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Neural Markers of Musical Memory in Young and Older Adults

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Abstract

Memory for music can be preserved in the presence of neurodegenerative disorders even when other memories are forgotten. However, understanding how the brain remembers music has proven difficult despite decades of research. The central goal of this thesis was to elucidate the neural correlates of musical memory by exploring how the presence of language and music information affect the way young and older adults remember music. To that end, I 1) used a controlled training paradigm to familiarize participants with novel stimuli that manipulated the presence of language and music, and 2) collected functional magnetic resonance imaging data to compare brain activity in response to stimuli that were identical except for their level of familiarity. First, I compared differences in neural activation based on familiarity in young adults using general linear model (GLM) and multivariate pattern analyses (Chapter 2). Contrary to the results of previous studies, there were no differences in the areas involved in processing novel and familiar music. Next, I used an intersubject synchrony analysis to assess the effect of familiarity on neural synchrony (Chapters 3 and 5). Synchrony is a new technique in the musical memory literature that correlates neural activation timecourses to a stimulus across individuals. Familiarity reduced synchrony in both young and older adults. Synchrony reduction is associated with increased idiosyncratic processing across participants. This reduction occurred after a single listen suggesting that each participant had a unique experience of the stimuli after only a single exposure. Finally, I used GLM and synchrony analyses together to characterize how musical stimuli with and without language are processed by healthy young and older adults (Chapter 4). Brain areas involved in processing music and language stimuli differed based on age group and stimuli, but in both groups language information induced more synchrony than stimuli without language. Altogether, these results suggest that 1) similarities in stimulus processing across individuals are directly related to the presence of language, and 2) the lack of clearly defined neural correlates of musical memory across previous studies may stem from the idiosyncrasies in processing that arise as individuals become familiar with musical stimuli.

Keywords: Musical memory, language, aging, fMRI, intersubject synchrony

Summary for the Lay Audience

Memory for music is unique in that it may be preserved in the presence of disorders such as dementia even when other memories are forgotten. However, the processes involved in musical memory are not completely understood. In this thesis, I aimed to gain a deeper understanding of how the brain stores musical memories. Specifically, I was interested in how the presence of language affects the way the brain remembers music and whether the mechanisms are similar in young and older adults. To that end, novel musical stimuli with and without language were used in these studies. Participants repeatedly listened to the novel stimuli to become familiar with the music. I used functional magnetic resonance imaging to collect brain activity data while young and older adults listened to the novel and familiar music. I then compared how brain activity changed when listening to identical pieces of music that differed only in their level of familiarity. A variety of analyses were used to investigate the brain areas involved in processing the novel and familiar music as well as the patterns of the fluctuations of the neural activation within those brain areas. Specifically, I characterized the similarity in the patterns of activation in response to the music across participants. The primary findings of this thesis were: 1) in contrast with previous studies, there were no differences in the brain areas involved in processing novel and familiar stimuli in young adults, 2) novel stimuli were processed more similarly than were familiar stimuli by both young and older adults, and 3) music with language was processed more similarly than music without language by participants in both age groups. Overall, the findings of this thesis contribute to the literature on musical memory by expanding existing knowledge on how young and older adults process novel and familiar music. Understanding how the brain processes music has potential implications for the development of therapeutic and clinical interventions that could improve the quality of life for individuals living with dementia.

Co-Authorship Statement

Chapter 2
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This paper has been published in the *Journal for Cognitive Neuroscience*. I designed the experiments alongside L. M. McGarry. I collected all of the data, performed the analyses, created the figures and tables, and wrote the manuscript. Dr. J. A. Grahn, and Dr. A. M. Owen provided assistance with experimental design, consultation on the analyses, and editing of the manuscript and revisions prior to publication.

Chapter 3
The effect of repetition on intersubject synchrony.

I designed the experiments alongside L. M. McGarry. I collected all of the data, performed the analyses, created the figures and tables, and wrote the manuscript. Dr. B. Stojanoski assisted with the analyses of the data. Dr. J. A. Grahn, and Dr. A. M. Owen provided assistance with experimental design, consultation on the analyses, and editing of the manuscript.

Chapter 4
The effects of language and age on intersubject synchrony.

I designed the experiments alongside L. M. McGarry. I collected all of the data, performed the analyses, created the figures and tables, and wrote the manuscript. Dr. J. A. Grahn, and Dr. A. M. Owen provided assistance with experimental design, consultation on the analyses, and editing of the manuscript.

Chapter 5
The effects of long-term familiarity on intersubject synchrony in older adults

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List of Abbreviations

AD	Alzheimer's disease
BOLD	Blood-oxygen-level dependent
EEG	Electroencephalography
ERP	Event-related potential
fMRI	Functional magnetic resonance imaging
GLM	General linear model
GSR	Galvanic skin response
IFG	Inferior frontal gyrus
MEG	Magnetoencephalography
SART	Sustained attention response task
SFG	Superior frontal gyrus
STG	Superior temporal gyrus

1 Introduction

Have you ever been driving when a song comes on the radio that you have not heard in 20 years and, much to your surprise, you can sing along with every lyric? Do you still know all the words to your favourite song from high school? These are just some examples of the robust nature of musical memory. Memory for music is also unique in that it seems to be preserved in some aging patients with dementia even when other semantic memories have been forgotten (Baird & Samson, 2009; Jacobsen et al., 2015). However, characterizing the neural substrates of musical memory has yielded mixed results despite numerous studies on the topic. Across 10 studies, 37 different brain areas in frontal, temporal and subcortical regions have been identified as involved in musical memory with, at most, four studies identifying the same region (see Table 1; Freitas et al., 2018). The recognition of familiar music may rely on a fronto-temporal network (Agustus et al., 2018; Groussard et al., 2009; Halpern & Zatorre, 1999; Herholz et al., 2012; Jacobsen et al., 2015; Plailly et al., 2007; Sikka et al., 2015; Slattery et al., 2019) along with supplementary motor areas (Agustus et al., 2018; Herholz et al., 2012; Pereira et al., 2011; Peretz et al., 2009; Slattery et al., 2019) and basal ganglia structures (Agustus et al., 2018; Pereira et al., 2011; Sikka et al., 2015). Musical memory researchers have employed a variety of experimental paradigms and musical stimuli in their attempts to identify these networks. As a result of the inconsistencies in experimental design across studies, there is little agreement about the network of areas necessary for musical memory.

In this thesis I aim to elucidate the neural correlates of musical memory. In the introduction I will identify and discuss how aspects of the experimental design of previous musical memory studies lack consistency. I will explain why consistency across musical memory studies is important and the clinical implications for the results from more highly controlled studies. I will describe important factors for building a solid understanding of the neural processes involved in musical memory for healthy adult participants before clinical applications

can be pursued. Previous studies have used traditional fMRI general linear model (GLM) approaches to identify musical networks. I will present why the use of intersubject synchrony analyses approaches the question of musical memory function in a novel way that capitalizes on the use of naturalistic stimuli like music. Finally, I will describe how this thesis aims to address the identified gaps and the expected results given the overview of the supporting literature.

Inconsistencies in existing research on musical memory

The inconsistencies in the brain areas identified as being involved in musical memory may be shaped by variable definitions of what constitutes familiarity with music. In some studies, musical memory is investigated by comparing unknown music to well-known music drawn from multiple genres, like folksongs (e.g., Alonso et al., 2016; Herholz et al., 2012; Saito et al., 2012; Schaal et al., 2015), popular music from the radio (e.g., Jacobsen et al., 2015; Pereira et al., 2011), or classical music excerpts (e.g., Agustus et al., 2018; Groussard et al., 2010). Participants are asked to rate their familiarity with the stimuli, but generally only one genre of well-known stimuli is used (i.e., folksongs or popular music). The difficulty in relying on only one genre of familiar music is that the stimulus genre may be confounded with the level of familiarity. For instance, a folksong learned in childhood may be much more familiar than a popular song released in the last year. Without direct comparisons between different types of familiar music it is difficult to know whether individuals are equally familiar with the stimuli used across different studies. In studies where brain activity is not compared between novel and familiar music, training and retrieval paradigms are used (Altenmüller et al., 2014; Klostermann et al., 2009; Nan et al., 2008). Participants learn short stimuli (musical excerpts or a series of computer-generated tones) during a training phase and perform an old versus new task to identify which stimuli were previously heard. However, long-term musical memory acquired over years of knowing a song is different from the short-term memory acquired within a single lab session (Ménard & Belleville, 2009). For example, short term memory for music has a much smaller capacity (approximately 10 notes long) than long-term memory (entire songs; Berz, 1995). These two memory systems may rely on different neural networks (Izquierdo et al., 1999) and studies investigating musical memory that do not differentiate between these two types of memory may be contributing to the inconsistencies in the literature. A consistent operational definition of familiarity is needed for clearer identification of the neural correlates of musical memory across studies.

Table 1. From Freitas et al, 2018: This table describes the identified anatomical regions and their activation likelihood estimate (ALE) for contrasts comparing familiar minus unfamiliar music across 10 studies investigating musical memory.

Cluster #	Volume (mm3)	ALE value	MNI			Side	Anatomical Region	BA	# of studies contributing to cluster
			x	*y*	*z*				
1	968	0.017	2	10	54	Left	Superior frontal gyrus	6	4/10
2	576	0.015	−10	−10	8	Left	Thalamus (ventral lateral nucleus)	–	3/10
3	440	0.015	0	0	64	Left	Medial surface of the superior frontal gyrus	6	2/10
4	424	0.012	−52	10	14	Left	Inferior frontal gyrus	44	3/10
5	352	0.014	−30	18	6	Left	Claustrum		2/10
6	336	0.012	−52	−42	24	Left	Superior temporal lobe	13	2/10
7	312	0.014	4	12	40	Right	Cingulate gyrus	32	2/10
8	280	0.013	−20	8	−12	Left	Lentiform nucleus. Putamen		2/10
9	280	0.013	50	−8	42	Right	Precentral Gyrus	4	2/10
10	256	0.012	−54	−22	−12	Left	Middle temporal gyrus	21	2/10
11	200	0.012	−4	58	2	Left	Medial frontal Gyrus	10	2/10
12	200	0.012	54	26	32	Right	Middle frontal gyrus	9	2/10
13	192	0.011	8	−26	−2	Right	Thalamus		2/10
14	176	0.011	−32	10	56	Left	Middle frontal gyrus	6	2/10
15	128	0.011	30	−18	−2	Right	Lentiform nucleus.		1/10
16	96	0.010	−42	22	4	Left	Insula	13	1/10
17	64	0.009	22	8	4	Right	Lentiform nucleus		1/10
18	64	0.010	36	42	24	Right	Middle frontal gyrus	9	1/10
19	64	0.009	−26	48	22	Left	Superior frontal gyrus	10	1/10
20	48	0.009	−10	−18	−10	Left	Subthalamic nucleus		1/10
21	40	0.009	−8	12	38	Left	Cingulate Gyrus	32	1/10
22	32	0.008	56	−6	−6	Right	Superior temporal gyrus	22	1/10
23	32	0.008	−32	−14	−4	Left	Lentiform nucleus		1/10
24	32	0.008	10	−8	4	Right	Thalamus		1/10
25	32	0.009	46	20	24	Right	Middle frontal gyrus	9	1/10
26	32	0.008	−50	−6	46	Left	Precentral gyrus	4	1/10
27	16	0.008	40	16	−16	Right	Extra-nuclear	13	1/10
28	16	0.009	−24	26	−8	Left	Claustrum		1/10
29	16	0.009	−4	−24	2	Left	Thalamus		1/10
30	16	0.009	−46	6	4	Left	Precentral gyrus	44	1/10
31	16	0.009	−22	6	4	Left	Lentiform nucleus		1/10
32	16	0.008	−46	26	6	Left	Inferior frontal gyrus	13	None
33	16	0.009	65	−34	14	Right	Superior temporal gyrus	42	1/10
34	16	0.009	−42	6	24	Left	Precentral gyrus	6	1/10
35	16	0.009	52	2	50	Right	Precentral gyrus	6	1/10
36	16	0.009	−44	−4	56	Left	Precentral gyrus	6	1/10
37	8	0.009	−22	52	22	Left	Superior frontal gyrus	10	None

ALE values for contrast 1. ALE values refer to the likelihood of obtaining activation evoked by listening to familiar music stimuli in a given voxel of the standard template MRI. Coordinates are in the MNI space. Cluster #,The clusters are ranked according to their size in millimeters cubed (mm3). BA, Brodmann area; x, medial-lateral; y, anterior posterior; z, superior-inferior.

Although musical memory is the topic of interest here, the presence or absence of lyrics (the words associated with music) may play a role in the discrepancies in the identified neural correlates of musical memory described above. Over the past twenty years, researchers have used computer generated music (e.g., Agustus et al., 2018; Slattery et al., 2019), unmodified pop- or rock-song excerpts with complex instrumentation and lyrics (e.g., El Haj et al., 2012; Jacobsen et al., 2015; Pereira et al., 2011), instrumental music excerpts with multiple instruments but without lyrics (e.g, Halpern & Zatorre, 1999; Sikka et al., 2015), and simple tonal melodies

played by a single instrument or single sung voice (e.g., Platel, 2005; Schaal et al., 2015). The reliance on musical stimuli with and without language makes it difficult to determine the role that language plays in musical memory. Although music and language are closely related, there is discussion in the literature regarding whether they rely on overlapping or distinct neural networks (Patel, 2011; Peretz & Coltheart, 2003). For example, Broca's area, the superior temporal sulcus, the superior temporal gyrus, the insula, and the frontal pole are known to be part of the language network and are also active in music processing (Fadiga et al., 2009; Hymers et al., 2015; Koelsch et al., 2002; Merrill et al., 2012; Schön et al., 2010; but see Chen et al., 2021). Evidence for distinct music and language networks is largely driven by clinical case studies of patients with a deficit in either music or language abilities that leaves the other ability intact. For example, individuals with acquired or congenital amusia recognize spoken words and lyrics but are unable to recognize tunes and melodies (Ayotte et al., 2002; Griffiths, 1997; Peretz et al., 1994; Piccirilli et al., 2000). In contrast, other individuals show evidence of verbal agnosia (word deafness) and are unable to recognize spoken words but are able to recognize nonverbal sounds, including music (Metz-Lutz & Dahl, 1984; Takahashi et al., 1992; Yaqub et al., 1988). There is also compelling evidence for a musical memory system that is distinct from that for language. Two patients with medial and lateral temporal lobe damage demonstrated severe deficits in visual and verbal memory, but intact musical memory (Esfahani-Bayerl et al., 2019; Finke et al., 2012) while a third patient experienced the opposite deficit: intact verbal memory with a severe, music specific memory deficit (Peretz, 1996). In the music familiarity literature, the presence of language has been manipulated in only one study on musical memory to characterize the neural networks involved in the recognition of musical stimuli with and without language (e.g., a sung folksong vs. the hummed melody of that same folksong; Saito et al., 2012). However, there was no language control condition that did not include music. Without controlling the presence of language in musical memory studies, it is not possible to differentiate which networks are responsible for processing musical, linguistic, or a combination of both aspects of the music stimuli.

The range of instrumentation present in the stimuli that are used in musical memory studies may also contribute to the inconsistencies in the literature. In some studies the stimuli consist of a simple computer-generated series of tones while in others the stimuli are excerpts taken from orchestral music and include multiple instruments (Halpern & Zatorre, 1999; Platel,

2005). There is also behavioural evidence to suggest that simple melodies involving a single stream of information are remembered better than more complex, polyphonic music that contains multiple streams of information (Demorest et al., 2016). These different stimuli may be processed by different networks of brain areas (Janata et al., 2002) but stimulus instrumentation has not been systematically manipulated in studies investigating musical memory. The difficulty in defining familiarity and the differences in stimulus features, like the presence of language or type of instrumentation, has made it difficult to compare findings across studies and limits the utility of these results in clinical settings outside of academic research.

Controlled musical memory research has clinical implications

Results from musical memory studies that carefully controlled familiarity and stimulus contents would have implications for using music for diagnostic or therapeutic purposes in patients with dementia. For instance, music can be used in clinical settings to reduce levels of agitation, increase social and emotional well-being, and enhance language skills (Wall & Duffy, 2010). However, the efficacy of musical interventions likely depends on how each type of dementia manifests in the brain. For example, Alzheimer's disease (AD) is characterized by levels of biomarkers like beta-amyloid and tau proteins as well as hippocampal atrophy (*Earlier Diagnosis*, 2021), frontotemporal dementia is characterized by focal frontal and temporal lobe atrophy (Omar, 2019), and semantic dementia is characterized by asymmetrical atrophy of the anterior temporal pole and anterior fusiform gyrus (Landin-Romero et al., 2016). These varying clinical profiles have distinct effects on how the brain processes music (Baird & Samson, 2015). Individuals with semantic dementia show greater deficits in recognizing musical emotions (Hsieh et al., 2012) and in recognizing famous melodies (Hsieh et al., 2011) than do patients with AD. Patients with AD readily report that a piece of music evokes autobiographical memories (Belfi et al., 2015), but patients with frontotemporal dementia require repeated exposure to a musical stimulus to trigger autobiographical memories (Baird et al., 2020). If clearly defined neural correlates from well-controlled musical memory studies are found, then musical stimuli could be tailored to an individual's disease type and progression to capitalize on spared areas of competence. Commonly used musical therapies in dementia include active singing interventions, passive listening in a group or individual setting, and playing musical instruments (Moreno-Morales et al., 2020), but depending on a patient's dementia diagnosis some of these therapies may be more effective than others. For example, a patient with semantic dementia who has

atrophy in language related networks may not receive the same benefit from music that includes language as a patient with AD with a different pattern of atrophy. As described above, it is unclear which areas of the brain are involved in musical memory due to the inconsistences across studies. Therefore, it is currently not possible to capitalize on the cortical areas spared by an individual's disease progression using music. Characterizing how familiarity and stimulus features affect the way the brain processes music may aid in the development of individualized therapies.

Effects of healthy aging on processing music

A thorough understanding of the changes in music processing that occur in dementia first requires knowledge of how music processing changes in healthy aging. Auditory processing in general is affected by aging both in the brain areas involved and in the intensity of the blood-oxygen level dependent (BOLD) activation within those areas. For example, aging is related to increased activation in occipital cortex during auditory word processing tasks (Kuchinsky et al., 2012) and in inferior frontal gyrus during sentence comprehension tasks (Peelle et al., 2010; Tyler et al., 2010). The differences in activity levels and activated brain areas are thought to reflect the recruitment of additional cognitive resources to make up for age-related losses in processing efficiency in the task-related regions seen in young adults (Peelle, 2019). In behavioural studies on music processing, older adults less accurately judge the length of musical rhythmic patterns (Ragot et al., 2002) and are slower to recognize familiar tunes than young adults (Dowling et al., 2008). Despite age-related differences in auditory and music processing, the neural correlates of musical memory have been almost exclusively explored in healthy young adults. A direct comparison of musical memory in young and older adults can be found in only one study (Sikka et al., 2015). Using excerpts from familiar and unfamiliar tunes that were recorded on computerized notation software, the researchers found that familiar melodies elicited more activity than unfamiliar melodies in the left superior temporal gyrus for young adults, and more activity in bilateral superior parietal gyri, left angular gyrus and the left superior frontal gyrus for older adults. Like previous studies exploring musical memory in young adults, the stimuli did not include any language and the instrumentation was a simple tonal melody, which is arguably not reflective of music listened to and remembered over a lifetime. Although this work sheds some light on age-related changes in the neural correlates of musical memory,

further research is needed that more tightly controls the definition of familiarity and the presence of language within the stimuli.

