPF when compared to individuals with PD (Figure 8), a main effect of Electrode (F (6.081, 237.152) = 6.972, p < 0.01, η^2=0.152) (see Appendix H for Bonferroni corrected pairwise comparisons), and an increasing trend for Time (F (1, 39) = 3.593, p = 0.065, η^2=0.084). Additionally, an interaction between Eye State and Group (F (1, 29) =36.589, p < 0.01, η^2=0.152) was revealed in which pairwise comparisons showed that the EO and EC conditions were not significantly different in PD (p_B =0.480) when compared to C_{ONS} in which the EC condition had a higher iAPF than the EO condition (p_B <0.01). An interaction between Time and Eye State (F (1, 39) = 5.965, p < 0.01, η^2=0.133) demonstrated that iAPF in the EO condition increased (p_B <0.01) from pre- to post- dance class whereas iAPF in the EC did not change as a result of dance (p_B =0.573). As there was an interaction between Eye state and Group, we investigated the Time x Eye State interaction in each Group. This analysis revealed that the Time x Eye state interaction was only present in the C_{ONS} group (F (1, 20) = 6.494, p < 0.05, η^2=0.245), in which only the iAPF in the EO condition increased from pre- to post- dance class (p_B <0.01), whereas the EC condition did not (p_B =0.329) (Figure 9). The PD group did not demonstrate a Time x Eye State interaction effect (F (1, 19) = 0.899, p = 0.355, η^2=0.045) (Figure 9).

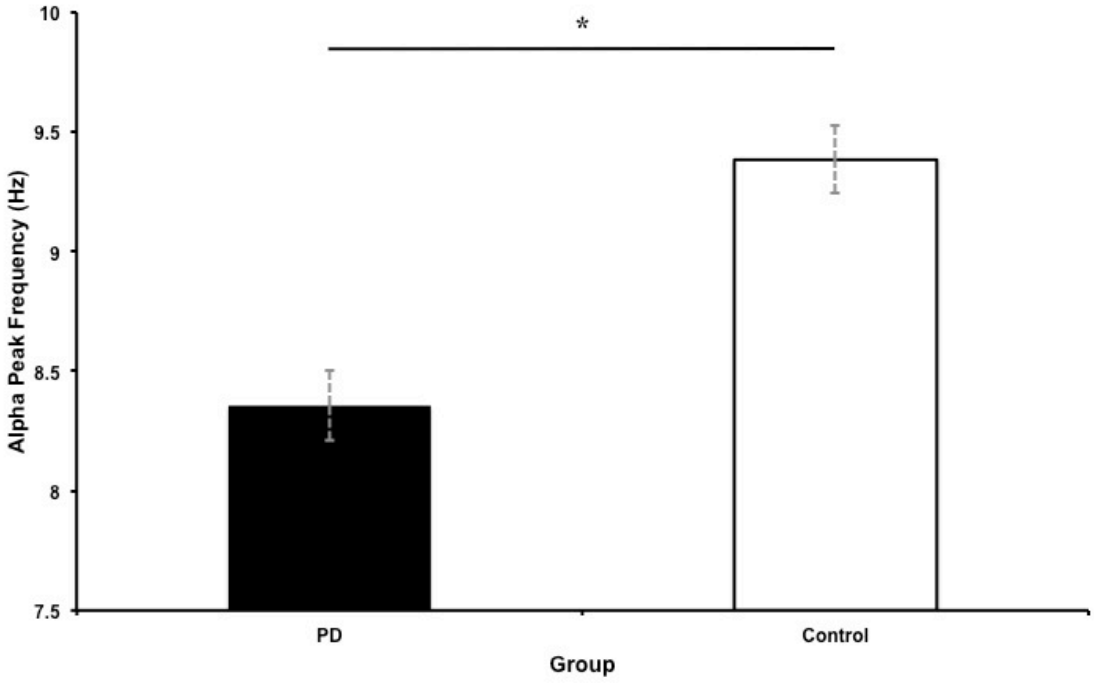


Figure 8. C_{ONS} exhibit a higher iAPF when compared to individuals with PD, when averaged across all electrodes (F (1, 39) = 25.863, $p < 0.01$, η^2=0.399). Bars = SEM.

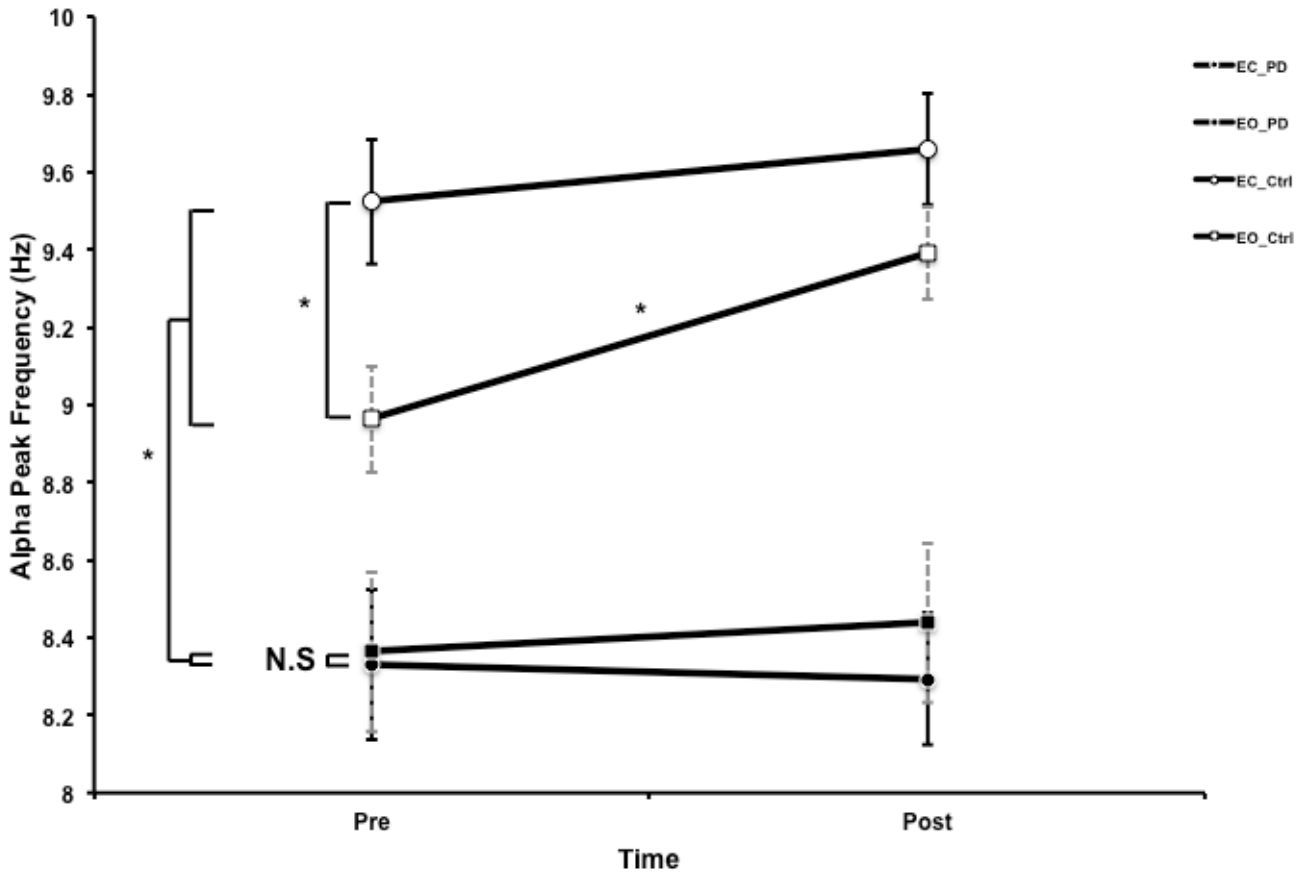


Figure 9. Time x Group x Eye State iAPF (averaged across all electrodes). C_{ONs} exhibited a higher resting iAPF when compared to individuals with PD (F (1, 39) = 25.863, p < 0.01, η^2=0.399). Additionally, individuals with PD did not demonstrate a significant difference between EO and EC iAPF (p_B =0.480), whereas C_{ONs} had higher iAPF in the EC condition when compared to EO (p_B <0.01). Finally, C_{ONs} demonstrated an increase in iAPF from pre- to post-dance class in the EO condition (p_B <0.01), whereas individuals with PD did not show any increases in either eye state. Black = PD, white = C_{ONs}, square = EO, circle = EC, bars = SEM.

3.2.2 Individual Alpha Peak Power

A 2 (Group) x 2 (Eye State) x 2 (Time) x 14 (Electrode) repeated measures ANOVA revealed a main effect of Group (F (1, 39) = 6.061, p < 0.05, η^2 = 0.135), in which individuals with PD exhibited higher iAPP when compared to C_{ONS}, a main effect of Electrode (F (4.758, 185.550) = 66.858, p < 0.01, η^2 = 0.632) (see Appendix I for Bonferroni corrected pairwise comparisons), a main effect of Time (F (1, 39) = 6.359, p

< 0.05, η^2 = 0.140) in which the post- condition showed greater iAPP when compared to the pre-condition, and a main effect of Eye State (F (1, 39) = 63.920, p < 0.01, η2 = 0.621) in which iAPP was stronger in the EC condition than in the EO condition. Additionally there was an interaction between Eye State and Electrode (F (5.808, 226.524) = 25.004, p < 0.01, η^2 = 0.391).

