COGNITIVE FLEXIBILITY AS A MECHANISM FOR COGNITIVE PROCESSING SPEED CHANGES FOLLOWING A PIANO TRAINING INTERVENTION IN OLDER ADULTS AT RISK FOR DEMENTIA

by

JADE DANDURAND

(Under the Direction of Lawrence H. Sweet)

ABSTRACT

Extant literature supports that music learning can improve or maintain aspects of cognitive function in older adults at risk for Alzheimer's Disease and related dementias (ADRD), but whether a core cognitive ability underlies change in more specific cognitive abilities has not been addressed. The present study examined the effects of a piano training intervention on cognitive processing speed performance and examined baseline level of cognitive flexibility as a moderator of expected training-related improvements in 41 older adults at risk for ADRD. Analyses revealed significant improvements in cognitive processing speed post-intervention and demonstrated that greater training time predicted greater improvements in cognitive processing speed. Baseline cognitive flexibility performance was not found to moderate this association nor degree of improvements in cognitive processing speed. Findings highlight the benefits of musical training for older adults in early stages of cognitive decline and warrant further investigation of moderators of training-related improvement in cognitive performance.

INDEX WORDS: Older adults; dementia risk; cognitive impairment; cognitive training; music learning; cognitive flexibility; processing speed

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CHAPTER ONE

INTRODUCTION

The ability to maintain cognitive function and delay expected age-related decline is an increasing public health priority, given the rapidly aging population in the United States (Mather et al., 2015) and high prevalence of neurogenerative processes slowing cognition among this age group. While some risk factors for cognitive decline and dementia are not modifiable (e.g., age), cognitive and behavioral risk factors can be changed, and therefore represent promising targets for intervention (Gatz et al., 2006; Baumgart et al., 2015). Cognitive training is one behavioral intervention approach that has demonstrated efficacy for both directly forestalling cognitive decline and indirectly improving modifiable risk factors for poor cognitive outcomes such as dementia (Yu et al., 2009; Moore et al., 2001; Reijnders et al., 2013). Defined as guided mental tasks intended to stimulate brain function, cognitive training is administered in a number of different forms, including crossword puzzles, computerized test platforms, and individual or group training sessions (Gates et al., 2011; Kelly et al., 2014). They are designed to challenge and ultimately improve—or at least attenuate decline of—specific cognitive functions, such as language, memory, cognitive flexibility, attention, and reasoning (Clare & Woods, 2004). The potential benefits of cognitive training rest on the general theory that the brain is plastic throughout the lifetime (Hertzog et al., 2008), thus creating the potential for positive change in functioning, even in older age and among people at risk for specific forms of dementia, such as Alzheimer’s disease.

A number of different forms of cognitive training exist, including strategy-based training, component-specific training, and multi-domain or multimodal training. Strategy-based training focuses on techniques aimed at compensating for age-related cognitive deficits and typically focuses on a single, complex mental ability (Lustig et al., 2009; Willis & Belleville, 2016), while component-specific training reduces the complexity of the task by focusing successively on different components of the task (Willis & Belleville, 2016). Multimodal training approaches, such as musical training, are more complex than strategy-based and component-specific approaches due the incorporation of simultaneous training in multiple domains. Multimodal training may include participation in classes that teach new skills, participation in volunteer work, or engagement in cognitively demanding activities. It is thought to provide a greater range of cognitive challenges and increased stimulation of cognitive plasticity, compared with single-domain training (Gates et al., 2011). Additionally, multimodal approaches often include a social component that is intended to be more enjoyable or socially meaningful for older adults, and therefore, increase the chances that they will maintain the activities after the formal training period (Lustig et al., 2009).

Cognitive training interventions are also delivered through a variety of mechanisms, including computerized and video game interventions. Technology-based interventions (e.g., computers, smartphones, video games) have a number of potential benefits, such as greater flexibility, cost-effectiveness, and a more personalized approach (Kueider et al., 2012). Specifically, they allow greater flexibility in dissemination to reach populations that would otherwise not have access to such interventions and a personalized approach, with potential for performance feedback and adjustment to the user’s ability level. Further, technology-based interventions are often more cost-effective than traditional face-to-face training programs.

Cognitive training programs are designed to target and subsequently assess effects in many cognitive domains, including memory, reasoning and problem solving, executive functioning, cognitive processing speed, reaction time, and attention. Unimodal cognitive training programs are often designed to target specific domains, such as training a specific memory strategy or training to improve processing speed (Lustig et al., 2009). Multimodal training programs, on the other hand, often target training in multiple cognitive domains. Outcomes are commonly assessed through performance on cognitive tests, with the expectation of improvement or at least maintenance of performance after the training intervention compared to pre-intervention.

Efficacy of cognitive training is typically determined by assessment of direct effects and indirect effects. Direct effects are measured by improvement on tasks or domains closely related to the training task itself, while indirect effects are measured by improvement on other tasks or domains not directly trained by the program, but thought to be theoretically related to the training task. This distinction is also referred to as “near transfer” and “far cognitive transfer,” respectively (Lustig et al., 2009). The underlying assumption of this transfer is that regular practice of a task has the potential to maintain or improve functioning in a given domain, and that any effects of practice may generalize beyond the specific training environment (Clare & Woods, 2004).

The idea that domain-specific training can produce enhancement in domain-general cognitive mechanisms has been consistently demonstrated and has been adopted in prominent theoretical models (Taatgen, 2021). Far cognitive transfer suggests that core cognitive systems have been enhanced that will subsequently have positive effects on downstream cognitive functions and generalize across cognitive domains. Far transfer effects are arguably more valuable than near transfer effects because improvements are expected in core domains essential to maintaining activities of daily living, such as working memory, cognitive processing speed, and executive functioning. Multimodal tasks that include high levels of task novelty and progressive difficulty, such as musical training, demonstrate greater likelihood of far transfer (Lustig et al., 2009).

Similarly, quality of life and overall well-being are also common far transfer targets of assessment. For example, some cognitive training programs specifically emphasize the importance of assessing far transfer effects on performance of instrumental activities of daily living (IADLs) in MCI populations, such as managing medications (Willis, 1996), as more "ecological" tests of cognitive functioning (Greenberg & Powers, 1987).

Some of the most prominent domains that are both targeted by cognitive training and assessed for near and far transfer outcomes are verbal memory, executive functioning, reasoning, and cognitive processing speed (Clare & Woods, 2004; Kueider et al., 2012; Butler et al., 2018). Processing speed is defined as the ability to receive and react to information in a temporal framework (Kail & Salthouse, 1994) and is a particularly important target of cognitive training. Decreased cognitive processing speed has been considered a primary general mechanism explaining age-related cognitive decline (Cerella, 1990; Salthouse, 1996) and has been found to mediate performance on many other cognitive measures, including reasoning, memory, verbal fluency, and executive functioning (Lindenberger et al., 1993; Liebel et al., 2017). Thus, interventions that focus on cognitive processing speed may be the most robust approach for preventing overall cognitive decline (Wolinsky et al., 2010). Additionally, cognitive processing speed holds great practical importance for maintaining instrumental activities of daily living (Bezdicek et al., 2016; Wadley et al., 2021; den Ouden et al., 2013).

Processing speed is thought to be comprised of several fundamental components, including sensory/perceptual, motor, and cognitive aspects. Thus, it can be measured in various sensory domains. Processing speed as a construct represents the efficiency of processing within cognitive networks to transmit information, as well as processing in networks responsible for the afferent transmission of sensory information and the efferent transmission of motor response commands (Clough et al., 2020). Prior work has proposed a differentiation of simple processing speed from complex processing speed, with the involvement of each type of processing dependent on the demands of the task (Chiaravalloti et al., 2003; DeLuca & Kalmar, 2007). Simple processing speed is posited to involve primarily sensory and motor processing networks, (e.g., simple reaction time), while complex processing speed similarly involves these networks, but additionally engages cognitive networks given the increased demands of the task (Clough et al., 2020). In attempts to isolate the cognitive aspect of processing speed, prior work has controlled for the sensory and motor aspects by using performance on a simple processing speed task (e.g., ocular motor tasks) to adjust performance on a task of complex processing speed (Cloug et al., 2020). Many modern methods stem from Donders' (1868) subtraction methods of comparing reaction times between tasks to estimate the duration of added mental processes involved in a task.

Executive functioning is another prominent target domain of cognitive training. Executive functions are a set of cognitive processes involved in the planning, managing, and regulation of cognition and behavior (Diamond, 2013; Diamond & Ling, 2017). Most models of executive functions describe three related components or dimensions: working memory updating, cognitive flexibility (also known as switching or shifting), and inhibitory control (Lehto et al, 2003; Miyake et al., 2000; Miyake & Friedman, 2012; Logue & Gould, 2014).

Because the ability to shift from one task to another has been identified as a primary marker of intact executive control and given evidence of age-associated reductions in executive control among older adults (Dempster, 1992; Royall et al., 2004; Prakash et al., 2009; Phillips & Henry, 2010), cognitive flexibility has been a common focus in research on cognitive training approaches for older adults.

Cognitive flexibility is the ability to switch attentional focus between multiple tasks or mental sets (Monsell, 1996), as well as the ability to adapt processing strategies to the meet the demands of a changing environment (Diamond, 2013; Glass et al., 2013; Canas et al., 2003). Cognitive flexibility is closely implicated in the ability to maintain ADLs and IADLs, given its involvement in planning and flexibility in problem-solving, as well as divergent thinking and ability to shift between tasks. These skills are required for performance of essential daily activities, such as driving, cooking, and managing finances and schedules. Evidence has suggested that executive functioning accounts for more variance in older adult ADL performance than demographic variables such as age, education level, and health status (Cahn-Weiner et al., 2000). Moreover, it has been suggested that decline in executive functioning associated with normal aging may be the best predictor of functional deterioration, over and above the contributions of other cognitive functions, such as memory, language, and spatial skills (Cahn-Weiner et al., 2000). Thus, maintenance and improvement of executive functions, particularly cognitive flexibility, is a promising target for cognitive training, as investigators have suggested that intact executive functions increase the chances that older adults will remain functionally independent (Grigsby et al., 1995; Grigsby et al., 1998).

