

Investigating the Neural Correlates of Social and Individual Singing in Persons with Dementia

Using Functional Near-Infrared Spectroscopy

by

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means, without the permission of the author.

I acknowledge and respect the lək̓ʷəŋən peoples on whose traditional territory the university stands and the Songhees, Esquimalt and W̱SÁNEĆ peoples whose historical relationships with the land continue to this day.

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Abstract

Introduction: While music interventions for persons with Alzheimer’s Disease and related dementias (ADRD) are increasingly utilized due to their documented cognitive and behavioral benefits, the neurological correlates underlying these advantages are largely unknown and under-researched. Using the advantages of functional near infrared spectroscopy (fNIRS), this study provided a preliminary investigation of the neural correlates and functional connectivity (FC) patterns associated with musical performance in both choral and individual contexts for persons with ADRD. **Objectives:** The objectives were to i) identify within-person patterns of cortical oxygenation in choral and individual singing, ii) explore how singing context (i.e., choral and individual) modulates patterns of functional connectivity (FC) within and across frontal and parietal cortices, and iii) leverage these neurological data as individual differences predictors of cognitive function in a series of discriminant function analyses (DFA). **Methods:** Participants included 13 persons with ADRD who volunteered from a larger, ongoing social-cognitive choir intervention. fNIRS data was collected via the TechEn Cw6 system, using a sampling frequency of 50 Hz, during both choral and individual singing. Paired sample t-tests were used to evaluate changes in neurological patterns observed across conditions and DFA were used to determine whether these neurological data, when used in conjunction with other gold-standard individual differences predictors, were predictive of between-person differences in cognitive impairment (proxied by performance on the Mini-Mental State Examination [MMSE]). **Results:** Significant differences in cerebral oxygenation were identified in the right anterior PFC (BA10), corresponding to one channel of the fNIRS frontal array; specifically, individual singing was associated with significantly greater oxygenation relative to social singing. Moreover, though not significant, individual singing was associated with broad bilateral increases in cortical

oxygenation across the majority of fNIRS channels, and increased FC, relative to choral singing.

Planned DFA were not significantly predictive of cognitive impairment status. **Conclusion:**

These findings yield tentative support for the notion that individual singing necessitates greater neocortical recruitment for persons with ADRD, and potentially increased FC, which is consistent with a body of literature detailing how increased stress and executive processing – likely enhanced in individual singing – facilitates greater neocortical recruitment. This is the first study to investigate differences in music cognition correlates across environmental contexts for persons with ADRD and may provide preliminary neurological evidence behind the advantages of group music interventions for persons with ADRD. That is, choral singing environments may alleviate the extraneous recruitment of neocortical systems found in individual performance systems which become increasingly impaired with dementia. This study motivates increasing utilization of fNIRS in music neuroscience research, especially in persons with ADRD, aimed at exploring the neurological mechanisms underlying the well-noted benefits of music interventions.

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List of Abbreviations

Abbreviation	Definition
ACTH	Adrenocorticotropic Hormone
ADRD	Alzheimer's Disease and Related Dementias
ANOVA	Analysis of Variance
BA	Brodmann Area
CORT	Cortisol
CRT	Choice Reaction Time
DFA	Discriminant Function Analysis
FC	Functional Connectivity
fMRI	Functional Magnetic Resonance Imaging
fNIRS	Functional Near Infrared Spectroscopy
HbO	Oxyhaemoglobin
HbR	Deoxyhaemoglobin
HRF	Haemodynamic Response Function
ISD	Intraindividual Standard Deviation
MA	Motion Artifact
MMSE	Mini-Mental State Examination
OXT	Oxytocin
PFC	Prefrontal Cortex
TMTA	Trail Making Task A
VIM	Voices in Motion

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Introduction

Music is a powerful stimulus - revered universally as a medium capable of imbuing unique cognitive, emotional, and social benefits to both its performers and partakers. While the value of music has long been appreciated, only recently are more rigorous investigations providing insights into its capacity as both a complex psycho-physiological stimulus and health-promoting tool. Specifically, due to the accessibility and widely-enjoyed nature of music, it is increasingly being studied and utilized in interventions – including for persons with Alzheimer’s Disease and related dementia’s (ADRD) - where several cognitive-behavioral benefits have been identified. Such benefits are often contextualized at the psychosocial level, where changes in cognition and behavior are attributed to the advantageous impacts of socialization (e.g., Leggieri et al., 2019; McDowell et al., 2022; Peck et al., 2016; Pongan et al., 2017; Särkämö et al., 2014). However, the burgeoning field of music neuroscience provides an opportunity to examine the biological mechanisms specific to music that underly its benefits in intervention contexts, including exploring the neural correlates of music and how they are differentially affected by disease and performance environment. Given the infancy of this field, there are many avenues yet unexplored. The present thesis aims to identify and investigate several of these avenues, using an innovative paradigm to monitor the cortical correlates of music cognition in persons with ADRD while singing in different environmental contexts (i.e., choral versus individual performance).

Psychosocial Benefits of Music Interventions

A growing number of randomized controlled trials have highlighted how various music-based interventions for persons with ADRD can significantly improve feelings of belonging and self-esteem (Cooke et al., 2010), emotional well-being (Cho, 2018), and overall quality of life

(Leggieri et al., 2019) while also attenuating the impact of deleterious dementia-related comorbidities (e.g., anxiety, loneliness, and depressive symptoms; Pongan et al., 2017; Särkämö et al., 2014). Musical performance, especially group performance, has also been shown to regulate biomarkers of health and socialization – stimulating endorphin production and modulating salivary oxytocin and cortisol concentrations, which can mollify pain and stress while increasing a sense of social bonding and empathy (e.g., Keeler et al., 2015; Pongan et al., 2017). Music-based interventions may foster these benefits through providing a sense of connection and alternative medium of expression for individuals experiencing increasing perturbations in social capacities (Cooke et al., 2010). Given these psycho-social advantages, music interventions are gaining popularity as an effective nonpharmacological treatment for individuals with varying degrees of dementia severity (Svansdottir & Snaedal, 2006).

Cognitive Benefits of Music

Music-based interventions have also shown to enhance cognitive functioning in persons with ADRD. Specifically, music interventions have demonstrated a positive impact on memory (Baird & Samson, 2009; Irish et al., 2006; Särkämö et al., 2014), attention, executive functioning, and global cognition in persons with ADRD (Leggieri et al., 2019; Särkämö et al., 2014; Thompson et al., 2005). While the mechanisms of these benefits are uncertain, these findings can be contextualized within the broader music cognition literature. Indeed, as a complex, domain-general neurological stimulus, music facilitates diverse and extensive recruitment of neural substrates and pathways which span a wide array of cognitive competencies – including, but not limited to, long-term planning, error monitoring, and both short- and long-term memory (Callan et al., 2006; Pongan et al., 2017). Further, prolonged musical engagement (e.g., music listening) or training has shown to facilitate neuroplasticity

(i.e., structural and/or functional changes within the brain [e.g., Hyde, 2009; Norton et al., 2005; Schlaug et al., 2005; Schlaug, 2015]). Music-acquired neuroplasticity may promote cognitive reserve – bolstering resilience against normative and pathological decline (e.g., Baird & Samson, 2015; Monaghan et al., 1998; Zatorre & McGill, 2005; Wan & Schlaug, 2010) – and provide transferable benefits to cognitive domains that rely on similar neural architecture such as verbal memory (Moreno, 2011), nonverbal memory, executive processes (Hannah-Pladdy & MacKay, 2011), spatial intelligence and abstract reasoning (Portowitz, 2009). Thus, the cognitive benefits realized by persons with ADRD in prolonged music interventions are likely resultant from a combination of music’s ability to stimulate and modify underlying neural tissue and functioning, in addition to its psychosocial impact on increasing personal autonomy and connection, comorbidity reduction, and parasympathetic modulation (e.g., increased mood; Leggieri et al., 2019; Peck et al., 2016). While neuroscientific investigations have yet to fully explore the neural mechanisms underlying the cognitive and behavioral benefits of music-based interventions, a growing body of research has begun categorizing the underlying processes of music cognition in persons with ADRD that provide a valuable template for understanding how music may foster neurological benefits in this population.