Although there was no interaction effect for Eye State x Time x Group, there were main effects for each variable and thus the interactions were investigated. When examining the Group x Eye State interaction within each Time variable, individuals with PD exhibited higher iAPP when compared to C_{ONS} in both the EC (p_B < 0.05) and EO (p_B < 0.01) conditions pre-dance class, whereas post-dance class, individuals with PD exhibited higher iAPP when compared to C_{ONS} only in the EO (p_B < 0.05) condition (Figure 10). When examining the Eye State x Time interaction within each Group, the PD group did not show any significant increases from pre- to post-dance class in either the EC (p_B =0.498) or Eyes EO (p_B =0.551) conditions, whereas the C_{ONS} group showed increases in iAPP from pre- to post-dance class in both EC (p_B < 0.01) and EO (p_B < 0.05) conditions (Figure 10). Finally, when examining the Time x Eye State interaction within each Group, both the PD group and the C_{ONS} group demonstrated stronger iAPP in the EC condition over the EO condition in both pre- and post-dance class (all p_B < 0.01) (Figure 10) (See Appendices D and E for corresponding headmaps).

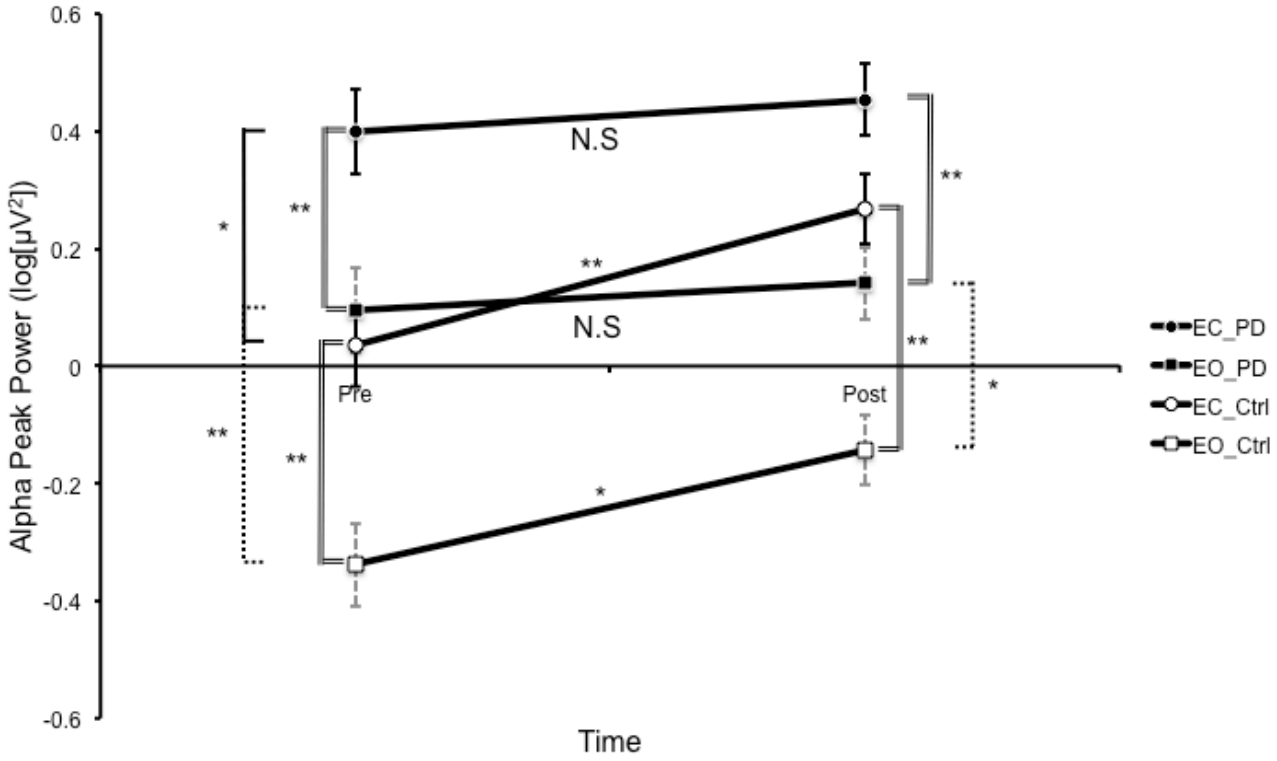


Figure 10. Time x Group x Eye State iAPP Interaction (averaged across all electrodes). Individuals with PD exhibit higher iAPP when compared to C_{ONs} in both the EC (p_B < 0.05) and EO (p_B < 0.01) conditions pre-dance class, whereas post-dance class, individuals with PD exhibited higher iAPP when compared to C_{ONs} only in the EO (p_B < 0.05) condition. Individuals with PD did not show any significant increases from pre- to post-dance class in either the EC (p_B =0.498) or EO (p_B =0.551) conditions, whereas the C_{ONs} showed increases in iAPP from pre- to post-dance class in both EC (p_B < 0.01) and EO (p_B < 0.05) conditions. Individuals with PD and C_{ONs} demonstrate stronger iAPP in the EC condition over the EO condition in both pre- and post-dance class (all p_B < 0.01). Bars = SEM. Black = PD, white = C_{ONs}, square = EO, circle = EC, bars = SEM.

3.2.3 FRONTAL INDIVIDUAL ALPHA PEAK POWER

In order to evaluate lateralized differences resulting from dance, an averaged frontal alpha power in the EC condition was computed for the left (F3 and F7 electrodes) and right (F4 and F8 electrodes) hemispheres. A 2 (Time) x 2 (Hemisphere) x 2 (Group) repeated measures ANOVA revealed a main effect of Time (F (1, 39) = 7.406, p < 0.01, η^2 = 0.160). Although this analysis only showed a trend towards significance between groups (F (1, 39) = 3.081, p = 0.087, η^2 = 0.073), groups were

then evaluated separately with the intent of uncovering differing dance-induced changes in frontal neural networks within each group. For each group, a 2 (Hemisphere) x 2 (Time) repeated measures ANOVA was performed. In the PD group, there was a main effect of Time (F (1, 19) = 6.650, $p < 0.05$, $\eta^2 = 0.259$) in which the post-dance condition elicited a higher frontal iAPP across both hemispheres. Although there was no significant Hemisphere x Time interaction (F (1, 19) = 0.052, $p = 0.822$, $\eta^2 = 0.003$), the purpose of this analysis was to evaluate asymmetric changes in frontal alpha power, and thus a pairwise comparison was performed, which revealed a significant increase in the right hemisphere from pre- to post-dance class ($p_B < 0.05$), and only an increasing trend towards significance in the left hemisphere ($p_B = 0.087$). The C_{ONS} group demonstrated a trend towards significance for the effect of Time (F (1, 20) = 3.847, $p = 0.067$, $\eta^2 = 0.158$), and a significant interaction effect for Hemisphere x Time (F (1, 20) = 7.177, $p < 0.05$, $\eta^2 = 0.264$), with pairwise comparisons revealing increases only in the left hemisphere from pre- to post- dance class ($p_B < 0.05$), and no significant increases in the right hemisphere ($p_B = 0.158$) (Figure 11).

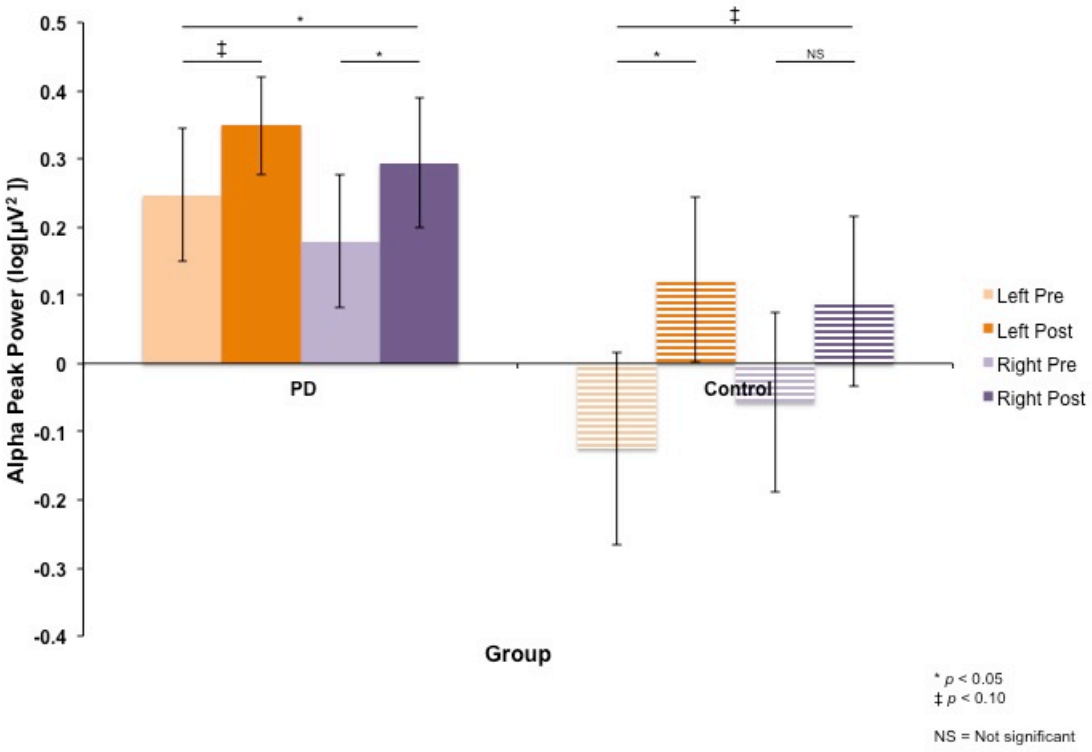


Figure 11. Lateralized dance induced increases in frontal iAPP. Individuals with PD demonstrated increases in right frontal iAPP (p_B <0.05) whereas C_{ONs} demonstrated increases in left frontal iAPP (p_B <0.05). Bars = SEM.