Musical cognitive training

Musical training has been supported conceptually and empirically as an effective form of cognitive training, as learning to play a musical instrument is a highly complex task that involves the integration of several modalities, including sensory and motor systems, and higher-order cognitive functions (Herholz & Zatorre, 2012; Jäncke, 2009; Wan & Schlaug, 2010). Conceptually, musical training is also known to engage cognitive reserve and neuroplasticity differently from other cognitive training forms, uniquely emphasizing the exercise of multiple cognitive domains including attention, memory, cognitive processing speed, and executive function (Herholz & Zatorre, 2012). Additional cognitive functions affected by musical training that are not typically targeted by other forms of training include psychomotor function, emotional processing, and opportunity for social engagement (Hanna-Pladdy & MacKay, 2011). This unique combination of complex skill learning, emotional processing, and social engagement has been proposed to yield greater efficacy than other forms of cognitive training (Särkämö et al., 2014; Bugos et al., 2007).

Likewise, at the underlying neural level, many studies suggest that age-related cognitive decline may also be associated with a level of dysconnectivity, or loss of the ability to functionally integrate multiple systems (Dixon et al., 2004). Thus, cognitive interventions such as musical training that have the capacity to simultaneously engage multiple neural networks may be particularly effective in mitigating or preventing age-related cognitive decline (Bugos et al., 2007).

Empirically, a number of studies have demonstrated a positive association between participation in musical activities and cognitive functioning, particularly later in life (Roman-Caballero et al., 2018). For example, results of a study examining cognitive differences among older healthy adults with differing instrumental musical experience revealed significantly better performance among high-activity musicians (participants with at least 10 years of musical experience) relative to non-musicians on measures of naming, nonverbal memory recall, visuomotor speed, visuomotor sequencing, and cognitive flexibility (Hanna-Pladdy & MacKay, 2011). Although investigators did not show statistically significant cognitive differences between low- and high-activity musicians, the cognitive performance of low-activity musicians fell in between that of non-musicians and high-activity musicians, illustrating a linear relationship between years of music activity and cognitive functioning. A recent meta-analysis showed that musically trained participants exhibit better long-term, short-term, and working memory performance than those not trained musically (Talamini et al., 2017). Other studies have reported improvements in global cognitive function and cognitive flexibility (i.e., Mini Mental State Examination, Trail Making Test) among older adults who engaged in training involving voice and percussion rhythm and improvisational exercises, compared to control participants who engaged in a non-musical exercise activity (Biasutti & Mangiacotti, 2018). Improvements in Trail Making Test performance among those who completed a short-term mallet (xylophone) training program, compared to a non-musical autobiographical discussion control group have also been reported (Bugos & Cooper, 2019).

In terms of a potential clinical intervention, a number of studies have demonstrated that engagement in regular musical activities provides cognitive benefits in domains of orientation, attention, executive function, short-term and working memory, as well as improvements in mood and perceived quality of life in patients with early dementia (Särkämö et al., 2014; Seinfield et al., 2013, Verghese et al., 2003; Geda et al., 2011). These findings are in line with evidence that playing a musical instrument improves structural and functional brain plasticity and increases white and grey matter volume (Jäncke, 2009; Herholz & Zatorre, 2012), and that adults with greater musical expertise tend to have increased grey matter density in brain regions associated with executive functioning and visuomotor coordination compared to adults with less musical expertise (Gaser & Schlaug, 2003).

A strong body of evidence specifically examining piano playing as a form of musical training has demonstrated improved performance in older adults in various cognitive domains. For instance, a 16-week piano training intervention has been associated with increases in verbal fluency, cognitive processing speed, and cognitive control in older adults with little to no formal prior musical training compared to a control group who participated in a music appreciation course (Bugos, 2010). Similarly, a short-term, intensive piano training program of 30 hours over 10 days yielded improvements in verbal fluency and cognitive processing speed in musically naïve older adults who served as their own controls (Bugos & Kochar, 2017). In a prior study, Bugos et al. (2007) had examined individualized piano instruction as a six-month cognitive intervention with 31 musically naïve healthy older adults, ranging from 60 to 85 years old. Findings indicated that the intervention group demonstrated significantly improved performance in multiple cognitive domains, such as cognitive processing speed, cognitive flexibility, and planning and working memory processes (i.e., Trail Making Test, Digit Symbol WAIS III subtest) compared to the control group, and the enhancements were sustained up to three months post-training. In a 2013 study, Seinfeld et al. examined the specific effects of musical training through the implementation of piano lessons over four months, compared to the effects of other leisure activities in older adults. Results showed a significant improvement of the piano training group on measures of executive function, inhibitory control, and divided attention. Participants in the piano intervention group also reported decreased depression and increased positive mood states, and improvement in some domains of quality of life (Seinfeld et al., 2013).

Far transfer effects in musical training

It has been shown that complex cognitive skills developed during musical training have the capacity to transfer to other cognitive domains (Brochard et al., 2004; Chan et al., 1998; Ho et al., 2003; Bugos & Mostafa, 2011). One domain that has been a major area of study for far transfer, particularly in musical training, is cognitive processing speed. Given the integration of temporal sequential processing of sensory and motor information that music training involves, cognitive processes such as cognitive processing speed may be enhanced with musical instruction (Bugos & Mostafa, 2011). Previous research has shown correlations between performance of complex musical tasks, such as musical sight reading, and cognitive processing speed (Kopiez et al., 2006), and a relationship between formal musical instruction and cognitive processing speed, as measured by recordings of saccadic eye movements in young children (Gruhn et al., 2003). The effect of musical training on cognitive processing speed has been studied in adult musicians and non-musicians, showing that individuals with formal musical training performed significantly better on measures of visual and auditory cognitive processing speed (Trail Making Test and Paced Auditory Serial Addition Task, respectively), suggesting that musical training can enhance information cognitive processing speed in visual and auditory domains (Bugos & Mostafa, 2011). A number of studies have shown similar findings, demonstrating increases in cognitive processing speed following musical training interventions or enhanced cognitive processing speed in musicians with formal musical training (Roden et al., 2014; Bugos & Mazuc, 2013; Bergman et al., 2014). Studies on older adult samples have demonstrated enhanced cognitive processing speed following participation in group piano instruction (Bugos, 2010) and mallet (xylophone) instruction (Bugos & Cooper, 2019).

Executive function is another cognitive domain that demonstrates improvement as a result of far transfer effects of musical training. A number of studies have shown enhanced performance on measures of executive functions in individuals who have had formal musical training and individuals who participate in musical training interventions. For example, transfer effects from musical training to executive functions have been shown on tasks of sustaining attention and cognitive control (Degé et al., 2011; George & Coch, 2011), working memory (Amer et al., 2013; Bugos et al., 2007; Hanna-Pladdy & Gajewski, 2012; Bergman et al., 2014), task switching and dual-task paradigms (Moradzadeh et al., 2015), and measures such as the Trail Making Test, which assesses cognitive flexibility (Hanna-Pladdy & MacKay, 2011; Bugos et al., 2007). In each of these studies, musicians outperformed age-matched non-musicians.

Within executive functions, cognitive flexibility is particularly relevant to musical training, given the dynamic nature of musical learning, requiring the coordination of several modalities, and the need for flexible control of behavior in response to varying information. As cognitive flexibility involves the ability to switch attentional focus between tasks and the ability to adapt strategies to meet the demands of a changing environment, this facet of executive control has been implicated in the constant adaptations that are required in the process of reading and playing music, such as in response to changes in key, tempo, time signature, or dynamics (Herrero & Carriedo, 2020; Gade & Schlemmer, 2021). Cognitive flexibility has been linked to several musical tasks, including musical improvisation (de Manzano & Ullén, 2012) and sight-reading (Herrero & Carriedo, 2020), which suggests a contribution of cognitive flexibility to performance of these tasks. Evidence also suggests that high performance on a set-shifting cognitive flexibility measure was linked to enhanced maturation of neural sound discrimination in both musically trained and non-trained children (Saarikivi et al., 2016). Specifically, in both the musically-trained and non-trained group, children that exhibited better performance on the set-shifting task showed evidence of greater age-related increase in sound discrimination than low-performing children, suggesting that individual differences in cognitive flexibility may influence training-related plasticity. Cognitive flexibility has also shown strong associations with academic achievement in areas including math and reading skills (Cole et al., 2014; Yeniad et al., 2013). Executive functions are known to influence learning in a multifaceted way (Bull et al., 2008; Best et al., 2011) and cognitive flexibility, as a core dimension of executive functions, allows readily for acquisition of new information, thus may provide benefits in a training or learning scenario.

Cognitive flexibility as a mechanism for far-transfer effects

Some commonly proposed mechanisms of cognitive training include protecting against brain volume loss, which is accelerated with age, in that consistent use of a brain area may protect against structural loss, and that the brain substrate may be altered by experiences such as stimulating environments and learning, reflecting training-induced structural plasticity (i.e., brain reserve; Satz, 1993; Stern, 2012). (Belleville & Bherer, 2012; Boyke et al., 2008). Other proposed mechanisms are improvement of neuroplasticity (e.g., Mahncke et al., 2006) and allowance of greater neural efficiency and more flexible strategy use through the ability to recruit alternate brain networks in the face of brain pathology (i.e., cognitive reserve; Stern, 2002; Stern, 2012; Wilson et al. 2003) (Clare & Woods, 2004; Gates et al., 2011). Thus, cognitive flexibility is likely an essential piece of the mechanism of far-transfer effects of cognitive training, in promoting use of flexible cognitive strategies for greater neural efficiency and potential for plasticity.

Similarly, cognitive flexibility represents a likely mechanism for the far-transfer effects of musical learning as a form of cognitive training. At the cognitive level, musical training involves learning to switch attention between notes, rhythm, tempo, and stylistic elements of a musical piece, translate and combine visual and auditory stimuli, such as notes and sounds, maintain multiple components of the musical piece in working memory, and inhibit interference from competing stimuli (Moradzadeh et al., 2015). Piano practice also engages multiple brain areas by requiring temporal and sequential control of finger movements (Krings et al., 2000). Given the multimodal nature of musical learning and the integration of multiple cognitive skills, cognitive flexibility may benefit the learner in the training process. The dynamic nature of musical training may demand cognitive flexibility resources to continuously adapt behavior to the information flow provided by musical notation and manage processing in multiple modalities (e.g., sensory, motor, higher cognitive functions). Thus, cognitive flexibility resources may moderate one's adaptation to musical training and influence training-related changes in other cognitive skills via far cognitive transfer. Therefore, it is possible that individual differences in cognitive flexibility, as a component of executive function, may influence the learning of a musical instrument and facilitate the corresponding transfer effects to other cognitive domains.