The previous work using fMRI to investigate musical processing in older adults used traditional general linear model (GLM) analyses to identify the brain regions that are active in responses to familiar and unfamiliar music. However, intersubject synchrony may be an additional useful method of identifying age-related changes in the temporal patterns of brain activity to musical stimuli. Intersubject synchrony is an analysis method that identifies similar temporal activation patterns across individuals by calculating voxel-wise correlations over time between two individuals, or between an individual and the average of a group of individuals (Hasson et al., 2004; Regev et al., 2019). Therefore, unlike GLM analyses, synchrony is well suited to using naturalistic stimuli, like music, that unfold over time. Highly synchronized brain activity is interpreted as the stimulus being experienced in a similar way across people, whereas low levels of synchrony indicate differences in stimulus processing. The only two studies of aging and intersubject synchrony found an age-related reduction in synchrony, indicating that older adults were more idiosyncratic in their brain activity than young adults. The authors concluded that older adults experienced a movie stimulus in more individualized ways than the young adults. Synchrony differences were found across broad frontal regions (inferior frontal gyrus, middle frontal gyrus and medial prefrontal gyrus) and auditory and visual networks identified using an independent component analysis (Campbell et al., 2015; Geerligs et al., 2018). The same audio-visual movie stimulus was used in both studies. As the prevalence of the intersubject synchrony technique grows and is used in more studies of aging and clinical populations (Anderson et al., 2013; Hasson et al., 2009; Huntley et al., In preparation; Lyons et al., 2020) it is important to take into account that patients in these groups are likely to have impaired vision. Inducing intersubject synchrony using audio-only stimuli such as music may be essential, but the characteristics of the synchrony induced by audio-only stimuli in healthy older adults or clinical populations are largely unknown. Characterizing age-related changes of intersubject synchrony using audio-only stimuli provides a novel approach to investigating the neural correlates of musical memory, however, the effects of familiarity and stimulus characteristics on synchrony have not yet been clearly defined.

Effects of familiarity and stimulus characteristics on intersubject synchrony

Two studies have shown that intersubject synchrony is affected by a participant's level of familiarity with a stimulus, but both studies used audio-visual movie clips rather than music. Intersubject synchrony in the posterior medial network, measured using fMRI, was shown to decrease from the first to the sixth consecutive viewing of 90 second movie clips (Aly et al., 2017, 2018). In a similar study using EEG, participants were presented with three short films that were each viewed twice (Dmochowski et al., 2012). EEG synchrony decreased between the first and second viewings. Neither of these studies fully characterized the timecourse of the synchrony decrease and since both studies used movie stimuli it is not known whether a similar decrease in synchrony would be found with other types of stimuli like music. If fully characterized, the reduction in synchrony reported in these two studies could follow one of two patterns: synchrony could either steadily decrease over multiple viewings or be steeply reduced after a single repetition followed by a plateau. If synchrony steadily decreases with multiple exposures, then this may introduce confounds into synchrony studies that use familiar stimuli. For example, if the level of familiarity of a stimulus differs systematically with the experimental manipulation, then it will not be possible to say whether any differences in synchrony are a result of the manipulation or a result of previous stimulus exposure. For example, the Child Mind Institute Healthy Brain Network databank includes fMRI data from hundreds of children in the New York area watching a 10-minute clip from the children's movie '*Despicable Me'* but does not include information on whether participants had seen the movie prior to the experiment (Alexander et al., 2017). Researchers that then use these data to measure intersubject synchrony are unable to control for the possible familiarity confound which could influence the conclusions they are able to draw from their results. On the other hand, if synchrony levels reach a plateau after a certain number of exposures, then researchers can remove the confound of familiarity by exposing all participants to the stimulus before the study begins. Until the pattern of synchrony reduction with familiarity and the types of stimuli that induce the reduction are fully characterized, it is important for researchers to use novel stimuli to avoid a familiarity confound.

Intersubject synchrony is sensitive to the contents of the stimuli that participants experience. Movie stimuli result in highly synchronized activity over large areas of the occipital and temporal lobes (Hasson et al., 2004), audio-only movie (Naci et al., 2017) and audiobook excerpts (Regev et al., 2019; Simony et al., 2016) induce synchrony in large fronto-temporal and

auditory networks, and instrumental music excerpts induce synchrony in primary auditory cortex as well as bilateral thalamus, and motor planning regions (Abrams et al., 2013; Naci et al., 2017). As movies include both visual and auditory information it is not surprising that visual and auditory brain areas were highly synchronized while auditory regions were synchronized during audio-only stimuli. Intersubject synchrony to different types of stimuli have been compared in only one study (Naci et al., 2017). The researchers found that there was more synchrony in stimuli with language after comparing synchrony induced by audio-visual movie clips, audio-only movie excerpts, and popular tv-show theme-songs without language. However, the presence of music and language was not systematically varied across the stimuli and no other studies have characterized synchrony changes across different types of stimuli. Intersubject synchrony is also related to how well stimuli are learned (Meshulam et al., 2021) with better learning associated with higher synchrony. If, for example, characterizing synchrony differences across stimulus types reveals that more synchrony is induced by stimuli containing both music and lyrics than by stimuli that contain only language, this may be an indication of differences in how the stimuli are remembered. Pursuing the mechanisms behind the differences in synchrony across stimulus types may present an opportunity to understand why there is preservation of memory for melodies and lyrics in some patients with dementia when memory for words is lost (Vanstone et al., 2009).

Research goals and hypotheses

There were three research goals of this thesis that attempted to address the gaps in the literature described in the previous sections. First, I aimed to identify the neural correlates of musical memory by directly monitoring participants' stimulus exposure and manipulating the presence of language and memory across stimuli. Using a controlled training paradigm, I defined familiarity as the number of times participants listened to each stimulus rather than asking them to subjectively rate their level of familiarity with previously known stimuli. To manipulate music and language content, eight novel stimuli were created that contained either music, language, or both (instrumental music only; spoken word only; sung lyrics without instrumental music; sung lyrics with instrumental music). By controlling familiarity and the presence of music and language in stimuli within the same study, I aimed to bring clarity to whether the discrepancies in the musical memory literature are due to differences in the definition of familiarity and the contents of stimuli used across studies.

To address the first research goal, young adult participants were asked to learn the novel musical and language stimuli over a training period of 3 weeks and participated in a fMRI scanning session before and after the training period. During the training period, young adult participants listened to half of the stimuli using an online music player that tracked the number of times they listened to each stimulus (details regarding the training implementation can be found in the methods section of Chapter 2). When participants returned to the lab for the second scanning session, they were presented with the same stimuli they had listened to in the first scanning session. The only difference between the two scanning sessions was participants' level of familiarity with half of the stimuli. A traditional fMRI general linear model (GLM) approach was used to identify brain areas where BOLD activity differed as a result of increased familiarity and the presence of music and language.

The second research goal aimed to understand whether the degree of intersubject synchrony across a group of individuals changes based on memory for music and language stimuli. To address this goal, a second set of eight stimuli were created that manipulated the presence of music and language in the same way as the first set and participants also trained on half of these stimuli during the controlled training paradigm. The same set of stimuli could not be used to address both the first and second research goals because intersubject synchrony requires participants to listen to stimuli that are longer, and therefore more representative of naturalistic listening scenarios, than those generally used in GLM analyses. Details summarizing which stimuli were used in which experimental chapters can be found in Appendix C.

I hypothesized that the inclusion of more information within a stimulus (music and language together) would induce stronger levels of synchrony than either music or language on their own in the same way that audio-visual movie stimuli were shown to induce more synchrony than audio-only theme-songs (Naci et al., 2017). By asking participants to train on novel stimuli I could characterize whether synchrony was affected by repeated exposure to music and language stimuli over an extended period of time. Using the data from the second scanning session, synchrony to stimuli that were heard multiple times (trained stimuli) and stimuli that were heard once before (not trained stimuli) could be compared. If intersubject synchrony gradually decreases with increased exposure I would expect to see differences between the trained and untrained stimuli in the second session. If intersubject synchrony reduces after a single listen,

followed by a plateau, I would not expect to see differences between the trained and untrained stimuli in the second session.

The third research goal was to understand whether the effects of familiarity, music, and language seen in young adult participants were consistent across the lifespan. By including a group of older adult participants, I explored whether the brain areas involved in processing familiar music and language stimuli (as identified by the controlled training paradigm in young adults) were consistent with age. I was also interested in understanding whether an age-related reduction in synchrony (Campbell et al., 2015; Geerligs et al., 2018) would be apparent when older adult participants were presented with audio-only music and language stimuli. To reduce the burden of participation and to reduce the length and the number of scanning sessions (one session rather than two) older adult participants did not train to become familiar with novel stimuli and one of the four stimulus categories was removed (stimuli composed of sung lyrics without background instrumentation were excluded). During a single scanning session, older adults were presented with the same novel stimuli presented to young adults alongside highly familiar stimuli they had known for more than 50 years (detailed in Chapter 5). The familiar stimuli also manipulated the presence of language and music. Although the familiar and unfamiliar stimuli were not identical (as in the young adult familiarity manipulation), I tried to equate the stimuli on characteristics like lead singer voice, instrumentation, and musical style. Presenting older adults with the same stimuli as the young adults allowed for an investigation into the similarities between the way older and young adults experience identical music and language. By comparing highly familiar stimuli in older adults to recently learned stimuli in young adults and to novel stimuli in both groups I could further characterize how intersubject synchrony changes as a result of repeated exposure over short (3 weeks) and long (50 years) periods of time.

Division of data across chapters

Across all chapters, the presented data were collected from a single group of 26 young adult participants and a single group of 15 older adult participants. Details regarding which stimuli were used in each chapter can be found in Appendix C.

In Chapter 2, I used univariate GLM analyses and multivariate analyses to examine neural responses to musical familiarity across young adult participants only. The data collected

while young adults listened to short 10-sec clips of stimuli in both scanning sessions were used for these analyses.

In Chapter 3, I used intersubject synchrony measures to investigate how repeated exposure to a stimulus changes the degree of synchrony across a group of young adult participants only. The data collected while young adults listened to 5-minute-long stimuli in both scanning sessions were used in the intersubject synchrony analyses.

In Chapter 4, I investigated age-related differences in how stimuli with music and language are processed in a second GLM analysis. I combined a subset of the young adult data from the first scanning session used in the GLM analysis described in Chapter 2 with the data collected while older adults listened to the same short 10-sec clips of stimuli. I also investigated how intersubject synchrony differed based on the presence of music and language and whether those differences were consistent across young and older adults. I combined a subset of the young adult data from the first scanning session used in the intersubject synchrony analysis described in Chapter 3 with the data collected while older adults listened to the same 5-minute-long stimuli.

Finally, in Chapter 5, I investigated whether the effects of long-term familiarity with a stimulus (more than 50 years) on synchrony in older adults were similar to the effects of shorter-term familiarity (3 weeks) on synchrony in young adults. I combined the data collected while older adult participants listened to the highly familiar stimuli with a subset of the data collected while older adults listened to the novel 5-minute-long stimuli used in Chapter 4. The results were compared to what was found in young adults in Chapter 3, but the young and older adult familiarity data were not combined into a single analysis.

Bibliography

Abrams, D. A., Ryali, S., Chen, T., Chordia, P., Khouzam, A., Levitin, D. J., & Menon, V. (2013). Inter-subject synchronization of brain responses during natural music listening. *European Journal of Neuroscience*, *37*(9), 1458–1469. https://doi.org/10.1111/ejn.12173

Agustus, J. L., Golden, H. L., Callaghan, M. F., Bond, R. L., Benhamou, E., Hailstone, J. C., Weiskopf, N., & Warren, J. D. (2018). Melody Processing Characterizes Functional Neuroanatomy in the Aging Brain. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00815

Alexander, L. M., Escalera, J., Ai, L., Andreotti, C., Febre, K., Mangone, A., Potler, N. V., Langer, N., Alexander, A., Kovacs, M., Litke, S., O'Hagan, B., Andersen, J., Bronstein, B., Bui, A., Bushey, M., Butler, H., Castagna, V., Camacho, N., … Milham, M. P. (2017). An open resource for transdiagnostic research in pediatric mental health and learning disorders. *BioRxiv*, 149369. https://doi.org/10.1101/149369

Alonso, I., Davachi, L., Valabrègue, R., Lambrecq, V., Dupont, S., & Samson, S. (2016). Neural correlates of binding lyrics and melodies for the encoding of new songs. *NeuroImage*, *127*, 333–345. https://doi.org/10.1016/j.neuroimage.2015.12.018

Altenmüller, E., Siggel, S., Mohammadi, B., Samii, A., & Münte, T. F. (2014). Play it again, Sam: Brain correlates of emotional music recognition. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.00114

Aly, M., Chen, J., Turk-Browne, N. B., & Hasson, U. (2017). Learning Naturalistic Temporal Structure in the Posterior Medial Network. *BioRxiv*. https://doi.org/10.1101/196287

Aly, M., Chen, J., Turk-Browne, N. B., & Hasson, U. (2018). Learning Naturalistic Temporal Structure in the Posterior Medial Network. *Journal of Cognitive Neuroscience*, *30*(9), 1345–1365. https://doi.org/10.1162/jocn_a_01308

Anderson, J. S., Nielsen, J. A., Ferguson, M. A., Burback, M. C., Cox, E. T., Dai, L., Gerig, G., Edgin, J. O., & Korenberg, J. R. (2013). Abnormal brain synchrony in Down Syndrome. *NeuroImage: Clinical*, *2*, 703–715. https://doi.org/10.1016/j.nicl.2013.05.006

Ayotte, J., Peretz, I., & Hyde, K. (2002). Congenital amusia. *Brain*, *125*(2), 238–251. https://doi.org/10.1093/brain/awf028

Baird, A., Gelding, R., Brancatisano, O., & Thompson, W. F. (2020). A Preliminary Exploration of the Stability of Music- and Photo-Evoked Autobiographical Memories in People with Alzheimer's and Behavioral Variant Frontotemporal Dementia. *Music & Science*, *3*, 2059204320957273. https://doi.org/10.1177/2059204320957273

Baird, A., & Samson, S. (2009). Memory for music in Alzheimer's disease: Unforgettable? *Neuropsychology Review*, *19*(1), 85–101. https://doi.org/10.1007/s11065-009-9085-2

Baird, A., & Samson, S. (2015). Music and Dementia. In *Progress in Brain Research* (Vol. 217, pp. 207–235).

Belfi, A. M., Karlan, B., & Tranel, D. (2015). Music evokes vivid autobiographical memories. *Memory*, *August 2015*, 1–11. https://doi.org/10.1080/09658211.2015.1061012

Berz, W. L. (1995). Working Memory in Music: A Theoretical Model. *Music Perception*, *12*(3), 353–364. https://doi.org/10.2307/40286188

Campbell, K. L., Shafto, M. A., Wright, P., Tsvetanov, K. A., Geerligs, L., Cusack, R., Tyler, L. K., Brayne, C., Bullmore, E., Calder, A., Dalgleish, T., Duncan, J., Henson, R., Matthews, F., Marslen-Wilson, W., Rowe, J., Cheung, T., Davis, S., Kievit, R., … Villis, L. (2015). Idiosyncratic responding during movie-watching predicted by age differences in attentional control. *Neurobiology of Aging*, *36*(11), 3045–3055. https://doi.org/10.1016/j.neurobiolaging.2015.07.028

Chen, X., Affourtit, J., Ryskin, R., Regev, T. I., Norman-Haignere, S., Jouravlev, O., Malik-Moraleda, S., Kean, H., Varley, R., & Fedorenko, E. (2021). The human language system does not support music processing. *BioRxiv*, 2021.06.01.446439. https://doi.org/10.1101/2021.06.01.446439

Demorest, S., Morrison, S., Nguyen, V., & Bodnar, E. (2016). The Influence of Contextual Cues on Cultural Bias in Music Memory. *Music Perception: An Interdisciplinary Journal*, *33*, 590–600. https://doi.org/10.1525/mp.2016.33.5.590

Dmochowski, J. P., Sajda, P., Dias, J., & Parra, L. C. (2012). Correlated Components of Ongoing EEG Point to Emotionally Laden Attention – A Possible Marker of Engagement? *Frontiers in Human Neuroscience*, *6*(May), 1–9. https://doi.org/10.3389/fnhum.2012.00112

Dowling, W. J., Bartlett, J. C., Halpern, A. R., & Andrews, M. W. (2008). Melody recognition at fast and slow tempos: Effects of age, experience, and familiarity. *Perception & Psychophysics*, *70*(3), 496–502. https://doi.org/10.3758/PP.70.3.496

Earlier Diagnosis. (2021). Alzheimer's Disease and Dementia. https://alz.org/alzheimers-dementia/research_progress/earlier-diagnosis

El Haj, M., Fasotti, L., & Allain, P. (2012). The involuntary nature of music-evoked autobiographical memories in Alzheimer's disease. *Consciousness and Cognition*, *21*(1), 238–246. https://doi.org/10.1016/j.concog.2011.12.005

Esfahani-Bayerl, N., Finke, C., Kopp, U., Moon, D.-U., & Ploner, C. J. (2019). Musical memory and hippocampus revisited: Evidence from a musical layperson with highly selective hippocampal damage. *Cortex*, *119*, 519–527. https://doi.org/10.1016/j.cortex.2018.12.023

Fadiga, L., Craighero, L., & D'Ausilio, A. (2009). Broca's area in language, action, and music. *Annals of the New York Academy of Sciences*, *1169*, 448–458. https://doi.org/10.1111/j.1749-6632.2009.04582.x

Finke, C., Esfahani, N. E., & Ploner, C. J. (2012). Preservation of musical memory in an amnesic professional cellist. *Current Biology*, *22*(15), R591–R592. https://doi.org/10.1016/j.cub.2012.05.041

Freitas, C., Manzato, E., Burini, A., Taylor, M. J., Lerch, J. P., & Anagnostou, E. (2018). Neural Correlates of Familiarity in Music Listening: A Systematic Review and a Neuroimaging Meta-Analysis. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00686

Geerligs, L., Cam-CAN, & Campbell, K. L. (2018). Age-related differences in information processing during movie watching. *Neurobiology of Aging*, *72*, 106–120. https://doi.org/10.1016/j.neurobiolaging.2018.07.025

Griffiths, T. D. (1997). Spatial and temporal auditory processing deficits following right hemisphere infarction. A psychophysical study. *Brain*, *120*(5), 785–794. https://doi.org/10.1093/brain/120.5.785

Groussard, M., Rauchs, G., Landeau, B., Viader, F., Desgranges, B., Eustache, F., & Platel, H. (2010). The neural substrates of musical memory revealed by fMRI and two semantic tasks. *NeuroImage*, *53*(4), 1301–1309. https://doi.org/10.1016/j.neuroimage.2010.07.013

Groussard, M., Viader, F., Landeau, B., Desgranges, B., Eustache, F., & Platel, H. (2009). Neural Correlates Underlying Musical Semantic Memory. *Annals of the New York Academy of Sciences*, *1169*(1), 278–281. https://doi.org/10.1111/j.1749-6632.2009.04784.x

Halpern, A. R., & Zatorre, R. J. (1999). When That Tune Runs Through Your Head: A PET Investigation of Auditory Imagery for Familiar Melodies. *Cerebral Cortex*, *9*(7), 697–704. https://doi.org/10.1093/cercor/9.7.697

Hasson, U., Avidan, G., Gelbard, H., Vallines, I., Harel, M., Minshew, N., & Behrmann, M. (2009). Shared and idiosyncratic cortical activation patterns in autism revealed under continuous real-life viewing conditions. *Autism Research*, *2*(4), 220–231. https://doi.org/10.1002/aur.89

Hasson, U., Nir, Y., Levy, I., Fuhrmann, G., & Malach, R. (2004). Intersubject Synchronization of Cortical Activity DuringNatural Vision. *Science*, *303*(5664), 1634–1640. https://doi.org/10.1126/science.1089506

Herholz, S., Halpern, A., & Zatorre, R. (2012). Neuronal correlates of perception, imagery, and memory for familiar tunes. *Journal of Cognitive Neuroscience*, *24*(6), 1382–1397. https://doi.org/10.1162/jocn_a_00216

Hsieh, S., Foxe, D., Leslie, F., Savage, S., Piguet, O., & Hodges, J. R. (2012). Grief and joy: Emotion word comprehension in the dementias. *Neuropsychology*, *26*(5), 624–630. https://doi.org/10.1037/a0029326

Hsieh, S., Hornberger, M., Piguet, O., & Hodges, J. R. (2011). Neural basis of music knowledge: Evidence from the dementias. *Brain*, *134*(9), 2523–2534. https://doi.org/10.1093/brain/awr190

Huntley, J., Bor, D., Fleming, S. M., Mancuso, M., Mediano, P., Naci, L., Owen, A. M., Rocci, L., Sternin, A., & Howard, R. (In preparation). *Assessing awareness in severe Alzheimer's disease*.