3.3 FRONTAL INDIVIDUAL ALPHA PEAK POWER CORRELATIONS

3.3.1 DEMOGRAPHIC

Correlations with frontal iAPP differences scores (post – pre dance class, left and right hemispheres separately) were investigated within each group for the variables of disease duration (PD only), age, gender, hours of weekly exercise, and use of visualization (all recorded in the Demographic Questionnaire – see Appendix A), in order to elucidate whether increases in frontal iAPP are enriched, exacerbated, or unaffected by these variables. To correct for multiple comparisons, an adjusted

significance value of p = 0.05/20 = 0.0025 was used. Only the following correlations were significant or showed a trend towards significance at the uncorrected value (p < 0.05); left iAPP difference scores showed a trend towards positive correlation with disease duration (r(18) = 0.397, p = 0.083), visualization use (r(18) = 0.434, p = 0.056) (Figure 12), and with right iAPP difference scores (r(18) = 0.394, p = 0.086). In the C_{ONS} group, significant positive correlations were found between left iAPP difference scores and hours of weekly exercise (r(18) = 0.471, p < 0.05) (Figure 13), between right iAPP difference scores and hours of weekly exercise (r(18) = 0.537, p < 0.05), and between left and right iAPP difference scores (r(19) = 0.937, p < 0.01).

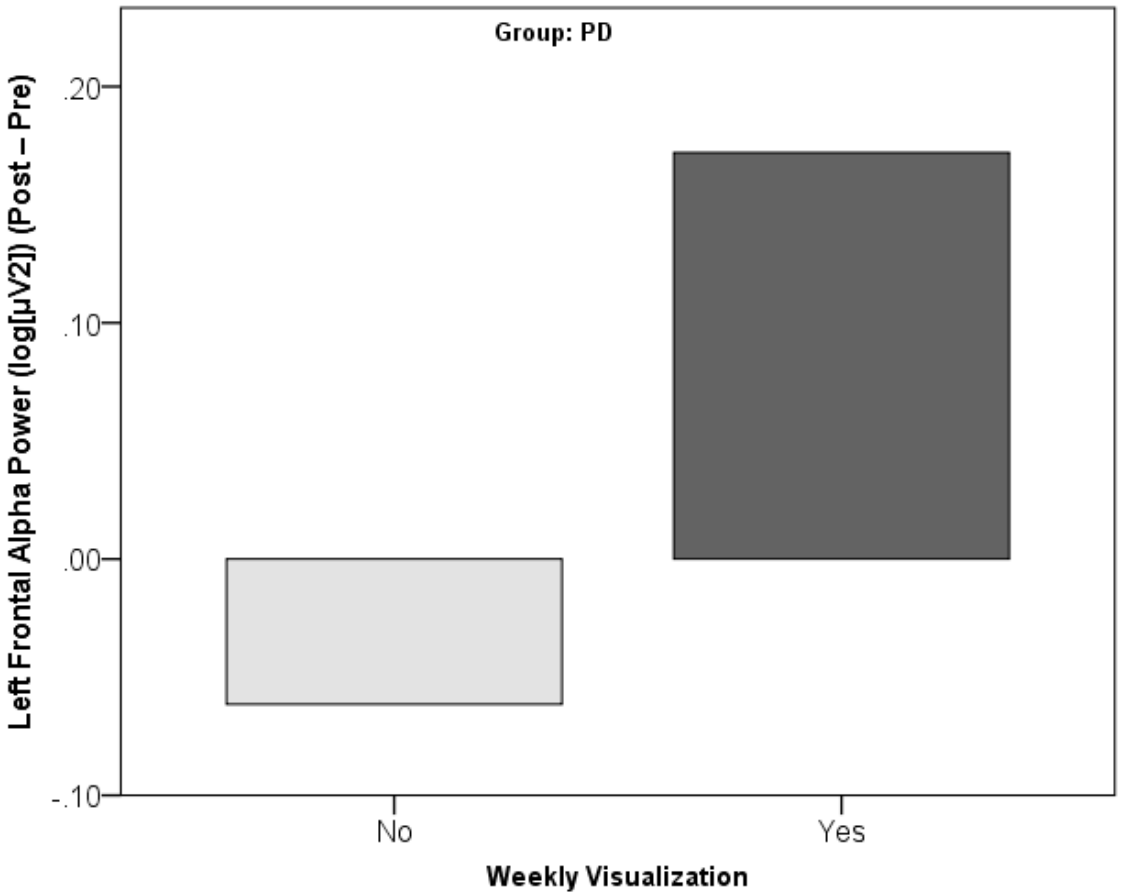


Figure 12. Left Frontal iAPP correlation trend with weekly visualization. Individuals with PD who visualize dancing outside of the dance class show greater dance-induced increases in left frontal iAPP (r(18) = 0.434, p = 0.056).

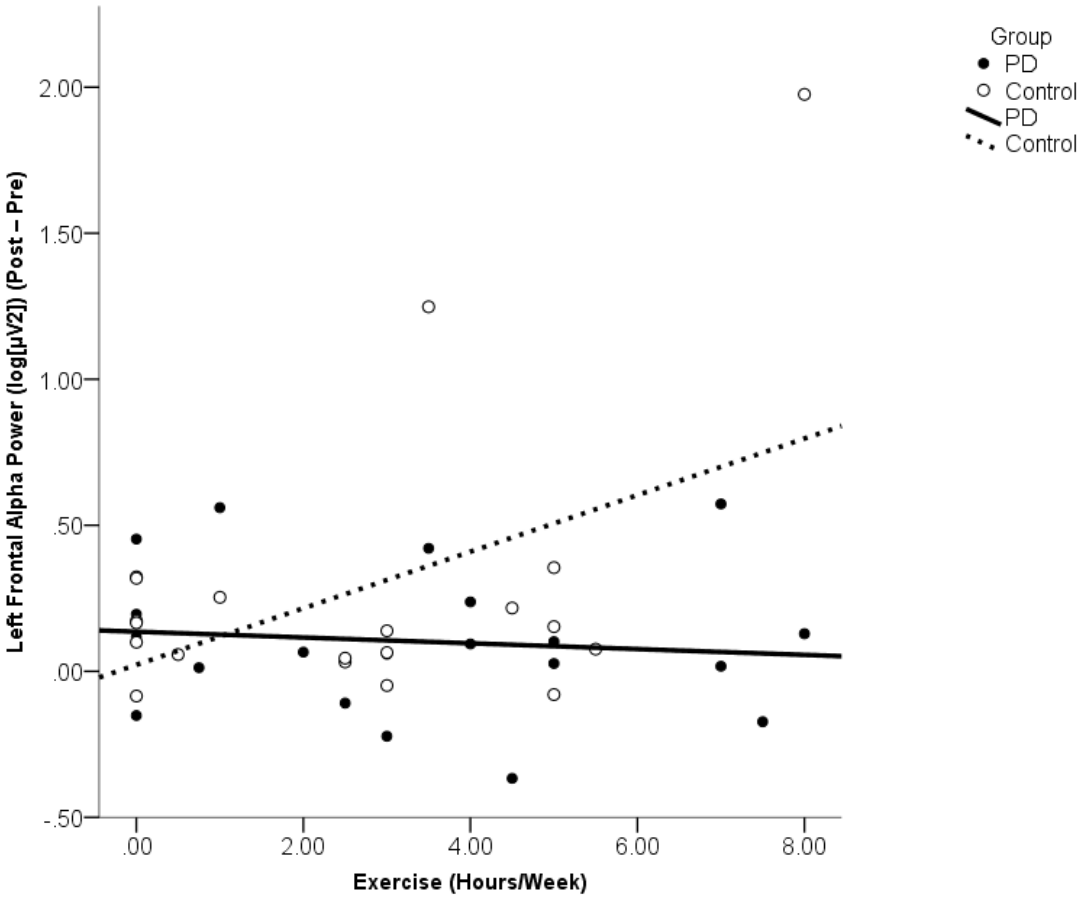


Figure 13. Left Frontal iAPP correlation with more weekly exercise in C_{ONs}. Greater number of weekly hours spent exercising correlated to greater changes in left frontal iAPP in C_{ONs} ($r(18) = 0.471$, $p < 0.05$). Bars = SEM.

