

## Abstract

### The Impact of Music Making on Dual-Task Performance in Healthy Older Adults

**Objective:** Music making is a unique, multifaceted activity that has been linked to improved cognitive functioning across numerous domains and related neuroanatomical changes in children and adults. However, the effect of music making on cognition in older adulthood has been relatively under-studied. Characterizing this relationship, including underlying neural mechanisms and particular associations with executive functioning, is essential for broadening our understanding of music's role in healthy aging. Additionally, exploring the relationship between music making and physical variables, as well as the moderating influence of sex, will serve to further define its potential benefits. Thus, the purpose of this study was to assess neural, cognitive, and physical correlates of music making in a sample of healthy older adults using an ecologically valid dual-task walking (DTW) paradigm.

**Methods:** Study participants (N=415) were identified as musicians if they currently played a musical instrument or sang on a weekly basis (n=70). A DTW paradigm that included functional near-infrared spectroscopy was used to measure neural activation in the prefrontal cortex, as well as cognitive performance and gait velocity. Improved neural efficiency was established by the presence of lower task-related brain activation in the context of similar or better behavioral performance. Linear mixed effects models (LMEM) were used to examine the impact of music making on neural activation and task performance in addition to moderating change from single to dual-task conditions, defined as dual-task costs. Stratified LMEMs were analyzed to assess the moderating effect of sex on associations between music making and study outcomes. **Results:** Findings clearly indicate that older adult musicians exhibit greater neural efficiency, as compared to non-musicians. Additionally, reduced dual-

task costs in musicians was consistently observed with an attenuated decrease in cognitive and gait performance from single- to dual-task conditions. Stratified LMEMs clarified that results were significant only for female musicians. **Potential Implications:** Study results support the benefit of music making for healthy aging through increased neural efficiency and relatedly enhanced cognitive reserve, particularly among women. This emphasizes music's utility across the lifespan, including its role as a recommended leisure activity and as a potential tailored intervention for specific candidates (e.g., older women).

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by

Sydney Jacobs, M.A.

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by  
Sydney Jacobs, M.A.

The committee for this doctoral dissertation consists of

Roe Holtzer, Ph.D., Ferkauf School of Graduate Psychology, Yeshiva University

Anne Elizabeth Hirky, Ph.D., Ferkauf School of Graduate Psychology, Yeshiva University

Andrea Weinberger, Ph.D., Ferkauf School of Graduate Psychology, Yeshiva University

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## **Dedication**

This dissertation is dedicated to my family, who has always modeled the intersection between art and science. Particular dedication goes to my mother, whose constant presence and support stretches over a lifetime, and to my husband, who has supported me through every step of my doctoral degree with kindness, understanding, and encouragement.

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## Chapter I: Introduction

As the aging population continually grows, with a projected 88.5 million older adults in 2050 and a relatedly increasing morbidity rate placing greater economic demands on countries (Hung et al., 2011; Jin et al., 2015), the concept of healthy aging has gained traction both in the community and as a public health initiative (CDC, 2007; Desai et al., 2010). While its conceptualization has evolved over the years, healthy aging has been most recently defined by the World Health Organization as the “process of developing and maintaining the functional ability that enables well-being in older age” (WHO, 2015). Stated as such, healthy aging does not assume absence of neurodegeneration or disease, but rather individual protection or compensation that allows for preserved functional ability in the context of typical or pathological age-related changes (Michel & Sadana, 2017). For example, while changes in brain morphology have been identified in typical aging, with neurodegeneration frequently observed in the frontal and temporal lobes specifically, there is notable variability between individuals regarding the extent of associated cognitive decline (Fjell & Walhovd, 2010; Lindenberger & von Oertzen, 2006). In a similar vein, rate of impairment linked to neuropathological changes related to disease processes such as Alzheimer’s has been found to vary significantly among individuals (Bennett et al., 2006; Price & Morris, 1999). This discrepancy between actual cognitive abilities and level of expected impairment based on age-related neuroanatomical changes is commonly referred to as cognitive reserve (Barulli & Stern, 2013). Although the exact underpinnings of cognitive reserve are unknown, it is thought to be influenced by a number of factors including

physiological health, neural reserve (i.e., plasticity, efficiency, compensation), and environmental factors such as education (Barulli & Stern, 2013; Vance & Crowe, 2006).

In pursuit of promoting cognitive reserve, ongoing research has attempted to more fully define its contributory factors. Of these, lifestyle variables are of significant interest given their modifiable quality. In fact, research has shown that a large percentage of adults endorse the belief that their cognition can be improved through lifestyle choices (Anderson et al., 2009) such as engagement in cognitively stimulating activities (e.g., reading, doing puzzles, playing games), which has been consistently shown in the literature to slow rates of cognitive decline in aging, and has even been linked to reduced risk of dementia and Alzheimer's disease (La Rue, 2010). Music in particular has been an area of clinical and research interest given its multidimensional nature that has the potential to contribute to healthy aging in a myriad of ways. Compared to other cognitively stimulating activities, music is uniquely composed of emotional, social, cognitive, and physiological elements (Cohen, 2009). Research has shown that listening to or playing music can facilitate social connectedness and emotional expression, influence mood states, and change physiological qualities such as pupil dilation, muscular tone, and respiratory rate (Hays et al., 2002). Numerous studies have established that the benefits of music span multiple domains related to healthy aging, including improved quality of life, sense of wellbeing, and overall health (Creech et al., 2013; Hallam, 2016). Additionally, music is an appealing intervention option for at-risk individuals or those diagnosed with a cognitive disorder given its intrinsic properties of motivation and reward (Altenmüller & Schlaug, 2013). While both music listening and music making have been studied, research has found that actively making music, in the form of playing a musical instrument or singing, provides the greatest benefits

across numerous domains including social, cognitive, and emotional factors (Creech et al., 2013).

While psychosocial aspects of music have been studied in older adults, there is relatively little research on its cognitive correlates in this population, which is particularly relevant given the significance of cognitive health for successful aging. Thus, the current study aimed to examine the cognitive benefits of music making in a healthy older adult population through the use of a dual-task walking paradigm which allows for the assessment of both behavioral performance and neural activation, with the latter contributing to our understanding of the mechanisms through which music making may support healthy aging. The following review of the literature will discuss current research on music and cognition, including neuroanatomical correlates; music and physical health; dual-task walking and the associated relationship between aging and mobility; and the potentially moderating contribution of sex to the relationship between music making and study variables.

### **Key Terms**

- Skill transfer: A concept in which training in one area (i.e., music) leads to improved performance in other domains which may either be related or unrelated from the original skill, termed near and far transfer, respectively.
- Cognitive reserve: Differences in cognitive ability that are established through numerous factors present across the lifespan (i.e., education, lifestyle activities) and contribute to individual variability in the level of functioning associated with aging or disease processes.
- Neuroplasticity: The brain's ability to change and reorganize, including both structural and functional adaptations (i.e., synaptic efficiency).



- Neural efficiency: Refers to the ability of individuals with greater cognitive capacity to complete tasks using lower brain activation. Its presence is frequently established in empirical studies through the assessment of neuroimaging in the context of behavioral performance (i.e., evidence of lower neural activation without detriment to performance).
- Dual-task walking (DTW): A condition in which an individual completes a cognitive task while simultaneously walking, with particular relevance for the aging population given age- and disease-related changes in mobility.
- Dual-task costs: The observed pattern of decline in performance during dual-task walking conditions as compared to single-task conditions (i.e., slowed gait velocity during dual-task walking compared to walking alone).
- Functional near-infrared spectroscopy (fNIRS): A portable neuroimaging technique that uses light to assess changes in blood oxygenation in the cerebral cortex. Often designed as a flexible band placed across the forehead, fNIRS is specifically sensitive to changes in the prefrontal cortex (PFC).

## **Background & Significance**

### ***Music Making and Cognition in Older Adulthood***

The act of making music, which relies on a multitude of skills such as bimanual fine-motor coordination, sight reading of musical notation, temporal rhythm discrimination, and monitoring of performance (Schlaug, 2015), engages various processing systems including sensorimotor processing and integration, visual-spatial processing, and executive functions and attention (Benz et al., 2016; Wilson, 2013). Relatedly, music training has been associated with numerous cognitive benefits in children and adults with evidence for improved language

(Moreno, 2009); nonverbal reasoning (Forgeard et al., 2008); memory (Talamini et al., 2017); academic abilities, particularly reading (Schlaug, 2015; Tierney & Kraus, 2013; Wetter et al., 2009); and specific aspects of executive functions such as working memory, cognitive control, and processing speed (Bergman Nutley et al., 2014; Okada & Slevc, 2018; Slevc et al., 2016; Zuk et al., 2014). Consistent findings of the positive relationship between music and specific cognitive functions indicate the presence of skill transfer, in which training in one area (i.e., music) leads to improvements in other domains that may be either directly related (i.e., pitch and rhythm discrimination) or indirectly related to the original skill (i.e., language) (Wan & Schlaug, 2010).

While the presence of widespread transfer effects has been consistently shown in children and adults with musical training, there is a relative lack of literature on music-related cognitive changes in older adults, frequently defined as those aged 65 years or older (WHO, 2010). Current studies on music and cognition in aging include examination of short-term (i.e., six months or less) music interventions as well as long-term (i.e., over six months) music training. Evidence for the relationship between music making and cognition in older adulthood largely resides in cross-sectional studies examining the effect of relatively long-term music training. In a recent meta-analysis of nine correlational studies examining healthy adults over the age of 59, researchers identified significant positive relationships between music training (occurring over the course of many years) and numerous cognitive domains consistent with those commonly observed in studies of younger adult musicians, including language, visual-spatial abilities, and executive functioning and attention (Román-Caballero et al., 2018). However, effect sizes associated with specific cognitive domains varied from small ( $g = 0.2-0.5$ ) to large ( $g > 0.8$ ) and there was notable heterogeneity among studies.

Whereas processing speed and attention had a small but consistent positive effect size, cognitive domains that demonstrated the largest effect sizes also had the highest level of heterogeneity, including inhibition, verbal working memory, and visual-spatial ability. Additionally, researchers identified a complexity effect in which larger effect sizes were found for tasks that were the most demanding within the same cognitive domain (i.e., compared to non-musicians, musicians performed better on a standard list learning task rather than a shortened version). Although this and other recent studies examining the effect of music making on objective cognitive performance (Gray & Gow, 2019; Pentikäinen et al., 2021; Strong & Mast, 2018) contributes evidence for music's positive relationship with specific cognitive domains in older adults, the use of various neuropsychological tasks that appear to have disparate sensitivity to cognitive differences leads to mixed results.

This variability in study findings extends to the literature on music and executive functioning in particular, which is a cognitive domain that is especially relevant to healthy aging (Spreng et al., 2017). Higher-order cognition plays a large role in numerous processes involved in making music and musical training has been associated with various aspects of executive functioning (e.g., working memory, inhibitory control) in children and adults (Okada & Slevc, 2016). Although this correlational relationship has not yet been adequately examined in older adults, a review of numerous experimental studies supports the use of music-based interventions to improve executive functioning in this population (Koshimori & Thaut, 2019). However, empirical research on this relationship overall remains mixed, which may be at least partially attributed to the multidimensional nature of executive functioning which consists of numerous components such as inhibition, cognitive control, set-shifting, and fluency, among others (Jurado & Rosselli, 2007). In an attempt to address this

multifaceted layer of executive functioning as well as the various neuropsychological tasks used to measure the domain, one study employed a latent variable approach to examine the impact of music on specific aspects of executive functioning in adults, as assessed through multiple measures (Okada & Slevc, 2018). Study results revealed significant positive associations between music and working memory updating specifically, with little evidence for similar correlations between music, inhibition, and set-shifting abilities. While this pattern of association has been seen in other studies and across both visual and auditory stimuli (Slevc et al., 2016; Zuk et al., 2014), variability among results still remain due to the use of differing cognitive tasks to operationalize study outcome. Despite evidence for a nuanced relationship between music making and executive functioning, as well as the importance of this domain for successful aging, this association has been largely understudied in older adults. Thus, more research is needed to parse out these specific relationships, with particular emphasis on the potential utility of non-traditional methods of assessing executive functioning rather than standard neuropsychological testing.

### ***Neuroanatomy of Music Making***

Underlying these changes in cognitive abilities are multiple structural and functional neuroanatomical differences associated with music making that are due largely to enhanced neuroplasticity or the brain's adaptive ability to change and reorganize (Demarin et al., 2014; Jäncke, 2009; Wan & Schlaug, 2010; Wilson, 2013). Indeed, musicians are often cited as ideal models for the study of neuroplasticity given the multimodal, complex nature of music making (Moreno & Bidelman, 2014; Münte et al., 2002; Schlaug, 2015). Studies of children and young adults have demonstrated numerous structural gray matter differences, with musicians typically displaying larger brain regions bilaterally in the prefrontal cortex (PFC)

and frontal lobe, motor and somatosensory areas, middle and inferior temporal gyrus, parietal regions, and the cerebellum (Wilson, 2013). Although structural changes are widespread throughout the brain, there is consistent evidence for a frontotemporal network involved with music making, including regions related to processing of both music and language such as the planum temporale, as well as those recruited for higher-order functions including the dorsolateral prefrontal cortex (dlPFC) (Bermudez et al., 2009). White matter differences have also been established including a larger anterior corpus callosum, which is thought to represent increased interhemispheric communication to support bimanual motor activity (Schlaug et al., 1995), as well as asymmetry (left greater than right) in the superior longitudinal fasciculus, a region involved in speech and music (Oechslin et al., 2010). Functional differences include greater left hemisphere specialization in musicians, enhanced information processing, and greater neural efficiency (Wilson, 2013).

Similar to the current literature on cognition and music making, neuroanatomical correlates of music in older adulthood have been relatively understudied, despite the wealth of information among children and adults. However, it has been postulated that music may protect against age-related cognitive decline primarily through relative preservation of the frontal lobes (Jäncke, 2013) due to music making's strong recruitment of executive functioning skills which are closely linked to this brain area, particularly prefrontal regions (Gilbert & Burgess, 2008). There is also some empirical evidence that music has neuroprotective benefits for cognitive health as the brain matures with one study demonstrating that, compared to non-musicians, adult musicians exhibited better "brain age," defined as the discrepancy between participants' chronological age and the age of their brains as assessed via magnetic resonance images (Rogenmoser et al., 2018). Authors highlight the

ability of music to modify and enhance neural activity, in addition to other physiological processes such as cerebral blood flow and metabolism, as a primary mechanism through which music may have “age-decelerating” effects on the brain. Although this study was conducted in a sample of adults (ranging in age from 17-39 years) it can be expected that older adult musicians would demonstrate structural and/or functional changes similar to their younger counterparts, given that neuroplasticity has been shown to extend into aging (Park et al., 2013). There is also existing evidence that neuroanatomical changes related to music are long-lasting (White-Schwoch et al., 2013), especially when engagement in music making is ongoing (Wilson, 2013).

Preliminary support of the direct relationship between music and neuroanatomical changes in older adulthood can be found in a recent intervention study examining the neuroplastic effects of music training in a sample of healthy older adults with limited prior music exposure (Alain et al., 2019). Following a 3-month music training program that consisted of both singing and playing a musical instrument, those in the music group exhibited functional brain changes (as assessed by electroencephalography) related to both auditory and inhibitory control processes in the auditory cortex and frontal regions, respectively. This provides evidence for improved post-intervention outcomes specific to music training as well as effects that were generalized to a higher-order cognitive function (i.e., cognitive control). Behavioral changes were also observed, in which performance on measures of processing speed improved in the music training group between pre- and post-intervention time points. While other music intervention studies have shown similar changes in behavioral performance (Bugos et al., 2007; Seinfeld et al., 2013), the accompanying neuroimaging results shown by Alain et al. (2019) provides empirical evidence for a causal

relationship between music and changes in neural activation in a healthy older adult population in response to both musical and nonmusical cognitive tasks. While more research is needed on the neural correlates of music making in older adults, this preliminary evidence combined with our knowledge of neuroplastic capabilities extending into older adulthood suggests that neuroanatomical changes are present in older adult musicians, even if length of previous music training is relatively brief.

### ***Music Making and Neural Efficiency***

A related construct to neuroplasticity is the concept of neural efficiency, which states that individuals with greater cognitive capacity are able to complete cognitive tasks using lower (and therefore, more efficient) brain activation (Neubauer & Fink, 2009). Empirically, neural efficiency is frequently established by interpreting neuroimaging results in the context of associated behavioral performance. For example, a number of studies have demonstrated that older adults exhibit an over-activation of the prefrontal cortex in response to executive functioning demands compared to younger individuals, which can subsequently be interpreted as relative neural inefficiency given that behavioral performance between older and younger adults remains comparable (Jordan et al., 2020; Nyberg et al., 2014). While neural efficiency typically declines with age, this is better preserved in individuals with higher levels of cognitive reserve (Barulli & Stern, 2013) and cognitive training has been shown to improve neural efficiency specifically related to executive functioning in older adults (Motes et al., 2018; Nguyen et al., 2019; Wang et al., 2011). These findings are particularly relevant given that decline in executive functioning is considered a core feature of cognitive aging (Spreng et al., 2017) and these higher-order functions are closely

associated with independent activities of daily living (Reuter-Lorenz et al., 2016). Thus, it is clinically pertinent to identify factors related to its protection in older adulthood.