The neurocognitive mechanisms of far transfer effects in music training remain under investigation. Some studies have suggested that musical training promotes 'metaplasticity' (e.g., Abraham & Bear, 1996), a greater potential for new short-term learning, by facilitating faster and more stable skill acquisition (Altenmüller & Furuya, 2016; Herholz & Zatorre, 2012). Studies have supported this notion by demonstrating structural (Hyde et al., 2009) and functional (Lahav et al., 2007; Chen et al., 2012) changes in brain networks following music training. This facilitation of learning is likely supported by flexibility in thinking, by allowing for generalization of training effects and subsequent improvement in other tasks.

Musical training is also an example of a multimodal approach that can provide both mental and social stimulation—through learning of musical content and interaction with an instructor. Social outcomes provide further evidence of the far transfer effects of musical training, as evidence has indicated that that musical experience and training can lead to benefits to social outcomes as well as cognitive processes (Gerry et al., 2012; Hays & Minichiello, 2005; Saarikallio, 2011; Särkämö, 2018; Schellenberg et al., 2015; Wu & Lu, 2021). Cognitive flexibility may also underlie positive social outcomes as a result of cognitive training, given its role in adapting behavior in new environments and the strong link cognitive flexibility has shown to social cognition and emotional understanding (Bock et al., 2015; Milders et al., 2008).

Utility of cognitive training to treat dementia risk

Cognitive training programs are often designed for people diagnosed with mild cognitive impairment (MCI), which is considered a transitional phase between normal cognitive aging and dementia (Gauthier et al., 2006). MCI is characterized by the presence of objective cognitive deficits in the context of preserved functional independence in activities of daily living (Petersen et al., 2001; Albert et al., 2013). It is believed that the MCI phase is a critical stage of cognitive decline during which interventions may be effective in slowing and potentially improving cognitive function, as compensatory processes, such as neuroplasticity, are still active and could be enhanced to delay manifestation of dementia (Clément & Belleville, 2010, 2012). Cognitive processing speed and executive functions, including cognitive flexibility, are frequently employed as training and target domains, as they decline at rates exceeding expected age-related changes among people with MCI (Sherman et al., 2017; Nordlund et al., 2005). They are also excellent candidates for broad far transfer effects because they are fundamental processes that support a wide range of higher order cognitive functions and instrumental activities of daily living (Liebel et al., 2017; Wolinsky et al., 2010; Salthouse, 1996).

Empirically, cognitive training has been moderately effective in improving cognitive function in older adults with MCI (Yu et al., 2009; Ball et al., 2002; Moore et al., 2001; Kelly et al., 2014; Belleville et al., 2006) and effective in reducing incidence of dementia in high-risk patients with MCI (Willis & Belleville, 2016). For instance, a 2011 meta-analysis of cognitive training, including memory training, in adults at risk of dementia suggests that training enhances cognitive function among MCI patients and may slow progression from MCI to dementia (Gates et al., 2011). In a cross-sectional study of older adults with normal cognitive aging and MCI, Geda et al. (2011) found that computer guided cognitive activities, craft activities (e.g., knitting, quilting), playing games, and reading books were associated with 30% to 50% decreased odds of having MCI, based on report of frequency of cognitive activities carried out within one year of interview.

Research has also shown that cognitive training can benefit older adults who present with subjective complaints of cognitive decline but appear normal on standardized cognitive testing. Subjective cognitive decline (SCD) has been characterized as a self-experienced, persistent decline in cognitive capacity that may represent the earliest stage of later MCI or dementia, despite objectively unimpaired performance on neuropsychological testing and in daily functioning (Jessen et al, 2014). Mounting evidence suggests that SCD may be a promising marker of preclinical Alzheimer's Disease (AD) (Buckley et al., 2016). For example, greater SCD has been related to greater levels of Aβ-amyloid burden (Amariglio et al., 2012; Mielke et al., 2012), a biomarker for AD, and other downstream markers of neurodegeneration (Chetelat et al., 2010; Jessen et al., 2006). Thus, SCD provides another ideal stage for cognitive training interventions, given its association with an increased risk of future objective cognitive decline, its increasing recognition as a preclinical phase of dementia, and its potential to relieve some level of subjective distress.

Prior research findings support the expectation that cognitive training is effective in enhancing the cognitive functioning of older adults with subjective memory complaints (Kwok et al., 2013; Canevelli et al., 2013). This includes a 2013 meta-analysis that indicated that most cognitive interventions examined yielded objectively improved cognitive performance in older SCD samples (Canevelli et al., 2013). Prior research studies have also suggested that participation in cognitively stimulating activities—including many of the activities utilized in cognitive training programs—are cognitively protective for older adults, regardless of baseline levels of cognitive or memory impairment (Wilson et al., 2002). The results of subsequent research on cognitively stimulating activities outside of formal cognitive training confirms that it can reduce the risk of lifetime MCI and AD development among samples who are specifically cognitively unimpaired at baseline (Sattler et al., 2012). Evidence from a four-year cohort study has also shown engagement in cognitively stimulating activities at least twice per week to be significantly associated with reduced risk of developing dementia in a sample of adults aged 65 and older who were dementia-free at baseline (Akbarly et al., 2009). Taken together, this evidence suggests benefits of regular practice of cognitively stimulating activities for older adults, including those with unimpaired cognition, subjective cognitive complaints, and MCI.

Although further research on the benefits of cognitive training is needed, cognitive training methods may provide a way to reduce the number of people who will develop AD and slow progression of early stages of the disease process, which could greatly improve quality of life and lower the burden of care placed on individuals and communities. The examination of the mechanisms underlying the effects of cognitive training interventions on older adults at risk for dementia, including those presenting with SCD, represents a gap in the literature in need of further study, particularly with regard to domain-specific effects in musical training.

The Current Study

The present study examines the relation between cognitive flexibility and the far-transfer effects of a piano training intervention on cognitive processing speed in older adults at risk for dementia. Overall, we expect high performance on measures of baseline cognitive flexibility (pre-intervention) to be related to larger training-related improvements in cognitive processing speed after six months of piano training (post-intervention) (See Figure 1). The primary hypothesis is that baseline cognitive processing speed and baseline cognitive flexibility each positively predict post-intervention cognitive processing speed. When statistically controlling the effects of baseline cognitive processing speed, baseline cognitive flexibility is expected to remain a significant unique predictor of post-intervention cognitive processing speed. Further, it is expected that the degree of pre-post change in cognitive processing speed will depend upon baseline levels of cognitive flexibility, such that lower levels of baseline cognitive flexibility will be associated with lower degrees of pre-post change in cognitive processing speed, while higher levels of baseline cognitive flexibility will be associated with greater degrees of pre-post change in cognitive processing speed (See Figure 2).

We also expect that the amount of time older adults spend engaging in the piano training intervention will affect the degree of pre-post change in cognitive processing speed, such that less amounts of time spent engaging in piano training will be associated with lower degrees of pre-post change in cognitive processing speed, while more time spent engaging in piano training will be associated with greater degrees of pre-post change in cognitive processing speed. We predict that baseline levels of cognitive flexibility will moderate this relationship, in that higher levels of baseline cognitive flexibility will be associated with greater degrees of pre-post change in cognitive processing speed (See Figure 3).

CHAPTER TWO

METHOD

Participants

As part of a larger clinical trial aimed at training a machine learning algorithm for a technology-based music learning cognitive training program, a total of 70 participants (*M* = 71.49± 7.69 years; 64% female; 87% White/European American, 10% Black, 1% Asian, 1% other) were recruited for this study from Athens, GA, and other communities within a 100 mile radius. The research team recruited participants using flyer postings, radio advertisements, and active participant referrals. Inclusion criteria required that adults were age 65 or older, fluent in English, had less than 3 years of experience playing a musical instrument, and scored between 24—37 out of 41 on the Telephone Interview for Cognitive Status (TICS; Brandt et al., 1988). The TICS score range was determined based on prior cutoff score recommendations for MCI detection (Graff-Radford et al., 2006; Cook est al., 2009) and the goal to include participants with a range of dementia risk. Participants were also required to be able to sit upright for two hours consecutively with occasional breaks, attend weekly visits to the study site, and identify an individual to serve as their study partner, in order to provide a collateral source of information on their cognitive functioning and activities of daily living. To capture a range of dementia risk and maintain generalizability, the sample included participants with subjective cognitive complaints and MCI.

Of the 70 participants who were recruited, 50 were screened and deemed eligible, 50 were randomized to the study interventions, and 41 (*M* = 72.71± 4.91 years; 66% female; 83%

White/European American, 12% Black, 2% Asian, 2% more than one race; See Table 1 for complete demographic characteristics of study participants) completed the entire clinical trial (27 study visits); see Figure 4.

All study procedures and materials were approved by the University of Georgia's Institutional Review Board (IRB), and the tenets of the Declaration of Helsinki were adhered to at all times during the study.

Procedures

Potential participants (*n* = 70) were screened over the phone. A total of 50 participants were deemed eligible and scheduled for a 2.5-hour in-person assessment visit. Given the fact that study participants presented with SCD at minimum, the investigator conducting informed consent completed a capacity to consent assessment before obtaining verbal and written informed consent. A total of 50 participants were deemed eligible after the in-person study visit and were consented. Once consented, participants were randomly assigned to one of two computerized intervention conditions that were the focus of the parent study —piano instruction from an autonomous socially assistive robotic instructor, or via a computerized platform with the same functionality as the socially assistive robot, but without embodiment.

The first study visit consisted of a clinical interview and the first of two baseline cognitive assessments. In total, a three-hour comprehensive neuropsychological test battery was given on two separate days over a period of approximately a week, in order to minimize cognitive fatigue of participants. The battery consisted of both paper-and-pencil and computerized tests. The cognitive domains that were analyzed in the current study are cognitive processing speed and cognitive flexibility.

Following the initial two visits, the research team delivered and installed a full 88-key Yamaha keyboard at the participant's home to use for at-home practice between training visits. Participants returned to the study site each week for 24 weeks for regular training visits, during which they engaged in a piano lesson delivered through the randomly assigned technology and completed questionnaires about their interaction with the technology platform.