3.3.2 BEHAVIORAL

Frontal iAPP difference values (post – pre dance class, left and right hemispheres separately) were correlated with changes in BBS_{avg} and GDS_{avg} scores within the PD group, and were correlated with changes in TUG_{avg} scores in the C_{ONS} group. A two-tailed Pearson's correlation revealed no significant correlations for either group, for any of the behavioral measures.

4. DISCUSSION

4.1 SUMMARY

Here we examined changes in balance, walking speed, depression scores, iAPF and iAPP in individuals with PD and C_{ONs} resulting from participation in a single 75-minute dance class. Our results showed improvement in balance and depression scores in the PD group and improvement in walking speed in C_{ONs}.

Global examination of iAPF revealed increases in EO iAPF in C_{ONs}, whereas EC iAPF did not increase from pre- to post-dance class in C_{ONs}. Dance did not change iAPF in the PD group in either EC or EO conditions. iAPF in C_{ONs} was significantly larger than iAPF in the PD group, and individuals with PD did not show eye state dependent modulation of iAPF, whereas the C_{ONs} showed larger EC iAPF when compared to EO iAPF.

Global iAPP increased after dance class, was greater in the PD group when compared to C_{ONS}, and greater in the EC condition when compared to the EO condition. When examining groups separately, further inspection revealed that iAPP only increased globally from pre- to post-dance class in the C_{ON} group for both EO and EC conditions, and not in the PD group for either the EO or EC conditions.

Examination of EC frontal iAPP lateralized differences revealed dance-induced increases in right frontal iAPP in the PD group (with an increasing trend in left iAPP), and increases in left frontal iAPP in C_{ONs}.

Additionally, changes in frontal iAPP were correlated with demographic and behavioral (balance, walking speed, depression) measures in the PD and C_{ON} groups. No significant correlations between changes in frontal iAPP and demographic measures

were found, however left iAPP showed a trend towards significantly correlating with visualization use in the positive direction. Finally, a significant positive correlation between left iAPP and hours of weekly exercise was demonstrated in the C_{ON} group. No correlations were found between frontal iAPP in PD and balance or depression scores, nor were there any correlations demonstrated between frontal iAPP in the C_{ON} group and walking speed scores.

4.2 IMPROVEMENTS IN BALANCE (PD) AND IN WALKING SPEED (C_{ONS})

4.2.1 BALANCE

Studies have shown that participation in dance class can result in improvements in balance in both elderly (Eyigor et al 2009; Hackney & Earhart 2009; de Dreu et al. 2012; da Silva Borges et al. 2014) and PD populations (Hackney & Earhart 2009), in partnered and unpartnered dance class (de Dreu et al. 2012), in short term and long term dance interventions. For example, da Silva Borges et al. (2014) showed significant improvements in balance, as measured by the Lizard stabilometric and posturometric platform after a 12 week ballroom dancing intervention, in which a group of healthy elderly individuals participated in a 50-minute dance class 3 times per week. Individuals in this study also showed a reduction in fall rate. In both healthy elderly individuals and individuals with PD, the immediate improvements in balance could have resulted from participants uncovering an ability they already had, for which the dance class served as a medium in which they were able to test, and build confidence in these skills (Houston & McGill 2011). Another mechanism underlying these improvements may stem from induced neuroplasticity from participation in exercise to music (Dhami et al. 2015) in the degenerating locomotor apparatus and sensory systems (da Silva Borges et al. 2014).

New neural connections between these regions could form from the novel learning associated with dance, enabling for better balance control. Additionally, exercise has been shown to promote angiogenesis (increased vasculature), which allows for greater distribution of nutrients in the motor cortex and cerebellum, two areas implicated in balance control (Dhami et al. 2015).

The reason we believe that we did not observe changes in balance in our elderly group was likely that the sample was too small to notice considerable changes (with an n=6). Additionally, ceiling and floor effects have been reported for the BBS when used with community dwelling older adults post-stroke, suggesting that the BBS may not be useful to detect meaningful changes in those with only mild impairments (Blum & Korner-Bitensky, 2008)

4.2.2 WALKING SPEED

In our study, there was no significant improvement in TUG scores in our PD group. In a similar study to ours, Hashimoto et al. (2015) assessed changes in TUG scores resulting from either 12 weeks of dance for PD, 12 weeks of exercise for PD, and 12 weeks of no intervention in a PD group. Their study showed improvements in TUG scores in all three conditions, which they attributed to a practice effect, having had a trial run in all three groups before performing the actual task. As there was no trial run in our study, another possible explanation is that the TUG may not have been a sensitive enough measure to detect changes in walking speed (Heiberger et al. 2011). To enhance our investigation, future examinations should additionally include step amount (i.e. how many steps taken to walk the 10 meters), as TUG step improvement

was larger in the PD group when compared to the exercise group in Hashimoto et al. (2015), indicating that it is a more sensitive measure.

4.3 INDIVIDUAL ALPHA PEAK FREQUENCY

4.3.1 DANCE-INDUCED INCREASE IN EYES OPEN INDIVIDUAL ALPHA PEAK FREQUENCY IN C_{ONs} BUT NOT IN PD

iAPF gradually changes with age, increasing up to adulthood and decreasing with older age (Haegens et al. 2014), however, it is usually very stable over long periods of time (i.e. over 6 months) in healthy adults up to 80 years of age (Grandy et al. 2013). Grandy et al. (2013) examined iAPF before and after an extensive 6-month cognitive intervention with both EO and EC rsEEG data, and demonstrated that although significant improvements in cognition ensued, iAPF showed no change longitudinally. Although it may not change in the long term, iAPF can change in the short-term with increasing cognitive load in healthy young adults (Haegens et al. 2014). Haegens et al. (2014) examined event-related changes in iAPF during EO rsEEG, passive visual stimulation, and an N-back working memory task in a group of young adults. Their study showed significant increases in iAPF in the N-back working memory task when compared to baseline and passive visual stimulation, suggesting that iAPF can be modulated in the short-term with increased cognitive load (Haegens et al. 2014). We postulate that the increase in iAPF in the elderly group could be attributed to an increase in cognitive demand during the dance class, as participation in dance class has been suggested to influence frontal lobe processing speed and efficiency (Hashimoto et al. 2015). Our dance class consisted of 75-minutes of engaging challenges to cognition including, but not limited to, learning (new movement

sequences, and controlling one's body in space), attention (watching the dance teacher, following instruction, and listening for/following the beat in the music), mental imagery (imagining a sequence of steps before executing them), memory (remembering a sequence of repeated movements), communication, perception, and emotion (Dhami et al. 2015). Hashimoto et al. (2015) hosted a similar DwP program in Japan and reported improvements in the Frontal Assessment Battery (FAB) in a group of individuals with PD after participation in a 12-week, weekly 60-minute dance class intervention. The FAB is a brief battery of six neuropsychological tasks specifically designed to assess frontal lobe function (Kopp et al. 2013). Participants also showed improvements in speed required to complete a mental rotation task, without changing the number of correct responses in this task. Taken together, we suggest that a DwP program may improve cognitive processing speed over 12-weeks, however these improvements may not necessarily be reflected in long-term iAPF changes. We may however observe improvements in cognition resulting from a single dance and correlate these to increased iAPF, though a follow up study would be needed to substantiate this hypothesis.

With regards to the PD group not demonstrating increased iAPF after a single dance class, a number of reasons could underlie this finding. One explanation, which will be addressed in section 4.3.3, is that individuals with PD have a malfunctioning iAPF in the EO condition, and thus it cannot be used as an indicator of changes to cognition. Additionally, an alternative explanation is that many of the C_{ONs} were participating in our dance class either for the first time, or did not participate regularly, which may have made the class more difficult, or cognitively demanding for this group.

The majority of the participants with PD had been regularly attending classes, some even before data collection began. Although the instructional material changed form week to week, the structure of each class remained the same, and participants may have became habituated, thereby reducing their short-term cognitive load. The next step in this line of research would be to investigate changes in cognition associated with participation in a single dance class, and to correlate these findings to changes in iAPF in both individuals with PD and C_{ONs}. Additionally, examining iAPF in *de novo* DwP PD participants taking part in their first DwP class could give weight to our hypothesis that increases in iAPF in the C_{ONS} were due to increased cognitive load resulting from unfamiliarity and difficulty level of the dance class. Finally, it would be interesting to replicate the Haegens et al. (2014) study in our PD group to better understand whether iAPF can in fact be modulated in this group with increased cognitive load.