Among the other neuroplastic changes found in the brains of musicians, current literature supports the association between music making and enhanced neural efficiency. Compared to non-musicians, adult musicians have been shown to use fewer neural resources across differing brain regions and in response to various stimuli (i.e., motor, auditory, etc.) while playing a musical instrument or singing (Merrett & Wilson, 2011). Additionally, there is evidence for greater neural efficiency when completing non-musical tasks, with adult musicians demonstrating lower brain activation in the superior PFC and dlPFC during an auditory working memory task (Alain et al., 2018). Although often hypothesized as a mechanism through which older adult musicians exhibit preserved cognitive functions (Amer et al., 2013; Moussard et al., 2016; Román-Caballero et al., 2018), the relationship between music making and neural efficiency has not yet been directly examined in aging. However, preliminary evidence for this association can be found in intervention studies examining the impact of brief music training on neural activation. For instance, one intervention study examining the effects of a 6-month singing program in a sample of older adults with Alzheimer's disease (aged 69-87 and 60% female) demonstrated significantly improved neural efficiency in the lingual and angular gyri while singing, as compared to pre-intervention assessment (Satoh et al., 2015).

Evidence for changes in neural efficiency related to non-musical tasks has also been observed in another study assessing the impact of a music intervention in healthy older adults who were aged 61-85 years and predominantly female, with no prior music experience (Guo et al., 2021). Following a 4-month program of weekly keyboard harmonica training, changes



in both behavioral and neural performance were evinced, including post-intervention improvements in verbal memory as assessed through neuropsychological task performance. Additionally, as compared to a control group, a significant post-intervention decrease in neural activation across multiple brain regions (i.e., temporal gyri, cerebellum, insula, superior parietal lobe) was observed via functional MRI during a visual working memory task. As working memory performance remained unchanged, authors interpreted these findings as evidence for the presence of improved neural efficiency. Interestingly, additional correlational findings linked improved verbal memory performance to reductions in functional connectivity between the left putamen and right superior temporal gyrus (areas of gray matter that are often found to be larger in musicians), further suggesting enhanced neural efficiency following music training. While this provides promising evidence that music making can improve neural efficiency in older adulthood, the effect of music making as a relatively long-term leisure activity rather than a brief targeted intervention has not yet been assessed.

### ***Music Making and Gait***

Just as music-related neuroanatomical changes underlie differences in cognitive functioning, there is also likely a similar effect on physical functioning. However, within the current literature, few studies have directly examined the relationship between music making and physical health. Music listening is often cited as an adjunct therapy to support exercise training programs, and there is evidence for its positive effect on treatment adherence as well as outcome measures such as physical endurance and walking velocity in older adults, including those with neurological disorders (Clark et al., 2016; de Dreu et al., 2012; Mathews et al., 2001; Rosseland, 2016). Theoretical mechanisms underlying music listening's positive

effect on exercise outcomes includes increased motivation, improved adherence, manipulation of physiological arousal, and rhythmic entrainment (Clark et al., 2016). Although limited, there is also preliminary evidence for the beneficial effects of music making. Intervention studies utilizing short-term (12- to 30-week programs) instrument playing and singing have demonstrated improved gait velocity and stride length from pre- to post-test assessment in older adults with mild cognitive impairment (MCI) (Domínguez-Chávez et al., 2019), as well as better overall physical health and fewer falls in healthy older adults (Cohen et al., 2006). While there is a notable gap in the literature with a lack of studies examining the impact of long-term music making on physical parameters such as gait, it is postulated that music making can protect against physical decline through psychoimmunoneurology effects related to increased sense of wellbeing and control, as well as neuroanatomical changes including neuroplasticity and greater interhemispheric symmetry (Cohen, 2009).

### ***Dual-Task Walking***

One method of assessing multiple factors related to music making, including neural activity, cognition, and gait, is through the use of a dual-task walking (DTW) paradigm in which an individual performs a series of tasks that include completing a motor and cognitive task simultaneously. Not only does this allow for concurrent assessment of various outcome measures, DTW paradigms are particularly relevant for the aging population with extensively supported ecological validity. This is reviewed further in the sections below along with literature supporting the potential moderating impact of music.

**Aging & Mobility.** Walking is a complex system that relies on attentional capacity and integration of information, and typically declines in older adulthood – a process that is

largely attributed to age-related neuroanatomical and cognitive changes (Beurskens & Bock, 2012). The cognitive control of locomotion has been well-established, with research consistently showing that cognition is highly correlated with gait changes, postural instability, and falls (Li et al., 2018). The intersection between cognition and mobility is frequently studied through DTW experiments in which an individual simultaneously walks and completes a cognitive task (i.e., reciting alternate letters of the alphabet). The DTW paradigm provides a unique, robust opportunity to study individual performance under lab conditions that resemble real-world activities, as distractions are often present while walking outside of a controlled lab environment (e.g., talking, texting) (Neider et al., 2011). Dual-task performance has been well-validated in the literature and is associated with fall risk, frailty status, and disability (Fuller et al., 2013; Guedes et al., 2014; Lamoth et al., 2011; Nordin et al., 2010; Sosnoff et al., 2011).

Frequently, performance during dual-task conditions declines in comparison to similar performance under single-task conditions (i.e., walking alone) (Holtzer, Wang, & Verghese, 2012, 2014), which is a phenomenon observed across populations, including in aging, and is termed “dual-task cost.” As expected, dual-task costs typically increase with age as the automaticity of walking becomes reduced (Beurskens & Bock, 2012; Clark, 2015), and are even more pronounced in individuals with neurological disorders such as dementia and Parkinson’s disease (Belghali et al., 2017), as well as those with MCI (Doi et al., 2014) and subclinical cognitive impairment (Hashimoto et al., 2014). While some individuals can attenuate dual-task costs by recruiting higher-order cognitive functions, this strategy is limited for those with reduced cognitive capacity (Holtzer, Wang, & Verghese, 2012, 2014; McFadyen et al., 2017). Thus, performance on DTW paradigms that, by their nature, require

multiple cognitive resources is often used to assess cognitive dysfunction, particularly deficits in executive functioning (McFadyen et al., 2017).

Executive functions are central to many theories of dual-task costs, including limited neural capacity to process multiple tasks which may lead to task switching, as well as uneven attentional allocation to one task over another (i.e., prioritizing postural stability) (McIsaac et al., 2015; Yogev-Seligmann et al., 2008). Multiple aspects of executive functioning, including executive attention and speed of processing, have been related to specific facets of DTW, with poorer cognitive performance in this domain related to worse gait variability, velocity, and step asymmetry during dual-task conditions (Holtzer et al., 2012; Sunderaraman et al., 2019). Similarly, a better hazard estimate, which is conceptualized as an aspect of executive function that may be engaged during DTW and involved with planning, self-monitoring, and risk assessment, has been correlated with faster gait speed and improved accuracy on a cognitive interference task during DTW conditions (Holtzer et al., 2014). Interestingly, language has also been positively correlated to dual-task performance, which may reflect the protective effect of cognitive reserve, as vocabulary knowledge is often used as a proxy for this construct (Sunderaraman et al., 2019).

**Neural Correlates of Mobility.** A complex neuroanatomical network associated with mobility, including cerebellar and spinal tracts, subcortical structures, and regions within the cerebral cortex, has been identified across various walking conditions and among different populations (Takakusaki, 2017). Research among older adults has established that both gray matter atrophy and decline in white matter integrity, particularly in frontal regions and the basal ganglia, are associated with poor gait (Wilson et al., 2019). However, the identification of specific neural correlates of walking is challenging given that traditional neuroimaging

techniques are not conducive to mobile conditions. Although magnetic resonance imaging (MRI), diffusion tensor imaging (DTI), and positron emission tomography (PET) have been used to assess brain structure and function related to walking, these techniques are limited to a correlative study design. Newer study methodology, however, has more recently allowed for the real-time assessment of neural activation during walking, including functional near-infrared spectroscopy (fNIRS), a noninvasive portable neuroimaging device that uses light to measure changes in oxygenated hemoglobin (HbO<sub>2</sub>) in the cerebral cortex, namely the PFC (Ferrari & Quaresima, 2012). Systematic review of the use of fNIRS to assess neural correlates of mobility have demonstrated its significant utility across various conditions within naturalistic environments including cycling, rowing, dancing, postural tasks, and walking (Herold et al., 2017; Leff et al., 2011; Quaresima & Ferrari, 2019). In addition to its applicability to real-world situations, other advantages to fNIRS includes its high temporal resolution as well as comprehensive assessment of the brain's hemodynamic response (Leff et al., 2011).

**DTW and Neural Efficiency.** Given the established demands on executive functioning, it is unsurprising that the PFC is heavily involved in DTW (Hamacher et al., 2015). Studies using fNIRS to examine HbO<sub>2</sub> levels during DTW paradigms have shown an increase in prefrontal activation during dual-task conditions compared to single-task (Holtzer et al., 2011; Mirelman et al., 2014). This increase is moderated by age and neurological status, indicating either underutilization or compensatory activity of the PFC during dual-task conditions (Beurskens et al., 2014; Holtzer et al., 2011, 2016; Verghese et al., 2017). The ability of the PFC to serve as a compensatory strategy for reductions in automatic walking is

thought to be influenced by overall executive functioning capabilities and this role may be less efficient in older adults (Nóbrega-Sousa et al., 2020).

Within the DTW paradigm, neural efficiency can be examined by assessing PFC activation in the context of behavioral performance. For example, older adults who display greater PFC activation during dual-task walking conditions while also demonstrating equivalent or worse behavioral performance (e.g., slower gait velocity), as compared to a control group, may be considered as exhibiting relative neural inefficiency. Indeed, previous research has identified associations between inefficient fNIRS-derived PFC activation during DTW and lower gray matter volume (Wagshul et al., 2020) and white matter integrity (Lucas et al., 2019). Additionally, there is evidence that DTW performance and related PFC efficiency (as assessed via fNIRS) can improve over one session of repeated dual-task trials (Holtzer, Izzetoglu, et al., 2019). Given evidence of structural and functional differences observed in the PFC of musicians, we would expect fNIRS-derived HbO<sub>2</sub> levels during the DTW paradigm to differ in older adult musicians, potentially indicating the presence of enhanced neural efficiency.

**DTW and Music.** Due to its clinical correlates, individual factors that may protect against poor dual-task performance are of particular interest. Previous research has shown that both cognition and routine physical activity can positively moderate dual-task performance, which may be further enhanced by positive affect and mental well-being (Hausdorff et al, 2008; Forte et al., 2019). Taken together, the current literature suggests that music making may impact dual-task performance through both indirect and direct pathways, the latter of which includes its role in preserving executive functioning. Preliminary support is found in dual-task training studies that utilize short-term music-based interventions to

improve performance. Following an eight-week rhythm-motor training program, which consisted of playing an instrument or singing while completing a concurrent motor task (either walking or bimanual tapping), healthy older adults demonstrated significant improvements in attentional control and gait (Kim & Yoo, 2019). Similarly, a study of older adults with dementia showed post-intervention improvements in attentional control in the musical dual-task training group only (Chen & Pei, 2018). Given that these music interventions led to significant improvements over a short period of time, it is logical to hypothesize that long-term music training would be associated with dual-task performance, and specifically, dual-task costs.

### *Sex Differences*

It is important to note the potential contributory influence of sex on the relationship between music making and dual-task performance, given a myriad of sex-related differences across study variables. First, it has been well-established that there are general sex differences in brain organization and activation due to various factors such as hormones and environmental influences (Jäncke, 2018). These neuroanatomical differences have been observed across the lifespan (Gong et al., 2011) and studies specifically examining healthy older adults have demonstrated sex-related differences in brain morphology, volumetric loss in specific brain structures, and activation in the PFC (Armstrong et al., 2019; Gur & Gur, 2002; Lemaître et al., 2005; Richter et al., 2007; Zhao et al., 2019). Studies examining neuroanatomical correlates of music making have also revealed some structural differences to be present only in male musicians, including a larger corpus callosum, greater cerebellar volume, and greater leftward asymmetry of the postcentral gyrus (Lee et al., 2003; Luders et al., 2004; Hutchinson et al., 2003). However, it is important to acknowledge the many

neuroimaging studies utilizing samples made up of both male and female musicians that have demonstrated significant results, suggesting that changes in brain structure and function are present in female musicians as well (Merrett et al., 2013). Thus, more research is needed to further define sex effects as they relate to specific neuroanatomical regions associated with music making.

Given the extent of these observed sex differences, it is unsurprising that previous research has identified specific elements of dual-task performance that differ by sex as well. For example, older adult men tend to display higher activation levels in the PFC during dual-task conditions (Holtzer et al., 2015). Similarly, sex differences in gait performance during dual-task walking has been shown, with older men demonstrating greater gait variability (Hollmann et al., 2011). Additionally, in a sample of young adults, there is evidence that men display different prioritization effects compared to women, in which they exhibit an attenuated change in gait speed when prompted to prioritize gait during dual-task conditions (Yogev-Seligmann et al., 2010). In light of these established sex differences among brain structure and function in both musicians and non-musicians, as well as performance during dual-task walking, it is expected that sex may moderate the relationship between music making and dual-task performance.

### **Rationale of Current Study**

Although much is known about the benefits of music making in children and adults, the impact of music on the aging brain is less well-characterized. Despite hypotheses that music may confer age-decelerating effects (Rogenmoser et al., 2017) and evidence that neuroanatomical changes related to music are long-lasting (White-Schwoch et al., 2013), the direct relationship between music and cognition in older adulthood requires further study.



Given the extent of neuroplastic changes associated with music making and preliminary evidence from music intervention studies suggesting modifiable functional neuroanatomy in older adults (Alain et al., 2019), it is reasonable to assume that ongoing engagement in music making as a leisure activity could lead to changes in neural activation. Specifically, adult musicians have been shown to exhibit improved neural efficiency across musical and non-musical tasks (Merrett & Wilson, 2011; Alain et al., 2018), however, this has been relatively understudied in older adults despite its relevance for aging. While neural efficiency typically declines in older adulthood (Barulli & Stern, 2013), this can be modified through cognitive training, which has been demonstrated particularly in relation to executive functions (Motes et al., 2018; Nguyen et al., 2019; Wang et al., 2011). Given that executive functioning is a critical aspect of successful aging and involved in the maintenance of functional ability (Spreng et al., 2017; Reuter-Lorenz et al., 2016), elucidating this relationship has important clinical applicability while also providing the opportunity to broaden our understanding of the mechanisms through which music making benefits cognitive health in late life.

Although music making has been linked to better executive functioning across the lifespan, study results often vary significantly due to the multifaceted nature of this cognitive domain as well as the variety of neuropsychological tasks used to assess it (Okada & Slevc, 2018). While research has linked music making to specific aspects of executive functioning, including working memory, this complex relationship has not been fully defined in older adults. Given evidence of notable variability in statistical significance and associated effect sizes in the current literature (Román-Caballero et al., 2018), expanding study methods outside of traditional cognitive testing to assess executive functioning is pertinent. Thus, this study focused on using a dual-task walking (DTW) paradigm to assess higher-order cognitive

functioning as a function of both dual-task costs as well as behavioral performance during the cognitive interference task, which taps specifically into working memory abilities.

In addition to cognition, this paradigm provides opportunities to examine physical parameters such as gait that have rarely been assessed in relation to music despite the presence of theoretical underpinnings for this association (Cohen, 2009). Furthermore, the use of portable neuroimaging techniques, such as functional near-infrared spectroscopy (fNIRS), allows for concurrent assessment of neural activation during all tasks within the DTW paradigm. In this way, differences in overall PFC activity between older adult musicians and non-musicians can be established, in addition to assessing for neural efficiency when framed by associated behavioral data (i.e., gait and cognitive performance). To our knowledge, this is the first study directly examining this relationship among older adults that is not within the context of a specific music intervention, and thus addresses a critical gap in the literature regarding the neural correlates of music making in aging.

Fully characterizing the neural, cognitive, and physical benefits of music making in older adulthood serves as a robust contribution to the current literature on music's influence across the lifespan. To this end, this study additionally explored the moderating effect of sex due to established sex differences in general neuroanatomy (Jäncke, 2018) and factors related to music making (Lee et al., 2003; Luder et al., 2004), as well as dual-task performance and related fNIRS-derived neural activation (Holtzer et al., 2015; Holtzer et al., 2017; Hollmann et al., 2011), thus providing the ability to more clearly define the relationship between music making and study variables. Due to previous research indicating that cognitive benefits of music making are more salient in samples of older adults who have not yet experienced cognitive decline, this study focused on a relatively healthy sample of older adults. The

practical clinical application of results is underscored by the study of older adults who currently endorse music making, which places emphasis on active music making rather than past music training. Not only does this enhance our ability to assess the moderating effect of music, as ongoing engagement has been shown to extend the greatest benefits, but it also supports its clinical utility as a recommended leisure activity that can bolster healthy aging, especially in individuals who may be at particular risk for cognitive and/or physical decline. Finally, assessing potential underlying neural mechanisms serves to strengthen our understanding of the therapeutic effect of music, which may lead to more sensitive identification of individuals who are ideal candidates for music interventions.