Neurological Correlates of Music in Persons with ADRD

Music cognition is relatively spared in persons with ADRD until late-stage disease process (e.g., Baird & Samson, 2009; Cuddy & Duffin, 2005). It is due to this preserved capacity that music-based interventions are an accessible and viable medium for persons with ADRD to attenuate dementia-related declines (e.g., Särkämö et al., 2014; Tamburri et al., 2019; McDowell et al., 2022). This relative preservation is likely related to the nature and location of ADRD progressive atrophy and how it overlaps with known areas of music cognition. Beginning with

the accumulation of neurological insults in the entorhinal cortices, within the medial temporal lobes, ADRD-related atrophy progresses to the hippocampal formation before spreading more diffusely to frontal and parietal cortices (Whitwell, 2010). This pattern of neurological decline results in the hallmark presentations of clinical symptomatology; namely, initial complaints in memory and other episodic deficits become increasingly supplemented by impairments in language, executive processes, behavioral dysregulation, sensorimotor declines, and global cognitive dysfunction (Cummings, 2012). However, despite these broader declines, persons with dementia have shown the capacity to identify and reproduce familiar music (Cuddy & Duffin, 2005; Simmons-Stern et al., 2010), produce music via singing or playing an instrument, and even learn new musical material (Baird & Samson, 2009). Further, music has been shown to evoke autobiographical memories (musically evoked autobiographical memories (MEAMs) in persons with ADRD despite their increasingly impaired episodic memory systems (e.g., Cuddy et al., 2015, 2017). These spared musical abilities highlight that some elements of music cognition must either preferentially utilize spared neural tissue and pathways (e.g., procedural memory systems) or uniquely stimulate cognitive processes that are otherwise increasingly impaired. For example, MEAMs are partially contingent on the deep emotional resonance of music – often coinciding with music popular during an individual’s reminiscence period (i.e., early adulthood) - alongside music’s ability to stimulate an exceptionally diverse array of neural networks. Thus, despite broad episodic memory declines, the qualities of music-evoked autobiographical memory retrieval may stimulate a different pattern of neural activation that potentially circumvents more common and increasingly impaired networks of episodic memory (Cuddy et al., 2015, 2017; Janata, 2009). Such music-related capacities and elicited responses for persons with ADRD

highlight the robustness of music as a neurological stimulus and help to better understand how it utilizes architecture within the brain.

However, music is not wholly spared from the neurological atrophy experienced by persons with ADRD; indeed, several elements of music cognition show signs of impairment even in the milder stages of dementia diagnosis. For example, while persons with ADRD generally show well-preserved implicit, procedural musical memory (the retained ability to perform music, cemented in well-trained motor circuits), musical episodic and semantic memory (the ability to recall details of music, specifically details of where or when it has been heard before) are typically impaired (Baird & Samson, 2015). These processes of musical episodic and semantic memory are largely contingent on the functioning of the medial temporal lobes, including the hippocampus, and their declining ability is likely due to the early accumulation of neurological insults in these regions associated with ADRD. Further, spared musical capacities are often related to the specific etiological subtype of dementia. That is, for persons with non-ADRD dementia diagnoses (e.g., frontotemporal dementia [FTD], semantic dementia), the differences in neurological atrophy associated with each subtype can exhibit vastly different patterns of musical sparing – with some persons diagnosed with FTD even experiencing music anhedonia: the lack of experiencing pleasure from music (Mas-Herrero et al., 2014). Thus, music, far from being an “island of preservation” unmediated by neuronal changes, answers chiefly to materialism and the underlying biochemical pathways and substrates of the brain.

The combined understandings of the neurological mechanisms behind both the spared and impaired abilities of music cognition in persons with ADRD helps to better structure music interventions targeted at persons with ADRD. Specifically, in better understanding the underlying neurological profile of intervention participants, and the impact this has on music

cognition, one can better design programs that optimally target a population's relative neurological strengths. Thus, the advent of music neuroscience has much to offer both in the academic context and in the field of nonpharmacological interventions; however, there are several notable gaps that should be addressed.

Current Gaps in the Music-Neuroscience Literature

With the well-documented benefits of music interventions for persons with ADRD, it is perhaps surprising that little is known of the specific neurological mechanisms underpinning these advantages. Indeed, while some research has investigated the modulatory effects of musical performance on neuropeptides and substrates (e.g., oxytocin, cortisol, and adrenocorticotrophic hormone [ACTH]; Keeler et al., 2015; Schladt et al., 2017) as a potential biological link between music and its psychosocial benefits (Chanda & Levitin, 2013), very little research has been dedicated towards exploring the potential neural correlates associated with music interventions – much less in persons with ADRD. This sparsity of research is, in part, due to the difficulty of utilizing neuroscientific methodologies to investigate neurological correlates during the music-making process. To be sure, functional magnetic resonance imaging (fMRI), positron emission tomography, and magnetoencephalography have all provided invaluable contributions to understanding both music cognition and dementia-related atrophy; however, these neuroimaging modalities are constrained by a lack of portability and sensitivity to motion which can hinder the ability to investigate neural correlates of music-production. Thus, certain design decisions must be imposed when using these modalities that may, at best, limit ecological validity and, at worst, negate the possibility of investigating certain neurological phenomena *in vivo*. Moreover, other neuroimaging techniques such as EEG, while more flexible to these natural constraints, proxy a neurological process (i.e., electrophysiological) that precludes adequate spatial resolution for

clarifying neural structures implicated in musical cognition. Cumulatively, these challenges make the measurement of neural correlates during music-making for persons with ADRD, especially under the broader context of intervention scenarios, more demanding, niche, and, consequently, under-researched.

Advantages of fNIRS

An innovative neuroimaging technique - functional near-infrared spectroscopy (fNIRS) – has garnered increasing popularity and utilization in music neuroscience research due in part to its increased amenability to the constraints imposed by monitoring music cognition during musical performance. fNIRS indexes the same biological process as fMRI (i.e., blood oxygen level dependent [BOLD] signal) and captures changes in cerebral hemodynamics as a way of proxying neurological activation (i.e., neurovascular coupling). This neuroimaging technique strikes a balance between temporal and spatial resolution, capable of monitoring neocortical activation patterns (with accuracy comparable to fMRI, up to 5mm deep [e.g., Duan et al., 2012, Sato et al., 2013]) at a temporal resolution of 50Hz – compared to fMRI's maximum frequency of ~12Hz. Furthermore, fNIRS is portable, making it useful for testing in more ecologically valid contexts, and is relatively robust to motion artifacts – often utilized in infant studies where motion is expected to occur (e.g., Wilcox & Biondi, 2015; Di Lorenzo et al., 2019). Given these advantages, increasing research has been investigating the cortical correlates of musical paradigms using fNIRS, including in novel inter-brain neural synchrony paradigms. For example, in a series of investigations by Osaka et al. (2014, 2015), researchers looked at whether neural synchronization occurred between two persons while singing or humming, cooperatively or individually, in face-to-face versus non-face-to-face conditions. In both humming and singing, whether persons were face-to-face or not, the left inferior frontal cortex showed an increase in

neural synchronization for cooperative as opposed to individual performance. These results are supported by the broader hyper-scanning literature, in which a recent meta-analysis identified that significant neural synchrony could occur during cooperative performance – with the largest effect sizes in both the frontal and temporoparietal areas (Czeszumski et al., 2022). In another study, Tachibana and colleagues (2019) evaluated changes in prefrontal cortex (PFC) activity during improvised guitar playing, identifying increased dorsolateral PFC (dlPFC) activity at the beginning and middle of an improvised sequence relative to the end – thus, capturing the temporal dynamics of cortical oxygenation during real-time musical performance. While other research leveraging fNIRS in musical paradigms exist, none of these studies involved monitoring persons with ADRD. With the continued exploration of novel research paradigms facilitated by fNIRS, there is a compelling opportunity and necessity to leverage the advantages of fNIRS to explore neural correlates of music in populations with ADRD, especially in the context of music-based interventions. Such investigations would provide more nuanced understandings of dementia-related and music cognition, as well as inform potential neurological mechanisms underpinning the benefits of music interventions for persons with ADRD. Therefore, the current thesis aims to capitalize on the relative strengths provided by fNIRS and investigate the neural correlates of music cognition in persons with ADRD engaged in a social-cognitive choral intervention -- evaluating how changes in intervention context (i.e., the difference between singing as a choir versus individually) modulate underlying neurological recruitment.

Current Study

The current thesis aims to provide a novel, preliminary exploration of the neural correlates of music-making in persons with persons with ADRD using an innovative fNIRS paradigm. In doing so, this study will expand on the current understandings of neurological

mechanisms behind the noted benefits of music-interventions for persons with ADRD. Further, given the increasing utilization of group music interventions for persons with ADRD, this thesis contrasts social (i.e., choral) and individual (i.e., solo performance with piano accompaniment) singing environments to explore the impact this may have on neurological recruitment.