Hymers, M., Prendergast, G., Liu, C., Schulze, A., Young, M. L., Wastling, S. J., Barker, G. J., & Millman, R. E. (2015). Neural mechanisms underlying song and speech perception can be differentiated using an illusory percept. *NeuroImage*, *108*, 225–233. https://doi.org/10.1016/j.neuroimage.2014.12.010

Izquierdo, I., Medina, J. H., Vianna, M. R. M., Izquierdo, L. A., & Barros, D. M. (1999). Separate mechanisms for short- and long-term memory. *Behavioural Brain Research*, *103*(1), 1–11. https://doi.org/10.1016/S0166-4328(99)00036-4

Jacobsen, J., Fritz, T., Stelzer, J., & Turner, R. (2015). Why musical memory can be preserved in advanced Alzheimer's disease. *Brain: A Journal of Neurology*, 1–13. https://doi.org/10.1093/awv148

Janata, P., Tillmann, B., & Bharucha, J. J. (2002). Listening to polyphonic music recruits domain-general attention and working memory circuits. *Cognitive, Affective & Behavioral Neuroscience*, *2*(2), 121–140. https://doi.org/10.3758/CABN.2.2.121

Klostermann, E. C., Loui, P., & Shimamura, A. P. (2009). Activation of right parietal cortex during memory retrieval of nonlinguistic auditory stimuli. *Cognitive, Affective, & Behavioral Neuroscience*, *9*(3), 242–248. https://doi.org/10.3758/CABN.9.3.242

Koelsch, S., Gunter, T., Cramon, D., Zysset, S., Lohmann, G., & Friederici, A. (2002). Bach Speaks: A Cortical "Language-Network" Serves the Processing of Music. *NeuroImage*, *17*, 956–966. https://doi.org/10.1006/nimg.2002.1154

Kuchinsky, S. E., Vaden, K. I., Jr, Keren, N. I., Harris, K. C., Ahlstrom, J. B., Dubno, J. R., & Eckert, M. A. (2012). Word Intelligibility and Age Predict Visual Cortex Activity during Word Listening. *Cerebral Cortex*, *22*(6), 1360–1371. https://doi.org/10.1093/cercor/bhr211

Landin-Romero, R., Tan, R., Hodges, J. R., & Kumfor, F. (2016). An update on semantic dementia: Genetics, imaging, and pathology. *Alzheimer's Research & Therapy*, *8*(1). https://doi.org/10.1186/s13195-016-0219-5

Lyons, K. M., Stevenson, R. A., Owen, A. M., & Stojanoski, B. (2020). Examining the relationship between measures of autistic traits and neural synchrony during movies in children with and without autism. *NeuroImage: Clinical*, *28*, 102477. https://doi.org/10.1016/j.nicl.2020.102477

Ménard, M.-C., & Belleville, S. (2009). Musical and verbal memory in Alzheimer's disease: A study of long-term and short-term memory. *Brain and Cognition*, *71*(1), 38–45. https://doi.org/10.1016/j.bandc.2009.03.008

Merrill, J., Sammler, D., Bangert, M., Goldhahn, D., Lohmann, G., Turner, R., & Friederici, A. D. (2012). Perception of Words and Pitch Patterns in Song and Speech. *Frontiers in Psychology*, *3*. https://doi.org/10.3389/fpsyg.2012.00076

Meshulam, M., Hasenfratz, L., Hillman, H., Liu, Y.-F., Nguyen, M., Norman, K. A., & Hasson, U. (2021). Neural alignment predicts learning outcomes in students taking an introduction to computer science course. *Nature Communications*, *12*(1), 1922. https://doi.org/10.1038/s41467-021-22202-3

Metz-Lutz, M.-N., & Dahl, E. (1984). Analysis of word comprehension in a case of pure word deafness. *Brain and Language*, *23*(1), 13–25. https://doi.org/10.1016/0093-934X(84)90002-6

Moreno-Morales, C., Calero, R., Moreno-Morales, P., & Pintado, C. (2020). Music Therapy in the Treatment of Dementia: A Systematic Review and Meta-Analysis. *Frontiers in Medicine*, *0*. https://doi.org/10.3389/fmed.2020.00160

Naci, L., Sinai, L., & Owen, A. M. (2017). Detecting and interpreting conscious experiences in behaviorally non-responsive patients. *NeuroImage*, *145*, 304–313. https://doi.org/10.1016/j.neuroimage.2015.11.059

Nan, Y., Knösche, T. R., Zysset, S., & Friederici, A. D. (2008). Cross-cultural music phrase processing: An fMRI study. *Human Brain Mapping*, *29*(3), 312–328.

Omar, R. (2019). Music Cognition in Frontotemporal Dementia and Non-Alzheimer's Dementias. *Music and Dementia: From Cognition to Therapy*, 88.

Patel, A. D. (2011). Why would Musical Training Benefit the Neural Encoding of Speech? The OPERA Hypothesis. *Frontiers in Psychology*, *0*. https://doi.org/10.3389/fpsyg.2011.00142

Peelle, J. E. (2019). Language and aging. In G. De Zubicaray I. & N. O. Schiller (Eds.), *The Oxford Handbook of Neurolinguistics*. Oxford University Press.

Peelle, J. E., Troiani, V., Wingfield, A., & Grossman, M. (2010). Neural Processing during Older Adults' Comprehension of Spoken Sentences: Age Differences in Resource Allocation and Connectivity | Cerebral Cortex | Oxford Academic. *Cerebral Cortex*, *20*(4). https://academic.oup.com/cercor/article/20/4/773/303007

Pereira, C. S., Teixeira, J., Figueiredo, P., Xavier, J., Castro, S. L., & Brattico, E. (2011). Music and Emotions in the Brain: Familiarity Matters. *PLoS ONE*, *6*(11). https://doi.org/10.1371/journal.pone.0027241

Peretz, I. (1996). Can we lose memory for music? A case of music agnosia in a nonmusician. *Journal of Cognitive Neuroscience*, *8*(6), 481–496. https://doi.org/10.1162/jocn.1996.8.6.481

Peretz, I., & Coltheart, M. (2003). Modularity of music processing. *Nature Neuroscience*, *6*(7), 688–691. https://doi.org/10.1038/nn1083

Peretz, I., Gosselin, N., Belin, P., Zatorre, R. J., Plailly, J., & Tillmann, B. (2009). Music lexical networks: The cortical organization of music recognition. *Annals of the New York Academy of Sciences*, *1169*, 256–265. https://doi.org/10.1111/j.1749-6632.2009.04557.x

Peretz, I., Kolinsky, R., Tramo, M., Labrecque, R., Hublet, C., Demeurisse, G., & Belleville, S. (1994). Functional dissociations following bilateral lesions of auditory cortex. *Brain*, *117*(6), 1283–1301. https://doi.org/10.1093/brain/117.6.1283

Piccirilli, M., Sciarma, T., & Luzzi, S. (2000). Modularity of music: Evidence from a case of pure amusia. *Journal of Neurology, Neurosurgery & Psychiatry*, *69*(4), 541–545. https://doi.org/10.1136/jnnp.69.4.541

Plailly, J., Tillmann, B., & Royet, J.-P. (2007). The Feeling of Familiarity of Music and Odors: The Same Neural Signature? *Cerebral Cortex*, *17*(11), 2650–2658. https://doi.org/10.1093/cercor/bhl173

Platel, H. (2005). Functional neuroimaging of semantic and episodic musical memory. *Annals of the New York Academy of Sciences*, *1060*(January 2006), 136–147. https://doi.org/10.1196/annals.1360.010

Ragot, R., Ferrandez, A.-M., & Pouthas, V. (2002). Time, music, and aging. *Psychomusicology: A Journal of Research in Music Cognition*, *18*(1–2), 28–45. https://doi.org/10.1037/h0094053

Regev, M., Simony, E., Lee, K., Tan, K. M., Chen, J., & Hasson, U. (2019). Propagation of information along the cortical hierarchy as a function of attention while reading and listening to stories. *Cerebral Cortex*, *29*(10), 291526. https://doi.org/10.1093/cercor/bhy282

Saito, Y., Ishii, K., Sakuma, N., Kawasaki, K., Oda, K., & Mizusawa, H. (2012). Neural Substrates for Semantic Memory of Familiar Songs: Is There an Interface between Lyrics and Melodies? *PLoS ONE*, *7*(9). https://doi.org/10.1371/journal.pone.0046354

Schaal, N. K., Javadi, A.-H., Halpern, A. R., Pollok, B., & Banissy, M. J. (2015). Right parietal cortex mediates recognition memory for melodies. *European Journal of Neuroscience*, *42*(February), n/a-n/a. https://doi.org/10.1111/ejn.12943

Schön, D., Gordon, R., Campagne, A., Magne, C., Astésano, C., Anton, J.-L., & Besson, M. (2010). Similar cerebral networks in language, music and song perception. *NeuroImage*, *51*(1), 450–461. https://doi.org/10.1016/j.neuroimage.2010.02.023

Sikka, R., Cuddy, L. L., Johnsrude, I. S., & Vanstone, A. D. (2015). An fMRI comparison of neural activity associated with recognition of familiar melodies in younger and older adults. *Frontiers in Neuroscience*, *9*(OCT), 1–10. https://doi.org/10.3389/fnins.2015.00356

Simony, E., Honey, C. J., Chen, J., Lositsky, O., Yeshurun, Y., Wiesel, A., & Hasson, U. (2016). Dynamic reconfiguration of the default mode network during narrative comprehension. *Nature Communications*, *7*(May 2015). https://doi.org/10.1038/ncomms12141

Slattery, C. F., Agustus, J. L., Paterson, R. W., McCallion, O., Foulkes, A. J. M., Macpherson, K., Carton, A. M., Harding, E., Golden, H. L., Jaisin, K., Mummery, C. J., Schott, J. M., & Warren, J. D. (2019). The functional neuroanatomy of musical memory in Alzheimer's disease. *Cortex*, *115*, 357–370. https://doi.org/10.1016/j.cortex.2019.02.003

Takahashi, N., Kawamura, M., Shinotou, H., Hirayama, K., Kaga, K., & Shindo, M. (1992). Pure Word Deafness due to Left Hemisphere Damage. *Cortex*, *28*(2), 295–303. https://doi.org/10.1016/S0010-9452(13)80056-1

Tyler, L. K., Shafto, M. A., Randall, B., Wright, P., Marslen-Wilson, W. D., & Stamatakis, E. A. (2010). Preserving Syntactic Processing across the Adult Life Span: The Modulation of the Frontotemporal Language System in the Context of Age-Related Atrophy. *Cerebral Cortex*, *20*(2), 352–364. https://doi.org/10.1093/cercor/bhp105

Vanstone, A., Cuddy, L., Duffin, J., & Alexander, E. (2009). Exceptional Preservation of Memory for Tunes and Lyrics Case Studies of Amusia, Profound Deafness, and Alzheimer's Disease. *Annals of the New York Academy of Sciences*, *1169*, 291–294. https://doi.org/10.1111/j.1749-6632.2009.04763.x

Wall, M., & Duffy, A. (2010). The effects of music therapy for older people with dementia. *British Journal of Nursing (Mark Allen Publishing)*, *19*, 108–113. https://doi.org/10.12968/bjon.2010.19.2.46295

Yaqub, B. A., Gascon, G. G., Nosha, M. A., & Whitaker, H. (1988). Pure word deafness (acquired verbal auditory agnosia) in an Arabic speaking patient. *Brain*, *111*(2), 457–466. https://doi.org/10.1093/brain/111.2.457

2 The effect of familiarity on neural representations of music and language

Sternin, A., McGarry, L.M., Owen, A.M., Grahn, J.A. (2021), *The Journal of Cognitive Neuroscience*, 33(8). doi:10.1162/jocn_a_01737

Introduction

Music and language abilities are closely related. At the sensory level, both music and language involve acoustic stimuli arranged in structurally meaningful ways. For example, both involve small units (music notes or words) that are combined using specific rules to create larger units (melodies/songs and sentences/stories). Cognitively, the comprehension of both music and language involves creating expectations about what comes next in a series of sounds (Patel, 2008), using learned rules (e.g. syntax) to interpret the input (Jackendoff, 2009; Jackendoff & Lerdahl, 2006), and requires the use of memory (Daneman & Merikle, 1996; Zatorre & Gandour, 2008). Although they rely on similar processes, there is evidence to suggest that both overlapping and distinct networks are involved in music and language.

Perceiving music and language activates overlapping brain networks. EEG data shows that words and music are closely related in the early stages of cognitive processing (within the first 300-500ms following the perception of the sound; Gordon et al., 2010) and fMRI studies provide evidence for anatomically similar networks. For example, Broca's area, the superior temporal sulcus, the superior temporal gyrus, the insula, and the frontal pole are known to be involved in the language network, and these areas are also active in music processing (Fadiga et al., 2009; Hymers et al., 2015; Koelsch et al., 2002; Merrill et al., 2012; Schön et al., 2010). One cognitive ability common to both music and language is memory. In the short term, language and music unfold over time and therefore require the initial inputs to be held in mind for subsequent inputs to be understood (Peretz & Zatorre, 2005). For example, to understand the end of this sentence you need to be able to remember what the beginning of the sentence was about (Daneman & Merikle, 1996). In music, individual or groups of notes need to be remembered to make sense of a melody. Long-term memory of music and language is responsible for our ability

to sing along with a song or recite a poem from memory. Similar to a 'word lexicon' that stores all of the words that we know (Mohanan, 1982), there is evidence for a 'musical lexicon' (Peretz & Coltheart, 2003) that contains representations of the music that we know. Long-term memory results from mapping a perceived sound, whether it is a melody or a sentence, onto a stored representation and making a decision about whether the sound is new or not. Therefore, both music and memory rely on short-term auditory memory to make sense of the components of a sound sequence, and on long-term stored representations to judge whether an incoming sequence is novel.

Evidence for distinct music and language networks is largely driven by clinical case studies of patients with a deficit in either music or language abilities that leaves the other ability intact. For example, individuals with acquired or congenital amusia recognize spoken words and lyrics but are unable to recognize tunes and melodies (Ayotte et al., 2002; Griffiths, 1997; Peretz et al., 1994; Piccirilli et al., 2000). The opposite deficit also exists. Some individuals with brain damage may have verbal agnosia (word deafness) and are unable to recognize spoken words but are able to recognize nonverbal sounds, including music (Metz-Lutz & Dahl, 1984; Takahashi et al., 1992; Yaqub et al., 1988). Further evidence for distinct networks for music and language comes from the speech-song illusion, in which the repetition of a spoken phrase creates the perception of a song (Deutsch et al., 2011). One study found that distinct areas in the fronto-temporal cortices are active when the repeated phrases are perceived as song but not when the same phrases are perceived as speech (Tierney et al., 2013) indicating that the neural difference is based on the perception of the phrase as language or music. Most recently, electrocorticography (ECoG) measured from the temporal cortex of individuals listening to a variety of sounds (e.g. birds chirping, individuals speaking, and music) found groups of neurons that responded specifically to songs and were distinct from those neurons that responded to language (Norman-Haignere et al., 2019).

There is also compelling evidence for a musical memory system that is distinct from that for language, despite the similar role that memory plays in these two abilities. Two patients with medial and lateral temporal lobe damage demonstrated severe deficits in visual and verbal memory, but intact musical memory (Esfahani-Bayerl et al., 2019; Finke et al., 2012) while a third patient experienced the opposite deficit: intact verbal memory with a severe, music specific

agnosia (Peretz, 1996). Musical memory is also spared in some individuals with neurodegenerative disorders such as Alzheimer's disease, even in the context of deteriorating semantic memories (Baird & Samson, 2009; Cuddy et al., 2012; Cuddy & Duffin, 2005; Jacobsen et al., 2015; Slattery et al., 2019; Vanstone & Cuddy, 2010). For example, patients with the expected grey matter atrophy profile associated with Alzheimer's Disease had impairments in semantic memory but intact musical memory, which was supported by a network that included bilateral supplementary motor cortex and left anterior superior temporal cortex (Slattery et al., 2019). The patterns of atrophy (whether from acute damage or a degenerative disorder) that selectively affect some memory systems more than others lends support to the idea that there are separate networks for musical and verbal memory.

Although there is general agreement that musical memories are spared in neurodegenerative disorders, a recent meta-analysis found little consistency in the brain areas involved in memory for music (Freitas et al., 2018). Generally, the recognition of familiar music appears to rely on a fronto-temporal network (Agustus et al., 2018; Groussard et al., 2009; Halpern & Zatorre, 1999; Herholz et al., 2012; Jacobsen et al., 2015; Plailly et al., 2007; Sikka et al., 2015; Slattery et al., 2019) along with supplementary motor areas (Agustus et al., 2018; Herholz et al., 2012; Pereira et al., 2011; Peretz et al., 2009; Slattery et al., 2019) and basal ganglia structures (Agustus et al., 2018; Pereira et al., 2011; Sikka et al., 2015). However, no two studies are in agreement about the brain areas necessary for musical memory.

In this study, we investigated which neural networks are responsible for the processing of music and language and how they are affected by memory for the stimuli. To our knowledge, only one other study has investigated how memory for music and memory for language interact (Saito et al., 2012). In that study, participants listened to familiar and unfamiliar children's songs (recreated on voice-synthesizing software) while undergoing an O^{15} PET activation scan. The analysis uncovered separate networks for the retrieval of familiar music and language. Familiar music stimuli recruited the right middle temporal sulcus and bilateral temporo-occipital cortices, and familiar language stimuli recruited the left fusiform gyrus and the left inferior occipital gyrus, adding to the disagreement in the literature regarding which areas are involved in musical memory.

To expand on previous work, the stimuli in the current study were designed to be as similar to what is heard 'in the real world' as possible and to manipulate the presence or absence of music and language. Previous experiments have differed in the type of stimuli used to probe musical memory with some stimuli containing music with language (e.g. songs with lyrics) and others containing music without language (e.g. classical musical excerpts), but it is unknown how the presence or absence of language influences memory for music. To understand how music and language interact during learning and memory formation, four stimulus conditions were created: (1) whole music (music and words together), (2) instrumental music without words, (3) a capella (sung words, no instruments), and (4) spoken words. This allowed for an assessment of whether the effect of memory differed based on music or language content and whether stimuli with more information (i.e. music AND language, rather than each independently) would be remembered differently.

Participants completed a strict training paradigm to control for their knowledge of the stimuli. This training process is in contrast to studies that compare novel music to music made familiar over a lifetime. Relying on lifetime exposure to a piece of music makes it impossible to control familiarity across participants and, therefore, to untangle the differences between memory for the music and the autobiographical memories linked to the music. Additionally, learning music shortly before a retrieval phase (e.g. Alonso et al., 2016; Esfahani-Bayerl et al., 2019) may not accurately produce the level of familiarity that occurs 'naturally' with repeated exposure over longer time periods. Therefore, the training paradigm in this study was designed to mimic exposure to music over time while carefully monitoring the amount of exposure. Participants listened to the music through a specialized music player that tracked the number of times a participant heard each stimulus. The training process created an objective measure of familiarity with the stimuli and allowed for comparisons between stimuli that differed only in the participant's degree of familiarity. By carefully manipulating the presence of language and the degree of familiarity, this study's aim was to bring some clarity to the disagreement in the field and to better understand the relationship between the neural networks responsible for music and language and how they interact with memory abilities.

Methods

Ethics

Ethics approval for this project was granted by the Health Sciences Research Ethics Board at The University of Western Ontario (#100606, #114263).

Participants

Twenty-six neurologically healthy, English-speaking participants (14 female) aged 18-39 (mean=24 years) were recruited at The University of Western Ontario. All participants had completed at least some post-secondary education and nine participants had completed some post-graduate education. Using the Goldsmith's Musical Sophistication Index (Müllensiefen et al., 2014), 17 participants reported having formal musical training (1-10yrs, mean=4.5yrs), but at the time of testing only 9 of them played instruments regularly. Seven participants were fluent in a second language. All participants reported listening to music regularly (average 1.5 hours per day) via a phone, computer, or car radio. No further data on the diversity of the participants' backgrounds were collected and therefore, no comment can be made on whether the results from the current sample of participants is generalizable to a more diverse sample.

Two individuals withdrew from the study following the first scan session and data from four individuals were not included in the analysis because the average scores on the behavioural memory tests (lyric modification and melody memory test – details below) were lower than 70% correct. FMRI data from 20 individuals were included in the analysis.