### **Aims and Hypotheses**

Given the current gaps in the literature, this study aimed to employ a dual-task walking paradigm in order to examine cognitive, physical, and neural correlates of music making in a community-dwelling sample of healthy older adults (aged 65 years or older). Those who endorsed currently playing a musical instrument or singing at least once a week were classified as a musician regardless of training length, as studies have shown benefits from both short- and long-term musical training (Rogenmoser et al., 2018). Cognitive performance was assessed through an alternate alphabet task, which was completed both as a single task and under dual-task conditions in which participants were prompted to simultaneously walk. In addition to behavioral performance across tasks, change in performance from single- to dual-task conditions was assessed in order to examine dual-task costs, which are characterized by decreased performance when engaging in two tasks simultaneously compared to one task alone. Finally, the role of sex as a moderator of the

relationship between music making and behavioral measures (including cognitive and physical performance) as well as brain activation was explored.

**Aim 1:** Examined whether music making is associated with levels of brain activation (fNIRS-derived HbO<sub>2</sub> levels) during task conditions (Single Task Alpha, Single Task Walk, and Dual Task Walk), as well as change in HbO<sub>2</sub> levels from single- to dual-task conditions. Behavioral performance was included as a covariate in order to interpret neural efficiency.

*Hypothesis 1:* Musicians (as compared to non-musicians) were expected to exhibit lower HbO<sub>2</sub> levels across task conditions and an attenuated increase in HbO<sub>2</sub> levels from single- to dual-task conditions.

**Aim 2:** Examined whether music making is associated with behavioral task performance in addition to moderating change in performance from single to dual-task conditions.

Aim 2A: Examined whether music making is associated with cognitive performance during single-task Alpha (STA) and dual-task (DTW) conditions, as well as change in cognitive performance from single- to dual-task conditions.

*Hypothesis 2A:* Musicians (as compared to non-musicians) were expected to demonstrate better cognitive performance across tasks and smaller dual-task costs.

Aim 2B: Examined whether music making is associated with gait performance during single-task walk (STW) and dual-task (DTW) conditions, as well as change in gait performance from single- to dual-task conditions.

*Hypothesis 2B:* Musicians (as compared to non-musicians) were expected to demonstrate better gait performance across tasks and smaller dual-task costs.

**Aim 3:** Given evidence for sex differences associated with music making, dual-task performance, and general neuroanatomy, we explored whether sex moderated the

relationship between music making and brain activation patterns as well as task performance, in addition to change in brain activation and task performance from single- to dual-task conditions.

Aim 3A: Explored whether sex moderated the association between music making and levels of brain activation (fNIRS-derived HbO<sub>2</sub> levels) during task conditions (STA, STW, DTW), as well as change in HbO<sub>2</sub> levels from single- to dual-task conditions. Behavioral performance was included as a covariate in order to interpret neural efficiency.

Aim 3B: Explored whether sex moderated the association between music making and cognitive performance during single-task Alpha (STA) and dual-task (DTW) conditions, as well as change in cognitive performance from single- to dual-task conditions.

Aim 3C: Explored whether sex moderated the association between music making and gait performance during single-task walk (STW) and dual-task (DTW) conditions, as well as change in gait performance from single- to dual-task conditions.

## **Chapter II: Methods**

### **Participants & Study Procedures**

Study participants were enrolled through the ‘Central Control of Mobility in Aging’ (CCMA) study, a longitudinal cohort study examining cognitive predictors of mobility function and decline in healthy older adults (Holtzer, Wang, & Verghese, 2014). Detailed review of the CCMA study protocol can be found in previous literature (Holtzer, Wang, & Verghese, 2014; Holtzer, Epstein, et al., 2014). Participants were community dwelling adults aged 65 years or older who were recruited from Westchester County, NY, through an institutional review board-approved letter and a follow-up telephone call consisting of an explanation of the study protocol and screener questions to determine study eligibility. Potential participants were excluded from the CCMA study if they reported the presence of severe or terminal illness, neurodegenerative disease, dementia, significant restrictions in mobility, impairment in vision or hearing that would negatively impact testing, and difficulty understanding or speaking English. Following study enrollment and subsequent data collection, further exclusion criteria for the current study sample included participants who were missing baseline data or with an established diagnosis of dementia as determined via diagnostic case conference.

Upon confirmation of CCMA study eligibility, participants were invited to the research clinic for two initial visits, typically scheduled within two weeks of one another and each lasting approximately three hours. The first visit consisted of a fixed battery of

neuropsychological tests, a dual-task walking paradigm integrating fNIRS (described in more detail below), and a number of questionnaires capturing an overview of medical, social, and psychological history, as well as current level of functioning. The second visit consisted of additional questionnaires, a neurological assessment, and mobility tasks designed to measure walking and balance. Written informed consent for the study protocol (approved by the Albert Einstein College of Medicine Institutional Review Board) was obtained from all participants during their first clinic visit. While CCMA participants were invited to return to the clinic each year following their initial visit in order to collect annual data for up to seven years, only data collected at baseline was utilized for the current study. Due to ongoing study recruitment, this baseline data was collected from participants between June 2011 and October 2017.

## **Measures**

### ***Music Making: Leisure Activity Questionnaire***

Group status was determined via response to a questionnaire evaluating common cognitive (e.g., reading, playing games, writing, playing a musical instrument, singing, visiting the museum or theater) and physical (e.g., tennis, golf, dancing, walking) activities. Participants were asked if they completed each activity on a weekly basis and if endorsed, they were subsequently asked *how often* they engaged in each activity, including number of days per week, number of hours per day, and for how many years. This questionnaire has been previously used to assess the relationship between leisure activities and risk of cognitive decline, including dementia (Verghese et al., 2003) and MCI (Verghese et al., 2006). For the purposes of this study, participants who endorsed either playing a musical instrument *or* singing at least once a week at baseline were categorized into a music making (or musician)

group. Significant differences between those who play a musical instrument versus singing was not expected given literature showing cognitive benefits and similar neuroanatomical changes related to both musical activities (Loui, 2015; Segado et al., 2018; Wan & Schlaug, 2010; Zatorre et al., 2007). Furthermore, the method of combining these groups into a single study sample has been employed in previous studies (Mansens et al., 2018; Nevriana et al., 2013).

### ***Quantitative Gait Assessment***

Gait was assessed via a 4 x 20 foot Zeno electronic walkway using ProtoKinetics Movement Analysis Software (PKMAS) for both STW and DTW conditions (Zenometrics, LLC; Peekskill, NY). Stride velocity (cm/s) was calculated based on the location and mathematical parameters between footfalls. Previous research has established excellent internal consistency for stride velocity measurements within task conditions with split-half intra-class correlations (ICC) falling at greater than 0.95 (Holtzer et al., 2015).

### ***Gait Paradigm***

Participants were instructed to complete two single-task conditions – single-task walk (STW) and a cognitive interference task (single-task Alpha; STA) – and one dual-task walk condition (DTW) during which participants walk and complete the cognitive interference task simultaneously. During STW, participants completed three consecutive loops around the electronic walkway and were directed to walk at their normal pace. The cognitive interference task (STA) was administered over 30 seconds during which participants were instructed to recite aloud alternate letters of the alphabet (i.e., A, C, E...) while standing in place. Responses were recorded by the examiner and rate of correct letter generation was calculated, which is a method of quantifying cognitive performance that has been used in



previous studies (Holtzer, Kraut, et al., 2019; Holtzer et al., 2017). Under the dual-task condition (DTW), participants were directed to walk around the electronic walkway at their normal pace while reciting alternate letters of the alphabet. They were stopped by the examiner when three loops were completed. In order to minimize task prioritization effects, participants were instructed to pay equal attention to both tasks (Holtzer, Wang, & Verghese, 2014). As in the single-task Alpha condition, responses were recorded and used to calculate the rate of correct letter generation. Task order was counterbalanced across participants in order to mitigate practice effects. The reliability and validity of this paradigm have been well-established in the literature (Holtzer, Wang, Lipton, & Verghese, 2012; Verghese et al., 2012).

### ***fNIRS Data Acquisition and Processing***

**fNIRS System.** Changes in oxygenated hemoglobin (HbO<sub>2</sub>) in the PFC was assessed using the fNIR Imager 1100 (fNIR Devices, LLC, Potomac, MD). The fNIRS system includes a sensor in the form of a flexible band that is placed on participants' foreheads and consists of 16 channels which include four LED light sources and ten photodetectors. A control box is used for data acquisition and a computer for data collection and storage, allowing for data to be collected at a sampling rate of 2Hz. The fNIRS sensor was worn during all task conditions of the gait paradigm and was placed on the forehead according to standard procedures. The sensor was situated so that it fell directly above the eyebrows according to the international 10-20 system, with the FP1 and FP2 marker locations positioned approximately on the bottom channel row level (Ayaz et al., 2006). The horizontal symmetry axis central (y-axis) coincided with the symmetry axis of the head, falling in between the eyes. The flexibility of the sensor allows for better adaptation to individual

contours, strengthening signals and light coupling efficiency. The fNIRS system has been validated in previous studies (Izzetoglu et al., 2005).

**Preprocessing and Hemodynamic Signal Extraction.** Data from the 16 fNIRS channels for all participants were visually inspected for saturation, dark current conditions, or extreme noise. In order to suppress spiky noise, wavelet denoising with Daubechies 5 (dv5) wavelet was then applied to the raw intensity measurements at 730 and 850 nm wavelengths. Once raw intensity measurements were cleaned of artifacts, changes in oxygenated hemoglobin (HbO<sub>2</sub>) were calculated used modified Beer-Lambert law (MBLL). In MBLL, wavelength and chromophore dependent molar extinction coefficients previously published by Prahl (1998), and differential pathlength factor (DPF) adjusted by age and wavelength were used. Spline filtering followed by a finite impulse response low-pass filter with a cut-off frequency of 0.08 Hz were used to remove possible baseline shifts and to suppress physiological artifacts (i.e., respiration and Mayer waves). The algorithms used to process current fNIRS data were chosen based on recently published data (Izzetoglu & Holtzer, 2020). HbO<sub>2</sub> was utilized rather than other fNIRS-derived measures (i.e., deoxygenated hemoglobin) due to evidence for its increased reliability and sensitivity to changes in cerebral oxygenation related to locomotion (Harada et al., 2009). In order to assess task-related changes in HbO<sub>2</sub> levels, data epochs in each condition were corrected relative to proximal 10-second baselines administered directly before each task condition (Holtzer et al., 2015, 2016, 2017).

**Epoch and Feature Extraction.** Individual mean HbO<sub>2</sub> data were separately extracted for each task within the gait paradigm. fNIRS and gait data acquisition were

synchronized using a centralized “hub” computer with E-Prime 2.0 software, as previously described (Holtzer et al., 2015, 2016, 2017).

**Reliability of fNIRS Measurements.** Split-half intra-class correlations of HbO<sub>2</sub> measurements within each task have been shown to be high for STW (0.830), STA (0.864) and DTW (0.849) conditions, demonstrating excellent internal consistency (Holtzer et al., 2015).

### *Covariates*

In addition to music making status indicating whether a participant regularly engaged in musical activity (i.e., playing a musical instrument and/or singing), the following covariates were included in analyses. Due to the previously described relationship between sex and study variables, including both music and dual-task performance, sex (assessed as either male or female) was included as a covariate. Another demographic covariate included age, which has been shown to significantly moderate dual-task walking with older individuals displaying greater decrements in dual-task performance compared to younger individuals, as assessed via brain activation and gait (Mirelman et al., 2017; Priest et al., 2008). A global health score (GHS) ranging from 0 to 10 that assessed the presence of diabetes, chronic heart failure, arthritis, hypertension, depression, stroke, Parkinson’s disease, chronic obstructive lung disease, angina, and myocardial infarction was included in analyses to control for significant health comorbidities, as has been used in previous studies (Holtzer et al., 2006; Holtzer, Wang, & Verghese, 2014). Additionally, given evidence that music making positively influences mood and depressive symptoms (Creech et al., 2013; Maratos et al., 2009), total score on the geriatric depression scale (GDS) was included. The GDS has been validated for use with healthy older adults, with an estimated 84% sensitivity in

detecting individuals with depression and a Cronbach's alpha of 0.94 (Montorio & Izal, 1996; Yesavage et al., 1982). Finally, total standard score on a screening measure of literacy, the Wide Range Achievement Test, 3<sup>rd</sup> Edition (WRAT-3) reading subtest, was used to control for premorbid intellectual ability and cognitive reserve, which has been widely implicated in the relationship between music and cognition in older adults (Hanna-Plady & Gajewski, 2012; Mansens et al., 2018; Moussard et al., 2016; Rogenmoser et al., 2018; Román-Caballero et al., 2018; Seinfeld et al., 2013). The WRAT-3 reading subtest is commonly used as an estimate for premorbid ability and adequate reliability has been demonstrated in samples of healthy older adults (Lezak et al., 2004; Ashendorf et al., 2009). Although not included in primary analyses, other demographic variables that were explored between study groups included race and years of education, both assessed via self-report.

### **Statistical Analysis**

Inclusion criteria for the current study consisted of completion of the above measures at baseline as well as the absence of dementia as determined by diagnostic case conference. Individuals missing case conference data were also excluded. Per these criteria, the final total study sample consisted of 415 participants, including 70 musicians. Prior to performing analyses, participant data were examined for missing data points, linearity, homogeneity of variance, and distribution of residuals in order to confirm required statistical assumptions. Descriptive statistics were calculated for demographic variables, covariates, and performance measures including gait velocity, rate of response generation, and HbO<sub>2</sub> levels. In addition to the overall sample, descriptive variables were stratified by primary group status (musicians versus non-musicians) as well as preliminary descriptive analysis stratified by sex and musician type (playing an instrument versus singing), and group differences were examined

via appropriate statistical analyses (i.e., *t*-test and chi-square test). Linear mixed effects models (LMEM) were used to analyze the influence of music making on behavioral performance measures. Chosen for their strength in analyzing repeated-measures data, LMEMs are especially useful in their estimation of missing data points, and their sensitivity to both group and individual-level variability (Cheng et al., 2010). All LMEMs described below specified a compound symmetry covariance matrix for repeated effects and a scaled identity covariance matrix for random effects. Models were fully adjusted for age, health status, depressive symptomology (GDS), cognitive function (WRAT-3), and sex (when applicable). Statistical analyses were conducted using IBM's Statistical Package for the Social Sciences (SPSS) version 25 (IBM, Somers, NY).

**Aim 1:** To determine the moderating effects of music making on PFC oxygenation, a conditional LMEM was run with music making as a two-level between-subjects variable (musicians vs. non-musicians). Task condition (STW vs. DTW; STA vs. DTW) was defined as a within-person repeated measures variable and PFC oxygenation (fNIRS-derived HbO<sub>2</sub> levels) was the dependent variable. fNIRS channels were included as a repeated random effect. The effect of music making on dual-task costs was examined through the two-way interaction of music making x task condition. In addition to other covariates, dual-task cognitive performance was included as a fixed effect in order to allow for interpretation of neural efficiency.

**Aims 2A:** To determine the moderating effects of music making on cognitive performance, a conditional LMEM was run with music making as a two-level between-subjects variable (musicians vs. non-musicians). Task condition (STA vs. DTW) was defined as a within-person repeated measures variable and cognitive performance (rate of correct

letter generation) was the dependent variable. The effect of music making on dual-task costs was examined through the two-way interaction of music making x task condition.

**Aim 2B:** To determine the moderating effects of music making on gait performance, a conditional LMEM was run with music making as a two-level between-subjects variable (musicians vs. non-musicians). Task condition (STW vs. DTW) was defined as a within-person repeated measures variable and gait performance (gait velocity) was the dependent variable. The effect of music making on dual-task costs was examined through the two-way interaction of music making x task condition.

**Aim 3:** To determine the moderating effect of sex on music making and brain activation as well as task performance, the above three LMEMs were run separately stratified by male and female participants. All covariates (except for sex) were included across models, and dual-task cognitive performance was additionally included as a fixed effect in the LMEMs examining brain activation as an outcome measure in order to allow for interpretation of neural efficiency.

**Sensitivity Analysis.** Given evidence that general engagement in cognitively stimulating activities is positively related to cognitive functioning in older adulthood (Newson & Kemps, 2005; Stern & Munn, 2010), sensitivity analyses were run that included overall engagement in cognitive lifestyle activities as a covariate. Overall engagement was calculated using the previously described Leisure Activity Questionnaire, with a total ranging from 1 to 19 based on the number of endorsed weekly cognitively stimulating activities (playing a musical instrument and singing were removed from the total score). While previous research has demonstrated that music making remains significantly correlated to cognition in older adults despite taking into account level of general activity (Hanna-Pladdy

& Gajewski, 2012), we acknowledge the importance of addressing this potential confounding factor. Finally, in order to thoroughly assess neural efficiency across dual-task paradigms, separate LMEMs examining the effects of music making on PFC oxygenation were run adjusted for single-task performance (i.e., single-task cognitive performance and gait velocity).

### **Power Analysis**

G\*power version 3.1 software was used to conduct power analyses. Given that LMEMs are not supported by this software due to their complexity, power analysis for linear multiple regression was used as a substitute. Because effect size has not been specified in previous research, we used a small effect size of 0.20, which has been recommended to test for practical significance (Ferguson, 2009). Based on a power of 0.95 (Cohen, 1977) and an alpha of 0.05, a sample size of 127 participants across study groups would be needed to achieve this effect size. Given the 415 participants in the current study sample, 70 of whom are classified as musicians, we are expected to achieve sufficient power in order to identify differences between groups at the specified effect size level.