Exploring the neurological recruitment patterns of choral versus individual singing may provide deeper insights into how social context modulates music cognition and why, for persons with ADRD, certain musical contexts may be more accessible than others.

Using an innovative research design, as well as leveraging the advantages of fNIRS, this thesis has three primary objectives: i) identify within-person patterns of cortical oxygenation in choral and individual singing, ii) explore how singing context (i.e., choral and individual) modulates patterns of functional connectivity (FC) within and across frontal and parietal cortices, and iii) utilize individual differences in these observed patterns of neurological function, alongside other gold-standard individual differences biomarkers, as predictors in a series of discriminant function analyses (DFA) aimed at discriminating individuals based on level of cognitive impairment.

Hypotheses

Though this study ultimately represents a new investigation of a previously unexplored phenomenon, a wide array of both music-related and non-music-related neuroscience exists upon which to foster *a priori* hypotheses.

Social versus Individual Singing

Music, and the singing of previously trained and well-known songs, requires the involvement of the procedural memory system; a network that has been extensively mapped with well-known correlates and expected patterns of activation. Specifically, increased automaticity –

or training on a particular task – is often associated with increased activation of subcortical regions (e.g., basal ganglia, striatum) and decreased activations of neocortical regions (e.g., PFC; see, Kassubek et al., 2001; Ono et al., 2015; Poldrack et al., 1999; 2005). Indeed, the implication of procedural memory systems in music is partly responsible for the behavioral and neural efficiency that is associated with training and practice (e.g., Baird & Samson, 2009; Herholz & Zatorre, 2012; Pinho et al., 2014). Moreover, procedural memory is relatively spared in persons with ADRD until late disease staging – a key feature relevant to the partially preserved musical competencies in persons with ADRD. However, altering the social/cooperative element of musical performance may lead to differential patterns of activation. Specifically, proceduralized patterns of activation (i.e., diminished frontal-cortical activation) can be perturbed by the influence of perceived task difficulty, novelty, stress, and performance pressure – all of which may facilitate increased activations of neocortical tissue and deleteriously affect performance. For instance, utilizing fNIRS to index PFC activity in a working memory task of varying difficulties under evaluative pressure, Ito et al. (2011) identified that increasing PFC activity was associated with both the hardest task difficulty and increasing evaluative pressure. Further, Shimizu et al. (2009) utilized fNIRS to monitor frontal cortical activity in a driving simulation task and observed increased activation of lateral frontal cortices in association with increased subjective task difficulty, and general increases in PFC activity correspondent to increased participant attention. Finally, concerning the adverse effects of stress on performance, a study by Lee & Grafton (2014) identified that ‘choking’ under pressure (i.e., failing to perform) in a motor task was associated with increased PFC activity, but found that increased FC between frontal cortices (e.g., PFC and primary motor cortex) was inversely related to performance choking. That is, increased regulation and cognitive control exerted by PFC on motor and sensorimotor

cortices – operationalized as increased FC - reduced participant's likelihood of choking under performance pressure. Thus, increasing performance pressure may manifest as increased prefrontal recruitment, while increases in FC may be indicative of healthy adaptations to task demands.

Given this context, there are several reasons to hypothesize that group singing would be an easier, more accessible mode of performance. In a social setting, individuals can more readily rely on others, relax the degree of conscious effort and control on performance regulation, and, consequently, may experience less performance pressure. For example, Keeler et al. (2015) showed significant modulation of ACTH concentrations in group singing -- a pattern attributed to the reduction of stress and arousal of group performance. Further evidence of the anxiolytic qualities of group singing have also been identified, as in a study by Schladt et al. (2017) who suggested that the reduction of stress and arousal in group singing was modulated by neuropeptides such as oxytocin. Therefore, there is precedent to suggest that group singing may not only foster a more relaxed and accessible environment but also modulate biological correlates of musical performance. As group singing is likely associated with a reduction of stress and performance pressure, and decreased reliance on cognitive control networks, it is anticipated that the individual singing condition will showcase greater cortical activation patterns relative to social singing; specifically, due to its increased involvement of the mechanisms implicated in executive processes (e.g., inhibition, performance regulation), arousal, and performance anxiety.

Patterns of Functional Connectivity

Music is known to facilitate broad FC between frontal and parietal cortices – an observation that holds true in improvisational and rehearsed performance, singing and

instrumental playing, and in novice and experienced musicians (Kleber et al., 2013; Segado et al., 2018; Zamorano et al., 2020; Zarate et al., 2010). Neural synchrony and connectivity analyses have been performed on individuals in musical contexts, with cooperative performance shown to increase both inter-brain synchrony and intra-brain connectivity (see Czeszumski et al., 2022, for review) – suggesting perhaps that choral singing would be associated with increased FC relative to individual performance. However, increased cognitive control and task novelty has also been associated with increased frontal-parietal connectivity (e.g., Cole et al., 2010); thus, FC may be expected to increase in individual relative to choral singing. Moreover, persons with ADRD experience alterations of FC in the default mode, executive control, and resting-state networks (Baird & Thompson, 2018; Sheline & Raichle, 2013; Weiler et al., 2014; 2016) that may also affect patterns of FC in musical contexts relative to healthy controls. Therefore, due to a lack of strong *a priori* evidence, and the novel paradigm and population in this thesis, FC research questions remain fundamentally exploratory.

Between-Persons Investigation

Given that this study involves persons with ADRD of varying disease stages, it is important to consider the pathological impact of dementia on music cognition and how this may impact neural activation. It is hypothesized that individual patterns of neural activation and connectivity will be modulated by increasing dementia-related impairment. Specifically, while neural atrophy for ADRD may initiate within the entorhinal cortex, the progressive pathology will begin affecting more superficial temporo-parietal and frontal cortices, manifesting as impairments in speech, behavioral disturbances, socialization, global cognition, and executive functioning. These impairments will also affect the functioning pathways of neural substrates, including dopaminergic pathways which are important in the context of musical pleasure,

reward-based learning, motivation, attentional regulation, and executive processing (e.g., Ferreri et al., 2019; Gebauer et al., 2012; Nieoullon, 2002). For these reasons, it is expected that greater disease burden will facilitate increased impairments on the underlying neural substrates in which musical performance is predicated upon. Specifically, if individual singing necessitates greater reliance on neural correlates and cognitive processes that are increasingly impaired in persons with ADRD (e.g., prefrontal regulation of stress, cognitive control, executive processes, etc.), persons with greater disease burden may require greater neurological activation to effectively perform. Increased activation of neocortical structures would not only be indicative of perturbed proceduralization, but of potential compensatory mechanisms necessary to maintain functioning in increasingly impaired persons. In contrast, increased ease and social support associated with choral singing may foster greater reliance on relatively spared musical cognition and procedural memory pathways -- potentially homogenizing between-person patterns of neural activation and minimizing differences attributable to increased impairment. Given these hypothesized patterns, between-person differences in cortical recruitment patterns for individual performance may serve as novel and valuable predictors of cognitive function, particularly when supplemented with other gold-standard individual differences variables.

FC patterns identified within-persons may also serve as useful individual differences predictors. While largely exploratory as to whether FC patterns will differ between contexts, both conditions will likely necessitate broad bilateral connectivity in order to successfully perform. Given the noted declines in functional connectivity in persons with ADRD, alongside findings that increased functional connectivity may be inversely related to performance choking, it may be that increasingly impaired individuals demonstrate lessened functional connectivity relative to their healthier peers. Therefore, it is anticipated that less functional connectivity will

be indicative of greater cognitive impairment, regardless of the musical context, and serve as a valuable predictor in discriminant analyses.

Methods

Participants

Participants consisted of 13 persons with ADRD, aged 69-87 ($m = 76.7$, $sd = 4.8$; 54% male) who volunteered from the broader, ongoing Voices in Motion (VIM) social-cognitive choral intervention. VIM was approved by the University of Victoria Human Research Ethics Boards and was conducted in accordance with institutional guidelines. Participants re-consented prior to being admitted into this current fNIRS study, had sufficient opportunity to ask questions, and were permitted to opt-out at anytime without any consequences extending to their participation in the broader VIM project. A detailed account of the demographic and exclusionary criteria for VIM participants, as well as the testing battery and measurement burst design, can be found in McDowell et al. (2022). No additional exclusionary criteria were imposed in the current fNIRS investigation to prevent persons from volunteering in the study. Participants were not compensated for their involvement; however, individuals who participated or helped facilitate fNIRS data collection (including accompanying caregivers and choral volunteers) were provided free breakfast, lunch, and snack foods.