Following 24 weeks of musical training, participants completed the same comprehensive neuropsychological test battery on two separate days over approximately a one-week period, as well as a final clinical interview. Participants were compensated $100 for their participation and were allowed to keep the keyboard that had been delivered to their home. A total of 41 participants completed all study visits.

Musical training intervention

The musical training intervention consisted of weekly piano lessons for 24 weeks in addition to at-home practice. Piano lesson content was created by the UGA research team in conjunction with Applied Universal Dynamics (Minneapolis, MN) and Vän Robotics (Columbia, SC) to be delivered via a computer interface. All participants received the same lesson content throughout the intervention. Classical music training was implemented in this cognitive training intervention because classical music has been shown previously to elicit positive cognitive changes (Mammerella et al., 2007; Bottirolli et al., 2014). The piano content utilized instructional materials adapted from *Hal Leonard Student Piano Library: Adult Piano Method* and *Alfred's Basic Adult Play Piano Now!*, along with supplemental pieces. Lesson content progressed in difficulty and was designed to be dynamic and challenging enough to likely promote lasting cognitive changes. During weekly training sessions, participants engaged in a piano lesson delivered through the computerized platform for approximately 45-50 minutes. Lesson content instructed participants in musical concepts including finger independence and hand coordination of playing separate bass and melody lines, rhythm and dynamics, and reading musical notation. Participants were provided with sheet music to practice at home between training sessions, consisting of exercises that mirrored their most recent lesson content. Participants were asked to practice the piano daily for 30 minutes, using the keyboard delivered to their home, and to record their practice sessions in a weekly tracking log.

Measures

CNS Vital Signs (CNS-VS)

CNS Vital Signs is a computerized neurocognitive assessment platform that measures a range of cognitive domains using normed subtests. The platform produces standardized domain scores based on participants' performance and demographic information. A neurocognition index (NCI) is also derived from the domain scores that represents the overall neurocognitive status of the participant. In the parent study, a standard assessment battery was administered to all participants that consisted of 10 cognitive tests and yielded raw and normed scores in 15 neurocognitive domains. The Symbol Digit Coding subtest raw score was used to measure cognitive processing speed in the current study.

Processing speed. Processing speed will be assessed with the Symbol Digit Coding Test (SDC), administered through the CNS-VS computerized test battery. The SDC used in CNS-VS is based on the Symbol Digit Modalities Test (Smith, 1973), which itself is a variant of the Wechsler Digit Symbol Substitution Test (Wechsler, 1955). The SDC consists of serial presentations of screens, each of which contains a bank of eight symbols above and eight empty boxes below. The participant is asked to type in the number (digits 2-9) on the number row that corresponds to the symbol that is highlighted. The participant is given 120 seconds to type in as many correct numbers as he/she can. Due to its good predictive validity and easy execution, the Symbol Digit Modalities Test and subsequent versions of the task, such as the SDC, are widely used for assessment of cognitive processing speed in a wide range of settings, including neurological and psychiatric clinics (Smith, 1968; Parmenter et al., 2007; Koh et al., 2011; Lee et al., 2011). The CNS-VS SDC has been found to exhibit a strong correlation with the WAIS Digit Symbol Substitution Test ($r = 0.79$) and has good test-retest reliability ($r = .84$) (Gualtieri & Johnson, 2006). The CNS-VS SDC score is calculated from correct responses minus errors (i.e., SDC Correct Responses - SDC Errors), and also represents the cognitive processing speed domain score for the battery. The variable used in all analyses was the SDC raw score, except age-corrected scaled score was used when reporting sample characteristics.

Finger tapping. Finger tapping will be assessed with the Finger Tapping Test (FTT), administered through the CNS-VS computerized test battery. Finger tapping is a task of motor speed, measuring how many times a subject can depress a keyboard key using the index finger of their dominant and nondominant hands. The FTT consists of three test trials, requiring the participant to press the space bar with their right index finger as many times as possible in 10 seconds. The test is repeated with the left hand. The CNS-VS FTT score is calculated from average right and left hand taps (Right Taps Average + Left Taps Average), and also represents the motor speed domain score for the battery. The variable used in all analyses was the baseline FTT raw score, except age-corrected scaled score was used when reporting sample characteristics.

Delis-Kaplan Executive Function System (D-KEFS)

The D-KEFS (Delis et a., 2001) is a neuropsychological test battery used to measure verbal and nonverbal executive functions across the lifespan (ages 8-89 years). It consists of nine individually administered tests that were designed to stand alone, many of which are modified versions of traditional measures (e.g., the Trail Making Test), along with some new subtests and indices (e.g., Word Context Test). The D-KEFS measures various executive functions, such as inhibition, problem-solving skills, concept formation, and cognitive flexibility, and provides performance scores for each of the nine tests as well as process scores that offer insight into performance scores. The Trail Making Test condition 4 (Number Letter Switching) subtest raw score was used to measure cognitive flexibility in the current study.

Cognitive flexibility. To assess the executive functioning domain of cognitive flexibility, the D-KEFS Trail Making Test (Delis et a., 2001) was used. Test-retest reliability for the D-KEFS Trail Making Test for adults aged 50 to 89 ranges from .37 to .74 (Delis, Kaplan, & Kramer, 2001). All of the D-KEFS tests have been normed and validated on a range of healthy and clinical populations of older adults (Wecker et al., 2000), including patients with mild cognitive impairment (Grant et al., in press, as cited in Delis et al., 2004).

The D-KEFS Trail Making Test involves sequencing of responses at varying levels of complexity, which are labeled as five conditions. In all conditions, the participant is given a shorter practice version of the task before being given the test version. Number Letter Switching (condition 4) is a measure of cognitive flexibility, and requires participants to alternate between connecting numbers in numerical order and letters in alphabetical order (e.g., 1-A-2-B, and so on). The number-letter switching task (condition 4) represents the main measure of the D-KEFS Trail Making Test and is a measure similar to the Trails B test (Trail Making Test Part B) originally developed by Partington (Brown & Partington, 1942; Partington & Leiter, 1949). The other four conditions of the D-KEFS Trail Making Test examine component processes of condition 4 individually. Number Sequencing (condition 2) is a measure of visual scanning, numeric sequencing, and visuomotor speed, and requires participants to connect numbers in numerical order—a measure similar to Trail Making Test Part A (Brown & Partington, 1942; Partington & Leiter, 1949).The variable of interest for the present study was the performance on condition 4, which aims to isolate set-shifting from other component skills such as letter sequencing and visual scanning. The number-letter switching task used in the Trails B test and the D-KEFS Trail Making Test has been commonly used to assess cognitive flexibility (Sánchez-Cubillo et al., 2009; Kortte et al., 2002). Another common method in prior work uses a difference score between condition 4 (set-shifting/Trails B) and condition 2 (numeric sequencing/Trails A) to further isolate the part of the score attributable to performance on cognitive switching (Bugos et al., 2007, MacRitchie et al., 2020). The variable used in all analyses will be the difference of the D-KEFS Trail Making Test condition 4 completion time in seconds and the D-KEFS Trail Making Test condition 2 completion time in seconds, in order to extract cognitive processing speed from the motor and visual scanning components of the task. However, summary sample characteristics will be presented as scaled scores.

Critical Flicker Fusion

Critical Flicker Fusion (CFF) is a measure of visual temporal processing speed. Temporal vision is defined as the rate at which one can perceive visual information that is changing over time. The upper limit of one's temporal processing capabilities is referred to as the critical flicker fusion threshold, which represents the fastest speed of flickering light that the visual system can perceive (Saint et al., 2017). CFF has often been regarded as a basic metric underlying higher order cognitive functions, as CFF thresholds have been shown to correlate positively with cognitive functions (Mewborn et al., 2015) and decline with age (Wooten et al., 2010).

CFF thresholds were collected during measurement of macular pigment at the initial and final study visits and were acquired in a completely dark room by an experimenter trained in psychophysical measurement using a customized device that has been previously described by Wooten et al. (2010). The stimulus was comprised of a 1° target surrounded by a 5.5° background. Both target and surround were composed of 660 nm (red) light, which is a wavelength that is not absorbed by macular pigment or crystalline lens and thus prevents individual differences in macular pigment optical density from confounding the measurements. The researcher oriented participants to the device and explained the procedure before turning off the lights. Participants sat in a chair and viewed the target through an eye-piece with a 3 mm artificial pupil (to obviate variations in luminance due to pupillary diameter). CFF thresholds were determined using a method of limits (1 Hz intervals) and were based on the average of two ascending trials (flicker frequency was increased until the stimulus fused) and two descending trials (flicker frequency was decreased until flickering was detected). Higher values (expressed in Hz) indicate better performance. Past studies using these conditions (Hammond & Wooten, 2005; Wooten et al., 2010) have shown CFF to be highly reliable (Cronbach's alpha = 0.95). The variable used in all analyses was the baseline CFF threshold value, which represented visual temporal processing speed.

Analytic Plan

Data were analyzed with IBM SPSS Statistics software (Version 28.0.0.0) and the PROCESS extension (Hayes, 2013). Means and standard deviations were computed for all study variables. All variables were examined for assumptions of parametric statistics and other quality control (e.g., outliers, normality).

In the first model, a linear regression was performed to test the primary hypothesis that, in addition to baseline level of cognitive processing speed, level of cognitive flexibility at baseline (pre-intervention) was related to cognitive processing speed and expected improvements in cognitive processing speed after six months of piano training. The independent measures were baseline scores on D-KEFS Number-Letter Sequencing and the CNS-VS SDC. Participant age and computer training interface were included as a priori covariates in all models. Zero-order correlations between the studied variables were inspected to determine whether other covariates were warranted in the regression model. The dependent measure was post-treatment CNS-VS SDC scores. Significant main effects of baseline cognitive processing speed and cognitive flexibility were expected, such that the latter also accounts for significant unique variance (change in R^2) in post-intervention cognitive processing speed. Moreover, the interaction of baseline cognitive processing speed and baseline cognitive flexibility was expected to account for significant variance in post-intervention processing speed. These analyses included examination of a moderation model using PROCESS (Hayes, 2013) to determine whether relations between baseline cognitive processing speed and post-training cognitive processing speed were moderated by baseline cognitive flexibility. Overall, these procedures were expected to reveal whether the expected far transfer effects of musical training on cognitive processing speed were associated with the level of baseline cognitive flexibility.