### **Ethics**

The current study falls within the longitudinal cohort CCMA study which is approved by the Albert Einstein College of Medicine institutional review board (IRB protocol #2010-224). Research personnel involved in the study are approved to work with human subjects by the Collaborative Institutional Training Initiative (CITI) program. As previously described, informed consent was collected upon initial study visit by all participants prior to data collection procedures. During this process, participants were informed of potential benefits

and risks, the latter of which were minimal and included frustration, fatigue, and performance anxiety.



## Chapter III: Results

### Participants

Descriptive statistics for all participants ( $N = 415$ ) are shown in Table 1. The overall study sample consisted of 53.3% women, were 83.9% White, had a mean age of 76 ( $\pm 6.55$ ) years, and reported a mean of 14.49 ( $\pm 2.93$ ) years of education. Global health assessments characterized participants as relatively healthy, shown by a low mean GHS of 1.62 ( $\pm 1.09$ ). Similarly, a low mean GDS score of 4.57 ( $\pm 3.75$ ) reflected minimal depression, while the mean total WRAT-3 standard score of 106.69 ( $\pm 9.92$ ) placed estimated premorbid levels of cognitive functioning within the average range. Further descriptive statistics for the study sample stratified by sex can be found in the Appendix (Supplemental Table 1). Overall, demographic variables did not significantly differ between male and female participants with the exception of years of education, which was slightly higher in men ( $p = 0.003$ ). Significant differences were observed on several outcome measures, with men exhibiting higher activation levels in the PFC during single-task walking and dual-task conditions ( $p < 0.001$ ) as well as a lower rate of correct letter generation during single-task Alpha ( $p = 0.010$ ).

### *Group Status*

Seventy musicians were identified within the study sample, including 19 participants who endorsed playing a musical instrument, 44 participants who endorsed singing, and 7 participants who endorsed participation in both musical activities. Descriptive statistics reported separately for non-musicians and musicians are listed in Table 1. Musicians reported regular engagement in musical activity for a mean of 3.14 ( $\pm 2.48$ ) days per week, 1.38

( $\pm 0.78$ ) hours per day, and over a mean of 39.44 ( $\pm 25.88$ ) years. Comparison between musicians and non-musicians did not significantly differ among demographic variables, including sex ( $p = 0.849$ ), age ( $p = 0.379$ ), race ( $p = 0.244$ ), and years of education ( $p = 0.147$ ), nor on any study covariates such as GHS score ( $p = 0.122$ ), GDS score ( $p = 0.38$ ), and WRAT-3 standard score ( $p = 0.644$ ). Furthermore, musicians and non-musicians did not significantly differ on outcome measures, including gait velocity across single-task ( $p = 0.116$ ) and dual-task conditions ( $p = 0.893$ ), as well as cognitive performance across single-task ( $p = 0.903$ ) and dual-task conditions ( $p = 0.304$ ). While levels of activation in the PFC did not differ between groups during single-task Alpha ( $p = 0.429$ ) and dual-task conditions ( $p = 0.241$ ), group differences trended in significance during the single-task walk condition ( $p = 0.052$ ) with musicians demonstrating lower HbO<sub>2</sub> levels compared to non-musicians.

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Insert Table 1

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Descriptive characteristics of non-musicians and musicians further stratified by sex are reported in Supplemental Table 2. The total percentage of musicians within the study sample were relatively evenly distributed among male (17.19%) and female (16.49%) participants, including similar distribution of musician type (i.e., playing an instrument versus singing). Additionally, when assessed separately within male and female study samples, musicians did not significantly differ from non-musicians across most study variables, with the exception of neural activation in the PFC during single-task walking which was observed to be somewhat lower in female musicians as compared to female non-musicians ( $p = 0.044$ ).

Descriptive statistics for all musicians stratified by musician type (plays an instrument, sings, or both) are reported in Supplemental Table 3. Given the relatively small sample size among each group of musicians, particularly those who engage in both kinds of musical activity, preliminary comparison between musicians who only play an instrument versus singers were explored. These descriptive analyses indicated no significant group differences among most demographic variables, including sex ( $p = 0.283$ ), race ( $p = 0.138$ ), age ( $p = 0.965$ ), general health status ( $p = 0.272$ ), and depressive symptoms ( $p = 0.253$ ). However, musicians who play an instrument reflected higher levels of premorbid cognitive functioning, as determined by a significantly higher WRAT-3 standard score ( $p = 0.046$ ), and they reported slightly greater years of education than singers, a difference which trended in significance ( $p = 0.056$ ). Most outcome measures were similar across musician groups, however, those playing an instrument demonstrated significantly higher rates of correct letter generation during both single- ( $p = 0.001$ ) and dual-task ( $p = 0.015$ ) conditions. Frequency of musical engagement also significantly differed between groups, with singers reporting a greater amount of hourly practice per day ( $p < 0.001$ ) over a longer period of years ( $p = 0.003$ ), while those playing an instrument endorsed participating in musical activity more days per week ( $p = 0.025$ ).

### **Aim 1: fNIRS-derived PFC Activation**

Hypotheses for the first study aim, which sought to examine the moderating effect of group status (musicians versus non-musicians) on brain activation during the dual-task walking paradigm, were partially confirmed. Results did not support the main effect of music making on fNIRS-derived HbO<sub>2</sub> levels during task conditions (estimate = -0.09;  $p = 0.148$ ). However, music making did moderate the change in HbO<sub>2</sub> levels from STA to DTW

(estimate = 0.1;  $p = 0.014$ ). Specifically, musicians demonstrated similar HbO<sub>2</sub> levels between task conditions, whereas non-musicians exhibited a significant increase in HbO<sub>2</sub> levels from STA to DTW (see Figure 1). This pattern was not observed in the change of HbO<sub>2</sub> levels from STW to DTW, as both groups displayed a similar increase in brain activation (estimate = 0.01;  $p = 0.812$ ). Results were similar across the unadjusted model and the model adjusted for all covariates, including dual-task cognitive performance (see Table 2).

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Insert Table 2

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Insert Figure 1

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## **Aim 2: Behavioral Performance**

The second study aim sought to examine the moderating effect of group status (musicians versus non-musicians) on cognitive and gait performance during the dual-task walking paradigm. Similar to the first aim, hypotheses were partially confirmed. Regarding cognitive performance, the main effect of music making approached significance in the fully adjusted model (estimate = 2.36;  $p = 0.066$ ), with musicians demonstrating a slightly higher rate of correct letter generation compared to non-musicians. Music making was also shown to moderate the change in cognitive performance from single-task Alpha (STA) to dual-task (DTW) conditions (estimate = -1.44;  $p < 0.001$ ), with musicians demonstrating an attenuated

decrease in rate of correct letter generation from STA to DTW compared to non-musicians (see Figure 2). Results across unadjusted and adjusted models are fully detailed in Table 3.

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Insert Table 3

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Insert Figure 2

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A similar pattern of results was shown in LMEMs examining music making's effect on gait performance (see Table 4). The main effect of music making was significant in the fully adjusted model (estimate = 4.4;  $p = 0.014$ ), with musicians demonstrating faster gait velocity compared to non-musicians. As shown in previous models, music making also moderated the change in gait velocity from single-task walk (STW) to DTW conditions (estimate = -3.14;  $p < 0.001$ ). Specifically, musicians displayed an attenuated decrease in gait velocity from STW to DTW compared to non-musicians (see Figure 3).

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Insert Table 4

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Insert Figure 3

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### **Aim 3: Sex Effects**

The third study aim examined the moderating effect of sex on the associations between music making and outcome measures, including brain activation and behavioral performance, through LMEMs stratified by male and female participants. Results revealed a number of significant sex differences that varied across study variables and are described in more detail below.

### ***Sex & PFC Activation***

Results of LMEMs examining the effect of music making on fNIRS-derived HbO<sub>2</sub> levels across task conditions did not reveal significant associations in male study participants. Neither the main effect of music making (estimate = -0.06;  $p = 0.585$ ) nor the moderating effect of music making on change in brain activation from STW to DTW (estimate = 0.04;  $p = 0.510$ ) and STA to DTW (estimate = -0.07;  $p = 0.280$ ) were significant in both unadjusted and adjusted models (see Table 5).

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Insert Table 5

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On the other hand, significant relationships between music making and brain activation were observed among female study participants. The main effect of music making was significant (estimate = -0.21;  $p = 0.003$ ) with female musicians displaying lower HbO<sub>2</sub> levels during the DTW condition compared to non-musicians (see Figure 4). Additionally, music making significantly moderated the change in HbO<sub>2</sub> levels from STA to DTW (estimate = 0.24;  $p < 0.001$ ). While female non-musicians did not demonstrate a change in HbO<sub>2</sub> levels between task conditions, female musicians exhibited a significant decrease in brain activation from STA to DTW. As observed in the overall study sample, there was no

significant moderating effect of music making on change in HbO<sub>2</sub> levels from STW to DTW (estimate = -0.02;  $p = 0.710$ ), as both groups exhibited a similar increase in PFC activation. Results were similar across unadjusted and adjusted models (see Table 6).

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Insert Table 6

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Insert Figure 4

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### *Sex & Cognitive Performance*

The relationship between music making and cognitive performance was again not significant for male participants. There was no main effect (estimate = 1.69;  $p = 0.371$ ) nor moderating effect (estimate = -0.35;  $p = 0.20$ ) of music making on cognitive performance across tasks for men in both unadjusted and adjusted models (see Table 7).

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Insert Table 7

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A different pattern of results emerged for female participants. While the main effect of music making did not reach level of significance (estimate = 3.0;  $p = 0.089$ ), music making was shown to significantly moderate the change in cognitive performance from STA to DTW (estimate = -2.41;  $p < 0.001$ ) (see Table 8). As seen in the overall study sample, female musicians exhibited an attenuated decrease in rate of correct letter generation from STA to DTW as compared to non-musicians (see Figure 5).

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Insert Table 8

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Insert Figure 5

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### *Sex & Gait Performance*

Results of stratified LMEMs examining music making's effect on gait velocity in male participants revealed no main effect of music making (estimate = 1.33;  $p = 0.606$ ), however, the moderation of music making on change in gait velocity from STW to DTW was significant (estimate = -3.92;  $p < 0.001$ ) (see Table 9). Upon visual inspection of data (see Figure 6), gait velocity during DTW was evinced to be similar between male musicians and non-musicians, however, male musicians displayed slower gait velocity during STW thus the expected decrease in gait velocity from single- to dual-task conditions was attenuated.

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Insert Table 9

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Insert Figure 6

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Results of unadjusted and adjusted LMEMs examining this same relationship in female participants mirrored previous patterns (see Table 10). A significant main effect of music making was observed (estimate = 6.60;  $p = 0.006$ ), with female musicians displaying



faster gait velocity compared to non-musicians. Additionally, music making moderated the change in gait velocity from STW to DTW (estimate = -2.47;  $p < 0.001$ ), with female musicians exhibiting an attenuated decrease in gait velocity across task conditions (see Figure 6).

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Insert Table 10

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### **Sensitivity Analyses**

Results of fully adjusted LMEMs that additionally controlled for overall engagement in cognitively stimulating activities were not materially different than their counterparts outlined above, including analyses of the overall study sample (see Table 11) as well as models stratified by sex (see Tables 12 and 13).

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Insert Table 11

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Insert Table 12

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Insert Table 13

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Similarly, adjusted LMEMs assessing HbO<sub>2</sub> levels as the outcome variable that additionally controlled for single-task performance demonstrated results that were similar to those evinced in models controlling for dual-task cognitive performance. Overall, results were not materially different when controlling for rate of correct letter generation during the single-task Alpha condition (see Table 14) nor gait velocity assessed during the single-task walk condition (see Table 15).

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Insert Table 14

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Insert Table 15

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## Chapter IV: Discussion

The purpose of this study was to characterize the benefits of music making on the healthy aging brain. Although neuroanatomical and cognitive changes have been established in children and adult musicians, these associations have been largely understudied in older adults. Despite consensus that music making has defined relationships with specific cognitive domains such as executive functioning, studies that have been conducted thus far primarily utilize neuropsychological tasks in order to assess cognition, which in turn leads to significantly variable results (Román-Caballero et al., 2018). Additionally, the use of these tasks does not allow for elucidation of changes in neural activity that may directly accompany behavioral performance. To address these limitations, this study used a dual-task walking paradigm to concurrently assess neural activation as well as cognitive and physical functioning.

The cognitive control of locomotion is founded largely in executive control processes, which has been shown in the current literature to have a nuanced relationship with music making, with positive associations found only with certain aspects of executive functions (Okada & Slevc, 2018). The dual-task paradigm used in this study assesses both cognitive control and working memory updating, both of which have been shown to have significant correlations with music making as assessed via neuropsychological tasks (Slevc et al., 2016; Zuk et al., 2014). Given that poor dual-task performance has numerous clinical implications, including relation to neurologic pathology (Hausdorff et al., 2003; Sheridan et al., 2003), assessing the potential impact of music making within this context provides the opportunity

to characterize the benefits of music making and its underlying mechanisms in a clinically relevant paradigm. Additionally, the moderating effect of sex was explored in order to further delineate the impact of music making given notable sex differences across study variables including neuroanatomy and dual-task performance (Holtzer et al., 2015; Hollmann et al., 2011; Hutchinson et al., 2003; Lee et al., 2003; Luders et al., 2004).

In light of the current literature, we hypothesized that music making would significantly moderate dual-task performance, including better cognitive and gait performance across tasks as well as attenuated dual-task costs, which was defined as decline in performance during dual-task conditions compared to single-task conditions. We also hypothesized that evidence for neural efficiency would be observed, as this has been established in younger musicians and literature suggests that older adults are likely to demonstrate the capability for similar neuroplastic changes (Park et al., 2013).

### **Summary of Major Findings**

Overall, study findings were partially confirmed with significant results demonstrated within the overall study sample as well as sex-stratified analyses which are discussed in more detail below. Primarily, there was evidence that older adult musicians demonstrated improved neural efficiency compared to non-musicians. Although the main effect of music making on study variables was inconsistently observed, there was a persistent moderating effect of music making on neural activation and behavioral performance in the comparison of single- to dual-task conditions, indicating reduced dual-task costs.

Non-musicians exhibited an expected increase in PFC activation from single- to dual-task conditions, and a similar pattern was observed in musicians when comparing single-task walking to dual-task walking. However, musicians demonstrated negligible change in brain

activation from single-task Alpha to dual-task walking. Given that analyses controlled for behavioral performance, including dual-task and single-task cognitive performance as well as single-task gait velocity, this can be interpreted as neural efficiency – performance was maintained at comparable (or improved) levels to non-musicians although musicians did not require a similar increase in neural activation. While this is consistent with literature showing increased neural efficiency in musicians while completing nonmusical tasks, including tasks of executive functions (Alain et al., 2018), to our knowledge, this is the first study to demonstrate this pattern in a sample of older adults. Similarly, although music intervention studies provide evidence of improved neural efficiency following short-term music training in older adults (Guo et al., 2021), this is the first study to demonstrate similar results in a sample of older adults who play a musical instrument or sing on an ongoing basis.

The main effect of music making on cognitive performance for the overall study sample only trended in significance which may have been due to the relatively small sample size of the musician group. That being said, music making significantly moderated change in cognitive performance from single-task Alpha to dual-task walking conditions, with musicians exhibiting an attenuated decline in the rate of correct letter generation as compared to non-musicians. This similar pattern was seen in analyses assessing gait velocity, with musicians displaying an attenuated decline in gait velocity from single- to dual-task walking. Furthermore, the main effect of music was significant in this analysis, with musicians demonstrating faster gait velocity during dual-task walking compared to non-musicians. This, combined with musicians demonstrating a slightly faster rate of correct letter generation during dual-task walking, further supports the presence of neural efficiency in the music making group, as behavioral performance under dual-task conditions were improved

compared to non-musicians. Overall, musicians clearly displayed attenuated dual-task costs. While this is consistent with results from musical dual-task training research (Kim & Yoo, 2019; Chen & Pei, 2018), this is the first non-intervention study to demonstrate better dual-task performance in individuals who engage in music as a leisure activity.

It is important to note the lack of main effects of music making on cognitive and gait performance outside of the dual-task context. Contrary to our hypothesis, musicians did not exhibit better performance on a working memory task nor faster gait velocity during single-task conditions. Although positive associations have been identified between music making and working memory as a singular domain (Okada & Slevc, 2018), research with children and adults have demonstrated that this relationship may be dependent upon the specific components of working memory being studied. For example, previous studies have shown that while music is related to dimensions of working memory such as visual scanning and processing speed, as well as central executive components, there is less support for its relationship with informational memory capacity (Roden et al., 2014; Suárez et al., 2015). Thus, it is possible that the specific element of working memory that was captured by our cognitive interference task is not sensitive to the effects of music making. Additionally, while the study of music making's effect on gait is novel, we hypothesized a positive association based on extrapolation of results from relevant music intervention studies. However, the effect on gait velocity in one music intervention study was found in sample of older adults diagnosed with mild cognitive impairment (Domínguez-Chávez et al., 2018) and has not been reported elsewhere. Therefore, while there does not appear to be an effect of music making on basic gait speed (as assessed under task conditions without additional demands) in healthy older adults, there may be an effect found in older adults with some degree of

cognitive impairment. This would not be surprising given that the automaticity of walking decreases with cognitive decline, thus increasing reliance on executive functioning processes that have been shown to be stronger in musicians (Okada & Slevc, 2016).