Procedure

Data for all participants were collected during a single day at the University of Victoria in a large lecture hall capable of comfortably housing all participants, their respective caregivers, and volunteers from the broader VIM project. Participants were tasked with singing in two separate contexts: a social context alongside their choral peers and in an individual context in which they performed alone with only piano accompaniment from the choir director. Half of the participants were tested in the morning while the other half were tested in the afternoon, such that participants did not have to perform or be present for the full day of data acquisition.

Whether participants performed in the morning or afternoon session was determined at random. Moreover, due to the size of VIM, the intervention was comprised of several smaller choral groups; thus, for the current study, participants evaluated in the choral context were done so alongside choristers from their corresponding VIM groups. Social and individual singing conditions were also counterbalanced between participants – such that the condition (social vs individual) a participant started with altered between each subsequent subject. Finally, in the breaks between social and individual data acquisition, all participants and volunteers who were not currently being evaluated were free to rest and eat in a separate room.

For participants initial setup, they were fitted with the fNIRS system, at which point researchers ensured adequate signal strength for each channel and used the Polhemus Fastrak digitizer system (Polhemus, Colchester, Vermont) to obtain 3-D digitized coordinates of both the participants head (corresponding to 10-20 system landmarks: Cz, Nz, Iz, Al, and Ar) and the fNIRS optode array. Participant's neural activity was then monitored during choral and individual singing conditions.

In the choral context, evaluated subjects were accompanied by a subset of their fellow participants, caregivers, and adult volunteers from the VIM project. Participants were seated to one side of the choir (to accommodate the fNIRS system) but were still naturally integrated and involved within the choral group. Under direction from the choral director, the entire choral group – including the evaluated participant - performed the song “I Love a Piano” -- a song which was part of the choir's well-trained repertoire. This song contains three natural blocks of ~60 second singing verses with 30 second instrumental rest periods, accommodating a block design commonly used in fNIRS studies, where manual inputs by the researcher could timestamp singing and listening conditions with the fNIRS system.

During the individual singing condition, the choir was instructed to move to a separate room where food and drinks were served while the participant was tasked with singing a medley of well-known nursery rhymes with piano accompaniment by the choir director. The medley comprised the songs “Twinkle, Twinkle, Little Star” “Baa, Baa, Black Sheep” and “ABCs (The alphabet song)”. This nursery rhyme medley was arranged to facilitate singing and listening blocks of 60 seconds and 30 seconds, respectively, to align with the natural segmentation of the social song.

Measures

Functional Near-Infrared Spectroscopy Recordings

fNIRS data were recorded using a continuous-wave TechEn CW6 system (TechEn Inc., Milford, Massachusetts) with a sampling frequency of 50 Hz (corresponding to one sampling image per 20ms). During both social and individual singing conditions, the fNIRS system recorded cortical hemodynamic responses that were time-locked to specific elements of the song, including the start, singing and instrumental (listening) periods, and end. Participants wore custom-built fNIRS headgear consisting of 36 channels which spanned the bilateral prefrontal cortex (PFC) and frontal-parietal cortices (Figure 1a). fNIRS data were collected at wavelengths of 690 nm and 830 nm to index deoxyhemoglobin (HbR) and oxyhemoglobin (HbO), respectively. The array was designed to evaluate broad frontal-parietal activity given the breadth of music cognition networks -- with specific relevance to the involvement of prefrontal and fronto-parietal networks of cognitive control, attentional regulation, stress and arousal, and other hypothesized cognitive constructs. The optical array was positioned relative to several 10-20 landmarks (i.e., Cz, Nz, Iz, Al, Ar) and 3-D coordinates of both person-specific scalp references, alongside optode locations, were obtained using a Polhemus Fastrak digitizer system (Polhemus,

Colchester, Vermont) to perform probabilistic spatial registration. To evaluate the extent and sensitivity of coverage facilitated by the fNIRS array, a sensitivity matrix was generated based on the Monte Carlo photon migration model (10^6 photons; Figure 1b). Following this procedure, Montreal Neurological Institute (MNI) coordinates were generated for the midpoint of each source-detector pair (i.e., channel), which were then converted to Brodmann's Areas (BA) using Talairach Client software to obtain microanatomical labels (Lancaster et al., 2000). From these conversions we established that the fNIRS array facilitated modest bilateral coverage of the PFC (with frontal channels spanning left to right dorsolateral PFC (BA46), anterior PFC (BA10)), and bilateral fronto-parietal cortices (encompassing primary motor (BA4), sensory (BA1), and premotor/supplementary motor cortices (BA6)).

Given the general involvement of frontal and parietal cortices in music cognition, this array does an adequate job of mapping the cortical surface, including regions of specific relevance to the current investigation.

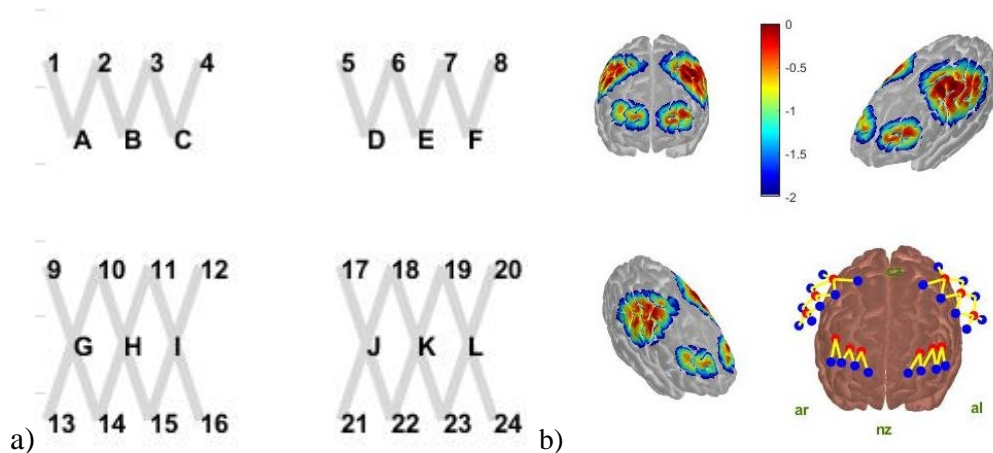


Figure 1. (a) A blank image of the fNIRS array depicting sources (letters), detectors (numbers), and their corresponding 36 channels. (b) A sensitivity profile based on the Monte Carlo photon migration model (10^6 photons) for the fNIRS array and corresponding probe projected over the cortex.

Preprocessing

Paired Sample T-tests

Preprocessing of fNIRS data was performed in MATLAB (2017b) using Homer2 software (Huppert et al., 2009; see Figure 2 for processing stream). First, raw fNIRS data was transformed into optical density values where motion was corrected for using a wavelet transformation algorithm described by Molavi & Dumont (2012) and incorporated in Homer2 as the *hmrMotionCorrectionWavelet* function. This wavelet filtering approach detects and corrects motion artifacts (MAs) channel-by-channel in a single step – decomposing the signal time-course of every channel as a series of wavelet coefficients characterized by a gaussian probability distribution, where physiological components are distributed around zero and MAs are identified as outliers. Specifically, wavelet coefficients that are outside a user-specified interquartile range are considered MAs and are set to 0 before reconstructing the signal with the inverse discrete wavelet transform. The current study used an interquartile range of 1.0 – a value previously evaluated as adequate for attenuating the influence of MAs in especially noisy datasets (e.g., Di Lorenzo et al., 2019) – which provided a version of our original fNIRS signal with MAs artifacts heavily reduced, as further confirmed by visual inspection. The decision to correct for MAs – including what methodology to use – was imperative in this study due to singing and musical performance likely facilitating larger fluctuations in fNIRS signal unrelated to the physiological mechanisms of interest. Additionally, to attenuate the influence of unwanted physiological information in the fNIRS signal (e.g., cardiac oscillations, respiration etc., Pinti et al., 2019), both high pass (0.01Hz) and low pass filters (0.1 Hz) were applied to the data. Optical density values were then converted to hemoglobin concentrations (HbO, HbR, and total hemoglobin (HbT)) by applying the modified Beer-Lambert law. Finally, the hemodynamic response

function (HRF) for HbO during singing segments within social and individual contexts was extracted for analysis using the HRF block average function within Homer2. The block average was computed in such a way to capture the peak HRF within singing segments – calculated as the average signal dynamics over a 22 second section from singing conditions. Given a 50 Hz sampling rate, this yielded 1100 samples per participant for each condition.