Stimuli

Stimuli were similar to those regularly encountered in the real world, and the presence of language and music were manipulated. Stimuli were created from the lyrics and music of eight different songs written and recorded by one of the authors (A.M.O) between 1997 and 2006 for an amateur rock band based in Cambridge, UK. Thus, all stimuli were completely novel to the Canadian participants. The original songs were all written in a similar style and instrumentation included a lead singer, bass, drums, guitar, string instruments, and backing vocals, each recorded on separate tracks. Stimuli from the band's original repertoire were selected based on having male vocals only (over some that included female vocals). All stimuli were recorded using the exact same equipment directly to digital hard drive using the Sonar software (by Cakewalk) and

a ShureSM58 microphone. Where the same instruments appear across stimuli (violin, cello, drums, guitar, etc.) the same physical instruments were used.

Four conditions were created by modifying the original eight songs to include only certain tracks: (1) whole music (music and words together in a fully intact version of each song), (2) instrumental music without words (all vocal parts were removed, leaving just the non-vocal instrumentation), (3) a capella (all non-vocal instrumentation was removed leaving just the lead and backing vocals), and (4) spoken words (the lyrics of each song were rerecorded in spoken form by the original lead singer to have a similar length, tempo, and emotional intonation as their original song counterparts). There were two different stimuli for each condition, and none of the original songs were used for more than one condition.

The stimuli varied in length from 3:00 - 4:03 minutes. However, during the fMRI scan sessions, participants heard only 10-s clips taken from the stimuli. Equal numbers of clips were taken from the beginning, middle, and end of the stimuli. Clips were taken from both verses and chorus and were chosen such that musical phrases were not interrupted within the clip. Each of the 10-s clips were normalized to equate their perceived loudness using the *Audacity* software (Audacity Team, 2020). Further details regarding the acoustic characteristics were determined using the Praat software (Boersma & Weenink, 2018) and can be found in Table 1. During the training period, participants listened to half of the stimuli (4 stimuli, 1 per condition) via an online audio player. The full stimuli, as well as the 10-s clips, can be found in the supplementary information.

Table 1. A summary of the average acoustic characteristics (as determined by Praat software) for the 10-s stimulus clips used in this experiment

	average pitch (Hz)	average pitch range (Hz)	average harmonicity (dB)	average tempo (bpm)
a capella music	229.79	398.14	11.82	135
instrumental music	146.71	524.86	4.36	162
spoken word	105.97	528.55	8.62	-
whole music	138.27	622.37	3.92	156

There were a total of four learning categories of stimuli: 'to be learned' refers to the novel stimuli heard in the first scanning session that the participant subsequently listened to over the training period; 'not to be learned' refers to the novel stimuli heard in the first scanning session that the participant *did not* listen to over the training period; 'learned' refers to the stimuli heard in the second scanning session that the participant listened to over the training period; and 'not learned' refers to the stimuli in the second scanning session that the participant *did not* listen to over the training period. The 'to be learned' and 'learned' stimuli were identical for each participant, as were the 'not to be learned' and 'not learned' stimuli. The sets of stimuli that were learned were counterbalanced across participants: half the participants familiarized with one half of the stimuli; the other half of the participants familiarized with the other half of the stimuli (Groups A and B; see Table 2).

Procedure

Participants completed two functional MRI scans that were separated by a stimulus training period (14-29 days; mean = 20 days). During both scans, participants passively listened to the stimuli. During the training period, participants listened to the stimuli via an online audio player (designed in-lab) that tracked the number of times each stimulus was played. Participants were asked to listen to the stimuli at least 5 times per week. To ensure participants were engaged while listening, the player presented a simple question about the stimulus (e.g. "*Were there lyrics present in the previous song?"*) at random between stimuli. A response was required to move to the next stimulus. Participants were encouraged to incorporate the music into their everyday lives (i.e. to listen while cooking or driving).

Behavioural familiarity tasks

Participants came to the lab every few days to complete a total of four behavioural testing sessions between their two scans. In each session, participants listened to the stimuli and completed a series of behavioural tasks. Each session lasted less than one hour, and the behavioural tasks described below were distributed across sessions.

We created two tests to track participants' familiarity with the stimuli. The first was a lyric modification task that visually presented participants with two sentences. One sentence was

a lyric taken directly from the participant's training stimuli group and the other sentence was a modified version of the same lyric. Participants indicated which of the sentences was correct. The correct and incorrect lyric pairs were tested for validity prior to the study to ensure that modified lyrics were chosen at least equally as often as original lyrics in naïve listeners. Two versions of the task were created to probe learning of the lyrics in the stimuli learned by groups A and B (see Table 2). Due to there being a larger number of word repetitions in the group A stimuli, more lyric pairs were included in the lyric modification task for group B to account for the larger number of unique words in the group B stimuli.

Before the first scan session, participants were tested on the full set of lyric pairs, but as they were not yet familiar with any of the stimuli, they were asked to indicate which lyric they believed was *most likely* to come from a real song. During the behavioural sessions, participants were presented with a randomly generated subset of 10 lyric pairs to track learning progress. Participants were tested on the full set of lyric pairs again after the second scan session. Only conditions that contained words (whole music, a capella, and spoken) were tested (see Table 2).

The second test of familiarity was a melody recognition task. After the second scan *only*, participants listened to 23 pairs of 2 sec clips taken from the stimuli. Three-four clips were taken from each stimulus and none of the clips contained any lyrics. Melodic information was extracted from the a capella stimuli using the *Praat* program (Boersma & Weenink, 2018). During the task, participants were presented with one clip taken from a stimulus the participant trained on and a second clip from a stimulus the participant did not train on (in a randomized order). Participants indicated which of the two clips was most familiar to them. Only conditions that contained melodies (whole music, a capella, and instrumental) were tested (see Table 2).

To ensure the familiar stimuli were truly familiar, any participant who scored an average of 70% correct or less across the two tasks was excluded from further analyses.

Preference ratings

In each lab session and after the second scan, participants rated from 1-5 how much they liked the stimuli, allowing us to track changes in preference with increased familiarity.

Table 2. Description of how the stimuli were counterbalanced across participants and how the behavioural tasks were designed to probe learning of both music and language.

Eight different stimuli	1	2	3	4	5	6	7	8
Conditions	a capella	instrumental music	spoken word	whole music	a capella	instrumental music	spoken word	whole music
Group A participants (N=11)	Learned				Not learned			
Group B participants (N=9)	Not learned				Learned			
Lyric modification task	x		x	x	x		x	x
	Group A task 21 lyric pairs (probing learning in stimuli with language)				Group B task 29 lyric pairs (probing learning in stimuli with language)			
Melody recognition task	x	x		x	x	x		x
	Group A task (probing learning in stimuli with music)				Group B task (probing learning in stimuli with music)			

Online Task Verification

A separate cohort of 32 participants completed an online version of the same lyric modification task described previously *without* training on the stimuli. The online study was used to determine whether an increase in scores from the first to last sessions could be attributed to training with the stimuli or simply due to exposure to the lyric modification task. The task was completed via online surveys that were emailed to participants at time intervals that mimicked the original study. Participants were asked to complete the surveys within 24 hours of receiving the email.

During the first session participants completed the full set of lyric pairs and then listened to all eight stimuli once. Participants were randomly assigned to one of two groups to match the counterbalanced training groups from the original study. In each of the subsequent four sessions, participants completed a short survey of 10 lyric pairs from the stimuli in their 'learning' group. In the final session, participants listened to all eight stimuli for a second time and completed the full set of lyric pairs mimicking the order of events from the original study. Participants only listened to the stimuli in the first and last online sessions and did not have

access to the stimuli in the interim period. No fMRI data was collected from participants completing the online study.

fMRI acquisition and analyses

Imaging was conducted at the Robarts Research Institute on a Siemens Magnetom 7 Tesla scanner with a 32-channel head coil. Functional scans were acquired with 54 slices per volume (TR = 1.25 s; TE = 20 ms; flip angle = 35°; FOV = 220 x 220 mm; voxel size = 2.5 mm^3). The two scan sessions (before and after the training period) were identical and included two 12-minute functional runs. Participants heard ten 10-second clips from each of the 8 stimuli (80 clips total) that were randomized across the two runs (40 clips in each run). Half of these clips were 'to be learned' in the first session, and 'learned' in the second session, while the other half were 'not to be learned' in the first session and 'not learned' in the second session. Between functional runs in the first session only, a whole-head anatomical scan was acquired (TR = 6s; TE = 2.69 ms; FOV = 240 x 240 mm; voxel size = 0.75 mm^3; 208 slices).

Data were processed using SPM12. Data were corrected for motion and coregistered to the participant's structural image. Images were normalized to MNI space and smoothing was done with a Gaussian kernel of 8 mm FWHM. Subject-specific first-level models combined data from all four runs (two from the first session and two from the second session) and included epochs representing each of the 10-second stimulus clips convolved by the canonical hemodynamic response function. Covariates of no interest, representing six motion parameters (x, y, z, translation and rotation) were also included. Serial correlations were accounted for using an autoregressive model and low-frequency noise was removed with a high-pass filter of 128s. Contrast images from single-participant models were created for each of the eight stimuli vs rest in each session for a total of 16 contrast images per subject. The 16 contrasts were then entered into a second-level full-factorial model for group level analysis. The second-level model factors were session (8 stimuli in the first session, 8 stimuli in the second), stimulus type (2 stimuli for each of the 4 types in each session), and learning condition (4 session one stimuli – to be learned, 4 session one stimuli – not to be learned, 4 session two stimuli – learned, 4 session two stimuli – not learned).

Contrasts probing differences in stimulus type, learning condition, and session were generated at the group level. To probe differences in memory, a 2(session) x 2(learning)

ANOVA was conducted within each of the four stimulus types. For each stimulus type, the main effect of session was calculated by comparing session 1 and session 2(e.g. [a capella not to be learned + a capella to be learned] vs.[a capella not learned + a capella learned]). These t-contrasts were calculated in both directions (session 1 > session 2; session 2 > session 1). The main effect of learning in each stimulus type was calculated both across sessions and within session 2. Learning across session compared session 1 to be learned with session 2 learned (e.g. a capella to be learned vs. a capella learned) and learning within session compared session 2 learned with session 2 not learned (e.g. a capella learned vs. a capella not learned). These t-contrasts were generated in both directions. Finally, interaction contrasts were generated within each stimulus type: ([to be learned – not to be learned] – [learned – not learned]). To probe differences in language, pairwise contrasts were created between each of the four stimulus categories (a capella vs. instrumental, a capella vs. spoken, a capella vs. whole, instrumental vs. spoken, instrumental vs. whole, and spoken vs. whole). These t-contrasts were generated separately in each session. Bayesian statistics were implemented using built-in SPM12 functions. To test for more subtle changes in the patterns of brain activation between conditions we used a multivariate representational similarity analysis (RSA). The RSA was implemented using The RSAToolbox (Diedrichsen et al., 2016) in 12 bilateral Harvard-Oxford defined regions of interest (ROIS; atlas distributed with the FSL software package http://fsl.fmrib.ox.ac.uk/fsl/). The ROIs were selected on the basis of a meta-analysis that identified these areas as being involved in memory for music (Freitas et al., 2018) (see Table 3).

Table 3. Areas identified by more than one study in the meta-analysis by Freitas, et al (2018) as being involved in memory for music. ROI templates from the Harvard-Oxford atlas were used.

Area Name	Harvard-Oxford division
Insular cortex	2
Superior frontal gyrus	3
Middle frontal gyrus	4
Inferior frontal gyrus (triangularis)	5
Inferior frontal gyrus (opercularis)	6
Precentral gyrus	7
Superior temporal lobe (anterior)	9
Superior temporal lobe (posterior)	10
Middle temporal gyrus (anterior)	11
Middle temporal gyrus (posterior)	12
Cingulate gyrus (anterior)	29
Cingulate gyrus (posterior)	30

Results

Participant Training

Participants listened to the stimuli an average of 13 times (from 6-20 listens) over an average of 20 days (from 14-29 days).

Behavioural familiarity tasks

Participants significantly improved on the lyric modification task over the training period (see Figure 1). During the first session participants scored an average of 36% correct, which was significantly lower than the average 82% correct score during the final session ($t(34) = -12.3$, $p<0.011$, $d=2.62$; with 3 participants scoring over 90%). The below-chance performance of individuals during the first session is due to how the lyric modification pairs were created. The lyric pairs were designed such that the modified lyrics were chosen at least as often as the original lyrics in naïve listeners. Often, to make the meaning of the new lyric seem *plausible*, we made choices that made the lyric seem more *likely* than the original (when songwriters write lyrics, word choices are often not made based on plausibility, but on intended meaning whether

plausible or not). Thus, as a result of finetuning our lyric pairs there were a number of modified lyrics that were initially chosen more often than the original.

There was no difference in average scores between the two learning groups in the final session (A: 80% vs. B: 85%; t(15)= -0.66, p=0.52, *d*=0.3). Scores from the first behavioural testing session 69% correct, *t(32)*= -3.2, *p*=0.003, *d*=0.86), the second behavioural testing session (71% correct, *t(30)*= -2.5, *p*=0.02, *d*=0.83), and the third behavioural testing session (70% correct, *t(30)*= -2.6, *p*=0.02, *d*=0.71) were also significantly lower than the scores recorded during the final testing session. The scores recorded in the fourth behavioural testing session did not significantly differ from the scores recorded during the final session (79% correct, *t*(30)=-0.7, *p*=0.49, *d*=0.18). Scores on the lyric modification task did not differ between the three conditions tested (spoken, whole, a capella).

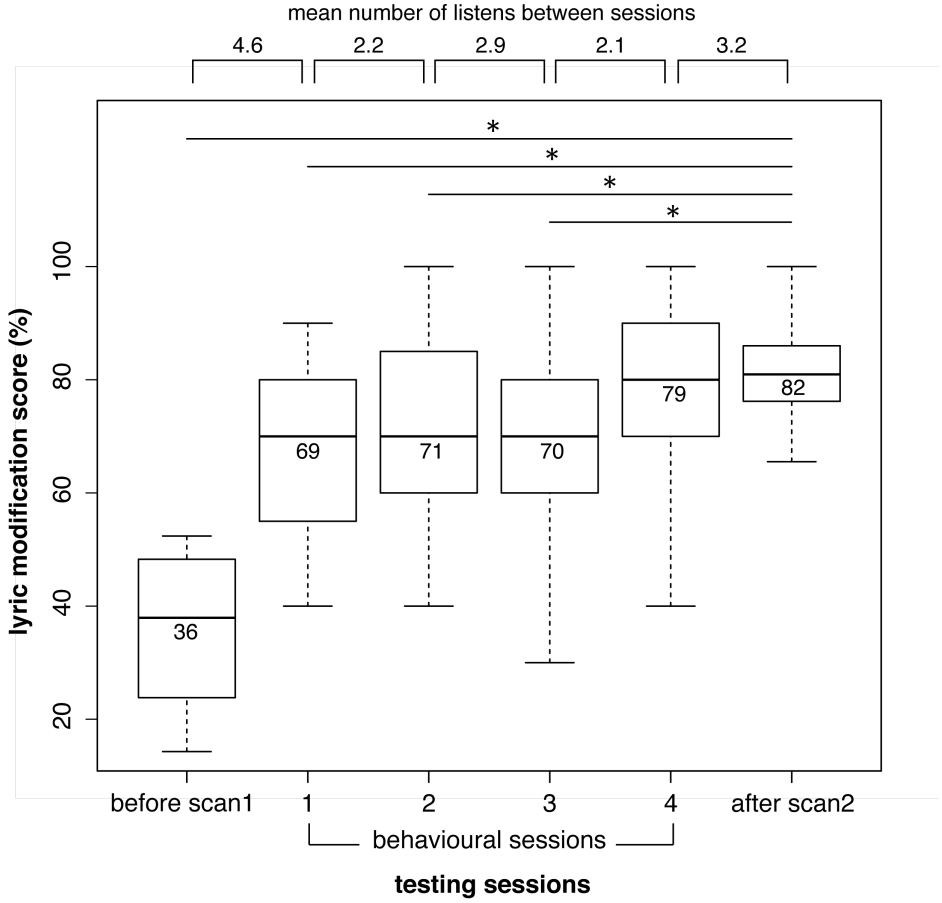


Figure 1. Scores on the lyric modification task across all sessions averaged across the two learning groups. Boxplots show the average, minimum, and maximum correct scores within each session. The average score in each session is listed within each box. The average number of times participants listened to the stimuli between each session is listed above the figure. Significant differences in scores between sessions are shown (* = p<0.05)

In the online task verification study, there was a significant increase from the first session (average 35%) to the last session (average 50%) ($t(121) = -6.30$, $p<0.001$, $d=0.84$; see Figure 2). However, when comparing the 'not learned' stimuli (i.e. Group A doing the group B task and Group B doing the group A task – outlined in red), and the 'learned' stimuli (i.e. Group A doing the group A task and Group B doing the group B task – outlined in blue), there was no interaction between learning and session.

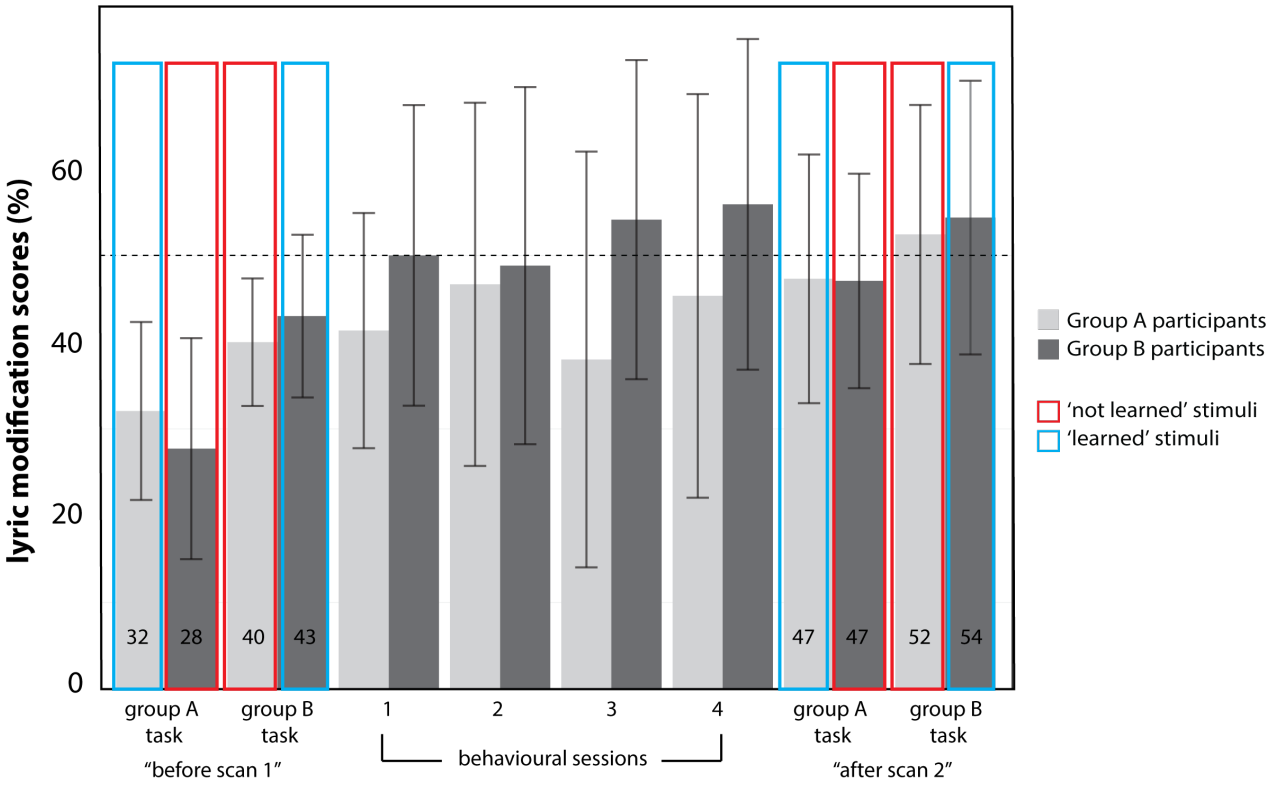


Figure 2. Thirty-two participants completed an online version of the lyric modification task *without training* on the stimuli to determine whether the increase in scores seen in the original experiment was due to exposure to the task itself rather than learning of the stimuli. Error bars represent plus/minus one standard deviation. Red and blue boxes highlight scores representing the 'not learned' or 'learned' stimuli respectively. Average scores are listed on the 'before scan 1' and 'after scan 2' bars directly.