### **Summary of the Effect of Sex on Study Results**

Although a number of significant relationships emerged in analyses of the overall study sample, these results were further clarified in LMEMs that explored the moderating effect of sex on the relationship between music making and study variables. Overall, the pattern of neural efficiency and reduced dual-task costs were evinced in female musicians only.

While no significant relationships were observed in analyses of PFC activation in male study participants, there was a significant main effect of music making on neural activation in female musicians, who displayed significantly lower activation levels during dual-task walking. While PFC activation increased from single-task walking to dual-task conditions for all study participants, female non-musicians did not exhibit a change in activation levels between single-task Alpha and dual-task walking. This is consistent with literature showing that women tend to show lower activation in general during dual-task walking compared to men (Holtzer et al., 2015), which may be related to evidence for greater gray matter degeneration in the PFC of men (Curiati et al., 2009). Female musicians, on the other hand, displayed a significant reduction in PFC activation during dual-task walking compared to single-task Alpha. This reduced neural activity under more challenging task conditions may be indicative of a complexity effect that has been identified in previous research on the relationship between music making and cognition. As mentioned previously, a recent meta-analysis has demonstrated that statistical analyses of the cognitive performance

of older adult musicians exhibit the largest effect sizes for more complex neuropsychological tasks (i.e., 120 versus 60 seconds of verbal fluency testing) (Román-Caballero et al., 2018). In general, cognitive performance becomes more effortful and recruits greater executive functioning resources as task demands increase. The associated pattern of relatively decreased performance for complex tasks is accentuated in older adults given this increased reliance on executive functioning (Verhaeghen et al., 2006), and it is perhaps unsurprising that this is mitigated in older adult musicians given the evidence for music making's association with higher-order cognitive functions.

Further stratified analyses demonstrated the presence of smaller dual-task costs in female musicians only. Reductions in both rate of correct letter generation and gait velocity from single- to dual-task conditions were attenuated in female musicians compared to non-musicians. While a similar interaction effect was identified for gait velocity in male musicians, this was primarily due to initial group disparities during the single-task walk condition. Given that this did not indicate differences in dual-task costs between musicians and non-musicians, these are not discussed further.

While some previous studies have demonstrated music-related neuroanatomical differences in men only (Lee et al., 2003; Luders et al., 2004; Hutchinson et al., 2003), the current pattern of results suggests that significantly increased neural efficiency and reduced dual-task costs emerged primarily in female musicians. Although the sample sizes of male and female musicians were similar, indicating equivalent statistical power, it is important to note that both sample sizes were relatively small. Therefore, results should be interpreted with caution and require replication in future studies in order to make more concrete conclusions. Nonetheless, this pattern of results is consistent with a number of music



intervention studies demonstrating improved neural efficiency and neuroplastic changes related to inhibitory control in study samples that consisted of a disproportionate number of female participants (Alain et al., 2019; Guo et al., 2021). The current study suggests that ongoing music making has a similar neuroplastic effect to what has been shown in relatively short-term intervention studies in female musicians.

Additionally, although somewhat debated, the current literature suggests that women may exhibit stronger working memory abilities specifically due to use of different strategies and/or differences in neuroanatomical development related to sex hormones (Grissom & Reyes, 2019). Furthermore, results from one functional neuroimaging study indicated that women recruited more prefrontal resources when completing working memory tasks as compared to men, who tended to rely on spatial brain regions such as the parietal lobe (Hill et al., 2014). Therefore, women may utilize the PFC differently during dual-task conditions. Indeed, while sex differences in dual-task costs have not been established, previous studies have found increased overall PFC activation and greater gait variability in men (as previously noted) which may contribute to a lessened effect of music making in this population. Another study utilizing fNIRS to assess HbO<sub>2</sub> levels in the PFC concluded that women displayed lower PFC activation during a verbal working memory task accompanied by equivalent behavioral performance to male participants, suggesting enhanced neural efficiency (Li et al., 2010). Taken together, it is possible that any combination of these factors may contribute to the emergence of significant results in female musicians only in the current study, however, future research examining sex differences is critical in further understanding the observed sex disparities in the relationship between music making and dual-task performance.

### **Limitations and Future Directions**

It is important to acknowledge the presence of some limitations associated with this study. While our study sample size was adequate to statistically examine the current study aims, the relatively small sample of musicians prohibited additional analyses such as assessing the possible impact of the length and frequency of music making. Additionally, although preliminary statistical comparison was explored, the ability to fully characterize differences between individuals who played a musical instrument versus singing, as well as musicians who engage in both types of musical activity, was limited. These variables may be of interest to include in future studies, as previous research examining the effect of music making frequency on cognitive functioning has indicated variable results (Hanna-Pladdy & MacKay, 2011; Rogenmoser et al., 2018), which may be in part due to associated stress levels. Relatedly, future studies may consider including assessment of self-perceived stress or biological factors that may indicate physiological effects of stress (e.g., increased cortisol). Indeed, given the multidimensional nature of music making (including mood, social, and physiological factors), mediation analyses that could identify the particular contribution of specific mechanisms through which music making may impact neural efficiency would be of interest to conduct. Additionally, given the design of the fNIRS system, assessment of neural activation was limited to the PFC. While the PFC has been heavily implicated in both music making and walking and, therefore, is of significant interest to assess, it is important to note that other brain regions involved in these processes were not directly evaluated. Future studies using multi-modal neuroimaging techniques are encouraged to more fully characterize neural correlates of music making and mobility, including brain regions that may moderate PFC activation, as has been demonstrated in other studies of DTW (Lucas et al., 2019; Wagshul et al., 2019; Ross et al., 2021).

Although confounding factors such as overall engagement in cognitively stimulating activities were controlled for in analyses, direct causality between music making and dual-task performance cannot be definitively established given the current correlational study design. The opportunity to examine these associations longitudinally in future studies by exploring changes in dual-task performance over time in musicians versus non-musicians will help establish the directionality of observed relationships. Finally, the relatively limited generalizability of our study sample should be noted, as participants were recruited from a single geographic area and the majority of participants were White and generally educated at or above a high school level. In a similar vein, given that individuals with a diagnosis of dementia were excluded, all study participants were characterized as relatively cognitively healthy. Therefore, the ability to extrapolate study results to older adults experiencing cognitive decline is limited. Future studies are encouraged to emphasize a diverse range of participants, in terms of both demographic factors and cognitive status, in order to more fully characterize study effects in various populations.

### **Clinical Implications**

A number of notable implications are associated with the current study results consistently demonstrating the presence of neural efficiency and reduced dual-task costs in musicians. Given that poor dual-task performance is associated with increased risk of falls and frailty (Guedes et al., 2014; Lamoth et al., 2011; Nordin et al., 2010), identifying a lifestyle factor that promotes better dual-task abilities may protect against these adverse health outcomes. Indeed, study results indicate improved executive functioning abilities (i.e., attentional control) which are consistently linked to preserved functional independence in aging (Reuter-Lorenz et al., 2016), thus suggesting that music making may enhance

functional outcomes and support aspects of cognition that are typically sensitive to age-related decline. Furthermore, the clinical application of study results is underscored by the unique composition of the study sample. All musicians were healthy, community-dwelling older adults who engaged in music making activity on a regular basis, the lengths of music training time notably varied, and musicians practiced largely outside of a professional capacity. This provides evidence for the practical recommendation of music making as an ongoing leisure activity that may be introduced at any age.

That being said, it is important to acknowledge potential barriers that may negatively interfere with musical engagement in late life, including limited access to resources and opportunity or lack of motivation. Additionally, certain individual characteristics may influence propensity for music making. For example, while music making's inherent feeling of reward and enjoyment may serve to support engagement (Altenmüller & Schlaug, 2013; Hallam et al., 2012), studies have identified several specific factors that are correlated with sustained musical activity, including preferences for certain musical styles and psychological factors such as sense of well-being and self-esteem (Krause et al., 2020; Krause et al., 2021). While demographic variables such as age and sex were not significantly related to continued musical engagement (Krause et al., 2020), these variables may influence initiation of music making as some studies have identified musical participants as predominantly female and White (Hallam et al., 2012; Creech et al., 2013). Further identification of variables that support both initiation and sustainment of musical engagement in older adulthood is an important component to the practical application of music as a recommended leisure activity. Moreover, characterization of accessibility to those with limited resources (e.g., money, time) and of diverse backgrounds should be a consideration for future studies.

In addition to musical engagement within the community, current results add to the preliminary evidence for the benefit of structured music intervention programs to prevent cognitive decline in healthy older adults. Prior intervention studies that employ short-term music training for healthy older adults have demonstrated post-intervention improvements in cognitive functioning, namely reasoning and visuoconstruction (Bugos et al., 2007; Seinfeld et al., 2013). Participants in these studies were aged 60 to 85 years, consisted of a higher proportion of women, and individuals with cognitive impairment were excluded. On the other hand, music interventions for individuals with cognitive dysfunction (e.g., dementia, MCI) provide less compelling evidence for its benefits on cognitive functioning (assessed both globally and within specific domains), with notable heterogeneity among studies (Li et al., 2015; Xu et al., 2017). In individuals with dementia specifically, there is poor evidence that short-term music training leads to better cognitive functioning (Fusar-Poli et al., 2019), although positive post-intervention outcomes indicating reduced anxiety and depressive symptoms, as well as decreased agitation have been observed (Pedersen et al., 2017; van der Steen et al., 2018). While preliminary evidence suggests that music intervention may promote cognitive improvement in older adults with MCI (Doi et al., 2017; Domínguez-Chávez et al., 2019), the positive association between short-term music training and cognition appears limited to healthy older adults who have not yet experienced significant cognitive decline. Further intervention studies are needed to determine the extent to which short-term music training may improve cognitive functioning, including assessment of potential sex differences.

While the current study indicates that results are significant for female musicians only, generalization of these findings should be approached with caution given the relatively

small sex-stratified sample size. Additionally, the scope of this study was focused on a dual-task design with limited assessment of neural activation in the PFC only, as discussed above. Therefore, potential cognitive and neural implications of music making in male participants should not be dismissed and may be revealed in further assessment of various brain regions and/or different cognitive tasks. In fact, previous research has already identified certain neuroanatomical differences in male musicians only that were observed in brain regions not examined in the current study, such as the corpus callosum, cerebellum, and postcentral gyrus (Lee et al., 2003; Luders et al., 2004; Hutchinson et al., 2003). Given that a number of existing study samples have been composed of predominantly women (Alain et al., 2019; Bugos et al., 2007; Guo et al., 2021; Seinfeld et al., 2013), future studies should underscore recruitment of both male and female participants. In order to more fully characterize potential sex-related discrepancies, future studies are encouraged to not only recruit balanced study samples but also to include statistical analysis of the potential moderating effect of sex, so as to reveal any sex-specific differences that may be masked in analyses of the total study sample.

Overall, the observation of enhanced neural efficiency in older adult musicians also contributes to our understanding of the multifaceted construct of cognitive reserve. As previously noted, the specific amalgamation of factors that comprise cognitive reserve remains undefined, however, efficiency is thought to be an integral component of the neural basis of cognitive reserve (Stern, 2009). Given that cognitive reserve remains a theoretical construct, it is empirically assessed through proxy measures that typically represent lifestyle factors thought to establish higher levels of reserve, such as education, occupational attainment, general intelligence, and socioeconomic status (Pettigrew & Soldan, 2019). The

validity of these factors in representing cognitive reserve has been consistently supported in the literature (Siedlecki et al., 2009) and the current study employed one of these proxies, normative performance on the Wide Range Assessment Test, 3<sup>rd</sup> Edition (WRAT-3) reading subtest, as a measure of literacy attainment to capture overall cognitive reserve. That being said, all analyses controlled for performance on the WRAT-3, which did not impact the significance of study results. Additionally, WRAT-3 standard scores and years of education (another common proxy measure of reserve) did not differ when compared between study groups.

While this would typically suggest that the cognitive reserve of musicians and non-musicians did not differ, analyses demonstrate that musicians exhibit better neural efficiency, providing support for the neuroprotective effect of music making and thereby bolstering cognitive reserve. This pattern of results speaks to the limitations of single proxies for a complex, multidimensional concept such as cognitive reserve, as well as the particular significance of music making for promoting reserve. Not only does this have implications for our conceptual understanding of cognitive reserve and how it may be assessed in empirical studies, but it also carries relevant clinical indications. While individuals with high levels of cognitive reserve are thought to better cope with neuropathology and delay the onset of related cognitive decline, there is also evidence that these individuals may exhibit steeper progression of symptoms once present (Stern, 2009). Thus, the knowledge that older adult musicians have the capacity for better neural efficiency and relatedly elevated levels of reserve may inform clinical monitoring and the predicted course of certain diagnoses.

## **Conclusion**

Overall, study results contribute significantly to our understanding of the cognitive benefits of music making in older adulthood, as well as the neural mechanisms through which it exerts its positive effect. Older adult musicians clearly displayed enhanced neural efficiency and reduced dual-task costs during a dual-task walking paradigm. These results remained significant when adjusting for a number of covariates, including overall engagement in cognitively stimulating activities, indicating the specific contribution of music making to outcomes variables. Moreover, moderation analyses revealed that results emerged only in female musicians. Although this is consistent with some available literature, the relatively small size of the music making sample when stratified by sex limits the ability to fully interpret these results. Therefore, while neural efficiency was observed only in female musicians in the current study, the potential benefits of music for men should not yet be discounted. Instead, future research is encouraged to consider the potential effect of sex on the relationship between music making and cognition. Taken together, the current pattern of study results supports the role of music making in promoting healthy aging and enhancing cognitive reserve. The current study provides a helpful framework for future research in music making and cognition in aging, as well as important clinical indications such as the role of music making as a recommended leisure activity for older adults.



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Table 1: Demographic characteristics of study sample stratified by group status.

	<u>All</u>	<u>Non-Musicians</u>	<u>Musicians</u>	<u>Non-Musicians vs. Musicians</u>
Participants (n)	415	345	70	
Plays an instrument only (%)	-	-	27.14	
Sings only (%)	-	-	62.86	
Both (%)	-	-	10	
Women: Number (%)	221 (53.3)	183 (53.0)	38 (54.3)	$p = 0.849$
Race: Number (% White)	348 (83.9)	294 (85.2)	54 (77.1)	$p = 0.244$
	Mean (SD)	Mean (SD)	Mean (SD)	$p$
Age	76.0 (6.55)	75.87 (6.49)	76.63 (6.86)	0.379
Education (years)	14.49 (2.93)	14.4 (2.98)	14.96 (2.67)	0.147
General Health Status	1.62 (1.09)	1.58 (1.09)	1.80 (1.04)	0.122
Geriatric Depression Scale	4.57 (3.75)	4.65 (3.82)	4.21 (3.41)	0.380
WRAT-3 Standard Score	106.69 (9.92)	106.79 (9.77)	106.19 (10.71)	0.644
STW: HbO <sub>2</sub> levels	0.16 (0.74)	0.19 (0.75)	-0.001 (0.72)	0.052
STA: HbO <sub>2</sub> levels	0.59 (0.69)	0.60 (0.69)	0.53 (0.67)	0.429
DTW: HbO <sub>2</sub> levels	0.66 (1.0)	0.69 (1.0)	0.53 (0.98)	0.241
STW: Gait velocity (cm/s)	70.09 (16.05)	70.04 (16.0)	70.32 (16.41)	0.893
DTW: Gait velocity (cm/s)	58.14 (16.33)	57.58 (16.24)	60.94 (16.65)	0.116
STA: Rate of correct response generation	33.24 (11.83)	33.21 (11.98)	33.40 (11.11)	0.903
DTW: Rate of correct response generation	30.06 (12.24)	29.78 (12.26)	31.43 (12.15)	0.304

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed. In order to examine group differences,  $t$  tests for independent samples and chi-square were used to assess continuous and categorical variables, respectively.



Table 2: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in HbO<sub>2</sub> levels across tasks.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STW vs. DTW	-0.54	0.02	-0.57 – -0.51	-33.33	<0.001
STA vs. DTW	-0.06	0.02	-0.10 – -0.03	-3.94	<0.001
Music	-0.11	0.07	-0.24 – 0.02	-1.63	0.104
Music x STW vs. DTW	0.01	0.04	-0.07 – 0.09	0.24	0.811
Music x STA vs. DTW	0.10	0.04	0.02 – 0.17	2.45	0.014
<b>Model 2</b>					
STW vs. DTW	-0.54	0.02	-0.57 – -0.51	-33.33	<0.001
STA vs. DTW	-0.06	0.02	-0.10 – -0.03	-3.95	<0.001
Music	-0.09	0.06	-0.22 – 0.03	-1.45	0.148
Music x STW vs. DTW	0.01	0.04	-0.07 – 0.09	0.24	0.812
Music x STA vs. DTW	0.10	0.04	0.02 – 0.18	2.45	0.014
Age	-0.01	0.003	-0.01 – 0.001	-1.78	0.075
General Health Status	-0.01	0.02	-0.05 – 0.04	-0.25	0.806
Sex	-0.29	0.04	-0.37 – -0.20	-6.53	<0.001
Geriatric Depression Scale	0.004	0.01	-0.01 – 0.02	0.68	0.498
WRAT-3 Standard Score	0.001	0.002	-0.004 – 0.01	0.26	0.796
DTW Cognitive Performance	-0.003	0.002	-0.01 – 0.001	-1.24	0.216

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.; DTW Cognitive Performance = rate of correct letter generation

Table 3: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in cognitive performance across tasks.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STA vs. DTW	3.41	0.08	3.25 – 3.57	42.37	<0.001
Music	1.62	1.49	-1.30 – 4.55	1.09	0.275
Music x STA vs. DTW	-1.44	0.20	-1.83 – -1.05	-7.28	< 0.001
<b>Model 2</b>					
STA vs. DTW	3.41	0.08	3.25 – 3.57	42.37	<0.001
Music	2.36	1.28	-0.15 – 4.86	1.84	0.066
Music x STA vs. DTW	-1.44	0.20	-1.83 – -1.05	-7.28	<0.001
Age	-0.13	0.07	-0.27 – 0.01	-1.77	0.078
General Health Status	-1.30	0.44	-2.17 – -0.43	-2.93	0.004
Sex	2.30	0.95	0.43 – 4.17	2.42	0.016
Geriatric Depression Scale	0.09	0.13	-0.16 – 0.34	0.70	0.482
WRAT-3 Standard Score	0.56	0.05	0.46 – 0.65	11.58	<0.001

*Note:* STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.