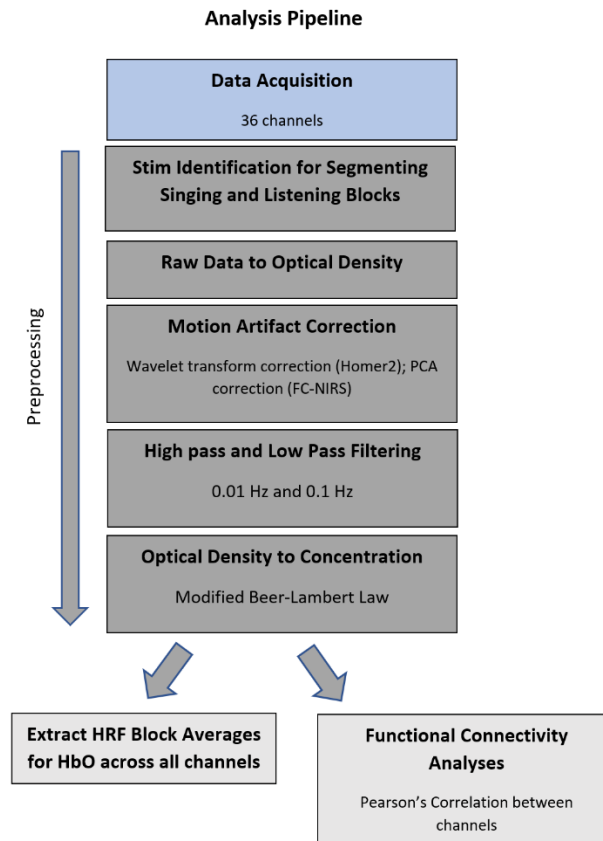


Figure 2. Pipeline of fNIRS data analysis. The outcome of the preprocessing approach resulted in data either being extracted via the Homer2 HRF block average function for paired sample t-test analysis or evaluated for channel-channel functional connectivity using Pearson's correlation coefficients computed via FC-NIRS software.

Functional Connectivity Analyses

Functional connectivity (FC) analyses were performed using FC-NIRS (Xu et al., 2015) – a software specifically designed to evaluate FC in fNIRS data. The preprocessing of fNIRS data

differed slightly from Homer2 preprocessing, given the different motion correction approaches available in FC-NIRS. Specifically, while equivalent high and low pass filters were applied to the data (0.01 Hz and 0.1 Hz, respectively), FC-NIRS provided both a spline interpolation and PCA driven approach for correcting MAs; this study leveraged the PFC method due to it providing greater attenuation of MAs in the fNIRS signal as confirmed by visual inspection. Further, a targeted PCA approach to motion correction has shown comparable effectiveness relative to the wavelet transform technique in correcting the influence of MAs (Di Lorenzo et al., 2019). Thus, the preprocessing of fNIRS data using FC-NIRS, while not identical to Homer2, was done to a comparable level of clarity as confirmed by visual inspection. After motion and physiological artifacts were removed, the preprocessed signal was converted into hemoglobin concentrations (HbO and HbR) using the modified Beer-Lambert law. The entire duration of participant performance, segmented by condition (i.e., choral vs individual performance) was utilized in the FC analyses to provide a wholistic index of FC patterns within both choral and individual performance. Further, FC was calculated on HbO only due to it showing a better signal-to-noise ratio (Pinti et al., 2019). Pearson's correlations were calculated between all channels, yielding a coefficient for each optode pairing in $C \times C$ matrices (36x36 channels; see Figure 3) for each condition and each participant. These global matrices were then extracted from MATLAB (2017b) and three average correlation coefficients were computed for fNIRS arrays corresponding to the prefrontal channels (i.e., PFC array), fronto-parietal channels (i.e., fronto-parietal array), and all channels. These averaged correlation coefficients were then used in subsequent paired sample and discriminant analyses.

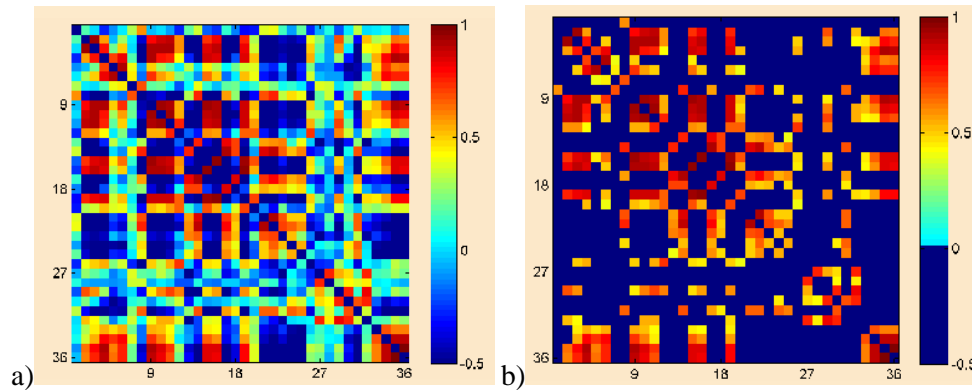


Figure 3. (a) Functional connectivity matrix for a random participant depicting channel-channel Pearson's correlations for all 36 channels during social performance. (b) Pearson's correlation matrix for random participant's social performance trial, trimmed at a threshold of Pearson's $r = 0.40$.

Cognitive and Behavioral Measures

In addition to neurological data, the planned DFA were contingent upon utilizing well-studied individual differences predictors. Specifically, this study leveraged participant data collected on the Mini-Mental State Examination (MMSE; Folstein et al., 1975), Trail Making Task A (TMTA; Lezak, 1995), Zarit Burden Interview (Zarit; Bedard et al., 2001), and Choice Reaction Time (CRT) variability tasks. These data were collected longitudinally as part of the broader VIM study; however, this study specifically made use of cross-sectional participant data taken from the closest assessment relative to the fNIRS data collection session.

Global Cognition

The MMSE is a well-validated tool and measure of global cognition for persons with dementia. The battery consists of verbally asking the participant questions about the world and orientation (e.g., what day is it? What street do you live on?) and assesses both memory and perceptual-motor skills. Participants received a score out of 30, with lower scores indicating

greater cognitive impairment. Performance in this sample indicated a mean MMSE score of 20.4 (SD = 6.4), with a range of 10 to 28.

Processing Speed

Trail Making Task A (TMTA) is a timed task measuring perceptual processing speed. The test consists of asking participants to draw a single line to connect 25 consecutive numbers without lifting pen from paper. Errors are corrected as needed and error time is included in total task completion time. In this study, TMTA is used as a putative measure of perceptual processing speed and a proxy for level of impaired cognition, with larger times indicating greater cognitive impairment. Cross-sectional scores on the TMTA have shown to provide valuable insights into between-person cognitive functioning (Sliwinski & Buschke, 1999). Descriptive statistics for this sample indicated a mean TMTA performance time of 117 (SD = 96.6) seconds, with a range of 32 to 347 seconds.

Caregiver Distress

The Zarit burden interview (Zarit) is a commonly used metric to index level of care partner distress. Research suggests that care partner distress may worsen with the increasing needs and impairment of the care recipient (e.g., Black et al., 2018; Rote et al., 2015). Therefore, in the context of the current study, Zarit scores were used as an indirect measure of care recipient impairment. Given that all VIM participants in this study were still living with their care partner, it is suspected that care partner distress may be a valuable variable in predicting level of impairment for their respective care recipients with ADRD. A score of 17 or more is considered high caregiver burden. Descriptive statistics for this sample indicated a mean Zarit score of 19 (SD = 18.5) with a range from 0 to 70, out of a total possible score of 88.

Cognitive Variability

Reaction time variability on a choice reaction time (CRT) task was also assessed. Participants were asked to respond to the color of a card (red or black) with either left or right key presses on a response box as quickly as possible as soon as a card appeared on a computer screen. Reaction time variability is increasingly being leveraged as a dissociable dimension of performance – relative to mean response time – that may better reflect changes and overall integrity of underlying physiological and cognitive processes (Hultsch et al., 2002; Dixon et al., 2007). Moreover, previous research has shown that within-person response time variability is a valuable individual differences predictor – sensitive to changes in cognitive status – with increased variability being most pronounced in subjects with more severe cognitive impairment (Strauss et al., 2007; MacDonald & Stawski, 2020). Variability in this study was indexed using residualized intraindividual standard deviation (ISD) estimates. For the full VIM population, residualized ISD estimates were computed across CRT trials for each session, across all sessions within each choral season, residualizing select confounds from the raw data by fitting a multilevel model to dissociate within- and between-sources of variation (MacDonald & Stawski, 2020). Removing these confounds yields variability estimates that are not conflated with mean age differences in response time or practice effects at the trial-to-trial level (Stawski et al., 2019; MacDonald & Stawski, 2020). The computed residualized ISD scores were then linearly transformed into standardized T scores ($M = 50$, $SD = 10$). This study leveraged ISD information from the most recent VIM assessment relative to fNIRS data collection.