The second model examined whether the time spent engaging in the training intervention was related to predicted changes in cognitive processing speed after six months of piano training, and included examination of a moderation model using PROCESS (Hayes, 2013) to determine whether relations between time engaging in training and pre-post cognitive processing speed changes were moderated by baseline cognitive flexibility.

Analyses were conducted in two separate regressions with predicted significant main effects and interaction. To establish significant interactions, models required a significant p-value within the model summary. Additionally, there needed to be a significant p-value for the interaction term and a confidence interval not containing the value zero as both indicate significance. If interactions were significant, simple slope analyses were used to probe the differing levels at which effects were observed. In line with previous work, we conceptualized results of simple slope analyses as indicating low, medium, and high levels of observed effects (Hayes, 2013). Power analyses were conducted using G-Power 3.1 for a multiple linear regression as a proxy for moderation analyses (Faul, 2009). Power analyses revealed that assuming statistical power of .80, a two-tailed alpha level of .05, and a sample of 50 participants yields a capacity to detect an effect size of .29. Thus, the analysis should be sufficiently powered, given that these effects are lower than the effect sizes expected from the literature.

A medium effect size of .4 (Cohen, 1988) was estimated for main effects based on extant literature on far transfer effects of musical training on cognitive processing speed (Roden et al., 2014; Helmbold et al., 2005; Bergman et al., 2014; Bugos & Kochar, 2017), as well as far transfer effects of musical training on other cognitive domains (IQ: Schellenberg, 2004; verbal fluency: Bugos & Kochar, 2017; working memory: Amer et al., 2013; Hanna-Pladdy & Gajewski, 2012; dual-task performance and task-switching: Moradzadeh et al., 2015; verbal memory: Taylor & Dewhurst, 2017). Given this literature, medium effect sizes ($d > .4$) were expected for main effects and a similar effect size was estimated for the interaction effect.

An exploratory analysis was conducted to address the components of processing speed that may have contributed to performance on the Symbol Digit Coding measure used in the analysis. Given that the Symbol Digit Coding Test requires processing on all three levels (sensory, motor, cognitive), in order to assess processing speed specific to cognitive processing, it may be necessary to parse out the sensory and motor aspects to isolate the cognitive aspect subserved by neural networks. An exploratory hierarchical multiple regression was conducted to account for the effects of sensory and motor aspects of processing speed in the SDC measure, by adding two covariates into the model that index sensory and motor processing speed (Critical Flicker Fusion; CFF and Finger Tapping Test; FTT, respectively), which were available in the dataset. This additional analysis was repeated for both of the original models.

An additional four participants were excluded from exploratory analyses due to missing data for the CFF and FTT variables. Given the available sample size and inclusion of additional covariates, it is acknowledged that this analysis was underpowered. It was conducted primarily for exploratory purposes, for the potential to explain obtained results.

CHAPTER 3

RESULTS

Data were checked for validity and distributions were checked for normality. K-S tests revealed acceptable distributions with skew and kurtosis between -1.00 and 1.18 after Winsorizing one outlier value in each, baseline SDC, Trail Making Test Number Sequencing and Number Letter Switching conditions, post-intervention SDC, and time spent on at-home piano practice. Two extreme FTT values were also Winsorized. Patterns of significance in the results did not change after Winsorizing outliers. One participant exhibited an invalid baseline SDC score, which was replaced with the group mean baseline SDC score.

Descriptive Statistics and Preliminary Analyses

Table 2 presents means and standard deviations for cognitive measures and Table 3 presents correlations between study variables. Mean baseline TICS performance of the sample at screening (M = 34.02± 1.82) was at or above several suggested score cutoffs of 29/30 and 32/33 used to detect MCI (Welsh et al., 1993; Watt et al., 2021). Mean baseline MoCA performance (M = 26.29± 2.40) was just above the score cutoff of 26 that is widely used to detect cognitive impairment (Nasreddine et al., 2005). There was a significant negative association between age and cognitive processing speed performance on SDC at baseline, r = -.35, p = .02, and post-intervention, r = -.39, p = .01. Additionally, total time spent engaging with the music learning intervention and change in cognitive processing speed were significantly positively correlated, r = .31, p = .047. Training interface was significantly positively associated with performance on D-KEFS Trail Making Test Condition 4 (Number-Letter Switching) at baseline, r = .37, p = .02, and with cognitive flexibility at baseline, *r* = .32, *p* = .04. Performance on D-KEFS Trail Making Test Condition 2 (Number-Sequencing) at baseline was significantly negatively correlated with cognitive processing speed performance on SDC at baseline, *r* = -.32, *p* = .04, and post-intervention, *r* = -.39, *p* = .01, as well as with performance on FTT, *r* = -.33, *p* = .04. There was a significant negative association between performance on D-KEFS Trail Making Test Condition 4 (Number-Letter Switching) at baseline and cognitive processing speed performance on SDC post-intervention, *r* = -.41, *p* = .01. Baseline cognitive flexibility was not significantly correlated with baseline or post-intervention cognitive processing speed. A paired t-test was conducted to test the effects of the music learning intervention on cognitive flexibility. Cognitive flexibility did not differ significantly between baseline and post-intervention, t(40) = 1.04, *p* = .15. The effect size, as measured by Cohen's *d*, was *d* = .16, indicating a very small effect. A paired t-test was also conducted to test the expected effects of the music learning intervention on cognitive processing speed prior to moderation analyses. Cognitive processing speed performance, as indexed by SDC scores, significantly increased between baseline and post-intervention, *t*(40) = -1.97, *p* = .03. The effect size, as measured by Cohen's *d*, was *d* = -.31, indicating a small to medium effect.

Moderation Analyses

Model 1 – Baseline Cognitive Processing Speed and Post-Intervention Cognitive Processing Speed Moderated by Baseline Cognitive Flexibility (see Figure 1)

The overall model was significant, R^2 = .33, *F*(5, 35) = 3.45, *p* = .01; however, baseline cognitive flexibility was not significantly associated with baseline (*r* = -.12, *p* = .46) or post-intervention (*r* = -.28, *p* = .07) cognitive processing speed, nor did it significantly moderate the association between baseline and post-intervention cognitive processing speed, *b* = .002, SE(*b*) =

0.005, *t*(40) = 0.34, *p* = .74, 95% CI [-0.01, .013]. Neither age (*b* = -0.36, *t*(35) = -1.70, *p* = .10, 95% CI [-0.78, 0.07]) nor training interface (*b* = 1.26, *t*(35) = 0.64, *p* = .53, 95% CI [-2.74, 5.25]) were significant covariates in the model.

Model 2 – Time Spent Engaging in Training Intervention and Pre-Post Intervention Change in Cognitive Processing Speed Moderated by Baseline Cognitive Flexibility

A linear regression indicated that the main effect of total time spent engaging in the intervention was a significant predictor of change in cognitive processing speed [F(1,39) = 4.20, p = .047] and explained 9.7% of the variation in cognitive processing speed change. When the moderation was included, the overall model was not significant, R^2 = .17, *F*(5, 35) = 1.47, *p* = .22., nor did baseline cognitive flexibility significantly moderate the association between time spent engaging in the intervention and change in cognitive processing speed. Neither age nor training interface were significant covariates in the model. See Table 4 for details of moderation analyses.

Exploratory Analyses

Two follow-up analyses were conducted to better understand the pattern of results observed during tests of hypotheses. Four additional participants were excluded from exploratory analyses due to missing or invalid scores on CFF and FTT measures, resulting in a sample of 37 participants. CFF and FTT were added as covariates to moderation models 1 and 2 above.

Exploratory Model 1 – Baseline Cognitive Processing Speed and Post-Intervention Cognitive Processing Speed Moderated by Baseline Cognitive Flexibility

The overall model was significant, R^2 = .51, *F*(7, 29) = 4.26, *p* = .002; however, baseline cognitive flexibility was not significantly associated with baseline (*r* = -.12, *p* = .46) or post-intervention (*r* = -.28, *p* = .07) cognitive processing speed, nor did it significantly moderate the association between baseline and post-intervention cognitive processing speed, *b* = .002, SE(*b*) = 0.005, *t*(36) = .44, *p* = .66, 95% CI [-.007, .01]. None of age (*b* = -.52, *t*(29) = -2.54, *p* = .02, 95% CI [-.93, -.10]), training interface, (*b* = 1.11, *t*(29) = .64, *p* = .52, 95% CI [-2.41, 4.62]), CFF (*b* = .15, *t*(29) = .45, *p* = .66, 95% CI [-.53, .82]), or FTT (*b* = .04, *t*(29) = .82, *p* = .42, 95% CI [-.06, .15]) were significant covariates in the model.

Exploratory Model 2 – Time Spent Engaging in Training Intervention and Pre-Post Intervention Change in Cognitive Processing Speed Moderated by Baseline Cognitive Flexibility

The overall model was not significant, $R^2 = .20$, $F(7, 29) = 1.04$, $p = .42$. See Table 5 for details of moderation analyses.

CHAPTER 4

DISCUSSION

Summary of rationale and primary findings

Music learning has been shown to be an effective form of cognitive training in older adults at risk for ADRD, with transfer effects beyond musical performance leading to maintained or improved performance in crucial cognitive domains such as processing speed (Bugos et al., 2007; Bugos, 2010), verbal fluency (Bugos & Kochar, 2017), and other executive functions (Seinfeld et al., 2013; Särkämö et al., 2014; Bugos & Cooper, 2019). However, the mechanisms underlying domain-specific effects of musical learning have been understudied in this population. Among the notable knowledge gaps is whether a core cognitive ability, such as cognitive flexibility, underlies benefits of music learning more frequently reported in other specific cognitive domains, such as processing speed. Therefore, this study examined the relation between cognitive flexibility and the far-transfer effects of a six month piano training intervention on cognitive processing speed in a sample of older adults at risk for ADRD. Specifically, cognitive flexibility was examined as a moderator of the expected improvements in post-intervention cognitive processing speed, and as a moderator of the association between time spent engaging in the music training and changes in cognitive processing speed. It was expected that better performance on measures of baseline (pre-intervention) cognitive flexibility would be related to larger training-related improvements in cognitive processing speed after six months of piano training (post-intervention). Additionally, it was predicted that the amount of time older adults spent engaging in the piano training would be associated with greater pre-post change in cognitive processing speed, and that higher baseline levels of cognitive flexibility would be associated with stronger effects of time spent learning on pre-post change in cognitive processing speed.