A 2x2 mixed measures ANOVA with session (first, last) and experiment (fMRI, online) was performed to compare learning in the fMRI and online experiments. There was a main effect of experiment, with participants performing better in the fMRI experiment ($F(1,164) = 45.5$,

$p<0.001$, $\eta^2=0.12$) and a main effect of session, with participants performing better in the final session ($F(1,164) = 124.7$, $p<0.001$, $\eta^2=0.33$). However, these must be interpreted in light of a statistically significant interaction between session and experiment ($F(1,164) = 46.2$, $p<0.001$, $\eta^2=0.12$, Figure 3).

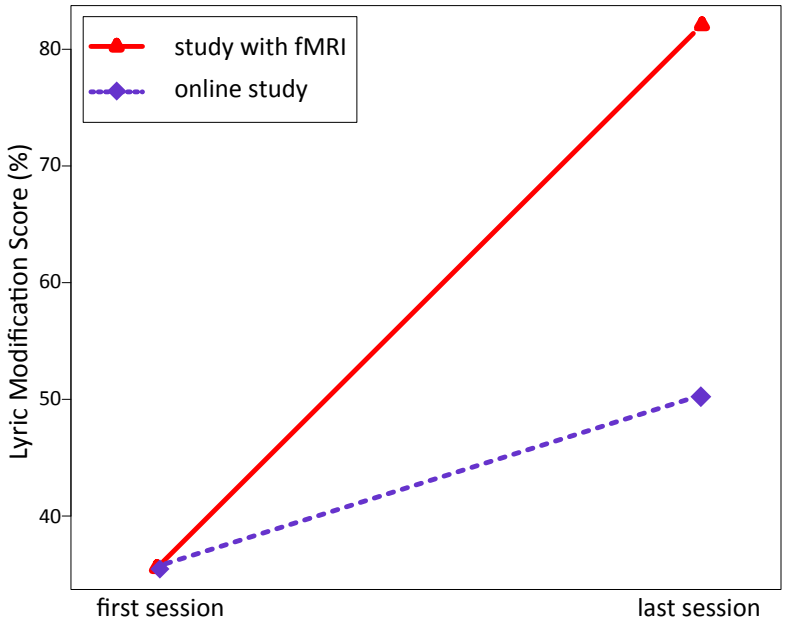


Figure 3. Lyric modification scores from the first and last sessions of the fMRI and online experiments.

Examination of mean scores in Figure 3 clearly shows that, while both groups of participants began at similar levels, the group who actively trained on the stimuli improved significantly more over time than the group who were merely tested repeatedly over the same timeframe. Thus, for the first session, scores from the online study did not differ from the fMRI study (36% vs 36%, $t(28)=0.04$, $p=0.97$, $d=0.01$), while, for the final session, scores from the online study were significantly lower than the fMRI study (50% vs. 82%, $t(47)= -11.2$, $p<0.001$, $d=2.34$; Figure 2). These results indicate that although exposure to the task alone did increase scores, it was not enough to explain the substantial improvement in the experimental group who trained on the stimuli over the same time period.

Participants scored an average of 92% (*SD*=6.4) on the melody memory task completed during the second session, indicating that they were near ceiling at recognizing the melodies of the stimuli they heard during the training period.

Before the training period, participants' preference ratings across all stimuli were an average of 2.9/5. After the training period there was no change in participants' preference ratings of the stimuli ($t(38)=-0.17$, $p=0.87$, $d=0.07$). This was true for all types of stimuli. Average preference ratings for each stimulus type over all testing sessions can be found in Table 4. There was a significant difference in preference based on the type of stimulus ($F(3,796)=93.82$, $p<0.001$, $\eta^2=0.26$). On average, the participants liked the whole stimuli significantly more than the a capella ($t(398)=9.19$, $p<0.001$, $d=1.02$) or the spoken stimuli ($t(398)=13.29$, $p<0.001$, $d=1.04$). Preferences for the instrumental stimuli did not differ from the whole stimuli ($t(396)=0.77$, $p=0.44$, $d=0.08$). Participants also preferred the instrumental stimuli over the a capella ($t(396)=9.64$, $p<0.001$, $d=0.97$) and spoken stimuli ($t(398)=13.61$, $p<0.001$, $d=0.95$). Participants preferred the a capella stimuli over the spoken stimuli ($t(398)=4.32$, $p<0.001$, $d=0.33$).

Table 4. Preference ratings for the stimuli averaged over all testing sessions

Stimulus type	Average preference rating
Whole	3.55 ± 1.07
Instrumental	3.64 ± 1.14
A capella	2.57 ± 1.06
Spoken	2.10 ± 1.11

fMRI Results

Memory

For each subject, all first-level contrasts for the 16 stimuli (8 different stimuli across 2 sessions) were entered into a second-level full-factorial model using SPM12. For each of the four stimulus types (whole, instrumental, a capella, and spoken) a 2x2 ANOVA was performed to test for significant effects of learning and session. Eight contrasts (two for each stimulus type) were created probing average stimulus differences in session 1 vs. session 2 (session 1 > session 2; session 2 > session 1). Eight contrasts (two for each stimulus type) were created probing learning

across session (session 1 to be learned > session 2 learned; session 2 learned > session 1 to be learned). Eight contrasts (two for each stimulus type) were created probing learning within session 2 (session 2 learned > session 2 not learned; session 2 not learned > session 2 learned). Four interaction contrasts (one for each stimulus type) were created probing the interaction between session and learning ([to be learned – not to be learned] – [learned – not learned]). There were no significant main effects or interactions between learning and session for any of the four stimulus types in any of the contrasts listed above (all: $t<3.7$, $p>0.6$).

We further investigated the pairwise comparisons' null results using the built-in Bayesian statistics toolbox in SPM12 (default Cohen's $d = 1.0$). The toolbox reports evidence in support of the alternative hypothesis (i.e. evidence in support of a significant difference between conditions). However, we were interested in the opposite evidence in support of the null hypothesis (i.e. evidence in support of *no* difference between conditions). Therefore, a custom script was created to extract areas which supported the null hypothesis at a Bayes Factor level of 1/50 (very strong evidence for the null; Stefan et al., 2019). Applying Bayesian statistics to the two pairwise contrasts described above showed that activity levels in several brain areas were very likely not to significantly differ between conditions. Thus, the areas highlighted in Figure 4 are statistically 50x more likely to not differ (i.e. in support of the null) than they are to differ.

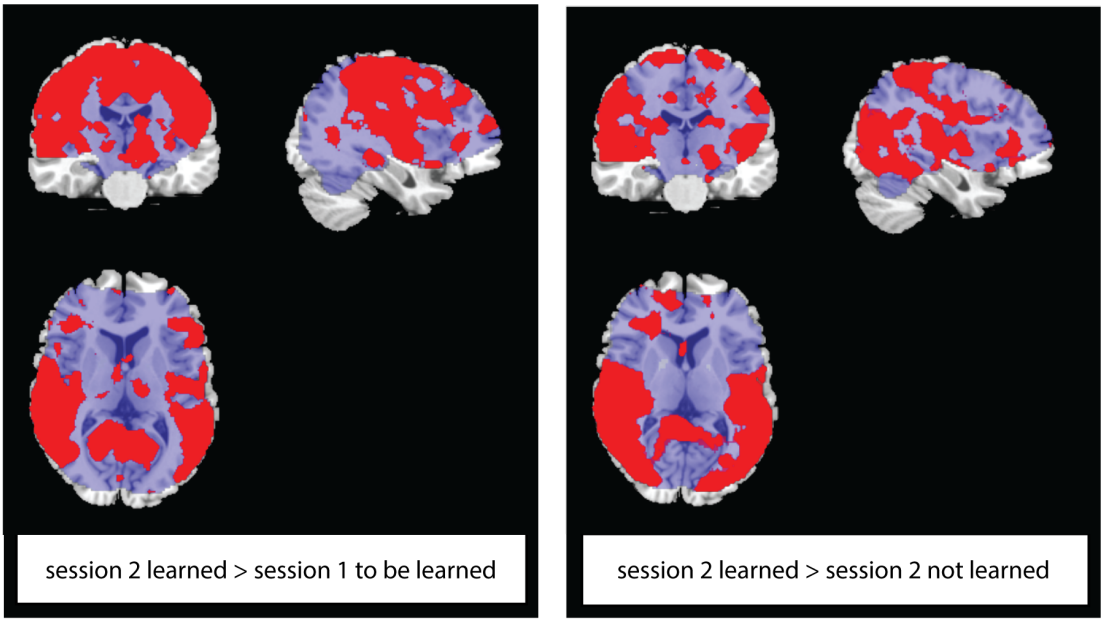


Figure 4. Bayesian statistical results for two contrasts at BF = 1/50. Left panel: session 2 learned stimuli > session 1 to be learned stimuli (identical stimuli differing in familiarity only). Right panel: session 2 learned stimuli > session 2 not learned stimuli (different stimuli). Bayesian statistics were only applied to areas of the brain in which data was acquired in all 20 participants (shown in blue). Thus, for example, the lack of statistics in the area of the basal ganglia reflects the fact that not all 20 participants contributed data in that area. Crosshairs are at x = 35, y = -18, z = 9.

Finally, a representational similarity analysis (RSA) probed for differences in voxel activity patterns generated by the learned and not learned stimulus conditions across the two 12-min functional runs in the second session. Within the 12 regions of interest, ß-weights for each individual and each stimulus type were extracted and spatially pre-whitened using an estimate of the overall noise-covariance matrix (Walther et al., 2016) resulting in the remaining noise in each voxel being approximately uncorrelated with the noise in other voxels (Diedrichsen et al., 2016; Diedrichsen & Kriegeskorte, 2017). We then quantified the difference between the pre-whitened patterns of activity using a "crossnobis estimator" (an unbiased method of determining the distance between patterns, as the estimator's average will be zero if two patterns differ only by noise). The resulting distances between the two patterns were plotted as a representational dissimilarity matrix (see Figure 5). We compared the four 'learned' and the four 'not learned' stimuli. Negative distances can be interpreted as zero distance, or no evidence of dissimilarity between stimulus categories. Mathematically, the negative distance is derived from whether or not the distance between the two conditions was consistent across the runs. In this case, there

were two runs included in the analysis and the negative distance is likely a result of the distance vectors between the conditions of interest (‘learned’ and ‘not learned’) being in slightly different space. When the inner product of the vectors from the two runs is taken, the resultant vector length is less than zero. There were no systematic RSA differences between the ‘learned’ and the ‘not learned’ stimuli across the 12 ROIs. There were RSA differences between the different stimulus categories in temporal auditory areas: bilateral anterior and posterior middle temporal gyrus and superior temporal gyrus.

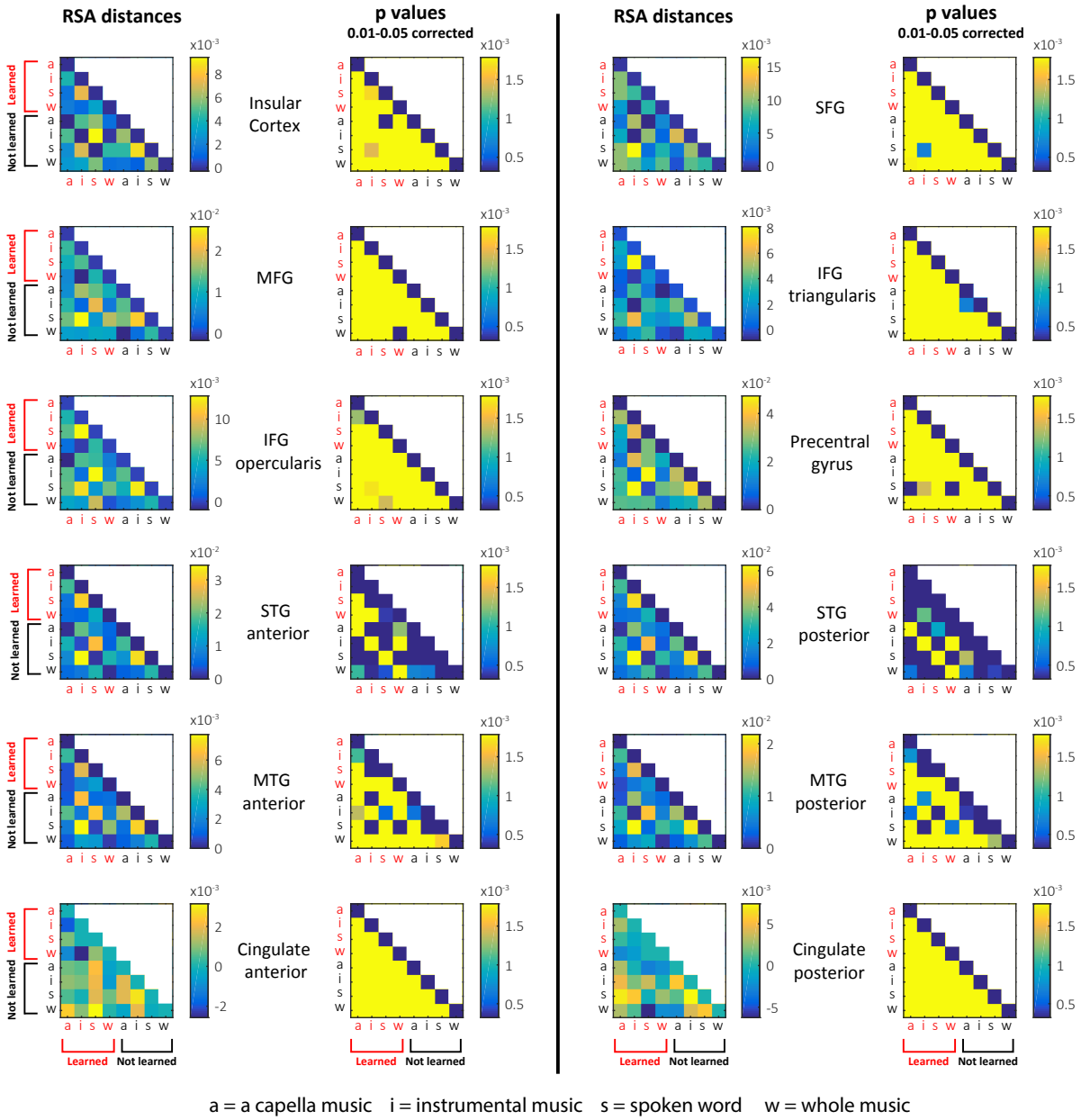


Figure 5. Distances between the patterns for the 'learned' (in red letters) and 'not learned' (in black letters) stimuli (from the second session), in 12 ROIs. The matrices in the left columns indicate the distance between patterns generated by each pair of stimuli. The matrices in the right columns are the corresponding p-values (Bonferroni corrected) from a 1-tailed t-test of those distances across all 20 participants. A yellow colour square in the right matrix indicates that the t-test on the corresponding square in the left matrix is not significant at a corrected $p \geq 0.05$ level. Any dark blue squares in the right matrices indicate significance at a level of $p \leq 0.01$. The diagonal of the lower left 4x4 corner of each matrix contains the direct comparisons between the learned and not learned conditions (i.e., a cappella learned vs. a capella not learned, instrumental learned vs. instrumental not learned, spoken learned vs spoken not learned, and whole learned vs. whole not learned).

Language

Given the lack of main effects or interactions resulting from familiarity with the stimuli, and the fact that the stimuli presented in the two scanning sessions were identical, the second session was treated as a replication of the first to investigate the reliability of the stimulus type differences between sessions. Using the same full-factorial model as described previously that contained all 16 first-level contrasts from each participant (8 different songs across 2 sessions), pairwise contrasts between each of the four stimulus categories (a capella, instrumental, spoken, whole) were calculated within each session. Brain areas with significant activity differences between stimulus types are listed in Table 5. Results from the two sessions are shown side-by-side to show the consistency between the two independently collected sessions. The statistical contrasts were only calculated in brain areas that contained data from all 20 participants (shown in blue in Figure 4)

A capella stimuli generated significantly more activity than other stimulus categories in auditory areas (posterior superior and middle temporal gyri, planum polare) and left motor areas (precentral gyrus) in both sessions (see Figure 6).

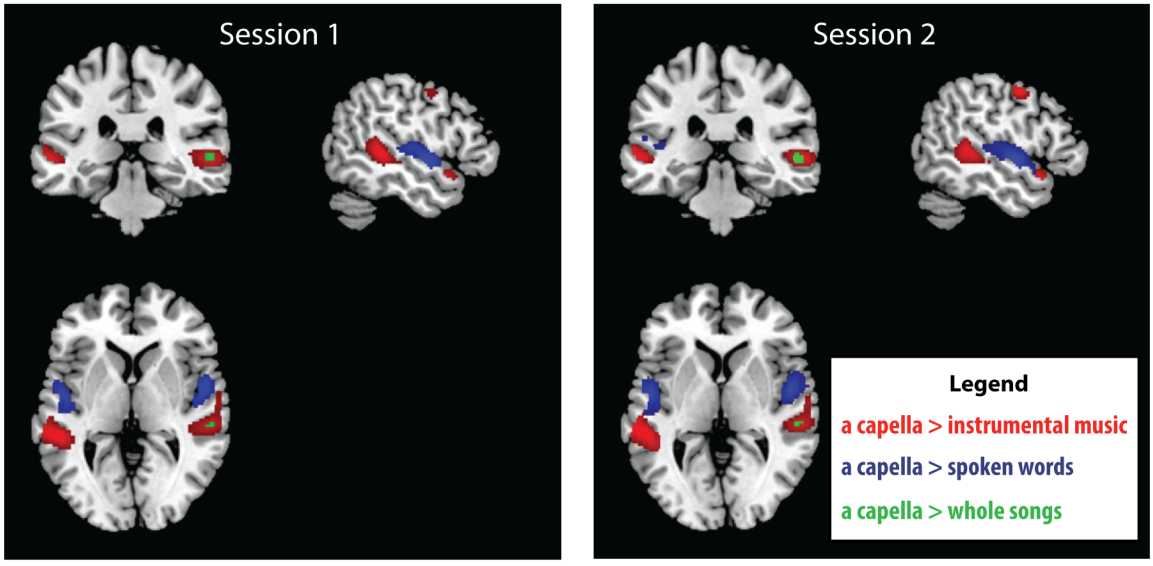


Figure 6. The left panel shows results from the first scan and the right panel shows results from the second scan. Three contrasts are shown: a capella > instrumental music (red), a capella > spoken words (blue), a capella > whole songs (green). Crosshairs are placed at x= -51, y= -30, z= 3.

Instrumental stimuli generated significantly more activity than spoken stimuli in bilateral auditory cortices (planum polare) in both sessions and in the left angular gyrus in the second session only (see Figure 7). Instrumental stimuli did not result in more activity than the a capella or whole stimuli in either session.

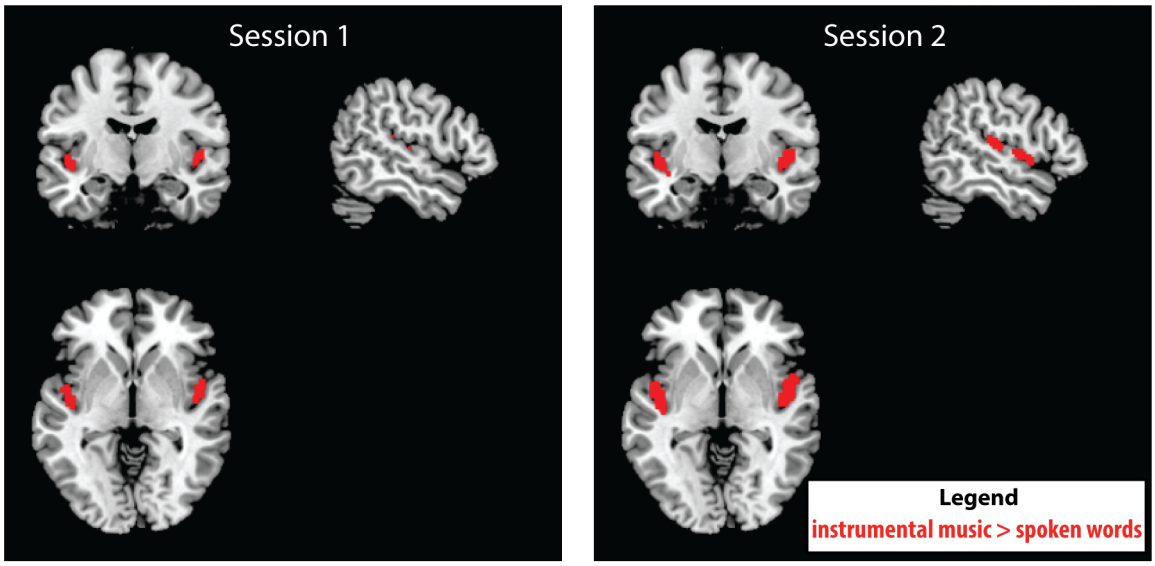


Figure 7. The left panel shows results from the first scan and the right panel shows results from the second scan. One contrast is shown: instrumental music > spoken words. Crosshairs are placed at x= -53, y= -8, z= 2.