Table 4: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in gait velocity across tasks.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STW vs. DTW	12.48	0.11	12.27 – 12.69	116.33	<0.001
Music	3.41	2.00	-0.53 – 7.35	1.70	0.089
Music x STW vs. DTW	-3.14	0.26	-3.66 – -2.62	-11.90	<0.001
<b>Model 2</b>					
STW vs. DTW	12.48	0.11	12.27 – 12.69	116.33	<0.001
Music	4.40	1.78	0.91 – 7.90	2.48	0.014
Music x STW vs. DTW	-3.14	0.26	-3.66 – -2.62	-11.90	<0.001
Age	-0.91	0.10	-1.11 – -0.71	-8.89	<0.001
General Health Status	-1.65	0.62	-2.86 – -0.43	-2.66	0.008
Sex	0.22	1.32	-2.38 – 2.82	0.17	0.868
Geriatric Depression Scale	-0.47	0.18	-0.82 – -0.11	-2.61	0.010
WRAT-3 Standard Score	0.25	0.07	0.12 – 0.38	3.69	<0.001

*Note:* STW = Single-Task Walk; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.

Table 5: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in HbO<sub>2</sub> levels across task conditions for men.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STW vs. DTW	-0.61	0.03	-0.66 – -0.56	-24.07	<0.001
STA vs. DTW	-0.18	0.03	-0.23 – -0.13	-6.97	<0.001
Music	0.03	0.11	-0.19 – 0.24	0.26	0.792
Music x STW vs. DTW	0.04	0.06	-0.08 – 0.16	0.66	0.510
Music x STA vs. DTW	-0.07	0.06	-0.19 – 0.05	-1.08	0.280
<b>Model 2</b>					
STW vs. DTW	-0.61	0.03	-0.66 – -0.56	-24.07	<0.001
STA vs. DTW	-0.18	0.03	-0.23 – -0.13	-6.98	<0.001
Music	-0.06	0.11	-0.17 – 0.28	0.55	0.585
Music x STW vs. DTW	0.04	0.06	-0.08 – 0.16	0.66	0.510
Music x STA vs. DTW	-0.07	0.06	-0.19 – 0.06	-1.08	0.280
Age	-0.01	0.01	-0.02 – 0.001	-2.05	0.042
General Health Status	0.01	0.04	-0.06 – 0.08	0.24	0.812
Geriatric Depression Scale	0.004	0.01	-0.02 – 0.02	0.41	0.685
WRAT-3 Standard Score	0.001	0.004	-0.01 – 0.01	0.20	0.839
DTW Cognitive Performance	-0.005	0.004	-0.01 – 0.002	-1.36	0.175

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.; DTW Cognitive Performance = rate of correct letter generation

Table 6: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in HbO<sub>2</sub> levels across task conditions for women.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STW vs. DTW	-0.48	0.02	-0.52 – -0.44	-23.18	<0.001
STA vs. DTW	0.04	0.02	-0.01 – 0.08	1.72	0.085
Music	-0.21	0.07	-0.35 – -0.08	-3.07	0.002
Music x STW vs. DTW	-0.02	0.05	-0.12 – 0.08	-0.37	0.710
Music x STA vs. DTW	0.24	0.05	0.14 – 0.34	4.74	<0.001
<b>Model 2</b>					
STW vs. DTW	-0.48	0.02	-0.52 – -0.44	-23.18	<0.001
STA vs. DTW	0.04	0.02	-0.005 – 0.08	1.72	0.085
Music	-0.21	0.07	-0.35 – -0.07	-2.95	0.003
Music x STW vs. DTW	-0.02	0.05	-0.12 – 0.08	-0.37	0.710
Music x STA vs. DTW	0.24	0.05	0.14 – 0.34	4.74	<0.001
Age	-0.002	0.004	-0.01 – 0.01	-0.42	0.675
General Health Status	-0.02	0.02	-0.06 – 0.03	-0.71	0.481
Geriatric Depression Scale	0.002	0.01	-0.01 – 0.02	0.33	0.741
WRAT-3 Standard Score	0.001	0.003	-0.005 – 0.01	0.24	0.809
DTW Cognitive Performance	-0.003	0.002	-0.01 – 0.004	-0.17	0.868

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.; DTW Cognitive Performance = rate of correct letter generation

Table 7: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in cognitive performance across task conditions for men.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STA vs. DTW	2.41	0.11	2.19 – 2.62	22.08	<0.001
Music	0.49	2.19	-3.83 – 4.82	0.23	0.823
Music x STA vs. DTW	-0.35	0.27	-0.87 – 0.18	-1.28	0.20
<b>Model 2</b>					
STA vs. DTW	2.41	0.11	2.19 – 2.62	22.08	<0.001
Music	1.69	1.89	-2.03 – 5.42	0.90	0.371
Music x STA vs. DTW	-0.35	0.27	-0.87 – 0.18	-1.28	0.20
Age	-0.17	0.11	-0.38 – 0.03	-1.66	0.099
General Health Status	-1.19	0.66	-2.50 – 0.12	-1.80	0.074
Geriatric Depression Scale	-0.06	0.19	-0.43 – 0.31	-0.34	0.736
WRAT-3 Standard Score	0.54	0.07	0.40 – 0.67	7.67	<0.001

*Note:* STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.

Table 8: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in cognitive performance across task conditions for women.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STA vs. DTW	4.30	0.12	4.07 – 4.53	37.06	<0.001
Music	2.56	2.01	-1.41 – 6.52	1.27	0.206
Music x STA vs. DTW	-2.41	0.28	-2.97 – -1.85	-8.48	<0.001
<b>Model 2</b>					
STA vs. DTW	4.30	0.12	4.07 – 4.53	37.06	<0.001
Music	3.00	1.76	-0.46 – 6.46	1.71	0.089
Music x STA vs. DTW	-2.41	0.28	-2.97 – -1.85	-8.49	<0.001
Age	-0.10	0.10	-0.30 – 0.11	-0.94	0.347
General Health Status	-1.42	0.61	-2.62 – -0.22	-2.33	0.021
Geriatric Depression Scale	0.22	0.18	-0.14 – 0.57	1.21	0.229
WRAT-3 Standard Score	0.57	0.07	0.43 – 0.70	8.37	<0.001

*Note:* STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.

Table 9: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in gait performance across task conditions for men.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STW vs. DTW	12.27	0.17	11.93 – 12.61	70.37	<0.001
Music	-0.13	2.77	-5.60 – 5.34	-0.05	0.963
Music x STW vs. DTW	-3.92	0.43	-4.76 – -3.07	-9.09	<0.001
<b>Model 2</b>					
STW vs. DTW	12.27	0.17	11.93 – 12.61	70.37	<0.001
Music	1.33	2.57	-3.74 – 6.40	0.52	0.606
Music x STW vs. DTW	-3.92	0.43	-4.76 – -3.07	-9.09	<0.001
Age	-0.63	0.14	-0.91 – -0.34	-4.38	<0.001
General Health Status	0.34	0.90	-1.45 – 2.11	0.36	0.716
Geriatric Depression Scale	-0.50	0.25	-0.99 – 0.01	-1.95	0.053
WRAT-3 Standard Score	0.32	0.10	0.14 – 0.51	3.40	0.001

*Note:* STW = Single-Task Walk; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.



Table 10: Unadjusted and adjusted LMEMs analyzing the contribution of group status to change in gait performance across task conditions for women.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1</b>					
STW vs. DTW	12.67	0.13	12.41 – 12.92	97.03	<0.001
Music	6.42	2.86	0.78 – 12.05	2.25	0.026
Music x STW vs. DTW	-2.47	0.32	-3.10 – -1.84	-7.72	<0.001
<b>Model 2</b>					
STW vs. DTW	12.67	0.13	12.41 – 12.92	97.03	<0.001
Music	6.60	2.40	1.87 – 11.33	2.75	0.006
Music x STW vs. DTW	-2.47	0.32	-3.10 – -1.84	-7.72	<0.001
Age	-1.15	0.14	-1.43 – -0.87	-8.06	<0.001
General Health Status	-3.29	0.83	-4.94 – -1.65	-3.94	<0.001
Geriatric Depression Scale	-0.40	0.25	-0.89 – 0.09	-1.61	0.109
WRAT-3 Standard Score	0.24	0.09	0.05 – 0.42	2.53	0.012

*Note:* STW = Single-Task Walk; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.

Table 11: Adjusted LMEMs analyzing the contribution of group status to change in outcome measures across tasks additionally controlling for overall cognitive engagement.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1: HbO<sub>2</sub> levels</b>					
STW vs. DTW	-0.54	0.02	-0.57 – -0.51	-33.33	<0.001
STA vs. DTW	-0.06	0.02	-0.10 – -0.03	-3.95	<0.001
Music	-0.09	0.06	-0.22 – 0.03	-1.49	0.138
Music x STW vs. DTW	0.01	0.04	-0.07 – 0.09	0.24	0.812
Music x STA vs. DTW	0.10	0.04	0.02 – 0.18	2.45	0.014
Age	-0.01	0.003	-0.01 – 0.001	-1.76	0.079
General Health Status	-0.01	0.02	-0.05 – 0.04	-0.23	0.819
Sex	-0.29	0.04	-0.38 – -0.20	-6.50	<0.001
Geriatric Depression Scale	0.004	0.01	-0.01 – 0.02	0.72	0.473
WRAT-3 Standard Score	0.001	0.003	-0.01 – 0.01	0.14	0.892
DTW Cognitive Performance	-0.003	0.002	-0.01 – 0.001	-1.26	0.208
Overall Cognitive Engagement	0.004	0.01	-0.02 – 0.02	0.42	0.675
<b>Model 2: Cognitive Performance</b>					
STA vs. DTW	3.41	0.08	3.25 – 3.57	42.37	<0.001
Music	1.99	1.28	-0.53 – 4.50	1.55	0.122
Music x STA vs. DTW	-1.44	0.20	-1.83 – -1.05	-7.28	<0.001
Age	-0.12	0.07	-0.27 – 0.02	-1.67	0.096
General Health Status	-1.25	0.44	-2.12 – -0.38	-2.82	0.005
Sex	1.92	0.96	0.03 – 3.81	1.99	0.047
Geriatric Depression Scale	0.12	0.13	-0.13 – 0.38	0.94	0.346
WRAT-3 Standard Score	0.52	0.05	0.42 – 0.62	10.27	<0.001
Overall Cognitive Engagement	0.48	0.21	0.06 – 0.90	2.24	0.025
<b>Model 3: Gait Velocity</b>					
STW vs. DTW	12.48	0.11	12.27 – 12.69	116.33	<0.001
Music	4.03	1.79	0.51 – 7.54	2.25	0.025
Music x STW vs. DTW	-3.14	0.26	-3.66 – -2.62	-11.90	<0.001
Age	-0.90	0.10	-1.10 – -0.70	-8.82	<0.001
General Health Status	-1.65	0.62	-2.81 – -0.38	-2.58	0.010
Sex	-0.18	1.34	-2.81 – 2.46	-0.13	0.896
Geriatric Depression Scale	-0.44	0.18	-0.79 – -0.08	-2.42	0.016
WRAT-3 Standard Score	0.21	0.07	0.07 – 0.35	2.96	0.003
Overall Cognitive Engagement	0.50	0.30	-0.09 – 1.08	1.65	0.099

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.; DTW Cognitive Performance = rate of correct letter generation

Table 12: Adjusted LMEMs analyzing the contribution of group status to change in outcome measures across tasks additionally controlling for overall cognitive engagement for men.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1: HbO<sub>2</sub> levels</b>					
STW vs. DTW	-0.61	0.03	-0.66 – -0.56	-24.07	<0.001
STA vs. DTW	-0.18	0.03	-0.23 – -0.13	-6.98	<0.001
Music	-0.06	0.11	-0.16 – 0.28	0.56	0.575
Music x STW vs. DTW	0.04	0.06	-0.08 – 0.16	0.66	0.510
Music x STA vs. DTW	-0.07	0.06	-0.19 – 0.06	-1.08	0.280
Age	-0.01	0.01	-0.02 – -0.001	-2.05	0.042
General Health Status	0.01	0.04	-0.06 – 0.08	0.24	0.811
Geriatric Depression Scale	0.004	0.01	-0.02 – 0.02	0.39	0.695
WRAT-3 Standard Score	0.001	0.004	-0.01 – 0.01	0.22	0.823
DTW Cognitive Performance	-0.01	0.004	-0.01 – 0.002	-1.31	0.191
Overall Cognitive Engagement	-0.003	0.02	-0.04 – 0.04	-0.14	0.887
<b>Model 2: Cognitive Performance</b>					
STA vs. DTW	2.41	0.11	2.19 – 2.62	22.08	<0.001
Music	0.88	1.89	-2.85 – 4.62	0.47	0.642
Music x STA vs. DTW	-0.35	0.27	-0.87 – 0.18	-1.28	0.199
Age	-0.15	0.10	-0.36 – 0.06	-1.43	0.153
General Health Status	-1.18	0.65	-2.47 – 0.11	-1.80	0.074
Geriatric Depression Scale	-0.03	0.19	-0.39 – 0.34	-0.14	0.892
WRAT-3 Standard Score	0.49	0.07	0.35 – 0.63	6.82	<0.001
Overall Cognitive Engagement	0.84	0.35	0.15 – 1.52	2.42	0.017
<b>Model 3: Gait Velocity</b>					
STW vs. DTW	12.27	0.17	11.93 – 12.61	70.37	<0.001
Music	0.65	2.61	-4.49 – 5.79	0.25	0.804
Music x STW vs. DTW	-3.92	0.43	-4.76 – -3.07	-9.09	<0.001
Age	-0.61	0.14	-0.89 – -0.32	-4.22	<0.001
General Health Status	0.34	0.90	-1.43 – 2.11	0.38	0.706
Geriatric Depression Scale	-0.46	0.25	-0.97 – 0.04	-1.82	0.070
WRAT-3 Standard Score	0.28	0.10	0.09 – 0.48	2.88	0.004
Overall Cognitive Engagement	0.70	0.48	-0.24 – 1.64	1.48	0.141

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.; DTW Cognitive Performance = rate of correct letter generation

Table 13: Adjusted LMEMs analyzing the contribution of group status to change in outcome measures across tasks additionally controlling for overall cognitive engagement for women.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1: HbO<sub>2</sub> levels</b>					
STW vs. DTW	-0.48	0.02	-0.52 – -0.44	-23.18	<0.001
STA vs. DTW	0.04	0.02	-0.005 – 0.08	1.72	0.085
Music	-0.21	0.07	-0.35 – -0.07	-2.99	0.003
Music x STW vs. DTW	-0.02	0.05	-0.12 – 0.08	-0.37	0.710
Music x STA vs. DTW	0.24	0.05	0.14 – 0.34	4.74	<0.001
Age	-0.002	0.004	-0.01 – 0.01	-0.41	0.684
General Health Status	-0.02	0.02	-0.06 – 0.03	-0.64	0.526
Geriatric Depression Scale	0.003	0.01	-0.01 – 0.02	0.42	0.674
WRAT-3 Standard Score	0.001	0.003	-0.006 – 0.01	-0.02	0.987
DTW Cognitive Performance	-0.003	0.002	-0.01 – 0.004	-0.16	0.871
Overall Cognitive Engagement	0.01	0.01	-0.01 – 0.03	-0.71	0.480
<b>Model 2: Cognitive Performance</b>					
STA vs. DTW	4.30	0.12	4.07 – 4.53	37.06	<0.001
Music	2.83	1.77	-0.65 – 6.31	1.60	0.110
Music x STA vs. DTW	-2.41	0.28	-2.97 – -1.85	-8.49	<0.001
Age	-0.10	0.10	-0.30 – 0.11	-0.93	0.355
General Health Status	-1.36	0.61	-2.57 – -0.15	-2.22	0.027
Geriatric Depression Scale	0.24	0.18	-0.12 – 0.60	1.32	0.187
WRAT-3 Standard Score	0.54	0.07	0.40 – 0.69	7.39	<0.001
Overall Cognitive Engagement	0.27	0.28	-0.28 – 0.82	0.97	0.333
<b>Model 3: Gait Velocity</b>					
STW vs. DTW	12.67	0.13	12.41 – 12.92	97.03	<0.001
Music	6.37	2.41	1.61 – 11.12	2.64	0.009
Music x STW vs. DTW	-2.47	0.32	-3.10 – -1.84	-7.72	<0.001
Age	-1.15	0.14	-1.43 – -0.87	-8.05	<0.001
General Health Status	-3.21	0.84	-4.87 – -1.56	-3.83	<0.001
Geriatric Depression Scale	-0.36	0.25	-0.86 – 0.13	-1.46	0.146
WRAT-3 Standard Score	0.20	0.10	0.0002 – 0.40	1.97	0.050
Overall Cognitive Engagement	0.38	0.38	-0.37 – 1.13	1.00	0.319