4.3.2 INDIVIDUAL ALPHA PEAK FREQUENCY IS LARGER IN C_{ONs} THAN IN PD

Our results suggest a global slowing of iAPF in individuals with PD when compared to C_{ONs}, consistent with what has been shown previously in the literature (Soikkeli et al. 1991; Moazami-Goudarzi, 2008). Lower iAPF in clinical populations has been correlated to lower scores in cognitive performance (Soikkeli et al. 1991; Angelakis et al. 2004), and individuals with PD are known to show impairments within executive functions such as working memory and attention (Troster & Fields 2008). Thus, the lower iAPF found in our PD group when compared to the C_{ONS}, in both EO and EC states may be reflective of impairment in underlying brain networks responsible for executive functions.

4.3.3 NO EYE STATE DEPENDENT MODULATION OF GLOBAL INDIVIDUAL ALPHA PEAK FREQUENCY IN PD

We have also demonstrated that individuals with PD do not show eye state dependent modulation of iAPF peaks in which the EO state elicits a lower iAPF than the EC state, a finding only noted once in the literature in healthy individuals (Bazanova 2011). This potential biomarker for PD could be the result of the disrupted dopaminergic processes in the retina, which behaves as though it is improperly dark-adapted (i.e. always in EC form) in individuals with PD (Wink & Harris 2000). In our C_{ONS} sample, the iAPF decreased in response to light input, whereas in the PD sample, it did not – a simple, yet striking indicator of PD. With a larger sample, a predictive model for PD based on rsEEG eye-state could be created, which would be an inexpensive diagnostic tool for PD. Researchers could search for a lack of within subject differences in EO and EC iAPF, in which a lower iAPF in the EO condition could be indicative of low dopamine levels in the retina and a predictive tool for PD. Our finding that there may be a disrupted network in EO rsEEG in individuals with PD has important methodological implications for future studies, as it indicates that perhaps only EC rsEEG should be used when examining rsEEG in PD.

4.4 INDIVIDUAL ALPHA PEAK POWER

4.4.1 LATERIALIZED DANCE-INDUCED INCREASE IN EYES CLOSED FRONTAL INDIVIDUAL ALPHA PEAK POWER

Our study is the first to demonstrate an exercise-induced iAPP increase in individuals with PD and in an elderly sample. Past literature examining exercise-induced iAPP changes have not shown significant increases in elderly samples (over age 60),

only in adults (between 20 to 30 years of age) (Moraes et al. 2011). Global increases in resting iAPP have been correlated to increases in rCBF in the basal frontal cortex and thalamus (Sadato et al. 1998; Goldman et al. 2002; Bazanova & Vernon, 2014), important areas implicated in the degenerated pathways of PD. When examining frontal iAPP specifically, frontal cortex differences and their relation to changes in emotional state have been studied extensively (Coan & Allen 2004). It is believed that frontal EEG activity reflects prefrontal cortex activity and one's ability to regulate emotions (Dennis & Solomon 2010). Emotion regulation refers to a set of strategies that individuals use in order to better control their emotions, including which emotions they experience and how they experience and express them (Grecucci et al. 2009). In our study, participation in a single dance class produced significant increases in left frontal iAPP in our C_{ONs}. Increases in left frontal iAPP are associated with positive emotions and enhanced emotion regulatory behavior, suggesting that the increases observed could be a result of positive emotions evoked during the dance class (Schneider et al. 2009; Dennis & Solomon, 2010; Fachner et al. 2013). Our PD group on the other hand, demonstrated significant increases in right frontal iAPP, with a trending increase in left frontal iAPP. Increases in right frontal activity are often associated with increased withdrawal behavior and increases in avoidance related negative emotions such as sadness, fear, and anxiety (Dennis & Solomon, 2010). Dennis & Solomon (2010) caution that greater right frontal activity could also represent the experience and regulation of negative emotions, in actuality representing a reduced negative affect. This rationale falls in line with our finding that individuals with PD showed improvements in depression scores (decreased negative feelings) after a single dance class. Additionally, the electrodes

averaged in our frontal iAPP analysis have been mapped to represent activity originating from the areas of the inferior frontal gyrus (F7 and F8), and middle frontal gyrus (F3 and F4) (Koessler et al. 2009), both of which are implicated in emotion regulation (Grecucci et al. 2013), a similar result to Kubitz & Pathakos (1997) who showed increases in low alpha power in left middle frontal gyrus immediately after exercising. A follow up study correlating same day dance-induced changes in affect with frontal alpha power in PD is underway (Biology Honours Thesis by Kelsi Smith 2015) and will help elucidate the significance of these observed asymmetrical changes.

4.4.2 PD: LEFT INDIVIDUAL ALPHA PEAK POWER CORRELATION TREND WITH VISUALIZATION

At the end of every dance class (last 15 minutes) the participants learned and rehearsed a piece of choreographed dance, building on it each week, and they were asked to practice visualizing their dance at home during the week. During data collection, participants were asked to report whether they visualized dancing their choreographed dance outside of class (Appendix A), and those who replied yes demonstrated the largest changes in their left frontal iAPP. This suggests that weekly visualization and dance class participation combined could elicit larger changes in left iAPP in our PD group, when compared to additional exercise (yielding no significant correlation in the PD group). As aforementioned, increased left iAPP is strongly tied to emotion regulation and positive emotions, thus additional practice at home could contribute to a boost in confidence, and resultantly greater positive emotion when performing dancing during class.

4.4.3 C_{ONS}: LEFT INDIVIDUAL ALPHA PEAK POWER CORRELATION WITH HOURS OF WEEKLY EXERCISE

C_{ONs} who exercised more on a weekly basis showed higher iAPP values in left frontal cortex. This suggests that there is a tie between regular exercise in elderly samples and better emotion regulation. What's interesting is that this correlation did not present in the PD group, which suggests that a different mechanism underlies the dance-induced changes observed in left frontal iAPP in the PD group and the C_{ON} group.

4.5 LIMITATIONS AND FUTURE WORK

We proposed that many of the spectral dance-induced changes observed stemmed from a high cognitive load during the dance class. PD is often associated with dementia, and so a limitation of this study would be that we did not test or control for dementia, which can contribute to a differing spectral profile in individuals with PD (Soikkeli et al. 1991; Stoffers et al. 2007). For instance, studies comparing spectral power in those with PD and in those with PD with dementia (PDD) report stronger power in lower frequencies for PDD (Soikkeli et al. 1991; Stoffers et al. 2007). Our participants did not show any overt signs of dementia, however we now control for this in our studies by administering the Mini Mental State Examination to all participants.

Another limitation would be that the motor and non-motor measures were collected on different dates than the rsEEG. Resultantly, we were unable to successfully correlate many expected changes in our behavioral measures with changes in rsEEG. This limitation is currently being addressed through the implementation of UPDRS-III, a comprehensive tool that measures changes in both motor and non-motor symptoms of

PD. We have trained multiple researchers in rsEEG and UPDRS-III so that both measures can be collected from 1-2 participants before and after a single dance class.

For future work, there are many directions that this study can take. For example, additional neurodegenerative groups can be investigated (i.e. Alzheimer's, PDD, dementia, etc.) in order to better understand the widespread effects of dance, and also to further examine the potential EC/EO rsEEG proposed biomarker. We could very well find that the EC/EO biomarker is specific to PD, or perhaps a more general indicator of neurodegenerative networks. Additionally, examining power in other frequency bands would be valuable, as collectively examining alpha, beta, and gamma according to activation theory (Kubitz & Pothakos, 1997) could elucidate whether changes observed are associated with increased or decreased brain activity. Finally, it would be interesting to examine whether movement-related beta desynchronization (i.e. neural processing speed leading up to making a movement) changes as a result of dance class.

5. CONCLUSION

In this study, we were able to demonstrate that dance is capable of improving balance and depression scores for individuals with PD, and walking speed for C_{ONS}. This is the first study to confirm that there is underlying neuromodulation associated with dance, as evidenced by alteration of iAPF and iAPP. We attribute increases in iAPF to high cognitive load during dance, whereas increases in iAPP were attributed to changes in affect, with increased left iAPP linked to more positive affect in C_{ONS}, and increased right iAPP linked to regulation of negative emotions in individuals with PD. Furthermore, we were able to demonstrate a correlation between hours of weekly exercise in C_{ONS} and increases in left iAPP. This correlation did not appear in individuals

with PD, suggesting that a different mechanism underlies changes in iAPP observed in individuals with PD when compared to C_{ONS}. Moreover, through the use of both EC and EO rsEEG, we uncovered a potential biomarker for PD. We hypothesize that the similarity between EC and EO iAPF in PD is due to improper visual encoding in the EO condition due to an erroneously dark-adapted retina. Taken all together, by examining both behavioral and neural changes associated with participation in a single dance class, our findings were able to strengthen and emphasize the importance of dance for individuals with PD and healthy elderly. We were able to hypothesize which aspects of dance may have contributed to the underlying neural changes, while identifying a potential biomarker for PD.

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APPENDIX A – DEMOGRAPHIC QUESTIONNAIRE

Date: _____

Please circle or answer the following questions as accurately as possible.