Statistical Procedures

Cognitive Status Classification

Individuals were classified into a dichotomous grouping of either non-clinical impairment or clinical impairment based on their most recent MMSE scores relative to fNIRS data

collection. These dichotomous groupings served as the outcome variable to-be-predicted in our DFA. Specifically, to best characterize participants based on literature informed MMSE cut-points, individuals with an MMSE score greater than or equal to 23 were categorized as non-clinically impaired, whereas those with scores less than 23 were denoted as clinically impaired (see, Anthony et al., 1982; Kochhann et al., 2010). Using this criterion, we obtained final group sizes of 7 (clinical impairment) and 6 (non-clinical impairment).

Statistical Analyses

Paired Sample Analyses

Within-person, channel-specific HbO HRF plots were extracted for social and solo singing conditions using Homer2. IBM SPSS Statistics for Windows Version 23 (IBM Corp., 2015) was used to compile these data, compute channel-specific HRF means for each condition and participant, and subsequently evaluate within-person differences in cortical oxygenation between conditions via paired sample t-tests. Significantly identified channel pairings were then evaluated in a series of DFA to further probe their utility as potential individual differences predictors. All analyses were conducted at a standard two-tailed $p < 0.05$ significance level.

Functional Connectivity Analyses

FC analyses were performed using the FC-NIRS software (Xu et al., 2015). After preprocessing data, Pearson's correlation coefficients were computed for each channel pair, within persons, across the full duration of either choral or individual performance. Three average correlation coefficients were computed from these respective global matrices, indexing FC between the fNIRS frontal array, fronto-parietal array, and the whole fNIRS array. These global FC averages were subsequently evaluated via paired sample t-tests and used in DFA.

Discriminant Function Analysis

Significantly identified channels from paired sample analyses and FC variables were further explored via DFA using SPSS (IBM Corp., 2015). Planned comparisons included leveraging significant paired sample HRF data and all FC variables in a series of DFA, alongside a combination of gold-standard individual differences predictors, aimed at classifying participants into their respective cognitive impairment groups as proxied by score on the MMSE (i.e. clinical impairment versus non-clinical impairment). Specifically, each DFA comprised one biological predictor (corresponding to FC or HbO concentration data obtained from either the social or individual singing condition), one cognitive predictor (either TMTA or CRT variability data), and a social predictor (i.e., Zarit data). This multivariate structure investigates the combined predictive utility of multimodal individual differences predictors – including the novel neuroimaging data – for discriminating groups based on cognitive impairment severity.

Results

Participant demographic and behavioral information, categorized by cognitive impairment grouping, is displayed in Table 1.

Table 1. Descriptive statistics for demographic and behavioral data

<i>Variable</i>	<i>Clinical Impairment</i> <i>N=7</i>	<i>Non-Clinical Impairment</i> <i>N=6</i>
<i>Age (years)</i>	75.9 (4.9)	77.7 (5.1)
<i>Sex (% male)</i>	43	67
<i>Education (% Secondary)</i>	71	83.3
<i>MMSE score</i>	15.9 (5.0)	25.7 (2.6)
<i>^a TMT-A score (seconds)</i>	165.6 (119.8)	68.4 (22.8)
<i>^a Zarit</i>	26.43 (21.3)	10.3 (10.4)
<i>^b CRT Variability</i>	8.9 (1.7)	7.1 (2.9)

*Note. MMSE = Mini Mental State Examination (Folstein et al., 1975).
TMT-A = Trail Making Task A (Lezak, 1995). CRT = Choice Reaction Time.
^a Computed based on a sample of 12 due to missing data.
^b Computed on a sample of 10 due to missing data.*

Paired Sample Analyses Between Social and Individual Singing

Within-persons comparisons of cortical oxygenation between choral and individual singing were compared to elucidate recruitment differences that may be attributable to social context. While individual singing was broadly associated with increased activations relative to choral singing – with bilateral increases in both the frontal and fronto-parietal fNIRS channels - only one channel yielded significant differences between conditions. Specifically, the frontal channel covering the right anterior PFC (BA10) showed a significant difference in activation between choral and individual singing, with individual singing showcasing increased HbO concentrations relative to choral singing, $t(12) = -2.36, p = 0.036$. No further significant differences were observed despite 22 of the remaining 35 channels showcasing greater activation during individual versus choral singing (all $ps > 0.05$).

Functional Connectivity Analyses

FC was proxied via Pearson's correlation coefficients, which were computed between frontal, fronto-parietal, and whole fNIRS array channels. The average FC for each of these regions was computed, for each condition, at the group level (Table 2). As is noted in Table 2, FC appeared to be most pronounced across the frontal array regardless of performance condition, and FC was slightly increased in individual relative to choral conditions for all FC measures. However, paired sample t-tests noted no significant differences in FC facilitated by changes in the performance context ($p > 0.05$).

Table 2. Functional connectivity means, standard deviations, and ranges for each condition conducted at the group level for the frontal array, parietal array, and whole fNIRS array.

	Range Pearson's r	Average Pearson's r (SD)
Frontal Array FC: Individual	.29-.92	.47 (.21)
Frontal Array FC: Choral	.22-.84	.44 (.18)
Parietal Array FC: Individual	.01-.62	.30 (.20)
Parietal Array FC: Choral	.08-.71	.28 (.19)
Whole Array FC: Individual	.05-.65	.31 (.20)
Whole Array FC: Choral	.10-.72	.30 (.18)

Discriminant Function Analyses

Except for the MMSE, one participant did not complete any cognitive data and were excluded from the subsequent analyses, leaving a final sample of 12 (N = 6 clinical impairment, N = 6 non-clinical impairment) for DFA. Further, two participants did not have data for the CRT variability measure and were thus excluded from such models. This left a final sample size of 10 participants for all models containing CRT variability (N= 5 clinical impairment, N= 5 non-clinical impairment).

DFA were run to further investigate the utility of fNIRS signal as an individual difference's predictor. Specifically, a combination of gold-standard individual differences

predictors in both cognitive (i.e., TMTA, CRT variability) and social (i.e., Zarit) domains were utilized, in tandem with the unique neurological data captured via fNIRS (i.e., FC and HRF data), to provide a novel multivariate evaluation of whether a linear combination of these measures could accurately discriminate participants based on their cognitive impairment status (i.e., clinically impaired vs non-clinically impaired). Using the significantly identified data from the paired sample HRF analyses, four models were run using a combination of the neurological, cognitive, and social predictors. Specifically, person-level mean HbO concentrations during both choral and individual singing were run in a series of models consisting of either TMTA and Zarit or CRT variability and Zarit. Furthermore, FC measures were also evaluated using DFA, where prefrontal, fronto-parietal, and whole fNIRS array FC were run in six separate models alongside a combination of either TMTA and Zarit or CRT variability and Zarit. None of these models yielded significant discriminative ability and, thus, their corresponding structural coefficients and accuracies are not reported (Wilk's $p > 0.05$).

Discussion

While neuroscience has provided invaluable insights into the mechanisms of music cognition and musical sparing in persons with ADRD, comparably little work has investigated the neural correlates of music interventions within this population. Given the documented psychosocial and cognitive benefits of music interventions for persons with ADRD, it is imperative to explore these benefits using neuroscientific methodology. Specifically, evaluating the distinction between neural correlates implicated in group intervention performance, relative to individual performance, may help elucidate some of the neurological mechanisms behind the benefits associated with different intervention contexts and why, for persons with ADRD, some contexts may be more advantageous than others. The current thesis attempted to address this question by exploring whether within-person differences in cortical activation (proxied via fNIRS) could be identified between choral and individual singing, and whether broad FC differences exist between choral and individual performance. Further, DFA were used to explore whether a linear combination of social (i.e., Zarit), cognitive (i.e., TMTA and CRT variability), and neurological data (i.e., HRF and FC) could accurately classify individuals based on their level of cognitive impairment. Such models were motivated by an interest in further evaluating the extent to which potential differences in neurological activity – when supplemented by other individual differences predictors - are indicative of between-person differences in cognitive impairment severity.