Spoken stimuli generated significantly more activity than instrumental and whole stimuli in auditory cortices (posterior superior and middle gyri) in both sessions. Spoken stimuli also resulted in significantly more activity than instrumental in the left inferior frontal area (pars triangularis) in the first session and in the temporal pole in the second session (see Figure 8).

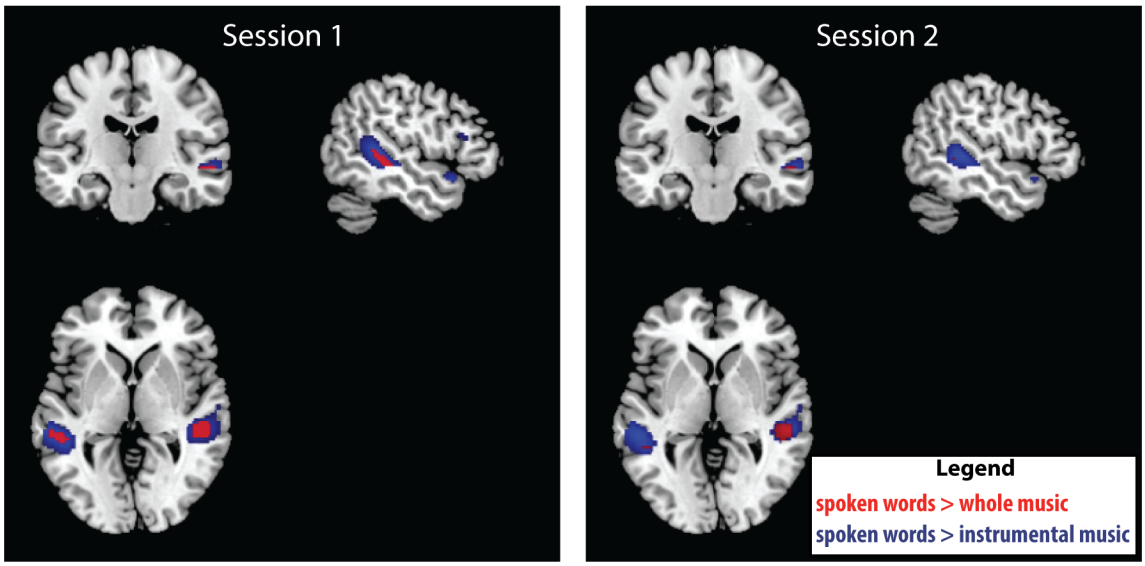


Figure 8. The left panel shows results from the first scan and the right panel shows results from the second scan. Two contrasts are shown: spoken words > whole music (red), spoken words > instrumental music (blue). Crosshairs are placed at x= -50, y= -18, z= 1.

Whole stimuli resulted in significantly more activity than instrumental and spoken stimuli in bilateral auditory cortices areas (posterior superior and middle temporal gyri, planum polare) in both sessions. Whole stimuli did not produce more activity than a capella stimuli in either session.

Table 5. Results from binary contrasts between all stimulus categories in both sessions. Significant clusters at FDR correction <0.05 are listed. Missing results indicate no significant clusters were found.

Contrast	Region	Session 1		Session 2	
		p FDR <0.05	Coordinates (x, y, z)	*p* FDR <0.05	Coordinates (x, y, z)
A capella > instrumental	L posterior temporal (superior gyrus)	<0.001	-52, -38, 2	<0.001	-54, -36, 2
	R posterior temporal (superior and middle gyri)	<0.001	58, -16, -6	<0.001	60, -26, -2
	L precentral gyrus	0.068	-52, -2, 46	0.006	-50, -2, 46
A capella > spoken	L planum polare	<0.001	-48, -2, -4	<0.001	-48, -4 ,-4
	R planum polare	<0.001	52, -2, 0	<0.001	50, -4, 0
A capella > whole	R posterior temporal (superior and middle gyri)	0.003	60, -18, -4	0.005	56, -28, -2
Instrumental > a capella	-	-	-	-	-
Instrumental > spoken	L planum polare	0.001	-46, -6, -4	<0.001	-46, -4, -6
	R planum polare	<0.001	48, 2, -6	<0.001	48, 2, - 8
	R planum temporale	0.003	62, -26, 16	-	-
	L angular gyrus	-	-	0.048	-58, -56, 38
Instrumental > whole	-	-	-	-	-
Spoken > a capella	-	-	-	-	-
Spoken > instrumental	L posterior temporal (superior gyrus)	<0.001	-52, -38, 2	<0.001	-54, -36, 2
	R posterior temporal (middle gyrus)	<0.001	48, -26, -4	<0.001	54, -30, -2
	L inferior frontal (pars triangularis)	0.014	-52, 22, 16	-	-
	Temporal pole	-	-	0.018	-50, 14, -16
Spoken > whole	L posterior temporal (middle gyrus)	<0.001	-54, -34, -2	-	-
	R posterior temporal (middle gyrus)	<0.001	52, -22, -6	<0.001	52, -30, -2
Whole > a capella	-	-	-	-	-
Whole > instrumental	L posterior temporal (superior and middle gyri)	<0.001	-52, -38, 2	<0.001	-54, -36, 2
	R anterior temporal (superior gyrus)	0.006	60, -4, -8	-	-
Whole > spoken	L planum polare	<0.001	-46, -6, -4	<0.001	-46, -2, -4
	R planum polare	<0.001	50, -2, 0	<0.001	48, 2, -8

Discussion

In the current study, we set out to understand the relationship between the neural networks responsible for music and language abilities and how they are influenced by memory. The four stimulus conditions allowed us to compare four combinations of music and language, namely, whole music, instrumental music, a capella, and spoken word. Using a novel methodological approach consisting of a strictly controlled training paradigm, we isolated natural exposure to music while controlling for autobiographical memory confounds. We monitored the number of times each stimulus was heard by participants, creating an objective measure of familiarity.

To track familiarity with the language component of the stimuli, participants identified correct lyrics in a forced choice paradigm. Scores on the lyric modification task improved during the training period (i.e. between the two fMRI scans), providing objective verification that the stimuli had, in fact, become more familiar over time. Moreover, the online follow-up study confirmed that performance improvement was the result of training exposure, rather than simply repeated exposure to the task itself. To track learning of the melodic component of the stimuli, participants identified familiar melodies in a forced choice task. This task was completed after the second fMRI scan session. Performance was near ceiling. The results from these two tests indicate that the participants became familiar with both the language and the musical components of the stimuli over the training period.

FMRI responses to the four stimulus types differed. This result can be seen in the representational similarity analysis in the anterior and posterior middle and superior temporal gyri as well as in the GLM contrast analyses. Because familiarity did not significantly affect activation to the stimuli, we treated the two scanning sessions separately in the GLM contrast analysis, replicating the comparisons between different stimulus types in each session. The three conditions that contained music (a capella, instrumental, and whole music) activated the bilateral planum polare more than the spoken condition did. The planum polare activity did not differ between the three musical conditions. The planum polare, along with the inferior frontal gyrus (IFG), has been shown to play a role in processing language and musical syntax, with increasing stimulus complexity resulting in more activation (Bookheimer, 2002; Brown et al., 2006; Constable et al., 2004; Griffiths et al., 1998; Merrill et al., 2012). It may be that the lack of

planum polare activation differences between the three music conditions is due to the highly controlled nature of the stimuli. The stimuli that contained music were written by the same individual and likely did not differ in musical complexity however, as these stimuli contained more musical information than the spoken condition, planum polare activation may have been greater as a result.

The left IFG was significantly more active in the spoken than in the instrumental condition. Despite the IFG's known involvement in musical and language syntax processing (Brown et al., 2006; Kunert et al., 2015; Merrill et al., 2012), the significant difference in activation was only seen in the one comparison (i.e. not seen in the a capella-instrumental or whole-instrumental comparisons). The activation difference between the spoken and instrumental conditions was in the opposite direction to that seen in the planum polare (where more activity to instrumental music than to spoken stimuli was found). A similar activation pattern was reported in another passive listening task that also directly compared music and language stimuli: greater activation in planum polare to stimuli with melodic pitch information than stimuli without pitch information, and greater activation in IFG to stimuli with language information over stimuli without language information (Merrill et al., 2012). In the current study, the need to process language syntax information was higher for the spoken stimuli than for the instrumental stimuli and is likely the reason for the difference in IFG activation. However, this reasoning does not explain why no differences were seen between either the a capella or the whole stimuli, which also contained language information, over the instrumental stimuli. It is possible that this pattern of results can be explained by an interaction between language and musical syntax processing. For example, Kunert et al. (2015) found that IFG activation only occurs when both the music and language components of the stimuli are syntactically challenging. In the current study, the two stimuli that were most different from each other in terms of both musical and language syntax were those in the spoken and instrumental conditions leading to the statistically significant difference in IFG activation.

All three conditions that contained language (a capella, spoken, whole) significantly activated bilateral posterior superior and middle temporal gyri more than the instrumental condition. These areas have been previously identified in passive listening tasks involving speech and non-speech stimuli (Tie et al., 2014; Tremblay et al., 2013) and are 'voice-selective'

(Belin et al., 2000; Fecteau et al., 2004). During passive listening to vocal (words, phrases, sentences, etc.) and non-vocal sounds (machine noises, nature sounds etc.), areas along the superior and middle temporal gyri are more active for stimuli with vocalizations than without vocalizations (Belin et al., 2000; Fecteau et al., 2004). In a direct comparison between speech and musical instruments, the posterior portions of the superior and middle temporal gyri were more active to human voice than to non-vocal sounds (Bethmann & Brechmann, 2014). In the current study, activity did not differ across the three different conditions involving the voice, confirming that these areas are generally active in response to the human voice.

The current experiment did not include a vocal no-language condition (e.g. humming), nor a language non-vocal condition (e.g. computerized language) to dissociate the presence of language from the presences of vocal sounds. Although the differences in the bilateral posterior superior and middle temporal gyri may be attributable to the presence of vocalizations, rather than language, the IFG and the planum polare are not known to be 'voice-selective' (Belin et al., 2000). Therefore, the activation differences in the IFG and planum polare are likely due to differences in language and syntax processing between stimulus categories (Merrill et al., 2012).

It is possible that the differences in acoustic characteristics across stimuli may have influenced the results. To mitigate any stimulus-specific effects, two stimuli were included in each of the four stimulus conditions, and the stimuli were counterbalanced across learning groups such that all stimuli were included in each of the four learning groups (to be learned, not to be learned, learned, not learned). Therefore, it is unlikely that a single stimulus could drive the differences between conditions, but we cannot definitively state that condition differences were completely uninfluenced by acoustic differences between conditions.

Although the behavioural task results confirmed that participants were more familiar with the stimuli during the second fMRI scan than the first, there were no corresponding neural changes associated with this behavioural improvement. The Bayesian statistics support this result at a Bayes Factor level of 1/50 (i.e. very strong evidence to support no difference between the 'learned' and 'not learned' conditions). A representational similarity analysis (a multivariate approach that takes into account the subtle pattern variations in brain activation to different stimuli) also showed no difference between the 'learned' and 'not learned' stimuli. One issue to consider is that the imaging data were collected at a 7-Tesla magnetic field strength. In high-

strength magnets, there can be signal loss in some brain areas. Here, signal dropout occurred in anterior temporal areas and basal ganglia across the majority of participants. However, primary auditory area activity was preserved. Effects of familiarity may be observed at lower field strengths in the areas where signal was lost in the current study. It is also possible that the null results found in the brain areas with consistent data across all participants were due to undetected true effects and an increase in stimulus trials or sample size could increase power.

The lack of difference between novel and familiar music is in contrast with the results of other studies (e.g. Freitas et al., 2018; Halpern & Zatorre, 1999; Herholz et al., 2012) and is likely related to procedural differences. In most previous studies, participants listened to stimuli that they already knew, such as children's songs or folksongs (e.g. Alonso et al., 2016; Herholz et al., 2012; Saito et al., 2012; Schaal et al., 2015), popular music from the radio charts (e.g. Jacobsen et al., 2015; Pereira et al., 2011), or music supplied by the participants (e.g. El Haj et al., 2012), and rated their familiarity with the stimuli. Using well-known music does not control for the amount of exposure to the stimuli but it does reflect the way individuals generally learn and become familiar with music 'in the real world'. In contrast, in the current study, participants learned novel stimuli by listening both in a 'sterile' lab environment, as well as out of the lab via an online music player and the number of exposures to the stimuli gave an objective measure of familiarity. Although participants were encouraged to incorporate the music into their everyday lives (i.e. to listen while cooking or driving), few participants reported having done so. Participants listened to the stimuli an average of 13 times over the course of the study, which is likely fewer times than a well-known song is heard over a lifetime. For example, the number one pop song in Canada is played over 5600 times per week across all Canadian radio stations (*World Airplay Radio Monitor: Real-Time Radio Tracking*, 2012). A person may encounter that song hundreds of times over the course of their life. Therefore, although the participants learned the current stimuli, they did not learn them to the same level as songs 'in the real world'.

In addition, the behavioural tests to probe music familiarity may have inflated measures of how well participants learned the stimuli because they relied on recognition rather than recollection memory. Recognition memory requires a more 'shallow' encoding of the stimuli being remembered than does recollection (Mandler, 2008). Although participants performed well on the recognition tests, we expect that if participants had been asked to sing the stimuli, their

recollection would be worse than if they sang a well-known song like, for example, a Christmas carol. However, assessing recall of musical information in participants, especially those who are not musicians, is difficult to do accurately as it requires the separation of deficits in recall from deficits in musical ability. For example, poor singing of a song could be caused by poor song recollection or poor singing ability. The reliance on recognition memory tests in the current study may have led us to believe that the differences in memory between the novel and familiar stimuli were more profound than in actuality.

When people listen to music in the real world, that listening is often connected with many other aspects of life (i.e. people, places, or experiences) making it difficult to separate the specific musical memory response in the brain from the neural response to the autobiographical memories evoked by that music. One study examined the overlap between musical and autobiographical memories evoked by music (Janata, 2009) and identified areas in which activation correlated with the degree of autobiographical salience above and beyond the degree of familiarity. These areas were located in prefrontal cortex in bilateral superior frontal gyrus (Brodmann areas 8 & 9) and in left inferior frontal gyrus (BA 45). These same regions have been identified as involved in musical memory in studies that presented individuals with well-known music (Groussard et al., 2009; Klostermann et al., 2009; Plailly et al., 2007). It is possible that the areas previously attributed to musical memory are in fact activated because of the autobiographical memories triggered by the music, rather than by memory for the music itself. In this study, the carefully controlled way in which participants learned the stimuli did not allow participants to create the autobiographical memories they would have if the music was learned ‘naturally’. Without such memories, the differences between the brain activity patterns for the ‘learned’ and ‘not learned’ stimuli are presumably reduced, limiting the ability to detect differences based on familiarity with the music alone.

Participant’s lack of preference for the stimuli, exacerbated by the way the stimuli were created, likely also contributed to the lack of familiarity results in the fMRI data. To create the different stimulus categories while controlling for as many features as possible, we deconstructed whole songs into their component parts. Although spoken word, instrumental music, and a capella music are all genres of their own, the way they were created in this study was not representative of these genres. For example, to create the instrumental and a capella music

stimuli we extracted only the specific lines of interest (instrumental or sung voice) from original whole songs. This process resulted in music that was not representative of instrumental and a capella music because each line was musically simpler and less interesting to listen to on its own, as originally, they were intended to be listened to as part of a larger whole. Similarly, the spoken word stimuli were created by recording song lyrics as spoken words. Although similar to poetry, the lyrics were not written to be experienced without music and participants informally reported that the repetitive nature of the lyrics was not pleasant to listen to as prose. In comparison, the whole stimuli were not modified. Participants' preferences mirrored the amount each stimulus was modified: participants preferred the stimuli that were modified the least over those modified the most. This pattern was not related to participants' memory for the stimuli as measured by the behavioural tasks. Interestingly, participants' enjoyment of the stimuli did not increase with exposure, as would be expected by the mere exposure effect (an increase in preference as a result of repeated exposure; Zajonc, 2001). Although there were no directly negative events associated with listening to the stimuli, the requirement to listen to the stimuli daily and the association with the lab environment may have been enough to override any mild positive reactions a participant may have had from the repeated stimulus exposure, resulting in no change in their preference ratings. Using stimuli intended to be experienced as poetry, a capella, or instrumental music (rather than deconstructing whole stimuli) may have increased participants' preference and memory for the stimuli, as preferred music is better remembered than non-preferred music (Eschrich et al., 2008; Samson et al., 2009; Stalinski & Schellenberg, 2013). However, using such existing stimuli would not have allowed control of similarity across the stimulus types (all stimuli were written by the same individual, with similar instrumentation, the same voice across all stimuli, and from a similar rock genre).

The present study isolated memory for music from the confounding factor of autobiographical memory by asking participants to train on highly controlled novel stimuli. As a result, we have come to understand a number of key components that are necessary for musical memory. The way individuals engage with music is important for creating a memory for that music. The degree of engagement during the learning of music, driven by preference or autobiographical memories associated with the music, may speak to why there is such a disagreement in the literature about the areas involved in musical memory as it is difficult to control for participants' engagement while maintaining a natural learning process. Further

investigations into how musical memory, emotional engagement, and language processing are related may be key to understanding what makes memory for music so unique and robust in the presence of neurodegenerative disorders such as Alzheimer's disease.