1. What are the initials of your first and last name? _____
2. Age: _____
3. At what age did you learn you had Parkinson's disease?
4. Sex: female / male
5. With which hand do you do the following actions?
   - Throw a ball R / L
   - Brush your teeth R / L
   - Eat soup with a spoon R / L
   - Comb your hair R / L
   - Cut bread with a knife R / L
   - Swing a racquet or bat R / L
   - Point accurately R / L
   - Write your name R / L
   - Hammer a nail R / L
   - Is there anything you do consistently with your left hand? _____
6. How many hours of sleep do you get per night? _____
7. Extend both arms in front of your body and place the hands together so as to make a small triangle between your thumbs and the first knuckle. With both of your eyes open, look through the triangle and focus on a specific small object. Close your left eye. If the object remains in view, you are right eye dominant. If your hands appear to move off the object and move to the left, then you are left-eye dominant

Date: _____

Eye dominance: R-eye / L-eye

8. Can you wink with your left eye? _____

   Can you wink with your right eye? _____

9. Corrected vision? Yes / No

10. Have you ever taken a dance class? Yes / No

11. If **yes**, what kind of dance class(es)? _____

    At what age did you start? _____

    At what age did you stop? _____

12. Have you ever participated in a dance for Parkinson's program? Yes / No

13. If **yes**, which program? _____

    Where was it held? _____

    Are you still participating in this program? Yes / No

    If yes, how many times per week? _____

14. Do you participate in any physical exercise programs besides dance? Yes / No

15. If **yes**, what kind of physical exercise (s) do you do? _____

    How many hours per week? _____

16. How many Dance for Parkinson's classes have you attended at Canada's National Ballet School? _____

17. Of the classes you attended, were you able to participate fully in them? Yes / No

    If no, how often did you have to sit out? _____

18. How many times per week do you practice visualizing the steps of the dance you are learning? _____

19. For how many minutes do you visualize? _____

APPENDIX B – MEDICATION QUESTIONNAIRE

Initials: _____ Date: _____

Medication Questionnaire

Please circle or answer the following questions as accurately as possible.

1. Are you taking any medications? Yes / No

   If **yes**, which medication(s)? Please list the medication name(s) and dosage(s).

_____

_____

_____

2. Do you take any medication(s) to be "on" for class? Yes / No

   If yes,

   a) What time do you take your medication for the 10 am class? _____
   b) What time does it become effective? _____
   c) What time does it wear off? _____

   If you participated in any of the pre- or post- class testing sessions,

   d) Did you take your medication(s) to be "on" for the test session? Yes / No
   e) What time did you take your medication for the test session? _____
   f) What time does it become effective? _____
   g) What time does it wear off? _____
   h) If you were tested before and after class, do you think your medication was equally effective before and after class? Yes / No
      If no, please explain_____
      _____

3. Has your medication or dosage recently changed? Yes / No

4. If **yes** above, when did the change occur? _____

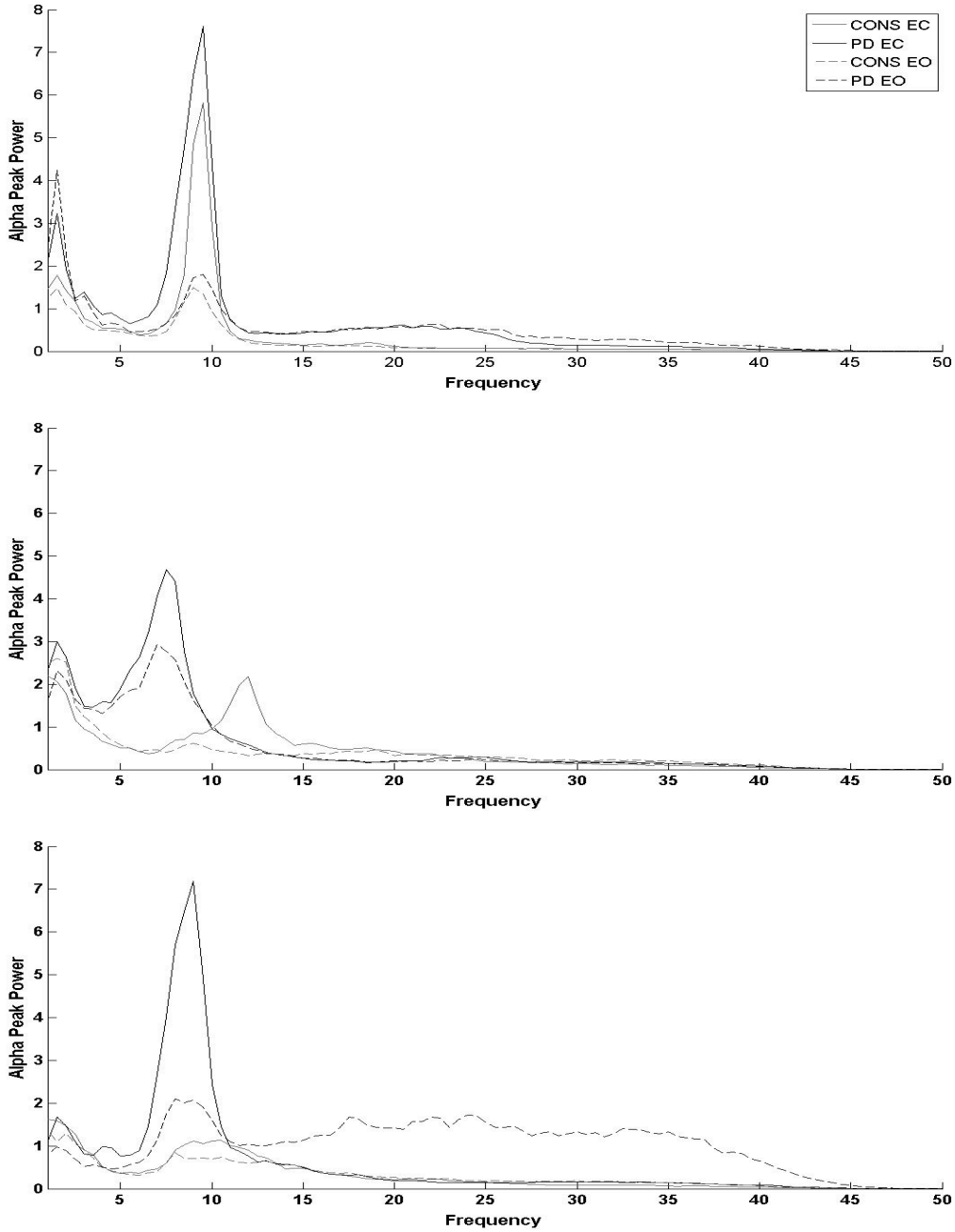
5. Is there any other information you would like to share with us about medication and performance on the motor tasks?

_____

_____

_____

APPENDIX C – SAMPLE POWERSPECTRA



Three pairs of powerspectra in the pre-dance class condition. Each panel shows powerspectra from one individual with PD and one C_{ON} that are age-matched and gender-matched. Top panel shows two male participants aged 52, middle panel shows two female participants aged 65, and bottom panel shows two female participants aged 88. Black line: PD (EC), gray line: C_{ONS} (EC), black dotted line: PD (EO), gray dotted line (EO). Frequency in Hz and Alpha Peak Power in μV^2.

APPENDIX D – IAPF MAIN EFFECT OF ELECTRODE: PAIRWISE COMPARISONS

Electrode L	Electrode J	Mean Difference (L-J)	Std. Error	Sig.[b]
AF3	O2	-.512*	.128	.025
F7	T7	-.480*	.115	.015
F7	O1	-.679*	.162	.014
F7	O2	-.718*	.141	.001
F7	T8	-.457*	.100	.005
F3	O2	-.550*	.131	.013
FC5	O2	-.601	.160	.052
P7	O1	-.374	.099	.050
P7	O2	-.413*	.087	.003
O1	F4	.726*	.150	.002
O1	AF4	.637*	.156	.019
O2	FC6	.417	.114	.072
O2	F4	.765*	.131	.000
O2	F8	.536*	.125	.011
O2	AF4	.675*	.142	.002

*. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.

Yellow indicates pairwise comparisons approaching significance.