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.; DTW Cognitive Performance = rate of correct letter generation

Table 14: Adjusted LMEMs analyzing the contribution of group status to change in HbO<sub>2</sub> levels across tasks controlling for single-task cognitive performance.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1: All Participants</b>					
STW vs. DTW	-0.54	0.02	-0.57 – -0.51	-33.33	<0.001
STA vs. DTW	-0.06	0.02	-0.10 – -0.03	-3.95	<0.001
Music	-0.10	0.06	-0.22 – 0.03	-1.53	0.128
Music x STW vs. DTW	0.01	0.04	-0.07 – 0.09	0.24	0.812
Music x STA vs. DTW	0.10	0.04	0.02 – 0.18	2.45	0.014
Age	-0.01	0.003	-0.01 – 0.001	-1.71	0.087
General Health Status	-0.004	0.02	-0.04 – 0.04	-0.17	0.863
Sex	-0.29	0.04	-0.37 – -0.20	-6.46	<0.001
Geriatric Depression Scale	0.004	0.01	-0.01 – 0.02	0.67	0.512
WRAT-3 Standard Score	0.001	0.003	-0.01 – 0.01	-0.01	0.996
STA Cognitive Performance	-0.001	0.002	-0.01 – 0.003	-0.57	0.570
<b>Model 2: Male Participants Only</b>					
STW vs. DTW	-0.61	0.03	-0.66 – -0.56	-24.07	<0.001
STA vs. DTW	-0.18	0.03	-0.23 – -0.13	-6.97	<0.001
Music	-0.06	0.11	-0.16 – 0.27	0.51	0.609
Music x STW vs. DTW	0.04	0.06	-0.08 – 0.16	0.66	0.510
Music x STA vs. DTW	-0.07	0.06	-0.19 – 0.05	-1.08	0.280
Age	-0.01	0.01	-0.02 – 0.001	-1.99	0.049
General Health Status	0.01	0.04	-0.06 – 0.08	0.33	0.745
Geriatric Depression Scale	0.01	0.01	-0.02 – 0.03	0.46	0.650
WRAT-3 Standard Score	0.001	0.004	-0.01 – 0.01	0.01	0.991
STA Cognitive Performance	-0.003	0.004	-0.01 – 0.005	-0.79	0.429
<b>Model 3: Female Participants Only</b>					
STW vs. DTW	-0.48	0.02	-0.52 – -0.44	-23.18	<0.001
STA vs. DTW	0.04	0.02	-0.005 – 0.08	1.72	0.085
Music	-0.21	0.07	-0.35 – -0.07	-2.97	0.003
Music x STW vs. DTW	-0.02	0.05	-0.12 – 0.08	-0.37	0.710
Music x STA vs. DTW	0.24	0.05	0.14 – 0.34	4.74	<0.001
Age	-0.002	0.004	-0.01 – 0.01	-0.41	0.682
General Health Status	-0.02	0.02	-0.06 – 0.03	-0.69	0.491
Geriatric Depression Scale	0.002	0.01	-0.01 – 0.02	0.32	0.750
WRAT-3 Standard Score	0.001	0.003	-0.005 – 0.01	0.19	0.851
STA Cognitive Performance	-0.0001	0.002	-0.01 – 0.004	-0.05	0.961

Note: STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.; STA Cognitive Performance = rate of correct letter generation

Table 15: Adjusted LMEMs analyzing the contribution of group status to change in HbO<sub>2</sub> levels across tasks controlling for single-task gait velocity.

Variable	Estimate	SE	95% CI	t	p
<b>Model 1: All Participants</b>					
STW vs. DTW	-0.54	0.02	-0.57 – -0.51	-33.33	<0.001
STA vs. DTW	-0.06	0.02	-0.10 – -0.03	-3.95	<0.001
Music	-0.10	0.06	-0.22 – 0.02	-1.60	0.111
Music x STW vs. DTW	0.01	0.04	-0.07 – 0.09	0.24	0.813
Music x STA vs. DTW	0.10	0.04	0.02 – 0.18	2.45	0.014
Age	-0.004	0.004	-0.01 – 0.004	-0.96	0.339
General Health Status	-0.003	0.02	-0.04 – 0.04	-0.14	0.886
Sex	-0.29	0.04	-0.38 – -0.21	-6.67	<0.001
Geriatric Depression Scale	0.01	0.01	-0.01 – 0.02	0.81	0.421
WRAT-3 Standard Score	-0.001	0.002	-0.01 – 0.003	-0.60	0.552
STW Gait Velocity	0.002	0.002	-0.001 – 0.01	1.50	0.136
<b>Model 2: Male Participants Only</b>					
STW vs. DTW	-0.61	0.03	-0.66 – -0.56	-24.07	<0.001
STA vs. DTW	-0.18	0.03	-0.23 – -0.13	-6.98	<0.001
Music	-0.06	0.11	-0.16 – 0.28	0.55	0.580
Music x STW vs. DTW	0.04	0.06	-0.08 – 0.16	0.66	0.510
Music x STA vs. DTW	-0.07	0.06	-0.19 – 0.06	-1.08	0.281
Age	-0.01	0.01	-0.02 – 0.003	-1.47	0.142
General Health Status	0.01	0.04	-0.06 – 0.09	0.41	0.686
Geriatric Depression Scale	0.01	0.01	-0.01 – 0.03	0.61	0.541
WRAT-3 Standard Score	-0.003	0.004	-0.01 – 0.005	-0.73	0.470
STW Gait Velocity	0.003	0.003	-0.002 – 0.01	1.26	0.208
<b>Model 3: Female Participants Only</b>					
STW vs. DTW	-0.48	0.02	-0.52 – -0.44	-23.18	<0.001
STA vs. DTW	0.04	0.02	-0.005 – 0.08	1.72	0.085
Music	-0.22	0.07	-0.36 – -0.08	-3.09	0.002
Music x STW vs. DTW	-0.02	0.05	-0.12 – 0.08	-0.37	0.709
Music x STA vs. DTW	0.24	0.05	0.14 – 0.34	4.74	<0.001
Age	-0.001	0.004	-0.01 – 0.01	0.20	0.846
General Health Status	-0.01	0.02	-0.05 – 0.04	-0.32	0.747
Geriatric Depression Scale	0.003	0.01	-0.01 – 0.02	0.43	0.668
WRAT-3 Standard Score	-0.0001	0.003	-0.005 – 0.01	-0.03	0.977
STW Gait Velocity	0.002	0.002	-0.001 – 0.01	1.15	0.253

Note: STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.

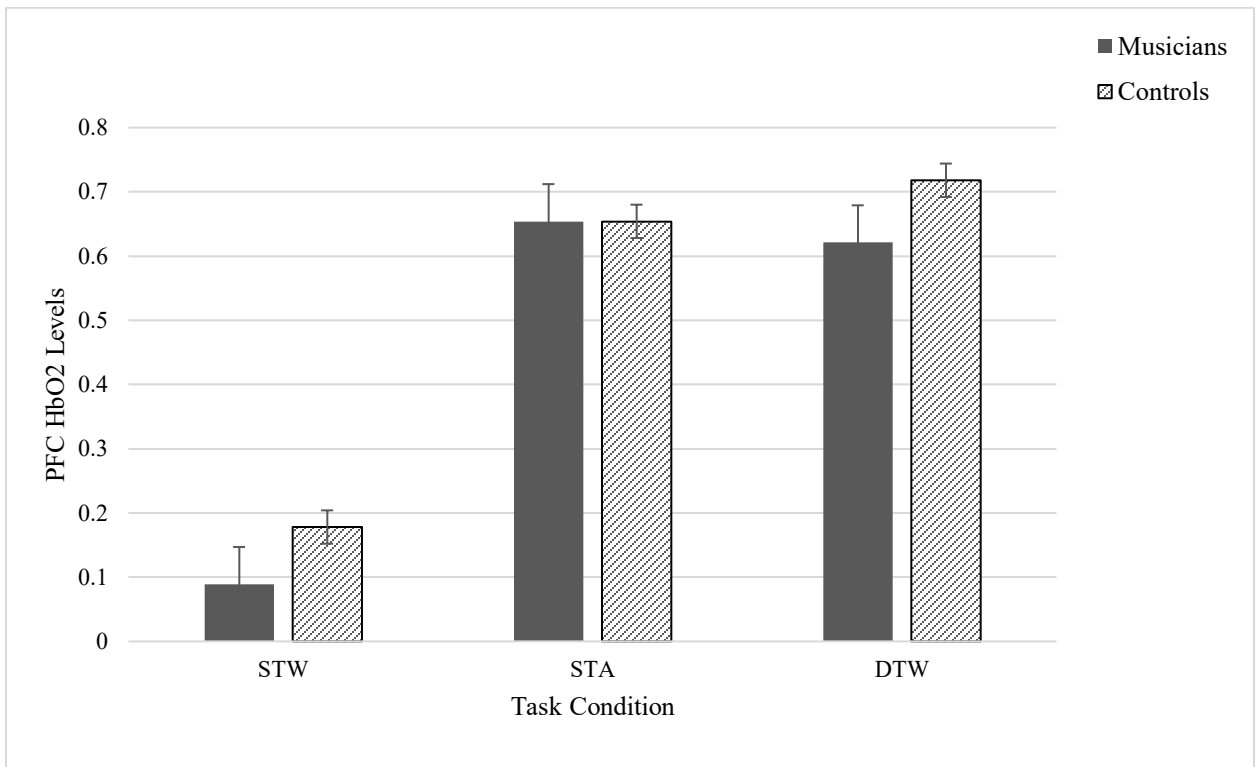


Figure 1: Contribution of group status to change in HbO<sub>2</sub> levels across tasks.

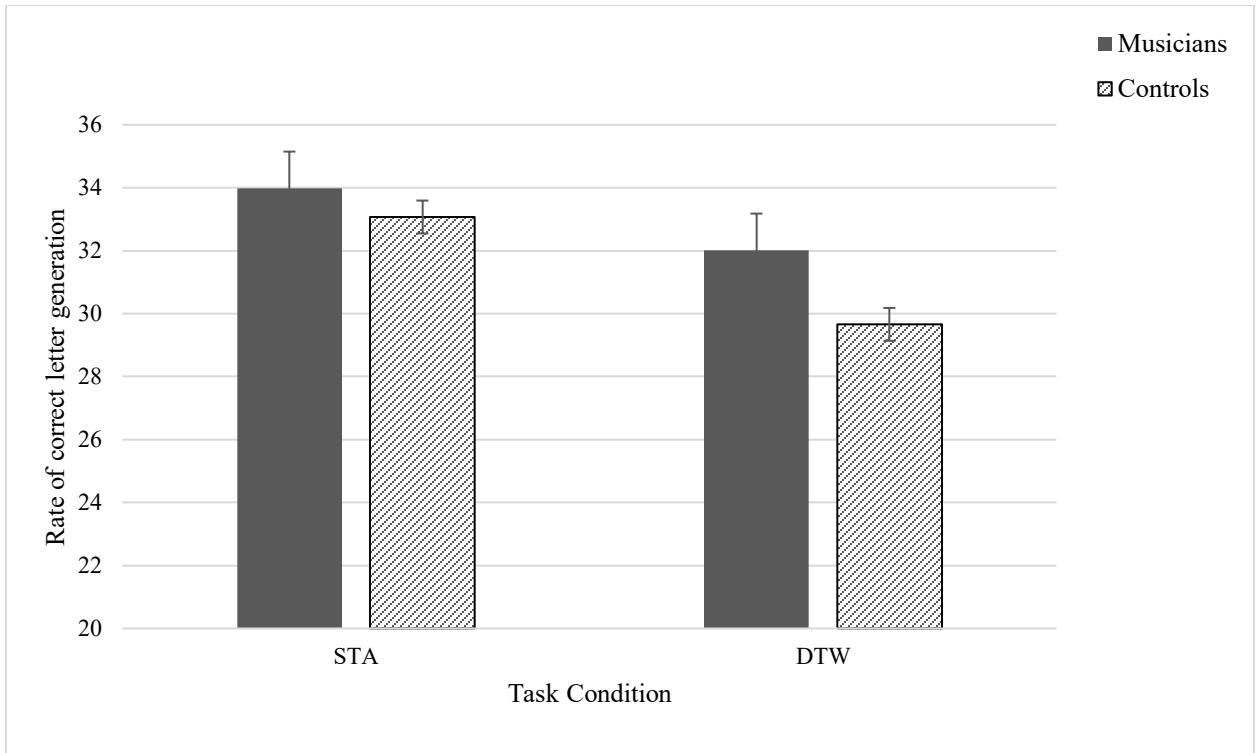


Figure 2: Contribution of group status to change in cognitive performance across tasks.



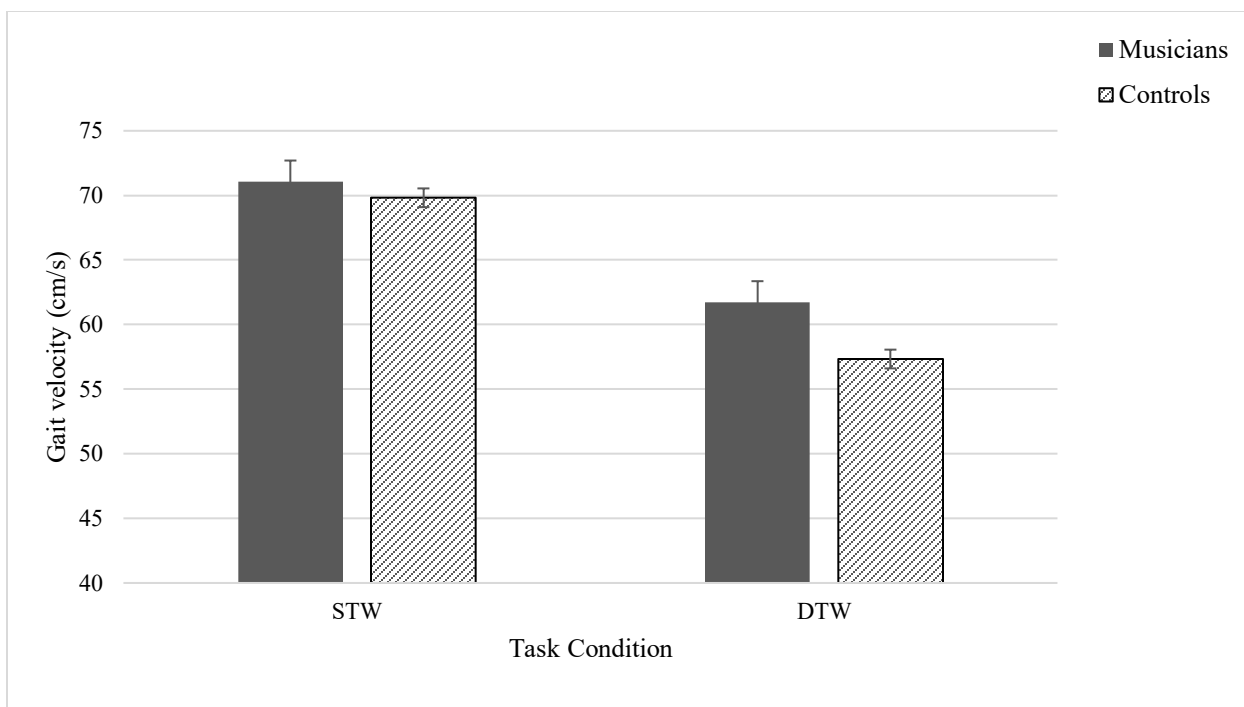


Figure 3: Contribution of group status to change in gait velocity across tasks.