Overall, analytic models revealed a significant post-intervention increase in observed cognitive processing speed and that the amount of time spent engaging in the music learning intervention was a significant predictor of this increase. However, baseline cognitive flexibility did not significantly moderate the association between baseline and post-intervention cognitive processing speed, or the association between time spent engaging in the intervention and change in cognitive processing speed. Therefore, support for specific hypotheses was mixed.

Specific hypotheses and integration of findings

The fundamental hypothesis that participants would show improvement in cognitive processing speed following the intervention was supported, as cognitive processing speed performance significantly increased between baseline and post-intervention, demonstrating a small to medium effect size. This finding builds on prior work showing improvement in cognitive processing speed performance in older adults following participation in piano training interventions (Bugos, 2010; Bugos & Kochar, 2017; Bugos et al., 2007) and supports the utility of piano learning as an effective, multimodal form of cognitive training for older adults at risk for ADRD.

Although not an a priori hypothesis, expected improvement in cognitive flexibility was observed following the intervention; however, it did not rise to the level of statistical significance. This is an unexpected finding, as prior studies have reported significant improvement on measures of executive function, including cognitive flexibility, in older adults who participated in piano training interventions for a similar duration (Seinfeld et al., 2013;

Bugos et al., 2007). The lack of significant improvement in the current sample may be attributed to high mean baseline performance on the measures assessing cognitive flexibility, resulting in a ceiling effect that may have limited accurate quantification of improvements due to the intervention. Other methodological differences from prior studies, such as intensity or duration of the intervention, may also have yielded smaller transfer effects on cognitive flexibility that were not statistically powered by design in the current study. Therefore, present results suggest a specificity of musical training to improving cognitive processing speed, or that there is a smaller transfer effect on cognitive flexibility.

The hypothesis that baseline cognitive processing speed and baseline cognitive flexibility would each positively predict post-intervention cognitive processing speed was supported for the former but not the latter. Baseline cognitive processing speed was strongly and positively associated with post-intervention cognitive processing speed, as would be expected given test-retest reliability of the tests, practice effects, and the hypothesized intervention effects in the within-subjects design. However, baseline cognitive flexibility was not significantly associated with baseline or post-intervention cognitive processing speed. It was also not a significant predictor of post-intervention cognitive processing speed after statistically controlling the effects of baseline cognitive processing speed. These null findings were unexpected, given evidence that performance on similar assessments of cognitive processing speed involves executive control and shifting processes (Albinet et al., 2012) and prior music learning studies that have reported improved executive functions, including cognitive flexibility (Hanna-Pladdy & MacKay, 2011; Biasutti & Mangiacotti, 2018; Bugos et al., 2007). Moreover, the lack of significant association between cognitive flexibility and processing speed appears to be the source of unexpected findings from the two transfer effect models tested.

The model used to investigate baseline cognitive flexibility as a moderator between baseline and post-intervention cognitive processing speed (Model 1) was significant due to the strong association between the processing speed measures; however, baseline cognitive flexibility did not significantly moderate this association as hypothesized. This finding was surprising given previously proposed mechanisms of cognitive training. One prominent theory asserts that when a person possesses the cognitive capacity, adaptive strategies such as recruiting alternate brain networks are used to attempt to maintain normal function in the face of neurocognitive decline or impairment (i.e., cognitive reserve; Stern, 2002; Clare & Woods, 2004; Gates et al., 2011; Stern, 2012; Wilson et al. 2003). It was predicted that successful adaptation, such as transfer effects of musical learning on cognitive processing speed, would imply a need for cognitive flexibility.

Given unexpected findings, the possibility of measurement error was explored. To measure cognitive flexibility in this sample, a well-validated difference score of D-KEFS Trail Making Test Condition 4 (equivalent of Trails B) and D-KEFS Trail Making Test Condition 2 (equivalent of Trails A) was used to isolate the performance variance attributable to cognitive switching (Bugos et al., 2007, MacRitchie et al., 2020). Data checking confirmed that the difference scores were normally distributed and free of outliers. Yet, due to the high variance in the difference scores relative to the mean, statistical models were repeated using Trail Making Test Condition 4 scores alone as a more traditional measure of cognitive flexibility. However, patterns of significance remained unchanged. Thus, the lack of support for this hypothesis was not likely due to a problem of restricted range or poor reliability of the Condition 4 minus Condition 2 difference scores.

The hypothesis that the amount of time spent engaging in piano training would affect the degree of pre-post change in cognitive processing speed was supported in the expected direction. Total time spent engaging in the intervention was associated with greater increases in pre-post change in cognitive processing speed. This is in line with prior published findings demonstrating that both younger and older adults who have more musical experience, such as formal musical training or participation in regular musical activities, demonstrate better performance on various cognitive measures, including cognitive processing speed (Hanna-Pladdy & MacKay, 2011; Talamini et al., 2017; Roman-Caballero et al., 2018).

Despite this significant direct effect indicated by the bivariate correlation and the direct effect in the multivariate model, overall Model 2 did not significantly predict change in processing speed, and the hypothesized moderation was not supported. Specifically, baseline level of cognitive flexibility did not significantly affect the strength of the association between time spent engaging in the intervention and change in cognitive processing speed. The significant direct effect suggests that the overall Model 2 might significantly predict change in processing speed with sufficient statistical power to accommodate the extra variables (i.e., moderator and covariates). However, it is unlikely that the lack of moderation effects from cognitive flexibility were due to statistical power alone, given the weak associations in bivariate and multivariate analyses, including Model 1.

Cognitive flexibility was anticipated to moderate the association between time spent engaging in the training intervention and cognitive processing speed change based on literature suggesting that executive functions, including cognitive flexibility, support a wide range of higher order cognitive functions that result in greater neural efficiency and potential for plasticity (Herrero & Carriedo, 2020; Bull et al., 2008). Further, as the need increases for neurocognitive adaptations to compensate for cognitive decline (e.g., aging), the need for flexibility in implementing them (e.g., apply cognitive reserve; Stern, 2012) would appear to increase. Thus, it was hypothesized that cognitive flexibility represents an essential piece of the mechanism of far-transfer effects, particularly among older adults.

The lack of empirical support for this hypothesis may be related to the characteristics of the study sample. While recruitment goals focused on enrolling a sample with a range of dementia risk and varied levels of cognitive decline, including MCI and SCD, the final sample demonstrated high baseline cognitive performance across study measures, including cognitive flexibility and cognitive processing speed. While the sample had subjectively declined to at least some degree from their baseline, based on self-report, they performed in the average range on objective cognitive measures and at or just above cutoff scores on cognitive screening measures. Although these mean scores suggest that cognitive performance is somewhat lower than would be expected from a sample in which the majority were college graduates, this uncertain decline from their individual baselines is modest. It is also possible that some participants may have been early on in the process of decline. Therefore, the potential effect of cognitive training may also be modest.

Relatedly, the sample showed a small degree of improvement in processing speed, which may have been a factor of high baseline performance, thus the restricted variance in processing speed change may have prevented detection of moderation effects, if they exist. A sample with a greater range of baseline cognitive performance and degree of cognitive decline would likely show greater variance in training-related improvements in cognitive performance, and the effects of cognitive flexibility as a moderator in this model may be better demonstrated. Future work should further examine the effects of cognitive training interventions in older adults at varying levels of cognitive decline to tease these differences apart with more granularity and determine more precise levels of decline at which cognitive training is most effective in maintaining and improving cognitive performance.

Conclusions, limitations, and future directions

Overall, the results of this study provide evidence that piano learning is an effective form of cognitive training for the maintenance and improvement of cognitive function, particularly cognitive processing speed, for older adults at risk for ADRD. This conclusion is based upon improvements in cognitive processing speed and cognitive flexibility performance, the a priori foci of this study, following six months of piano training. Although only the processing speed effect was statistically significant, absolute increases may be of clinical significance, as this at-risk sample might be expected to decline over six months in the absence of an intervention.

Findings also suggest that the amount of time spent engaging in musical cognitive training, including time spent learning and practicing content, is an important predictor of the degree of improvement in cognitive performance, particularly cognitive processing speed. Future research may inform musical learning interventions by determining whether this represents a linear dose-response relationship or how the association may change at greater levels of cognitive decline. This would likely help developers of intervention protocols to optimize intensity and duration of music learning, as well as practice (e.g., identify critical points of diminishing returns). More frequent timepoints of cognitive assessment during a similar longitudinal intervention design would allow this relationship to be examined more thoroughly.

Importantly, findings also indicated that baseline level of cognitive flexibility is not significantly related to training-related improvements in cognitive processing speed, and, therefore, does not appear to represent a core cognitive ability that underlies the transfer effect of musical training to cognitive processing speed. This preliminary novel finding on specific mechanisms underlying the cognitive benefits of music training needs replication in a larger sample with increased statistical power to address Type II error. Therefore, future research should examine this model in a similar longitudinal design with larger sample of older adults who exhibit a larger range of baseline cognitive functioning. Future investigations might also explore other core cognitive domains that may be underlying far-transfer effects, such as vigilance, and potentially cognitive processing speed as a moderator.

A notable strength of the current study was the longitudinal within-subjects design, which allowed comparisons to be made of cognitive performance pre- and post- training, with participants serving as their own controls for baseline cognitive performance. Another strength was the duration of the six-month piano training intervention and the frequency of weekly piano lessons. New content was introduced weekly and practiced daily, allowing for sufficient time intensity engaging with the training to likely promote cognitive change.

Despite numerous strengths, this study had limitations. In addition to the noted sample characteristics of high baseline cognitive performance and a modest degree of decline, which limits generalizability, the sample size is a limitation that hampers interpretation of null findings and may have prevented some medium effects from reaching statistical significance. This also may have prevented moderation effects from being demonstrated, despite the powerful within-subjects design. Our sample also did not allow investigation into differences in cognitive performance change between participants with varying levels of cognitive decline (e.g., MCI, SCD). Future studies using larger samples should examine how musical training interventions may impact the cognitive performance of these groups differently, and, ideally, compared to a control group.