APPENDIX E – IAPP MAIN EFFECT OF ELECTRODE: PAIRWISE COMPARISONS

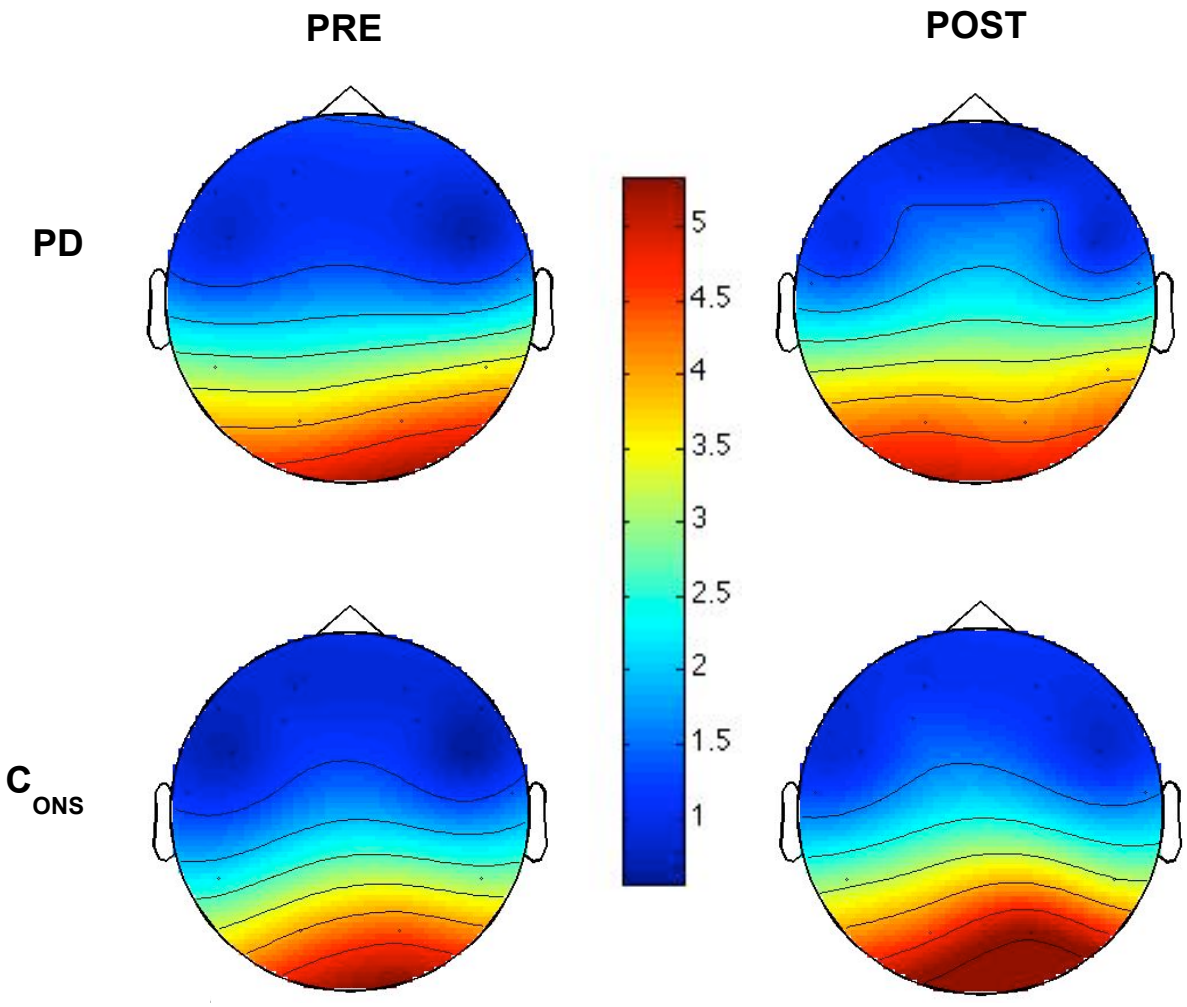
Electrode L	Electrode J	Difference (L-J)	Std. Error	Sig.[b]
AF3	F3	-.130*	.026	.001
AF3	T7	-.259*	.049	.000
AF3	P7	-.509*	.036	.000
AF3	O1	-.565*	.037	.000
AF3	O2	-.569*	.032	.000
AF3	P8	-.538*	.033	.000
AF3	T8	-.336*	.050	.000
F7	T7	-.170*	.039	.008
F7	P7	-.421*	.034	.000
F7	O1	-.477*	.043	.000
F7	O2	-.481*	.042	.000
F7	P8	-.450*	.037	.000
F7	T8	-.248*	.040	.000
F3	P7	-.380*	.029	.000
F3	O1	-.435*	.040	.000
F3	O2	-.440*	.039	.000
F3	P8	-.408*	.029	.000
F3	T8	-.206*	.041	.001
F3	FC6	.131*	.032	.017
F3	AF4	.120*	.027	.006
FC5	T7	-.186*	.029	.000
FC5	P7	-.436*	.034	.000
FC5	O1	-.492*	.045	.000
FC5	O2	-.497*	.042	.000
FC5	P8	-.465*	.031	.000
FC5	T8	-.263*	.036	.000

Electrode L	Electrode J	Difference (L-J)	Std. Error	Sig.[b]
T7	P7	-.251*	.036	.000
T7	O1	-.307*	.060	.001
T7	O2	-.311*	.060	.001
T7	P8	-.279*	.040	.000
T7	FC6	.260*	.039	.000
T7	F4	.149*	.034	.008
T7	F8	.205*	.048	.011
T7	AF4	.249*	.050	.001
P7	T8	.173*	.041	.014
P7	FC6	.510*	.034	.000
P7	F4	.400*	.026	.000
P7	F8	.456*	.040	.000
P7	AF4	.500*	.030	.000
O1	T8	.229	.063	.068
O1	FC6	.566*	.047	.000
O1	F4	.456*	.042	.000
O1	F8	.512*	.044	.000
O1	AF4	.556*	.029	.000
O2	T8	.233	.063	.056
O2	FC6	.571*	.049	.000
O2	F4	.460*	.044	.000
O2	F8	.516*	.048	.000
O2	AF4	.560*	.034	.000
P8	T8	.202*	.043	.003
P8	FC6	.539*	.039	.000
P8	F4	.428*	.030	.000
P8	F8	.484*	.044	.000
P8	AF4	.528*	.038	.000
T8	FC6	.337*	.045	.000
T8	F4	.226*	.040	.000
T8	F8	.283*	.048	.000
T8	AF4	.326*	.053	.000
FC6	F4	-.111	.030	.071

*. The mean difference is significant at the .05 level.
b. Adjustment for multiple comparisons: Bonferroni.

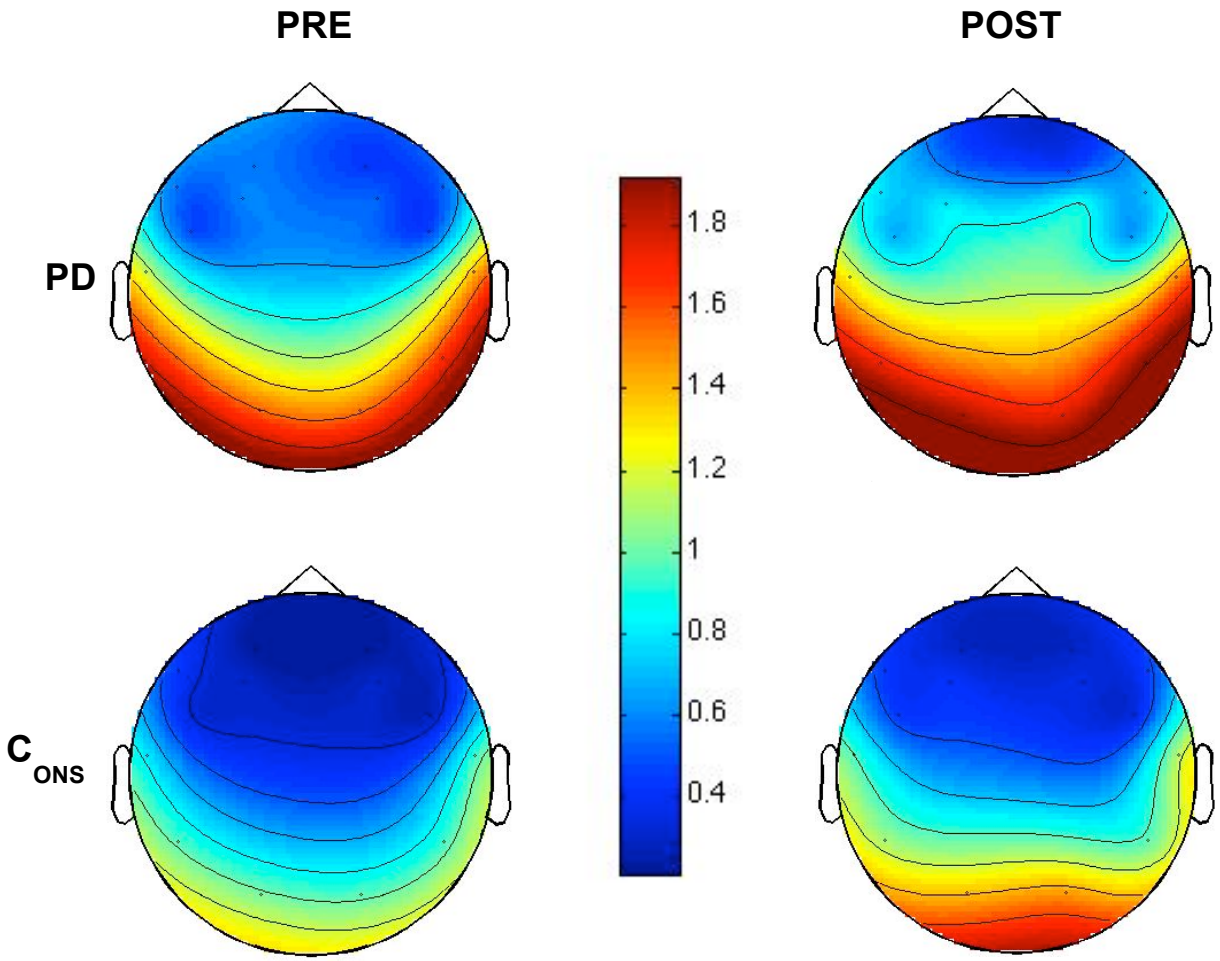
Yellow indicates pairwise comparisons approaching significance.