Within-Person Differences in Activation and FC in Choral vs Individual Performance

Individual singing was associated with broad, bilateral increases in frontal-parietal activation relative to choral singing, with one fNIRS channel yielding significant differences between contexts - corresponding to the right anterior PFC (BA10). Specifically, individual

singing was associated with significantly greater recruitment of the right anterior PFC relative to choral singing. Moreover, while nonsignificant, nine of the remaining eleven frontal channels, and seventeen of the twenty-four fronto-parietal channels, displayed patterns of increased cortical recruitment in individual relative to choral performance. This modest pattern of results provides preliminary evidence supporting *a priori* expectations that individual singing may place greater demands on frontal-parietal cortices relative to group singing. Specifically, broad increases in neocortical activation may be indicative of the increased cognitive (e.g., cognitive control, inhibition, attentional regulation) and psychosocial (e.g., performance anxiety) demands necessitated by individual singing. The reduced activations found broadly in choral singing are also interpretable within the context of the broader literature, as the anxiolytic qualities of group performance (e.g., Schladt et al., 2017) may have facilitated both increasingly efficient reliance on procedural networks (i.e., less frontal activation) and less cognitively demanding processes.

Further, while investigations of FC failed to exhibit significant differences between social and individual singing, each of the FC metrics showcased increased connectivity in individual relative to social performance. While this observation may be inconsistent with some FC patterns identified within social/music neuroscience suggesting that cooperative experience may increase FC (e.g., Czeszumski et al., 2022; Osaka et al., 2014, 2015), the pattern obtained in this study is consistent with previous literature investigating the fronto-parietal network (FPN) -- which plays a central role in a variety of cognitive tasks including working memory, attention, and shifting (Chenot et al., 2021; Niendam et al., 2012). Specifically, the FPN is a network of high connectivity that increases in FC commensurate with increased task novelty and demands on cognitive control (Cole & Schneider, 2007; Cole et al., 2012). Thus, scaffolding on the hypothesis that the increases in cortical oxygenation pursuant to individual singing are due to

increases in task demands, patterns of increased FC in individual singing may be related to an increase in task novelty and greater reliance on cognitive control networks. However, as the FC data yielded no significant differences, future research is recommended to investigate whether these nonsignificant patterns could surpass statistical significance in a larger sample size with greater statistical power.

Although the majority of the planned analyses did not reach statistical significance, the cumulative patterns – including the identified significant paired sample result – suggest that individual singing necessitates broadly increased frontal-parietal activation in persons with ADRD. Furthermore, these patterns can also be interpreted in the inverse, where group performance may have provided a context that eased the relative involvement of neocortical structures, potentially facilitating greater recruitment of procedural systems previously identified in neuroimaging work (e.g., Kassubek et al., 2001; Ono et al., 2015; Poldrack et al., 1999; 2005). In either of these interpretations, this research points towards a potential neurological correlate regarding the benefits of group-based music interventions for persons with ADRD. Specifically, that the cognitive (e.g., alleviation of comorbidities) and social (e.g., increasing social engagement and arousal) benefits of group music interventions may be further described by changes in neocortical activation patterns. That is, by capitalizing on the neurological strengths of persons with ADRD (e.g., relatively spared procedural memory), and avoiding excessive involvement of the regions and cognitive processes that are more frequently and progressively impaired (e.g., executive processes, cognitive control), group contexts facilitated more efficient and reduced demands on cognition in a population with increasingly limited cognitive resources.

Discriminant Function Analyses

If individual singing is associated with increased activation of neural architecture and cognitive processes that are progressively impaired in persons with ADRD, the extent of within-person neural activation in individual, or even social singing, may hold unique value as both a within- and between-person predictor of cognitive health. For example, individuals with greater cognitive impairment may necessitate greater activation within individual singing contexts to accurately perform the task. Moreover, due to the increasing impairments of dementia-related declines on FC, patterns of FC may also be valuable individual differences predictors yielding unique information about an individual's level of cognitive health. Given the small sample size, and the novelty of this fNIRS signal, we decided to leverage a multivariate approach to compare the relative predictivity of fNIRS data (including both FC and significant HRF data), alongside other gold-standard individual differences predictors, in a series of DFA attempting to classify participants based on level of cognitive impairment. Further, in dichotomizing participants based on clinical cut-points of MMSE data (i.e., clinically impaired versus non-clinically impaired) we facilitated an extreme-groups comparison whereby largely disparate groups were evaluated within the same analytic model (see Table 1) – bolstering an ability to detect significant functions classifying groups.

Despite efforts to leverage fNIRS signals as individual differences predictors in a series of DFA, none of the models were significant. Nevertheless, this represents an initial step in which future studies, with increased sample sizes and statistical power, may be better structured to evaluate between-person comparisons. Given the tentative promise of this thesis' within-person analyses, and previous research highlighting the utility of different operationalizations of the fNIRS signal as individual differences predictors (e.g., Halliday et al., 2017), between-person comparisons would facilitate a more direct investigation of the potential mechanisms underlying

the differential impact that dementia severity has on the neural correlates of music cognition within intervention contexts.

Implications and Future Directions

This study provided a preliminary investigation of a novel paradigm within the music neuroscience literature; specifically, investigating the neural correlates of singing and music cognition in persons with ADRD across social (i.e., choral) and individual performance contexts. This is the first study to investigate the neurological correlates of persons with ADRD under the context of a music intervention. The lack of research in this domain is due, in part, to the difficulty of using existing neuroimaging modalities to capture the neural correlates of music cognition during performance. Thus, this thesis leveraged the advantages of fNIRS to investigate the cortical correlates, and FC, of singing during both choral and individual contexts in persons with ADRD. In doing so, despite modest results, this study highlights the advantages of using fNIRS in increasingly nuanced designs, with increasingly varied populations, and demonstrated preliminary evidence that individual singing may be associated with increased cortical activation and FC patterns relative to social performance. This pattern may highlight a neurological advantage of group music interventions for persons with ADRD. Namely, the mitigation of fronto-parietal recruitment may be associated with a reduced dependency on more cognitively demanding processes (e.g., executive functioning and cognitive control, modulation of psychological stress) which are known to become increasingly impaired in persons with dementia. Given the promise of these findings, a key implication of this research is to stimulate increased utilization of neuroscientific modalities to investigate how music interventions confer social-cognitive and neurological benefits to persons with ADRD.

Demonstrating the utility of neuroscientific investigations for persons with ADRD in intervention contexts has several implications for the health and well-being of performers, caregivers, and the healthcare system at large. In better understanding how musical context

modulates neurological recruitment strategies for persons with ADRD, intervention programs can leverage this information to provide a more comfortable and accessible environment tailored towards the neurological competencies of their target population. Further, by providing increasing evidence of the value and benefits of music interventions, and informing adaptations that can potentially improve their effectiveness, these non-pharmaceutical interventions can continue growing as a viable treatment option for persons with ADRD. The benefits of such nonpharmacological interventions extend beyond the immediate performers, as the improvements in quality of life and mood of persons with ADRD may confer advantages to their caregivers, and the relative inexpensiveness of these interventions provides a cheaper alternative – or supplement – to pharmaceutical treatments. Moreover, given the evidence of group-based interventions slowing cognitive and behavioral declines in persons with ADRD, they provide considerable healthcare savings by delaying the transition of persons with ADRD to subsequent levels of long-term care. By increasing the amount of innovative research aimed at better understanding why these interventions are beneficial, and how they can improve, persons with ADRD and healthcare collaboratives can be increasingly assured of the utility that group-based music programs have as an effective non-pharmaceutical intervention option.

For these implications to be realized, several avenues of future research need to be explored. Primarily, there is a need to replicate and extend upon this study's design with a larger sample. Increased statistical power would help elucidate whether the currently identified within-person patterns of cortical activity are robust while also bolstering the viability of between-person comparisons; the latter of which would help to identify whether differences in neural correlates between intervention contexts (e.g., group versus individual) are associated with different levels of dementia-related impairment. If such patterns are identified, not only would

this be suggestive of potential neurological mechanisms underlying the cognitive-behavioral benefits of music interventions, but it would also help to inform and structure intervention approaches in a way that better accommodates participants neurological strengths.

Future research using fNIRS in musical contexts may also look towards evaluating the neural correlates of music cognition in persons with ADRD across repeated assessments. Such longitudinal, repeated measures designs would increase statistical power and allow researchers to evaluate the cortical correlates of musical training in addition to how within-person changes in cognitive function – pursuant to the progressive impairments of dementia pathology – modulate the neural correlates of music cognition. Further, while the current research project is primarily concerned with populations of ADRD, this thesis highlights the ability for fNIRS to be utilized in increasingly novel musical paradigms – where the neural correlates of music cognition, both during and across musical performance conditions, can be evaluated in a larger diversity of populations. Specifically, there would be value in using fNIRS to expand upon the neurobiological work done by Keeler et al. (2015) and Schladt et al. (2017), who discussed how differences in improvised versus pre-composed singing and in group versus individual singing modulated neuropeptides related to social bonding, stress, and positive social experiences (i.e., OXT, CORT, ACTH). It would be valuable to explore whether these contexts also modulated patterns of cortical activation, or FC, using fNIRS in healthy populations.