A control group would have allowed better experimental control over potentially confounding factors such as experimenter rapport (e.g., use of a placebo group/attention control) and practice effects (e.g., use of a waitlist control), and improved interpretation of expected change over time (e.g., use of a waitlist control). Inherent in the study design are potential effects of rapport with study personnel on cognitive performance at the final assessment timepoint. Given that participants interacted with study personnel on a weekly basis throughout the course of the intervention and developed familiarity with personnel, increased rapport at the final cognitive assessment visit compared to the initial assessment visit may have contributed modestly to improved performance on the final assessment. Practice effects are also a relevant consideration for the repeated measures study design that was used. This problem may be mitigated somewhat because the outcome cognitive measure of cognitive processing speed has been shown to have good test-retest reliability (CNS-VS: $r = .84$, Gualtieri & Johnson, 2006).

Importantly, the present study did not allow comparison of musical training effects on cognitive performance to repeated six-month performance of a control group receiving no intervention. A well-matched no-intervention control group would have improved expectations for the intervention group in quantitative and qualitative terms and could have enhanced statistical and clinical significance. For instance, had a control group declined in performance over six months (as expected in an at-risk sample), the observed improvements in the musical learning group would be more remarkable. Thus, replications of the present study and future work would greatly benefit from inclusion of a control group in the longitudinal design to compare expected improvements in cognitive performance with participation in a musical training intervention to expected declines in cognitive performance.

Variable attention during cognitive assessments, particularly the computer-based assessments (CNS-VS), which were self-paced, may also have impacted performance on cognitive measures. Future research may benefit from controlling this factor, to promote optimal attention to assessment procedures.

In addition, given that some participants received the computerized piano instruction from an autonomous socially assistive robotic instructor, as a condition of the parent study, the addition of the robotic instructor may have affected participants' engagement with the lesson content and motivation to practice differently than instruction from the computerized platform without embodiment. Though controls were put in place to account for this in analysis (e.g., including training interface as a covariate), future research might further examine the effects of musical training interventions that implement social stimulation in a larger sample with greater power to compare these experimental conditions. The inclusion of the two experimental conditions may also have contributed to the null findings produced by the models. The addition of the robotic instructor may have introduced increased variance in the data, thus the need to add another covariate into the model, further decreasing statistical power to detect effects.

It will also be important to further examine the specificity of musical training interventions to improve performance in various cognitive domains, including cognitive processing speed and cognitive flexibility, as well as other domains that commonly show decline in older adults at risk for Alzheimer's disease and related dementias, such as working memory, reasoning, and other components of executive functioning. Future investigation comparing the strength of improvements in these domains would help establish the specificity of musical training compared to other forms of cognitive training and may help clarify the contexts in which musical training can be most effective as an intervention.

Final conclusions

Using a longitudinal, within-subjects design, we examined the effects of a six-month musical training intervention on cognitive processing speed performance in older adults at risk for ADRD and discern how cognitive flexibility may moderate training-related change. Our findings illustrated significant improvements in cognitive processing speed following the piano training intervention and demonstrated that greater time spent engaging in the training activities led to greater training-related improvements in cognitive processing speed performance. Baseline cognitive flexibility performance was neither found to moderate this association, nor moderate the degree of improvement in cognitive processing speed. Future investigation may identify alternative moderators of cognitive processing speed improvement to help elucidate mechanisms underlying far-transfer training effects. Additionally, future investigation should focus on further examining the specificity of musical training for improving performance in cognitive processing speed and other cognitive domains, and the specificity for groups in various stages of early cognitive decline, to inform intervention efforts and better equip individuals to harness the benefits of cognitive training most effectively.

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Tables and Figures

Table 1

Participant Characteristics

Variable	*Mean (SD) or %*	*N*
Age (mean)	72.71 (4.91)	41
Sex (%)		
Female	65.9	27
Male	34.1	14
Race (%)		
White/European American	82.9	34
Black or African American	12.2	5
Asian	2.4	1
More than one race	2.4	1
Education (%)		
Secondary level education/GED	7.3	3
Some college	9.8	4
Associate’s degree	9.8	4
Bachelor’s degree or higher	53.7	22
Not reported	19.5	8
Employment (%)		
Not currently employed	26.8	11
Employed part time	9.8	4
Retired	43.9	18
Not reported	19.5	8
Income Range (%)		
$12,000-19,999	2.4	1
$20,000-39,999	17.1	7
$40,000-59,999	14.6	6

$60,000-79,999	19.5	8
$80,000-99,999	14.6	6
Not reported	31.7	13
Handedness (%)		
Right	80.5	33
Left	19.5	8
Total time spent engaging in music training intervention (mean)	76.67 (37.77)	41

Note. Total time spent engaging in music training intervention is in hours, over the course of the intervention period (24 weeks).

Table 2

Descriptive Statistics of Cognitive Measures

Variable	*Mean*	*SD*
TICS (baseline)	34.02	1.82
MoCA (baseline)	26.29	2.40
Symbol Digit Coding (baseline)	101.44	11.24
Symbol Digit Coding (post-intervention)	105.41	10.48
Processing Speed Change	3.98	10.13
D-KEFS Trails 2 (Number Sequencing) (baseline)	11.05	2.73
D-KEFS Trails 4 (Number-Letter Sequencing) (baseline)	11.29	3.02
Cognitive Flexibility (baseline)	0.20	3.09
Cognitive Flexibility (post-intervention)	0.68	2.98
Critical Flicker Fusion (baseline)	21.07	2.79
Finger Tapping Test (baseline)	91.16	23.82

Note. TICS, MoCA, and Critical Flicker Fusion means are based on raw scores. Although raw scores were used in hypothesis testing, test means are presented here in age-corrected standard scores or scaled scores, when norms are available, for ease of interpretability. Processing Speed Change is the standard score difference between baseline and post-intervention Symbol Digit Coding scores. Cognitive Flexibility is the scaled score difference between D-KEFS Trails 4 and D-KEFS Trails 2.

Table 3

Correlations of Study Variables

Variable	1	2	3	4	5	6	7	8	9	10	11
1. Age	--										
2. Interface	-.03	--									
3. Total Time	.10	-.21	--								
4. SDC1	.35*	.08	-.21	--							
5. SDC2	-.39*	.04	.12	.45**	--						
6. PS Change	-.07	-.03	.31*	-.46**	.58**	--					
7. Trails2	.12	.22	.17	-.32*	-.39*	-.10	--				
8. Trails4	.07	.37*	.005	-.24	-.41**	-.19	.56**	--			
9. CF1	.02	.32*	-.09	-.12	-.28	-.17	.14	.90**	--		
10. CF2	.13	.13	-.05	.02	-.17	-.18	.29	.43**	.36 *	--	
11. CFF	-.35*	-.12	.24	.04	.15	.11	.13	.05	-.004	.14	--
12. FTT	.05	.06	-.12	-.04	-.09	-.05	-.33*	.12	.32 *	.06	-.07

Note. Interface (1 = Robot-Assisted; 2 = Computer); Total Time = Total time spent engaging in music learning intervention in hours; SDC1 = baseline Symbol Digit Coding; SDC2 = post-intervention Symbol Digit Coding; PS Change = Processing Speed change; Trails2 = D-KEFS Trail Making Test Condition 2 (Number Sequencing); Trails4 = D-KEFS Trail Making Test Condition 4 (Number-Letter Switching); CF1= baseline Cognitive Flexibility; CF2 = post-intervention Cognitive Flexibility; CFF = baseline Critical Flicker Fusion; FTT = baseline Finger Tapping Test.

$^{*}p < .05$, $^{**}p < .01$.

Table 4

Moderation Analyses: Hypothesis testing

Outcome Variable	R^2	*F*	*df*	*b*	SE	95% CI
Model 1						
SDC2	.33	3.45*	(5,35)			
SDC1				.26	.30	-.36, .87
CF1				-.13	.21	-.56, .29
SDC 1 x CF1				.002	.005	-.009, .01
Age				-.36	.21	-.78, .07
TrInt				1.26	1.97	-2.74, 5.25
Model 2						
PSChange	.17	1.47	(5,35)			
TimeTot				.002	.001	.002, .004
CF1				.08	.10	-.13, .30
TimeTot x CF1				.000	.000	-.0001, .000
Age				-.12	.21	-.55, .31
TrInt				.74	2.26	-3.85, 5.33

Note. SDC1 = Symbol Digit Coding (baseline); SDC2 = Symbol Digit Coding (post-intervention); CF1 = cognitive flexibility (baseline); TrInt = training interface (robot-assisted or computer); PSChange = Processing speed change; TimeTot = total time spent engaging in music learning intervention.

$^*p < .05$.

Table 5

Moderation Analyses: Exploratory analyses

Outcome Variable	R^2	*F*	*df*	*b*	SE	95% CI
<u>*Model 1*</u>						
SDC2	.51	4.26	(7,29)			
SDC1				.13	.27	-.42, .69
CF1				-.17	.18	-.54, .20
SDC 1 x CF1				.002	.005	-.007, .01
Age				-.52	.20	-.93, -.10
TrInt				1.11	1.72	-2.41, 4.62
CFF				.15	.33	-.53, .82
FTT				.04	.05	-.06, .15
<u>*Model 2*</u>						
PSChange	.20	1.04	(7,29)			
TimeTot				.002	.009	-.0002, .003
CF1				.06	.11	-.16, .28
TimeTot x CF1				.000	.000	-.0001, .000
Age				-.10	.24	-.60, .39
TrInt				.85	2.32	-3.89, 5.58
CFF				.30	.47	-.65, 1.25
FTT				.04	.07	-.10, .17

Note. SDC1 = Symbol Digit Coding (baseline); SDC2 = Symbol Digit Coding (post-intervention); CF1 = cognitive flexibility (baseline); PSChange = Processing speed change; TimeTot = total time spent engaging in music learning intervention.

$^{*}p < .05$.