APPENDIX F – EYES CLOSED HEADMAPS



Eyes closed headmaps averaged across participants in each group. Middle bar indicates range in alpha peak power measured in μV^2.

APPENDIX G – EYES OPEN HEADMAPS



Eyes open headmaps averaged across participants in each group. Middle bar indicates range in alpha peak power measured in μV^2.

APPENDIX H – INFORMED CONSENT

The effects of motor learning and rehearsal: an fMRI study comparing people with Parkinson's disease, classical ballet dancers, and age-matched controls

Consent Form

We are a team of researchers at York University, comprising of Dr. Joseph DeSouza, Rachel Bar, Gabriella Levkov, and Larissa Vingilis-Jaremko. We can be contacted at dancestudy.yorku@gmail.com.

We are planning to study the effects of rehearsal on the brain, and to do so we will need to collect functional Magnetic Resonance Imaging (MRI) scans from participants' brains, electroencephalographic (EEG) brain signals, attention, working memory, and motor test results, and lastly some questionnaire responses, on three different dates, over three months.

We are therefore asking if you would agree to participate in our research by undergoing fMRI scans, and EEG tests, in addition to participating in attention, working memory, and motor tests, and questionnaires on three different dates over the next three months. As well, there will be one initial 45-minute workshop, which you will be required to participate in before the study begins.

Each MRI scan should take about ten minutes to complete and will occur at the Sherman Health Science Research Centre at York University's Keele Campus. The EEG test should take about thirty minutes to complete and will occur either at the National Ballet School or in a testing room at the Sherman Health Science Research Centre. The attention and working memory tests should take about fifteen minutes to complete, and the motor tasks and questionnaires should take about thirty minutes to complete. Both will take place at either at the National Ballet School or at York University's Keele Campus. For testing occurring at York University, you will be compensated for travel expenses to and from the campus.

You do not have to participate at all, or, even if you agree now, you can terminate your participation at any time without prejudice. Your name will not be attached to the research at all and we will ensure that your participation remains confidential. Refusal to participate or to answer any particular questions, or decision to withdraw from the study, will not affect your relationship with the researchers, York University, or any other group associated with this project. If you withdraw from the study, all associated data collected will be immediately destroyed wherever possible.

We can tell you that the results of your scans and tests may be included in a research publication; however, your scans and results would be anonymous and nobody could connect your scans or results with you as an individual.

A benefit you may experience by participating in this study is greater knowledge about the benefits observed from dance, as well as expanding your knowledge about magnetic resonance imaging (MRI) technology and EEG. Also, you will receive a printed anatomical scan of your brain.

What Is Involved in the Study?

MRI: Your participation will involve measuring the anatomy and activity of your brain using magnetic resonance imaging (MRI). MRI scanners image your brain using radio waves and very strong magnetic fields. You will be asked to fill out a safety screening form to assess whether it

is safe for you to enter the MR room. It is important that you provide us with an accurate and up-to-date medical history, and when unsure to ask clarifying questions so that we can proceed safely. You will then be asked to remove any metallic objects you may be carrying (for example, wallets, watches, earrings or piercings) and possibly to change clothing into a gown that we will provide (if deemed necessary because of large zippers etc.). You will be required to lie completely still on the patient bed that will slide into the bore of the MRI scanner. You will be able to communicate with us at all times via a built-in intercom. You will be holding an emergency bulb that you can squeeze at any time to let us know you want to come out of the MRI scanner. The MRI scans will only be administered by qualified personnel.

This is Not a Clinical Evaluation

The images of your brain collected in this study are not intended to reveal any disease state, in part because this MRI protocol is not designed for clinical diagnosis. Thus, your brain images will not be routinely examined by a clinical radiologist. The personnel at the Neuroimaging Laboratory are not qualified to medically evaluate your images. However, if in the course of collecting images of your brain we have any concerns, we may show your scans to a clinical radiologist, who may suggest that you obtain further diagnostic tests.
At the investigator's discretion, you may view your brain images and receive digital copies of them. However, you should be aware that brain structures within the normal population are highly variable, and that it is difficult to draw any conclusions from your images; you should be aware of the potential distress or discomfort that may occur by viewing your own images. Do not rely on this research MRI to detect or screen for brain abnormalities.

While in the MRI scanner, you will be asked to do tasks such as listen to music, visualize yourself dancing to the music, to view visual stimuli, and to wiggle your toes.

EEG: Your participation will involve measuring brain waves recorded while you participate in a variety of different activities. EEG involves recording naturally occurring electric and magnetic fields generated by firing neurons from the surface of your scalp. These will be recorded using small electrodes, which are part of a portable EEG cap, namely the EMOTIV 14-channel head cap. A researcher will place the EEG cap on your scalp. Your hair and scalp may get slightly wet due to the saline solution located on the 14 electrodes, however saline solution is completely non-toxic, and will dry shortly after the EEG cap is removed. During the EEG session, you will be asked to sit quietly and let your mind wander while we measure your resting state brain waves.

Attention and Working Memory: You will be asked to participate in two game-like simulations on a portable laptop. During these tasks, you will be asked to perform simple mathematical operations in your head, to remember letters that were previously presented, and to view faces and words that depict various emotions. We will be looking at the rate with which you respond during these two tasks, as well as the number of errors you make, which will indicate the strength of your attention and working memory capacities.

Motor Tasks and Questionnaires: You will be asked to perform several motor movements to test skills such as balance, gait, and transfers. Questionnaires will be administered in which you will be asked to indicate your opinion regarding various aspects of your own life.

De-identified data will be kept indefinitely.

What Are the Risks of the Study?

Metal: The MRI scanner produces a constant strong magnetic field, which may cause any metal implants and/or clips within your body to shift position. The magnetic field may also cause any implanted medical devices to malfunction. Thus, if you have any implanted metal, clips or devices, it is hazardous to your health to participate in this study. Please provide us with as much information as you can, for example if you had surgery in the past, so that we may decide whether it is safe for you to be a subject. Metallic objects brought into the MRI environment can become hazardous projectiles. Metal earrings, body piercings, and necklaces must be removed prior to the study.

Pregnancy: Exposure to MRI scanning might be harmful to a pregnant female or an unborn child. Although there are no established guidelines at this time about MR and pregnancy, you should be informed that there is a possibility of a yet undiscovered pregnancy related risk. If you know or suspect you may be pregnant or if you do not want to expose yourself to this risk, we recommend that you do not participate in this study.

Inner ear damage: MRI scanning produces loud noises that can cause damage to the inner ear if appropriate sound protection is not used. Earplugs and/or headphones will be provided to protect your ears. The earplugs will reduce but not eliminate the MRI noise.

Claustrophobia: When you are inside the MRI scanner, the MRI scanner surrounds your body and your head will also be positioned inside a close-fitting scanning coil. If you feel anxious in confined spaces you may not want to participate. If you decide to participate and begin to feel claustrophobic later, you will be able to tell us via the intercom and we will discontinue the study immediately.

Burns: In rare cases, contact with the MRI transmitting and receiving coil, conductive materials such as wires or other metallic objects, or skin-to-skin contact that forms conductive loops may result in excessive heating and burns during the experiment. The operators of the MRI scanner will take steps, such as using foam pads when necessary, to minimize this risk. Tattoos with metallic inks can also potentially cause burns. Any heating or burning sensations during a scan in progress should be reported to the operators immediately and we will discontinue the scan. Besides the risks listed above, there are no other known risks from the magnetic field or radio waves at this time. Although functional MRI scanning has been used for more than 15 years, long-term effects are unknown. If new findings about the risks of the MRI technique become available within a year of your participation, we will let you know about them.

Tiredness: You may find participating in all of these tasks in one day tiring.

What about Confidentiality?

All information obtained during the study will be held in strict confidence to the fullest extent possible by law. In no case will your personal information be shared with any other individuals or groups without your expressed written consent. Your brain images will be stored on secured computer servers and will be archived indefinitely. The experimental data acquired in this study may (in an anonymized form, that cannot be connected to you), be used for teaching purposes, be presented at meetings, published, shared with other scientific researchers or used in future studies. Your name or other identifying information will not be used in any publication or teaching materials without your specific permission.

If you have questions about the research in general or about your role in the study, please feel free to contact principal investigator Dr. Joseph DeSouza either by telephone (416 736 2100 Ext.

22946) or email (desouza@yorku.ca). This research has been reviewed by the Human Participants Review Committee, York University's Ethics Review Board and conforms to the standards of the Canadian Tri-council Research ethics guidelines. If you have any questions about this process, or about your rights as a participant in the study, please contact the Sr. Manager & Policy Advisor for the Office of Research Ethics, 5th Floor, York Research Tower, York University (telephone 416-736-5914 or e-mail ore@yorku.ca).

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Participant signature Date

_____ _____

Researcher Signature Date