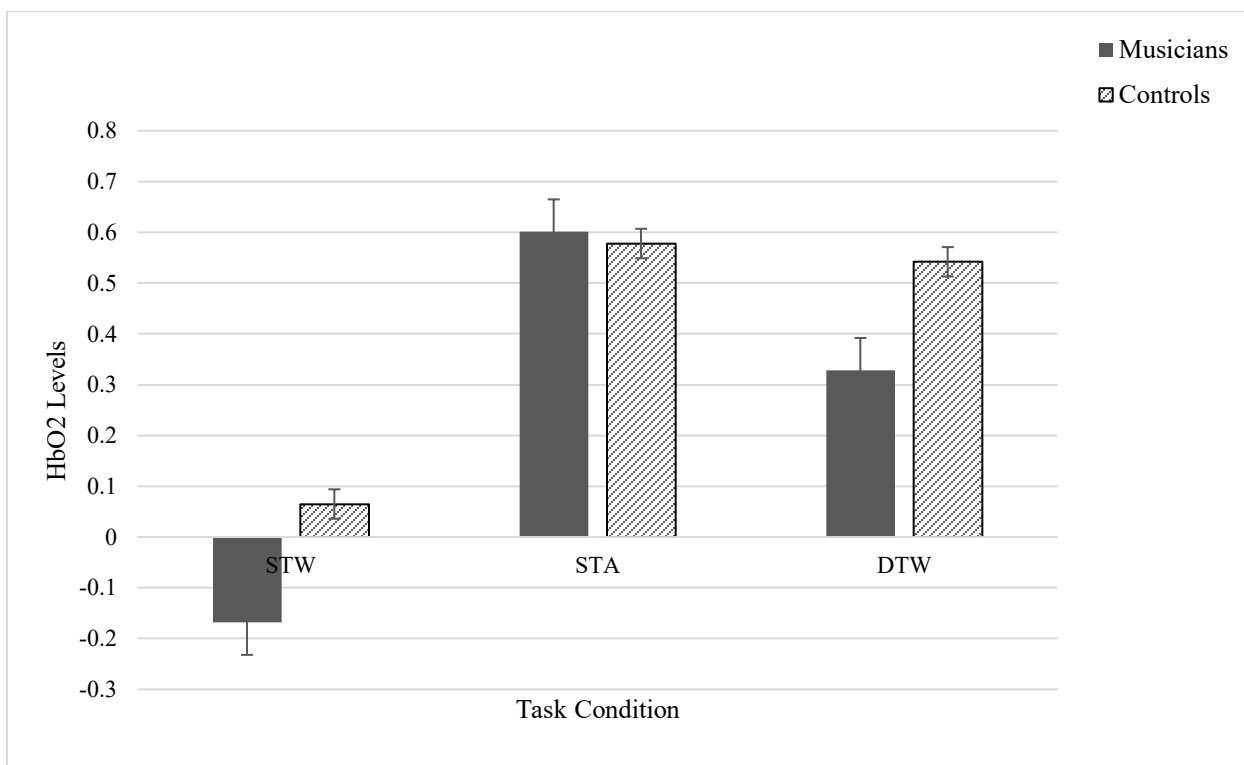


Figure 4: Contribution of group status to change in HbO<sub>2</sub> levels across tasks in women.

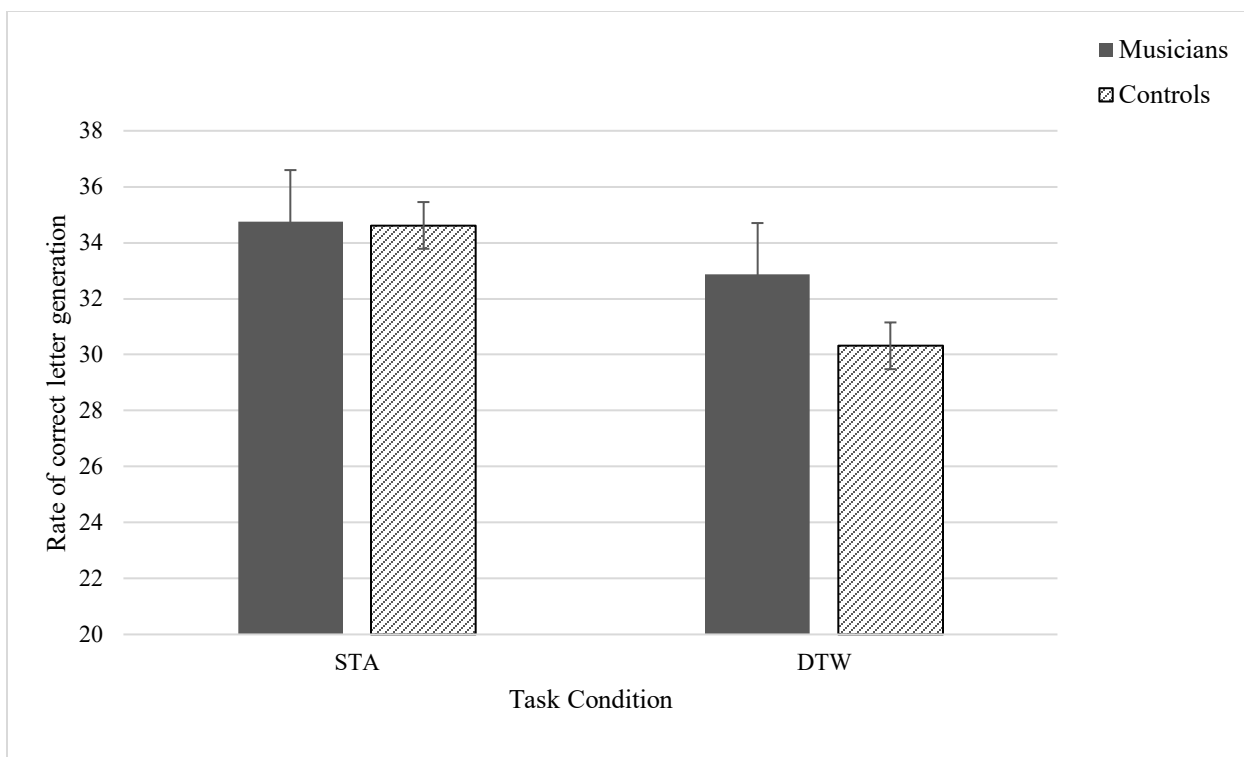


Figure 5: Contribution of group status to change in cognitive performance across tasks in women.

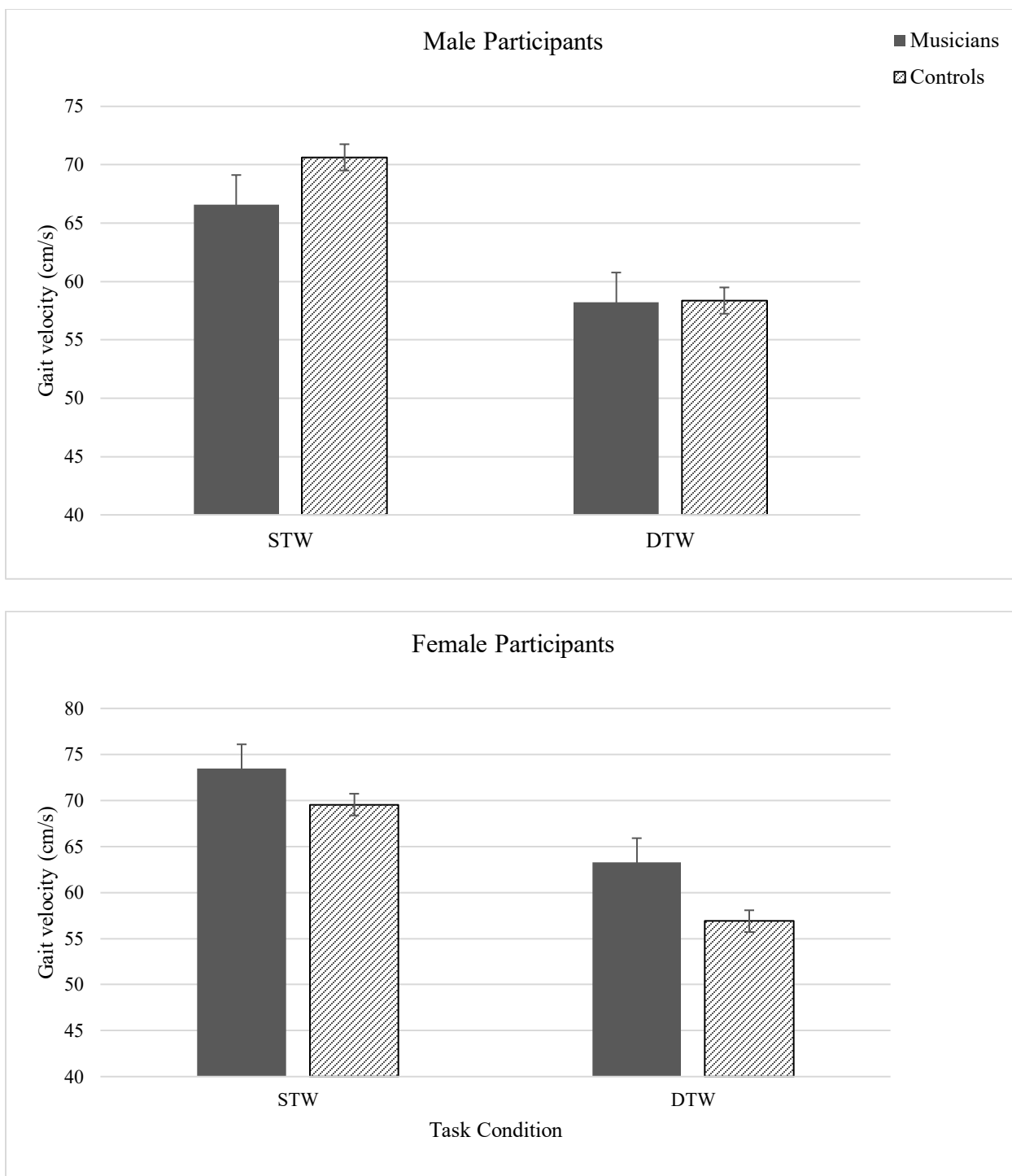


Figure 6: Contribution of group status to change in gait velocity across tasks stratified by men and women.

## Appendix

Supplemental Table 1: Demographic characteristics of study sample stratified by sex.

	<u>Women</u>	<u>Men</u>	<u>Men vs. Women</u>
Participants (n)	221	194	
Musicians (n)	38	32	
Plays an instrument only (%)	21.05	34.38	$p = 0.319$
Sings only (%)	65.79	59.38	$p = 0.616$
Both (%)	13.16	6.25	$p = 0.331$
Race: Number (% White)	175 (79.2)	173 (89.2)	$p = 0.103$
	Mean (SD)	Mean (SD)	$p$
Age	76.04 (6.43)	75.96 (6.71)	0.905
Education (years)	14.1 (2.75)	14.94 (3.07)	0.003
General Health Status	1.65 (1.10)	1.58 (1.08)	0.546
Geriatric Depression Scale	4.67 (3.75)	4.46 (3.76)	0.578
WRAT-3 Standard Score	106.67 (9.73)	106.7 (10.16)	0.978
STW: HbO <sub>2</sub> levels	0.03 (0.69)	0.30 (0.77)	< 0.001
STA: HbO <sub>2</sub> levels	0.53 (0.63)	0.66 (0.74)	0.052
DTW: HbO <sub>2</sub> levels	0.44 (0.90)	0.91 (1.05)	< 0.001
STW: Gait velocity (cm/s)	70.21 (16.81)	69.95 (15.18)	0.866
DTW: Gait velocity (cm/s)	58.0 (16.78)	58.31 (15.86)	0.851
STA: Rate of correct response generation	34.64 (12.01)	31.65 (11.43)	0.010
DTW: Rate of correct response generation	30.71 (12.08)	29.31 (12.41)	0.247
Music Frequency: Days per week	3.16 (2.57)	3.13 (2.42)	0.951
Music Frequency: Hours per day	1.40 (0.75)	1.35 (0.83)	0.788
Music Frequency: Years	44.29 (24.89)	33.69 (26.24)	0.088

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed. In order to examine group differences,  $t$  tests for independent samples and chi-square were used to assess continuous and categorical variables, respectively.

Supplemental Table 2: Demographic characteristics of study sample stratified by sex and musician status.

Female Participants			
	<u>Non-Musicians</u>	<u>Musicians</u>	<u>Non-Musicians vs. Musicians</u>
Participants (n)	183	38	
Plays an instrument only (%)	-	21.05	
Sings only (%)	-	65.79	
Both (%)	-	13.16	
Race: Number (% White)	147 (80.3)	28 (73.7)	$p = 0.591$
	Mean (SD)	Mean (SD)	$p$
Age	76.13 (6.44)	75.61 (6.43)	0.651
Education (years)	13.97 (2.85)	14.74 (2.14)	0.117
General Health Status	1.60 (1.12)	1.87 (0.94)	0.172
Geriatric Depression Scale	4.72 (3.75)	4.42 (3.76)	0.654
WRAT-3 Standard Score	106.69 (9.41)	106.61 (11.3)	0.962
STW: HbO <sub>2</sub> levels	0.08 (0.70)	-0.17 (0.63)	0.044
STA: HbO <sub>2</sub> levels	0.53 (0.64)	0.52 (0.58)	0.888
DTW: HbO <sub>2</sub> levels	0.49 (0.93)	0.22 (0.70)	0.088
STW: Gait velocity (cm/s)	69.53 (16.25)	73.51 (19.17)	0.185
DTW: Gait velocity (cm/s)	56.91 (15.85)	63.28 (20.08)	0.072
STA: Rate of correct response generation	34.62 (12.23)	34.74 (11.04)	0.958
DTW: Rate of correct response generation	30.26 (12.41)	32.86 (10.23)	0.228
Male Participants			
	<u>Non-Musicians</u>	<u>Musicians</u>	<u>Non-Musicians vs. Musicians</u>
Participants (n)	162	32	
Plays an instrument only (%)	-	34.38	
Sings only (%)	-	59.38	
Both (%)	-	6.25	
Race: Number (% White)	147 (90.7)	26 (81.3)	$p = 0.206$
	Mean (SD)	Mean (SD)	$p$
Age	75.59 (6.56)	77.84 (7.25)	0.082
Education (years)	14.89 (3.05)	15.22 (3.20)	0.613
General Health Status	1.56 (1.06)	1.72 (1.17)	0.434
Geriatric Depression Scale	4.56 (3.89)	3.97 (2.99)	0.416
WRAT-3 Standard Score	106.9 (10.18)	105.69 (10.13)	0.538
STW: HbO <sub>2</sub> levels	0.32 (0.78)	0.20 (0.77)	0.446
STA: HbO <sub>2</sub> levels	0.68 (0.73)	0.55 (0.78)	0.351
DTW: HbO <sub>2</sub> levels	0.91 (1.04)	0.91 (1.14)	0.981
STW: Gait velocity (cm/s)	70.62 (15.74)	66.55 (11.57)	0.166

DTW: Gait velocity (cm/s)	58.33 (16.68)	58.17 (10.99)	0.943
STA: Rate of correct response generation	31.62 (11.52)	31.81 (11.17)	0.930
DTW: Rate of correct response generation	29.23 (12.1)	29.73 (14.08)	0.837

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*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed.

Supplemental Table 3: Demographic characteristics of musician group stratified by musician type.

	<u>All</u>	<u>Plays an Instrument</u>	<u>Sings</u>	<u>Both</u>	<u>Plays an instrument vs. Sings</u>
Participants (n)	70	19	44	7	
Women: Number (%)	38 (54.3)	18 (94.7)	25 (56.8)	5 (71.4)	$p = 0.283$
Race: Number (% White)	54 (77.1)	8 (42.1)	32 (72.7)	4 (57.1)	$p = 0.138$
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	$p$
Age	76.63 (6.86)	77.16 (7.92)	77.07 (6.22)	72.43 (7.25)	0.965
Education (years)	14.96 (2.67)	16.0 (2.13)	14.59 (2.82)	14.43 (2.51)	0.056
General Health Status	1.80 (1.04)	2.05 (1.31)	1.73 (0.95)	1.57 (0.79)	0.272
Geriatric Depression Scale	4.21 (3.41)	4.95 (3.29)	3.82 (3.67)	4.71 (1.25)	0.253
WRAT-3 Standard Score	106.19 (10.71)	110.53 (8.70)	104.61 (11.23)	104.29 (10.32)	0.046
STW: HbO <sub>2</sub> levels	-0.001 (0.72)	-0.10 (0.60)	0.06 (0.79)	-0.11 (0.57)	0.422
STA: HbO <sub>2</sub> levels	0.53 (0.67)	0.36 (0.73)	0.65 (0.68)	0.28 (0.22)	0.129
DTW: HbO <sub>2</sub> levels	0.53 (0.98)	0.38 (1.05)	0.65 (1.0)	0.19 (0.55)	0.336
STW: Gait velocity (cm/s)	70.32 (16.41)	64.03 (14.47)	70.33 (15.82)	87.42 (14.5)	0.142
DTW: Gait velocity (cm/s)	60.94 (16.65)	57.19 (14.05)	60.26 (17.06)	75.44 (14.68)	0.493
STA: Rate of correct response generation	33.40 (11.11)	37.26 (5.04)	29.91 (11.56)	44.86 (9.86)	0.001
DTW: Rate of correct response generation	31.43 (12.15)	35.59 (8.82)	28.06 (11.8)	41.31 (14.61)	0.015
Music Frequency: Days per week	3.14 (2.48)	4.05 (2.71)	2.41 (2.2)	4.86 (2.12)	0.025
Music Frequency: Hours per day	1.38 (0.78)	0.91 (0.34)	1.48 (0.8)	2.0 (0.97)	< 0.001
Music Frequency: Years	39.44 (25.88)	25.05 (26.01)	45.91 (24.14)	37.86 (23.07)	0.003

*Note:* STW = Single-Task Walk; STA = Single-Task Alpha; DTW = Dual-Task Walk; WRAT-3 = Wide Range Achievement Test (reading standard score), 3<sup>rd</sup> ed. In order to examine group differences,  $t$  tests for independent samples and chi-square were used to assess continuous and categorical variables, respectively.