Moreover, while this study utilized two operationalizations of the fNIRS signal (i.e., hemodynamic response function (HRF) and FC), there is potentially valuable information in other elements of the BOLD response. Specifically, variability in neural activity proxied by fNIRS has been previously identified as a significant individual differences predictor of performance in standard cognitive control tasks (i.e., MSIT; Halliday et al., 2017). Thus, there is

value in exploring patterns of neural variability during musical performance and how they relate to within- and between-person functioning. Additionally, while this study evaluated FC by computing averaged Pearson's correlation coefficients – which characterizes a linear relationship between two signals by evaluating their covariances standardized by standard deviation – additional operationalizations of FC can account for different sources of information and may yield differential predictions. Specifically, future research on this dataset, or on evaluating intra-brain connectivity for persons with ADRD more generally, may wish to utilize other FC measures; including Spearman rank correlations, which characterizes non-linear relationships between signals, or wavelet transform coherence, which evaluates a localized correlation coefficient in time frequency space. While this latter approach specifically considers both time and phase-locked oscillations of the fNIRS signal, either approach would facilitate slightly different operationalizations of FC which may be of future interest. To be sure, using Pearson's correlations has proved a robust method for evaluating FC in fNIRS data (Chenot et al., 2021; Hennrich et al., 2015), but exploring these other metrics may better suit different research objectives and help contribute to the relative lack of FC studies using fNIRS data. The evaluation of FC during task states for persons with ADRD (especially during musical performance) is also a novel application of FC analysis – where a preponderance of research is concerned with resting-state FC; as such, this phenomenon should be explored using different FC approaches.

Lastly, concerning the existing dataset, future research would benefit from evaluating how different preprocessing approaches affect the patterns of FC and HRF. It is important to re-emphasize the novelty of this design and the potential problems it poses on data acquisition. Specifically, the prospect of singing during musical performance will necessarily evoke individual differences both in movement of the head, face, and body. In such a circumstance,

where motion is not only a salient concern but also manifests differently between participants, using a uniform preprocessing stream may lead to inconsistencies in artifact correction between persons and condition. Specifically, due to a user-specified interquartile range parameter in the wavelet filtering function, while all wavelet coefficients and MAs are parameterized around a condition-specific gaussian distribution, this inter-quartile value may not best reflect all person's data. To be sure, while previous research has detailed that using a consistent preprocessing approach is ideal, and that using motion correction approaches – especially wavelet filtering – is consistently superior to trial rejection techniques (e.g., Cooper et al., 2012; Selb et al., 2015), it is likely worthwhile to pursue a combination of both MA correction and rejection techniques given some equivocal results within the fNIRS literature using especially noisy data. For example, in a recent preprocessing comparison between motion correction versus rejection techniques for infant fNIRS data – where MAs are frequently problematic – Gemingnani & Gervain (2021) observed that, while artifact correction techniques (e.g., wavelet filtering) retained larger amounts of data, they also attenuated the HRF amplitude. Artifact rejection techniques, however, while resulting in a higher exclusion rate, more faithfully preserved the characteristics of the HRF. Thus, a combination of motion correction methods (e.g., wavelet filtering, spline interpolation), combined with person-to-person MA rejection based on the largest spike-like motion artifacts would be a useful consideration for continued use with this dataset. Person-to-person artifact correction may be a suboptimal strategy for most designs due to lacking a uniform motion correction criterion, but it is important to note that all fNIRS preprocessing contains a level of subjectivity. What is more important than rule-of-thumb preprocessing decisions is in ensuring overall data completeness and clarity for each subject. Thus, while the preprocessing options utilized in the current study were based upon literature-recommended criteria, which was

further informed by visual inspection of the current data, it is valuable to pursue a combination of both motion correction and trial rejection approaches – so long as they are justified and specified prior to viewing results. Specifically, if a wavelet filtering approach significantly attenuates the HRF signal, in a dataset with a smaller sample size this may have affected our ability to detect significant differences in neural activation between conditions.

Strengths and Limitations

This thesis represents an innovative study in which the paradigm and research questions are novel contributions to the music neuroscience and music intervention literature. Notably, this is the first study to investigate the neural correlates of singing in persons with ADRD, leveraging the advantages of fNIRS to explore how these correlates are modulated by changes in musical performance context. This innovative application of fNIRS provides further evidence of its strengths and flexibility as a neuroimaging modality, with the hopes that more researchers will be compelled to utilize these strengths to investigate both novel and well-documented phenomena in increasingly diverse contexts and populations. Specifically, research investigating the potential neurological mechanisms underpinning the benefits of music interventions for persons with ADRD are lacking relative to the research focused on exploring cognitive and social benefits. There is a clear need to continue researching the neurological correlates of different styles of music interventions as doing so will help better understand and augment them to optimally serve their target populations.

To be sure, this study is not without its limitations. The most critical concern pertains to sample size and statistical power. While the within-person comparisons were better structured to accommodate more modest sample sizes, this sample is still notably small. This concern is especially relevant for the between-persons comparisons using DFA. While this study attempted

to leverage the benefits of an extreme-groups comparison - where individuals of disparate cognitive capacities were evaluated in the same analytical model (i.e., clinically impaired vs non-clinically impaired) - and utilized a multivariate approach relative to running univariate ANOVAs on the target variables of interest, drawing firm conclusions from these between-person results would be imprudent considering our sample size. However, given this study was conducted on a cohort of volunteer persons with ADRD involved in an ongoing music intervention, a larger sample could not be achieved at time of testing – nevertheless, it is certainly a possibility for future research. The novelty of this paradigm, and the merits of this study, are worth disseminating despite the notable small sample size concerns. Notably, despite a small sample size, this study both identified a significant paired-sample result and observed consistent neurological trends in the expected directions based on previous research; thus, there is good precedent to conduct a follow up on this research with a larger sample.

This study also chose to adopt a loose contrast where the performed song differed between social and individual contexts – a decision informed by our small sample to maximize potential detectable differences. However, differences in musical material, while holding all other variables constant, may facilitate disparate activation patterns unrelated to the phenomena of interest. Notwithstanding, we utilized a block design that is consistent with a vast majority of existing fNIRS research recommendations (Yücel et al., 2021) and time-locked the singing and listening blocks between songs in each condition. Furthermore, the songs performed by participants were both well-known, reducing the potential influence that material novelty or difficulty might have in terms of evoking differential neural recruitment. Nevertheless, changes in musical stimuli may present an extraneous influence on within-person patterns of cortical activations, and studies with larger sample sizes could adopt a tighter contrast between

conditions to provide a more thorough investigation of the differences evoked from changes in environmental context.

Conclusion

The neurological correlates underlying the advantages of music interventions for persons with ADRD are largely unknown and under-researched. Using the advantages of fNIRS, this study provided a preliminary investigation of the neural correlates and FC patterns associated with musical performance in both choral and individual contexts for persons with ADRD. Significant differences in cerebral oxygenation were identified in the right anterior PFC (BA10) corresponding to one channel of the fNIRS frontal array; specifically, individual singing was associated with significantly greater cortical oxygenation relative to social singing. Moreover, individual singing was associated with (non-significant) broad bilateral increases in cortical oxygenation across the majority of fNIRS channels, and increased FC, relative to choral singing. In sum, though modest, these findings yield tentative support for the notion that individual singing may necessitate greater neocortical recruitment for persons with ADRD, and potentially increased FC, which is consistent with a body of literature that details how increased stress and utilization of higher-order cognitive processes likely accompany individual performance. However, these results need to be re-evaluated with a larger sample to clarify their robustness and replicability. Notwithstanding, this is the first study to investigate differences in music cognition correlates across environmental contexts for persons with ADRD and, should these patterns be replicable, may provide preliminary neurological evidence underscoring potential advantages of group music interventions for persons with ADRD. Namely, group singing environments foster a reduced and more efficient recruitment of cognitive resources relative to individual singing, reducing demand on increasingly impaired neocortical systems for persons with ADRD. In doing so, group contexts may provide a more accessible and enjoyable environment from which persons with ADRD can extract cognitive and behavioral benefits.

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