Supplementary Information

The full stimuli and the 10-s clips used during this experiment can be found at the following url: https://owenlab.uwo.ca/research/research_tools.html

Bibliography

Agustus, J. L., Golden, H. L., Callaghan, M. F., Bond, R. L., Benhamou, E., Hailstone, J. C., Weiskopf, N., & Warren, J. D. (2018). Melody Processing Characterizes Functional Neuroanatomy in the Aging Brain. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00815

Alonso, I., Davachi, L., Valabrègue, R., Lambrecq, V., Dupont, S., & Samson, S. (2016). Neural correlates of binding lyrics and melodies for the encoding of new songs. *NeuroImage*, *127*, 333–345. https://doi.org/10.1016/j.neuroimage.2015.12.018

Audacity Team. (2020). *Audacity(R): Free Audio Editor and Recorder*. https://audacityteam.org/

Ayotte, J., Peretz, I., & Hyde, K. (2002). Congenital amusia. *Brain*, *125*(2), 238–251. https://doi.org/10.1093/brain/awf028

Baird, A., & Samson, S. (2009). Memory for music in Alzheimer's disease: Unforgettable? *Neuropsychology Review*, *19*(1), 85–101. https://doi.org/10.1007/s11065-009-9085-2

Belin, P., Zatorre, R. J., Lafaille, P., Ahad, P., & Pike, B. (2000). Voice-selective areas in human auditory cortex. *Nature*, *403*(6767), 309–312. https://doi.org/10.1038/35002078

Bethmann, A., & Brechmann, A. (2014). On the definition and interpretation of voice selective activation in the temporal cortex. *Frontiers in Human Neuroscience*, *8*. https://doi.org/10.3389/fnhum.2014.00499

Boersma, P., & Weenink, D. (2018). *Praat: Doing phonetics by computer* (6.0.37) [Computer software]. Celemony. www.praat.org

Bookheimer, S. (2002). Functional MRI of Language: New Approaches to Understanding the Cortical Organization of Semantic Processing. *Annual Review of Neuroscience*, *25*(1), 151–188. https://doi.org/10.1146/annurev.neuro.25.112701.142946

Brown, S., Martinez, M. J., & Parsons, L. M. (2006). Music and language side by side in the brain: A PET study of the generation of melodies and sentences. *European Journal of Neuroscience*, *23*(10), 2791–2803. https://doi.org/10.1111/j.1460-9568.2006.04785.x

Constable, R. T., Pugh, K. R., Berroya, E., Mencl, W. E., Westerveld, M., Ni, W., & Shankweiler, D. (2004). Sentence complexity and input modality effects in sentence comprehension: An fMRI study. *NeuroImage*, *22*(1), 11–21. https://doi.org/10.1016/j.neuroimage.2004.01.001

Cuddy, L. L., & Duffin, J. (2005). Music, memory, and Alzheimer's disease: Is music recognition spared in dementia, and how can it be assessed? *Medical Hypotheses*, *64*(2), 229–235. https://doi.org/10.1016/j.mehy.2004.09.005

Cuddy, L. L., Duffin, J. M., Gill, S. S., Brown, C. L., Sikka, R., & Vanstone, A. D. (2012). Memory for Melodies and Lyrics in Alzheimer's Disease. *Music Perception: An Interdisciplinary Journal*, *29*(5), 479–491. https://doi.org/10.1525/mp.2012.29.5.479

Daneman, M., & Merikle, P. M. (1996). Working memory and language comprehension: A meta-analysis. *Psychonomic Bulletin & Review*, *3*(4), 422–433. https://doi.org/10.3758/BF03214546

Deutsch, D., Henthorn, T., & Lapidis, R. (2011). Illusory transformation from speech to song. *The Journal of the Acoustical Society of America*, *129*(4), 2245–2252. https://doi.org/10.1121/1.3562174

Diedrichsen, J., & Kriegeskorte, N. (2017). Representational models: A common framework for understanding encoding, pattern-component, and representational-similarity analysis. *PLOS Computational Biology*, *13*(4), e1005508. https://doi.org/10.1371/journal.pcbi.1005508

Diedrichsen, J., Provost, S., & Zareamoghaddam, H. (2016). On the distribution of cross-validated Mahalanobis distances. *ArXiv:1607.01371 [Stat]*. http://arxiv.org/abs/1607.01371

El Haj, M., Fasotti, L., & Allain, P. (2012). The involuntary nature of music-evoked autobiographical memories in Alzheimer's disease. *Consciousness and Cognition*, *21*(1), 238–246. https://doi.org/10.1016/j.concog.2011.12.005

Eschrich, S., Münte, T. F., & Altenmüller, E. O. (2008). Unforgettable film music: The role of emotion in episodic long-term memory for music. *BMC Neuroscience*, *9*(1), 48. https://doi.org/10.1186/1471-2202-9-48

Esfahani-Bayerl, N., Finke, C., Kopp, U., Moon, D.-U., & Ploner, C. J. (2019). Musical memory and hippocampus revisited: Evidence from a musical layperson with highly selective hippocampal damage. *Cortex*, *119*, 519–527. https://doi.org/10.1016/j.cortex.2018.12.023

Fadiga, L., Craighero, L., & D'Ausilio, A. (2009). Broca's area in language, action, and music. *Annals of the New York Academy of Sciences*, *1169*, 448–458. https://doi.org/10.1111/j.1749-6632.2009.04582.x

Fecteau, S., Armony, J. L., Joanette, Y., & Belin, P. (2004). Is voice processing species-specific in human auditory cortex? An fMRI study. *Neuroimage*, *23*(3), 840–848. https://doi.org/10.1016/j.neuroimage.2004.09.019

Finke, C., Esfahani, N. E., & Ploner, C. J. (2012). Preservation of musical memory in an amnesic professional cellist. *Current Biology*, *22*(15), R591–R592. https://doi.org/10.1016/j.cub.2012.05.041

Freitas, C., Manzato, E., Burini, A., Taylor, M. J., Lerch, J. P., & Anagnostou, E. (2018). Neural Correlates of Familiarity in Music Listening: A Systematic Review and a Neuroimaging Meta-Analysis. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00686

Gordon, R. L., Schön, D., Magne, C., Astésano, C., & Besson, M. (2010). Words and Melody Are Intertwined in Perception of Sung Words: EEG and Behavioral Evidence. *PLoS ONE*, *5*(3). https://doi.org/10.1371/journal.pone.0009889

Griffiths, T. D. (1997). Spatial and temporal auditory processing deficits following right hemisphere infarction. A psychophysical study. *Brain*, *120*(5), 785–794. https://doi.org/10.1093/brain/120.5.785

Griffiths, T. D., Büchel, C., Frackowiak, R. S. J., & Patterson, R. D. (1998). Analysis of temporal structure in sound by the human brain. *Nature Neuroscience*, *1*(5), 422–427. https://doi.org/10.1038/1637

Groussard, M., Viader, F., Landeau, B., Desgranges, B., Eustache, F., & Platel, H. (2009). Neural Correlates Underlying Musical Semantic Memory. *Annals of the New York Academy of Sciences*, *1169*(1), 278–281. https://doi.org/10.1111/j.1749-6632.2009.04784.x

Halpern, A. R., & Zatorre, R. J. (1999). When That Tune Runs Through Your Head: A PET Investigation of Auditory Imagery for Familiar Melodies. *Cerebral Cortex*, *9*(7), 697–704. https://doi.org/10.1093/cercor/9.7.697

Herholz, S., Halpern, A., & Zatorre, R. (2012). Neuronal correlates of perception, imagery, and memory for familiar tunes. *Journal of Cognitive Neuroscience*, *24*(6), 1382–1397. https://doi.org/10.1162/jocn_a_00216

Hymers, M., Prendergast, G., Liu, C., Schulze, A., Young, M. L., Wastling, S. J., Barker, G. J., & Millman, R. E. (2015). Neural mechanisms underlying song and speech perception can be

differentiated using an illusory percept. *NeuroImage*, *108*, 225–233. https://doi.org/10.1016/j.neuroimage.2014.12.010

Jackendoff, R. (2009). Parallels and Nonparallels between Language and Music. *Music Perception: An Interdisciplinary Journal*, *26*(3), 195–204. https://doi.org/10.1525/mp.2009.26.3.195

Jackendoff, R., & Lerdahl, F. (2006). The capacity for music: What is it, and what's special about it? *Cognition*, *100*(1), 33–72. https://doi.org/10.1016/j.cognition.2005.11.005

Jacobsen, J., Fritz, T., Stelzer, J., & Turner, R. (2015). Why musical memory can be preserved in advanced Alzheimer's disease. *Brain: A Journal of Neurology*, 1–13. https://doi.org/10.1093/awv148

Janata, P. (2009). The neural architecture of music-evoked autobiographical memories. *Cerebral Cortex*, *19*(11), 2579–2594. https://doi.org/10.1093/cercor/bhp008

Klostermann, E. C., Loui, P., & Shimamura, A. P. (2009). Activation of right parietal cortex during memory retrieval of nonlinguistic auditory stimuli. *Cognitive, Affective, & Behavioral Neuroscience*, *9*(3), 242–248. https://doi.org/10.3758/CABN.9.3.242

Koelsch, S., Gunter, T., Cramon, D., Zysset, S., Lohmann, G., & Friederici, A. (2002). Bach Speaks: A Cortical "Language-Network" Serves the Processing of Music. *NeuroImage*, *17*, 956–966. https://doi.org/10.1006/nimg.2002.1154

Kunert, R., Willems, R. M., Casasanto, D., Patel, A. D., & Hagoort, P. (2015). Music and Language Syntax Interact in Broca's Area: An fMRI Study. *PLOS ONE*, *10*(11), e0141069. https://doi.org/10.1371/journal.pone.0141069

Mandler, G. (2008). Familiarity Breeds Attempts: A Critical Review of Dual-Process Theories of Recognition. *Perspectives on Psychological Science*, *3*(5), 390–399. https://doi.org/10.1111/j.1745-6924.2008.00087.x

Merrill, J., Sammler, D., Bangert, M., Goldhahn, D., Lohmann, G., Turner, R., & Friederici, A. D. (2012). Perception of Words and Pitch Patterns in Song and Speech. *Frontiers in Psychology*, *3*. https://doi.org/10.3389/fpsyg.2012.00076

Metz-Lutz, M.-N., & Dahl, E. (1984). Analysis of word comprehension in a case of pure word deafness. *Brain and Language*, *23*(1), 13–25. https://doi.org/10.1016/0093-934X(84)90002-6

Mohanan, M., Karuvannur Puthanveettil. (1982). *Lexical phonology* [PhD]. Massachusetts Institute of Technology.

Müllensiefen, D., Gingras, B., Musil, J., & Stewart, L. (2014). The Musicality of Non-Musicians: An Index for Assessing Musical Sophistication in the General Population. *PLoS ONE*, *9*(2). https://doi.org/10.1371/journal.pone.0089642

Norman-Haignere, S. V., Feather, J., Brunner, P., Ritaccio, A., McDermott, J. H., Schalk, G., & Kanwisher, N. (2019). *Intracranial recordings from human auditory cortex reveal a neural population selective for musical song* [Preprint]. Neuroscience. https://doi.org/10.1101/696161

Patel, A. D. (2008). *Music, Language, and the Brain*. Oxford University Press, USA.

Pereira, C. S., Teixeira, J., Figueiredo, P., Xavier, J., Castro, S. L., & Brattico, E. (2011). Music and Emotions in the Brain: Familiarity Matters. *PLoS ONE*, *6*(11). https://doi.org/10.1371/journal.pone.0027241

Peretz, I. (1996). Can we lose memory for music? A case of music agnosia in a nonmusician. *Journal of Cognitive Neuroscience*, *8*(6), 481–496. https://doi.org/10.1162/jocn.1996.8.6.481

Peretz, I., & Coltheart, M. (2003). Modularity of music processing. *Nature Neuroscience*, *6*(7), 688–691. https://doi.org/10.1038/nn1083

Peretz, I., Gosselin, N., Belin, P., Zatorre, R. J., Plailly, J., & Tillmann, B. (2009). Music lexical networks: The cortical organization of music recognition. *Annals of the New York Academy of Sciences*, *1169*, 256–265. https://doi.org/10.1111/j.1749-6632.2009.04557.x

Peretz, I., Kolinsky, R., Tramo, M., Labrecque, R., Hublet, C., Demeurisse, G., & Belleville, S. (1994). Functional dissociations following bilateral lesions of auditory cortex. *Brain*, *117*(6), 1283–1301. https://doi.org/10.1093/brain/117.6.1283

Peretz, I., & Zatorre, R. J. (2005). Brain Organization for Music Processing. *Annual Review of Psychology*, *56*(1), 89–114. https://doi.org/10.1146/annurev.psych.56.091103.070225

Piccirilli, M., Sciarma, T., & Luzzi, S. (2000). Modularity of music: Evidence from a case of pure amusia. *Journal of Neurology, Neurosurgery & Psychiatry*, *69*(4), 541–545. https://doi.org/10.1136/jnnp.69.4.541

Plailly, J., Tillmann, B., & Royet, J.-P. (2007). The Feeling of Familiarity of Music and Odors: The Same Neural Signature? *Cerebral Cortex*, *17*(11), 2650–2658. https://doi.org/10.1093/cercor/bhl173

Saito, Y., Ishii, K., Sakuma, N., Kawasaki, K., Oda, K., & Mizusawa, H. (2012). Neural Substrates for Semantic Memory of Familiar Songs: Is There an Interface between Lyrics and Melodies? *PLoS ONE*, *7*(9). https://doi.org/10.1371/journal.pone.0046354

Samson, S., Dellacherie, D., & Platel, H. (2009). Emotional Power of Music in Patients with Memory Disorders: Clinical Implications of Cognitive Neuroscience. *Annals of the New York Academy of Sciences*, *1169*(1), 245–255. https://doi.org/10.1111/j.1749-6632.2009.04555.x

Schaal, N. K., Javadi, A.-H., Halpern, A. R., Pollok, B., & Banissy, M. J. (2015). Right parietal cortex mediates recognition memory for melodies. *European Journal of Neuroscience*, *42*(February), n/a-n/a. https://doi.org/10.1111/ejn.12943

Schön, D., Gordon, R., Campagne, A., Magne, C., Astésano, C., Anton, J.-L., & Besson, M. (2010). Similar cerebral networks in language, music and song perception. *NeuroImage*, *51*(1), 450–461. https://doi.org/10.1016/j.neuroimage.2010.02.023

Sikka, R., Cuddy, L. L., Johnsrude, I. S., & Vanstone, A. D. (2015). An fMRI comparison of neural activity associated with recognition of familiar melodies in younger and older adults. *Frontiers in Neuroscience*, *9*(OCT), 1–10. https://doi.org/10.3389/fnins.2015.00356

Slattery, C. F., Agustus, J. L., Paterson, R. W., McCallion, O., Foulkes, A. J. M., Macpherson, K., Carton, A. M., Harding, E., Golden, H. L., Jaisin, K., Mummery, C. J., Schott, J. M., & Warren, J. D. (2019). The functional neuroanatomy of musical memory in Alzheimer's disease. *Cortex*, *115*, 357–370. https://doi.org/10.1016/j.cortex.2019.02.003

Stalinski, S. M., & Schellenberg, E. G. (2013). Listeners remember music they like. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *39*(3), 700–716. https://doi.org/10.1037/a0029671

Stefan, A. M., Gronau, Q. F., Schönbrodt, F. D., & Wagenmakers, E.-J. (2019). A tutorial on Bayes Factor Design Analysis using an informed prior. *Behavior Research Methods*, *51*(3), 1042–1058. https://doi.org/10.3758/s13428-018-01189-8

Takahashi, N., Kawamura, M., Shinotou, H., Hirayama, K., Kaga, K., & Shindo, M. (1992). Pure Word Deafness due to Left Hemisphere Damage. *Cortex*, *28*(2), 295–303. https://doi.org/10.1016/S0010-9452(13)80056-1

Tie, Y., Rigolo, L., Norton, I. H., Huang, R. Y., Wu, W., Orringer, D., Mukundan, S., & Golby, A. J. (2014). Defining language networks from resting-state fMRI for surgical planning—A feasibility study. *Human Brain Mapping*, *35*(3), 1018–1030. https://doi.org/10.1002/hbm.22231

Tierney, A., Dick, F., Deutsch, D., & Sereno, M. (2013). Speech versus Song: Multiple Pitch-Sensitive Areas Revealed by a Naturally Occurring Musical Illusion. *Cerebral Cortex*, *23*(2), 249–254. https://doi.org/10.1093/cercor/bhs003

Tremblay, P., Baroni, M., & Hasson, U. (2013). Processing of speech and non-speech sounds in the supratemporal plane: Auditory input preference does not predict sensitivity to statistical structure. *NeuroImage*, *66*, 318–332. https://doi.org/10.1016/j.neuroimage.2012.10.055

Vanstone, A. D., & Cuddy, L. L. (2010). Musical memory in Alzheimer disease. *Neuropsychology, Development, and Cognition. Section B, Aging, Neuropsychology and Cognition*, *17*(1), 108–128. https://doi.org/10.1080/13825580903042676

Walther, A., Nili, H., Ejaz, N., Alink, A., Kriegeskorte, N., & Diedrichsen, J. (2016). Reliability of dissimilarity measures for multi-voxel pattern analysis. *NeuroImage*, *137*, 188–200. https://doi.org/10.1016/j.neuroimage.2015.12.012

World Airplay Radio Monitor: Real-Time Radio Tracking. (2012). https://warmmusic.net

Yaqub, B. A., Gascon, G. G., Nosha, M. A., & Whitaker, H. (1988). Pure word deafness (acquired verbal auditory agnosia) in an Arabic speaking patient. *Brain*, *111*(2), 457–466. https://doi.org/10.1093/brain/111.2.457

Zajonc, R. B. (2001). Mere Exposure: A Gateway to the Subliminal. *Current Directions in Psychological Science*, *10*(6), 5.

Zatorre, R. J., & Gandour, J. T. (2008). Neural specializations for speech and pitch: Moving beyond the dichotomies. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *363*(1493), 1087–1104. https://doi.org/10.1098/rstb.2007.2161

3 The effect of repetition on intersubject synchrony

Introduction

There is a growing trend in neuroscience to study the human brain using stimuli that contain naturalistic complexity rather than artificially constructed laboratory stimuli. Stimuli such as movies, audiobooks, or music enhance the ecological validity of studies examining brain function. These naturalistic stimuli unfold over time, and therefore require an analysis technique that is sensitive to temporal structure. This sensitivity can be gained with neuroimaging analyses (EEG, fMRI, or fNIRS) that use intersubject synchrony to detect common stimulus-driven brain activity across individuals over time. Intersubject synchrony was first introduced by Hasson et al. (2004) to study visual perception during movie viewing using fMRI. Brain areas with similar patterns of activity across participants were identified by calculating voxel-wise correlations between pairs of participants. They found that activity in large areas of the occipital and temporal lobes was correlated across participants over the course of the movie. Since this seminal paper, intersubject synchrony has been used to study attention (Ki et al., 2016), memory (Furman et al., 2007; Hasson et al., 2008), emotion (Trost et al., 2015), speech processing (Wilson et al., 2008), music perception (Abrams et al., 2013), consciousness (Naci et al., 2014), and brain function in clinical populations (Anderson et al., 2013; Hasson et al., 2009; Lyons et al., 2020). Intersubject synchrony analyses of naturalistic stimuli provide novel insight into how the brain functions in the world outside of the laboratory, but the way stimulus characteristics affect synchrony have not been fully characterized.

The contents of a stimulus, like the presence of language, affects intersubject synchrony. Audio-only movie (Naci et al., 2017) or audiobook excerpts (Regev et al., 2019; Simony et al., 2016) have successfully induced intersubject synchrony in fronto-temporal networks related to the cognitive processing of the stimulus. In contrast, instrumental music (e.g. theme songs from movies) produced synchrony in primary auditory cortex as well as bilateral

thalamus, and motor planning regions (Abrams et al., 2013; Naci et al., 2017). Thus, different stimuli (e.g., music, stories, movies) elicit intersubject synchrony in different brain areas, but only one study has included a direct comparison of the effects of different stimulus types on synchrony (Naci et al., 2017). In this study, the researchers found that there was more synchrony to stimuli with language than to stimuli without language when comparing synchrony to audio-visual movie clips, audio-only movie excerpts, and tv-show theme songs. However, the presence of language and other stimulus characteristics (like visual information or music) were not systematically varied and the data were not collected from the same group of participants. Further evidence for the role of language in inducing intersubject synchrony was found when participants watched two different audio-visual stimuli and greater synchrony was observed to the Alfred Hitchcock movie 'Bang! You're dead' (a highly suspenseful film with a coherent narrative) than to a real-life video of people walking through Washington Square Park (Hasson et al., 2010). The reproducible effect of the presence of language on intersubject synchrony suggest that stimulus characteristics are important for inducing synchrony and reveals the lack of existing research that systematically characterizes how synchrony measures react under different conditions.

The number of times an individual has experienced a stimulus may be an important aspect of stimuli that should be accounted for in synchrony studies. Synchrony strength is interpreted as being a marker of how similarly individuals experience a stimulus (Hasson et al., 2004) and that experience may be influenced by the number of exposures to the stimulus. For example, an individual's first experience of a song is likely very different from their hundredth experience of that song when they can sing along with all of the words. In support of the idea that experience of a stimulus changes with exposure, there is a small amount of evidence to show that intersubject synchrony is reduced with increased exposure. Synchrony, measured using fMRI data, in the posterior medial network decreased from the first to the sixth consecutive viewing of 90 second movie clips (Aly et al., 2017, 2018). In a similar study using EEG, participants were presented with three short films that were each viewed twice (Dmochowski et al., 2012) and synchrony decreased between the first and second viewings. However, neither of these studies fully characterized the timecourse of the synchrony decrease; for example, whether synchrony steadily decreased over multiple viewings or was steeply reduced after a single repetition followed by a plateau. If synchrony steadily decreases with increased exposure and

exposure differs systematically with an experimental manipulation, then researchers using intersubject synchrony analyses need to take stimulus exposure into account to reduce the possibility of confounds in their results. On the other hand, if synchrony is reduced after a single viewing followed by a plateau then researchers can avoid confounds by exposing all participants to the stimuli before starting the study. Characterizing how synchrony is affected by prior exposure is important for understanding how best to design studies that minimize the confound of exposure differences across participants.