Figure 1

Theoretical Model 1: Baseline Cognitive Flexibility as a Moderator of Training-Related Change in Cognitive Processing Speed

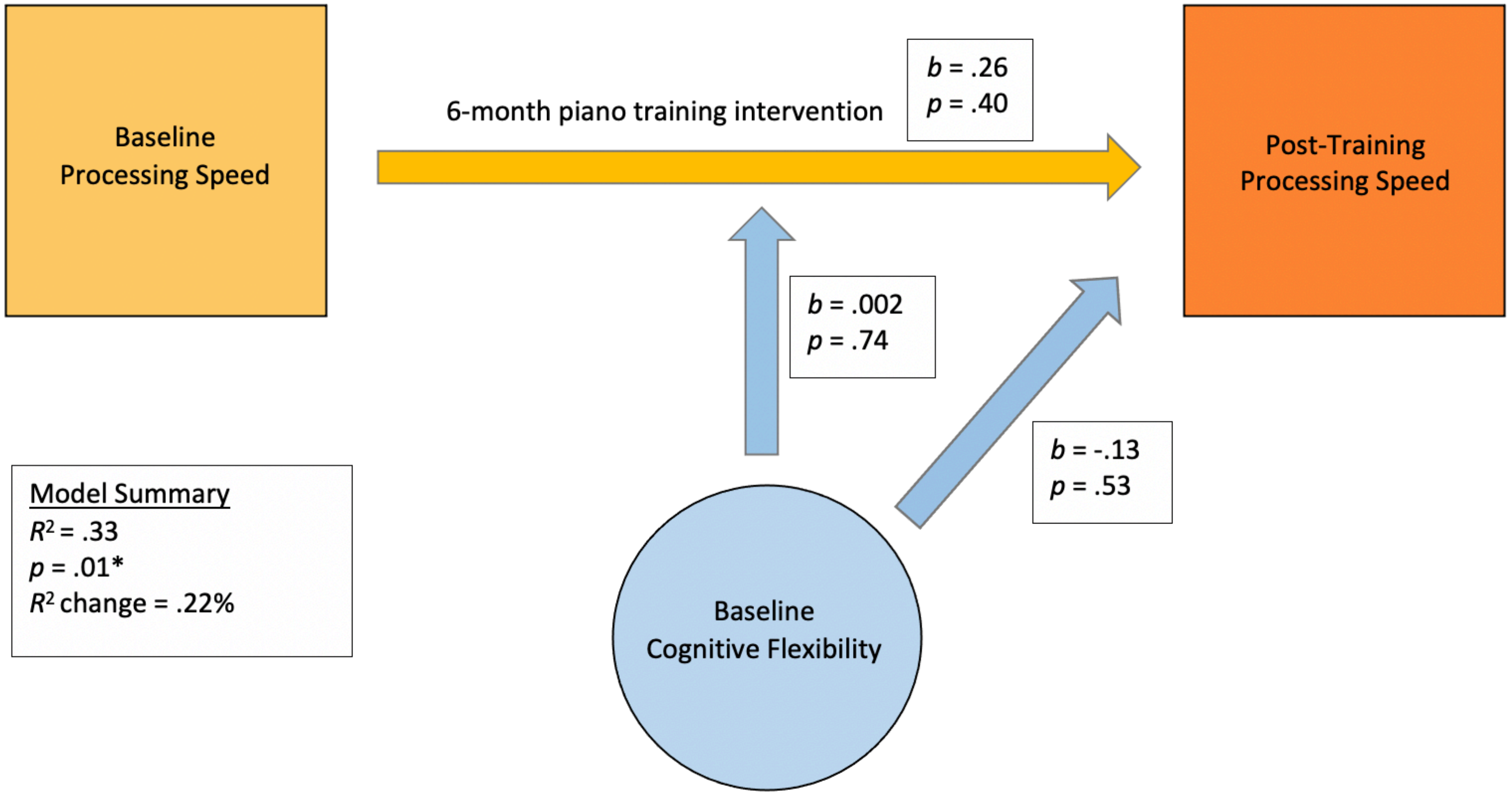

Figure 2

Interaction Effects of Baseline Cognitive Flexibility and Baseline Cognitive Processing Speed on Post-Training Cognitive Processing Speed

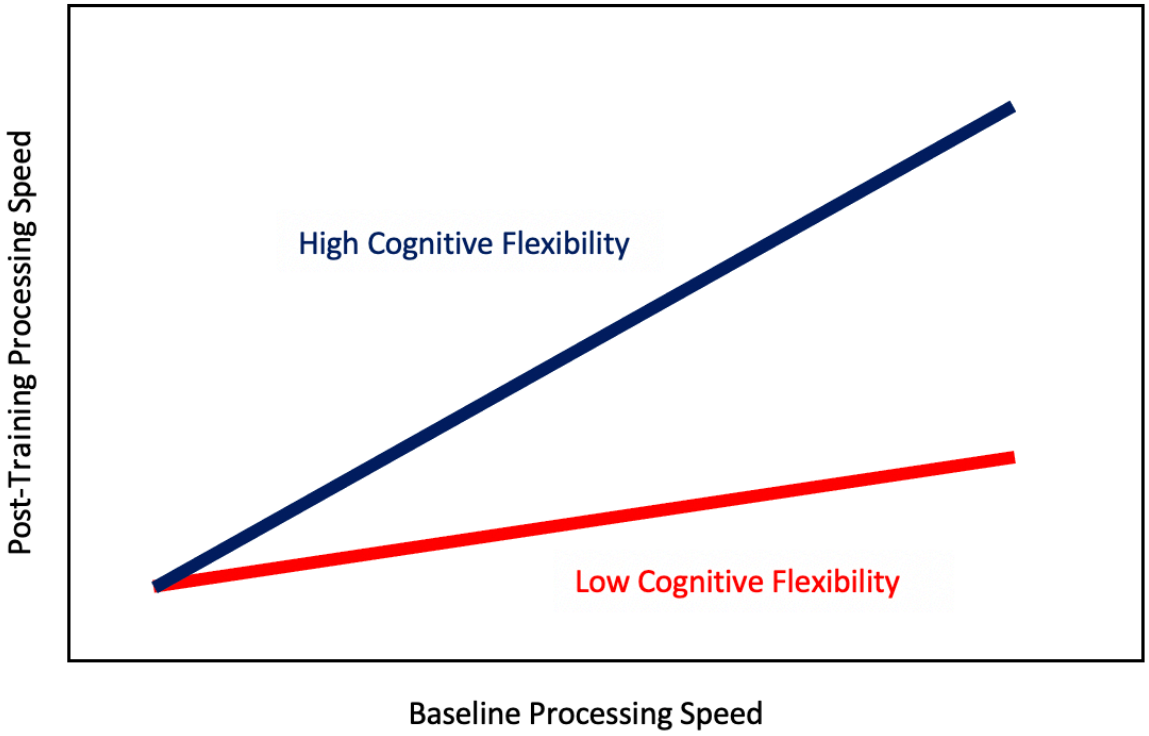

Figure 3

Theoretical Model 2: Baseline Cognitive Flexibility as a Moderator of the Relation between Time Spent Engaging in Intervention and Change in Cognitive Processing Speed

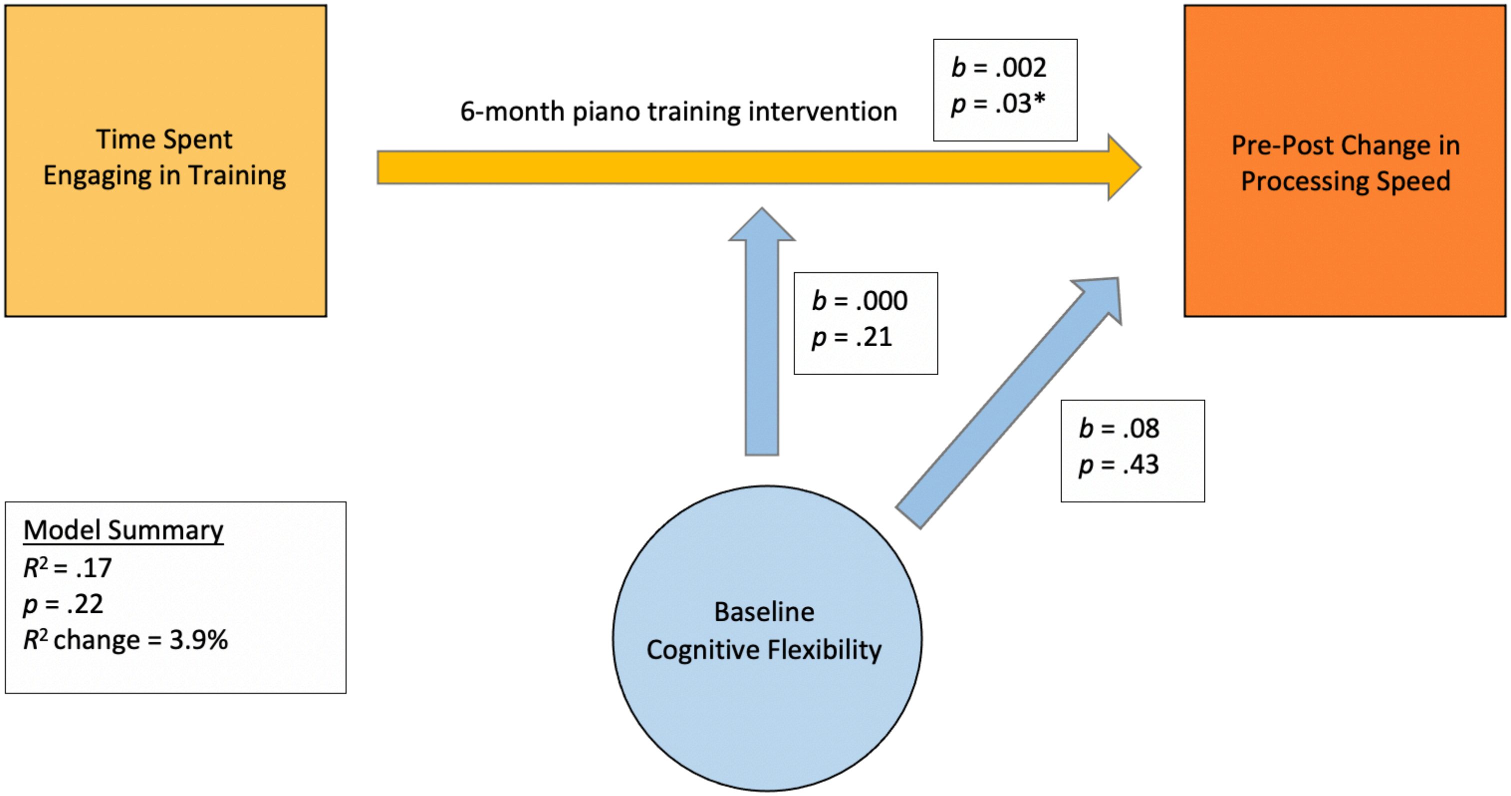

Figure 4

CONSORT diagram: Flowchart of Participants' Disposition throughout the Study