The goal of this study was to systematically examine how exposure to audio-only stimuli influences intersubject synchrony. In this experiment, a training paradigm was used to objectively define prior experience with a series of auditory stimuli. Participants were presented with stimuli in two scanning sessions: before and after a training period. During training, participants listened to 50% of the stimuli heard during the first scanning session through an online audio player that tracked the number of times each stimulus was played. When they returned for the second scanning session participants were very familiar with 50% of the stimuli. The stimuli presented in the second scanning session were otherwise identical to those presented in the first scanning session. Based on the previous research described above, we expected to see a decrease in synchrony based on stimulus exposure. If synchrony steadily decreases with repeated exposure, we expect there to be less synchrony to the 50% of the stimuli in the second session that were trained on when compared to the 50% of the stimuli that were not trained on. If, instead, synchrony is reduced after a single viewing followed by a plateau, we should see a reduction in synchrony between the first and second session, but no differences in synchrony between the 50% of the stimuli that were trained on and the 50% of the stimuli that were heard once in the first session. Characterizing how synchrony changes as a result of exposure may affect the types of stimuli chosen by researchers in future studies measuring intersubject synchrony to naturalistic stimuli.

Methods

Ethics

Ethics approval for this project was granted by the Health Sciences Research Ethics Board at The University of Western Ontario (#100606, #114263).

Participants

Twenty-six neurologically normal, English-speaking participants (14 female) aged 18-39 (mean=24 years) were recruited at The University of Western Ontario. All participants had completed at least some post-secondary education and nine participants had completed some post-graduate education. According to the Goldsmith's Musical Sophistication Index (Müllensiefen et al., 2014), 17 participants reported having formal musical training (1-10yrs, mean=4.5yrs), but at the time of testing only nine of them played instruments regularly. Seven participants were fluent in a second language. All participants reported listening to music regularly in their daily lives (average 1.5 hours per day) via a phone, computer, or car radio.

Stimuli

Eight stimuli were created from the lyrics and music of eight different songs written and recorded by a member of the research team between 1997 and 2006 for an amateur rock band based in Cambridge, UK. Thus, all stimuli were completely novel to the Canadian participants. The original songs were written in a similar style and instrumentation included a lead singer, bass, drums, guitar, string instruments, and backing vocals, each recorded on separate tracks. All stimuli were recorded using the same equipment directly to digital hard drive using the Sonar software (by Cakewalk) and a Shure SM58 microphone.

Four conditions were created by modifying the original songs to include or exclude certain tracks: (1) whole music (all tracks, with music and sung lyrics), (2) instrumental music without words (all vocal tracks removed, leaving only non-vocal instrument tracks), (3) a capella (all non-vocal instrument tracks removed, leaving only lead and backing vocals) and (4) spoken words (lyrics of each song rerecorded in spoken form by the original lead singer to have a similar length, tempo, and emotional intonation as their original song counterparts). There were two different stimuli for each condition, and none of the original songs were used for more than one condition. Although the design of the current experiment, directly mirrors the design of the experiment described in Chapter 2, the eight stimuli used here were different from the eight stimuli used in Chapter 2. Please see Appendix C for a detailed description of which stimuli were used in each experiment.

The stimuli were modified (e.g., lengthened by adding additional repetitions of the chorus) to each be five minutes long. During the fMRI scan sessions, participants heard the

entire 5-minute stimulus. Each stimulus was normalized to equate perceived loudness using the *Audacity* software (Audacity Team, 2020). During the training period, participants listened to half of the stimuli (4 stimuli, 1 per condition) via an online audio player.

There were four learning conditions: 'to be learned' refers to the novel stimuli heard in the first scanning session that the participant subsequently listened to over the training period; 'not to be learned' refers to the novel stimuli heard in the first scanning session that the participant *did not* listen to over the training period; 'learned' refers to the stimuli heard in the second scanning session that the participant listened to over the training period; and 'not learned' refers to the stimuli in the second scanning session that the participant *did not* listen to over the training period. The 'to be learned' and 'learned' stimuli were identical for each participant, as were the 'not to be learned' and 'not learned' stimuli. The sets of stimuli that were learned were counterbalanced across participants: half the participants familiarized with one half of the stimuli; the other half of the participants familiarized with the other half of the stimuli (Groups A and B; see Chapter 2, Table 2).

Procedure

Participants completed two functional MRI scans that were separated by a stimulus training period (14-29 days; mean = 20 days). During both scans, participants passively listened to the stimuli. During the training period, participants listened to the stimuli via an online player (designed in-lab) that tracked the number of times each stimulus was played. Participants were asked to listen to the stimuli at least 5 times per week. To ensure participants were engaged while listening, the player presented a simple question about the stimulus (e.g. "*Were there lyrics present in the previous song?"*) at random between stimuli. A response was required to move to the next stimulus. Participants were encouraged to incorporate the music into their everyday lives (i.e. to listen while cooking or driving).

Behavioural Familiarity Tasks

Please see Chapter 2, Methods for a full description of the behavioural familiarity tasks used.

fMRI acquisition and analyses

Imaging was conducted at the Robarts Research Institute on a Siemens Magnetom 7 Tesla scanner with a 32-channel head coil. Functional scans were acquired with 54 slices per volume (TR = 1.25 s; TE = 20 ms; flip angle = 35°; FOV = 220 x 220 mm; voxel size = 2.5 mm^3). The two scan sessions (before and after the training period) were identical and included eight 5-minute functional runs. During each of the runs, participants passively listened to the stimuli in their entirety. Stimulus order was randomized for each participant and in each scan session. Half of the 5-minute stimuli were 'to be learned' in the first session, and 'learned' in the second session, while the other half were 'not to be learned' in the first session and 'not learned' in the second session. Between functional runs in the first session only, a whole-head anatomical scan was acquired (TR = 6s; TE = 2.69 ms; FOV = 240 x 240 mm; voxel size = 0.75 mm^3; 208 slices).

Data from the 5 minute runs were processed using automatic analysis (version 4.1; Aly et al., 2017, 2018; Cusack et al., 2015; Dmochowski et al., 2012): a MATLAB based processing and analysis pipeline that integrates with Statistical Parametric mapping (SPM12). Three 'dummy' scans were excluded from the beginning of every run to allow stabilization of the signal. Images were realigned to the first image in the first run using six motion parameters (x,y,z, translation and rotation). Data were normalized to MNI space and smoothing was done with a Gaussian kernel of 10mm FWHM. Low-frequency noise (e.g., drift) was removed with a high-pass filter of 128s. Data were denoised using cerebrospinal fluid, white matter signals, motion parameters, their lag-3 2nd-order Volterra expansion (Friston et al., 2000), and "spikes" (>3 standard deviations based on mean signal variance across volumes) as nuisance regressors. The data were then further cleaned by running a group ICA (Calhoun et al., 2001) within each stimulus and removing 1-2 components that spatially correlated with a mask of the ventricles to remove non-brain related activity.

Intersubject synchrony

Whole brain analysis

Intersubject synchrony across the whole brain was calculated separately in each session and for each stimulus using a leave-one-out approach. Synchrony was only ever calculated between identical stimuli. For each stimulus in session one, the timecourse of every voxel in

each participant was correlated (Pearson and then Fisher z-transformed) with the mean timecourse of every corresponding voxel from the rest of the participants' session 1 data, minus that participant (N-1). This process created an *r*-value for each voxel, for each participant, that described the correlation between that participant's voxel and the same voxel in all other participants, for that stimulus in session 1. To look for differences in synchrony across sessions, these 'within session 1' synchrony values for each stimulus were then compared to synchrony values for the same stimulus in session 2.

The second session synchrony values were calculated 'within session 2' in the same way that synchrony was calculated in session 1. That is, for each stimulus in session 2, the timecourse of every voxel in each participant was correlated (Pearson and then Fisher z-transformed) with the mean timecourse of every corresponding voxel from the rest of the participants' session 2 data, minus that participant (N-1). This process created an *r*-value for each voxel, for each participant, that described the correlation between that participant's voxel and the same voxel in all other participants, for that stimulus in session 2. Because different stimuli were 'learned' by Group A and Group B, synchrony was calculated separately within Group A and Group B to obtain synchrony values for the four stimulus types while maintaining the integrity of the 'learned' and 'not learned' conditions in the second session. For example, stimulus 1 was learned by Group A but not Group B (see Chapter 2, Table 2). Calculating synchrony for stimulus 1 by combining data from Group A and B would average across learning conditions. Therefore, during the session 2 leave-one-out procedure, an individual's data was only correlated with data from the rest of the participants (N-1) in their group.

Before comparing synchrony values across sessions, we investigated whether there were initial synchrony differences between the stimuli that were assigned to be learned in Group A and the stimuli assigned to be learned in Group B. The individual correlation values from the first session, calculated as described above, were entered into a second-level flexible factorial model using SPM12 (see Supplementary Figure 1 for a visual depiction of the model). This model labeled learning group (Group A and B) and took subject effects into account. Two t-contrasts were run in SPM to determine whether session 1 synchrony differed between the four Group A and four Group B stimuli (Group A > Group B; Group B > Group A). The two stimulus groups were designed to be similar, and indeed, the analysis confirmed that no significant clusters survived correction. In subsequent analyses the synchrony values from all participants

(in Group A and Group B) were labeled based on learning condition, not based on which physical stimulus was heard (i.e. stimulus 1 synchrony values were 'learned' for Group A and 'not learned' for Group B, and stimulus 5 synchrony values were 'learned' for Group B and 'not learned' for Group A, see Chapter 2, Table 2).

Individual correlation values for the eight stimuli in session 1 (using the 'within session 1 values') and eight stimuli in session 2 (using the 'within session 2' values) were entered into a second-level flexible-factorial model using SPM12 to probe how learning affected synchrony across the entire group of participants. This model labeled learning condition (4 to be learned stimuli in session 1, 4 not to be learned stimuli in session 1, 4 learned stimuli in session 2, 4 not learned stimuli in session 2), and took subject effects into account (see Supplementary Figure 2 for a visual depiction of the model). As a result of the counterbalanced design, all eight stimuli were present within each of the four learning conditions across participants.

To probe changes in synchrony due to learning across the two sessions, a 2(session 1/session 2) x 2(trained/not trained stimuli) ANOVA was conducted using the 'within session 1' and 'within session 2' synchrony values. The 'to be learned' stimuli in session 1 and the 'learned' stimuli in session 2 were labeled as part of the 'trained' category. The 'not to be learned' stimuli in session 1 and the 'not learned' stimuli in session 2 were labeled as part of the 'not trained' category. *F*-contrasts were run in SPM to investigate main effects of stimulus training set, session, and the stimulus training set by session interaction. *T*-contrasts were then conducted to further investigate the significant main effect of session: session 1 > session 2; session 2 > session 1. For each contrast, the cluster-forming threshold was specified at FWE p=.0001 uncorrected (Roiser et al., 2016) to determine the extent threshold. Clusters were defined using the extent threshold and peak coordinates are reported at a corrected cluster level FWE p<.05.

Region of interest analysis

Within the 2(session 1/session 2) x 2(trained/not trained stimuli) ANOVA, half of the stimuli included in the trained category were in fact not yet trained (the 'to be learned' stimuli) and a significant difference between the trained and not trained stimuli may have been compromised by this mixing of stimuli from different levels of training. Therefore, the six clusters identified by the significant main effect of session in the 2(session1/session 2) x

2(trained/not trained stimuli) ANOVA described above were extracted and used as regions of interest. The 'within session 1' and the 'within session 2' synchrony values, averaged across each region's voxels, were extracted using MarsBAR (Brett et al., 2002) and further analyses were conducted in R (R Core Team, 2013) to probe changes in synchrony without combining stimuli from different levels of training.

The synchrony values from the session 1 to be learned and session 1 not to be learned stimuli were combined to create an 'all session 1 stimuli' category that consisted of synchrony values to all of the novel stimuli. We conducted a one-way ANOVA in R (R Core Team, 2013) to investigate synchrony differences between the three learning conditions across sessions (all session 1/session 2 not learned/session 2 learned). This ANOVA was conducted within each of the six ROIs defined by the main effect of session from the 2(session1/session 2) x 2(trained/not trained stimuli) ANOVA described above. Post-hoc tests between the three learning conditions were conducted in ROIs when a significant effect of training was found.

If there were significant results that could be attributed to general differences between sessions, rather than related to learning, it is possible that these differences may have been a result of familiarization with the scanner environment and therefore may have emerged over the course of session 1. If this were the case, we would expect to see less synchrony to the stimuli heard in the second half of the scanning session than to those heard in the first half. Therefore, to understand whether any significant learning effects seen across the sessions were due to the amount of time participants spent in the scanner, we conducted a one-way ANOVA to investigate synchrony differences between the two halves of session 1 (session 1 first half/session 1 second half).

Synchrony changes within an individual

The analysis described above used synchrony values that compared the degree of synchrony between an individual and the rest of the participants to probe whether there were group level changes in synchrony as a result of repeated exposure to the stimuli. However, it was also possible to investigate whether there were changes in synchrony at the individual level. An additional set of synchrony values were calculated for each stimulus within each participant. The 'individual changes' synchrony values were defined by calculating the voxel-wise correlations between session 2 and session 1 for each individual's data within each of the six defined regions.

That is, for each stimulus in session 2, the voxel timecourse in each region of interest in every participant was correlated (Pearson and then Fisher z-transformed) with the timecourse of every corresponding voxel of that same participant's session 1 data. This process created an *r*-value for each voxel, for each participant, that described the degree to which that participant's voxel during session 2 was correlated with their own data while listening to the same stimulus in session 1. The 'individual changes' synchrony values allowed us to probe how each individual's brain activity changed with learning in the second session as compared to their own data in the first session. The 'individual changes' synchrony values, averaged across each region's voxels, were also extracted from the same six ROIs described in the previous section using MarsBAR (Brett et al., 2002) for further analyses using R (R Core Team, 2013). To investigate the individual changes in synchrony between sessions, we conducted a one-way ANOVA to investigate synchrony differences between the session 2 learned and session 2 not learned stimuli using the 'individual changes' synchrony values.

Finally, to determine whether synchrony to the learned stimuli was related to behavioural scores on the memory tasks, both sets of second session synchrony values ('within session 2' and 'individual changes' synchrony values) for all of the learned stimuli in session 2 in each ROI were correlated with each individual's average score on the lyric modification and melody memory tasks.

Results

Participants

Two individuals withdrew from the study following the first scan session and data from four individuals were not included in the analysis because their average scores on the two behavioural memory tests were lower than 70% correct. FMRI data from 20 individuals were included in the analysis.

Participants listened to each stimuli an average of 13 times (from 6-20 listens) over an average of 20 days (from 14-29 days).

Behavioural familiarity tasks

Please see Chapter 2, Results (page 31) for a full description of the results from the behavioural familiarity tasks.

Intersubject synchrony

Whole brain analysis

The 2(session 1/session 2) x 2(trained/not trained stimuli) ANOVA using the 'within session 1' and the 'within session 2' synchrony values revealed a significant main effect of session in six clusters within bilateral temporal areas, frontal, occipital, and precentral gyrus (see Table 1 and Figure 1). The threshold was set to the FWEc value (=43) and clusters were defined at $p<.05$ FWE corrected. The two post-hoc t-contrasts conducted to determine how synchrony differed across the two sessions showed that there was significantly more synchrony within the first session than in the second session in largely the same regions identified by the *F*-contrast describing the main effect of session (see Table 1). There were no brain areas with more synchrony in the second session than the first. There was no significant difference between the set of stimuli that were trained and the set of stimuli that were not trained and no session by stimulus training set interaction.

Table 1. Cluster locations in which synchrony significantly differed between sessions as identified using a 2(session) x 2(stimulus training set) ANOVA. Reported peaks within each cluster are >4mm apart. The extent threshold was set for each contrast separately. All *p*-values <.001 unless otherwise specified (FWE corrected).

Harvard-Oxford Atlas labels	(x,y,z) coordinates	Main effect of session extent = 43 *F*-value	Session 1 > Session 2 extent = 53 *t*-value
** Planum temporale	-52,-20, 0	105.35	14.51
Planum temporale	-62, -34, 8	73.43	12.07
Posterior STG	-58, -36, 10	74.56	-
Posterior STG	-56, -34, 8	-	12.18
Posterior STG	-68, -22, 2	52.05	10.16
** Planum temporale	56, -20, 6	78.00	12.49
Planum temporale	60, -18, 6	77.63	-
Planum temporale	60, -16, 4	-	12.45
Posterior STG	68, -28, 6	76.58	12.31
Posterior STG	66, -24, 8	72.69	12.02
Heschl's gyrus	38, -26, 10	47.11	9.63
Temporal pole	62, 8, -10	38.90	8.76
Anterior STG	62, 4, -8	38.74	8.74
** Frontal orbital cortex	-12, 6, -22	30.33	7.78
Frontal orbital cortex	-12, 14, -20	25.16	7.09
Parahippocampal gyrus (anterior div.)	-14, 0, -26	23.70	6.84
Frontal orbital cortex	-16, 12, -24	22.95	6.77
Subcallosal cortex	-12, 22, -18	20.31	6.08
Parahippocampal gyrus (anterior div.)	-14, -4, -28	16.82	5.79 *p*=.002
** Precentral gyrus	58, 4, 46	27.06	7.27
** Occipital pole	40, -90, 24	23.73	6.87
Lateral occipital cortex (inferior div.)	46, -84, 18	17.75	5.95 *p*=.001
Lateral occipital cortex (inferior div.)	54, -72, 10	-	5.75 *p*=.002
Lateral occipital cortex (inferior div.)	56, -74, 6	-	5.45 *p*=.009
Lateral occipital cortex (inferior div.)	52, -72, 4	-	5.37 *p*=.013
** Occipital pole	34, -92, 4	23.67	-
Occipital pole	32, -96, 6	22.25	-
Parahippocampal gyrus (anterior div.)	16, -14, -22	-	6.25
Frontal orbital cortex	14, 8, -14	-	6.01 *p*=.001
Frontal orbital cortex	16, 12, -14	-	5.82 *p*=.002
Frontal orbital cortex	14, 10, -24	-	5.78 *p*=.002

** denotes the six clusters extracted and used as regions of interest in further analyses

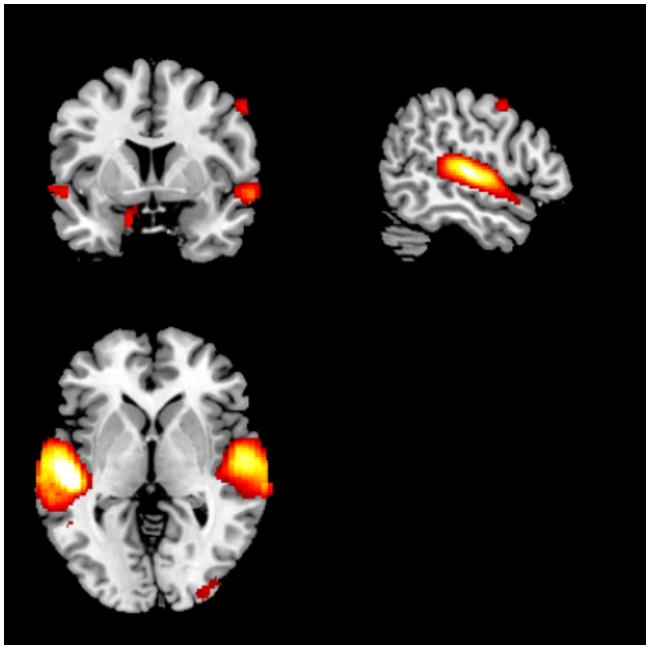


Figure 1. Brain regions in which intersubject synchrony differed between session 1 and session 2. These areas were identified using an *F*-contrast describing a main effect of session from a 2(session) x 2(stimulus training set) ANOVA. The six regions depicted (and described in Table 1) were extracted for use as regions of interest in further analyses. Extent threshold = 43. Displayed slices are at x=53, y=5, z=0.

Region of interest analysis

The one-way ANOVA investigating synchrony differences between the three learning conditions across sessions (all session 1/session 2 not learned/session 2 learned) performed in each ROI found a significant effect of learning on synchrony across all six clusters (see Figure 2 and Table 2, row 1 for full statistics).

A Tukey post-hoc test was done in each cluster to uncover where the differences between the three learning conditions existed (see Table 2, rows 2-4). There were no differences in synchrony between the session 2 not learned and the session 2 learned stimuli ($p>.05$ in all clusters). There were differences in synchrony between the session 1 stimuli and the session 2 learned stimuli ($p<.001$ in all clusters), however there were also differences in synchrony between the session 1 stimuli and the session 2 not learned stimuli ($p<.001$ in all clusters). These results suggest that any differences between learned and not learned stimuli were due to a general effect of session rather than a specific effect of learning, especially as there was no difference between session 2 learned and session 2 not learned stimuli.

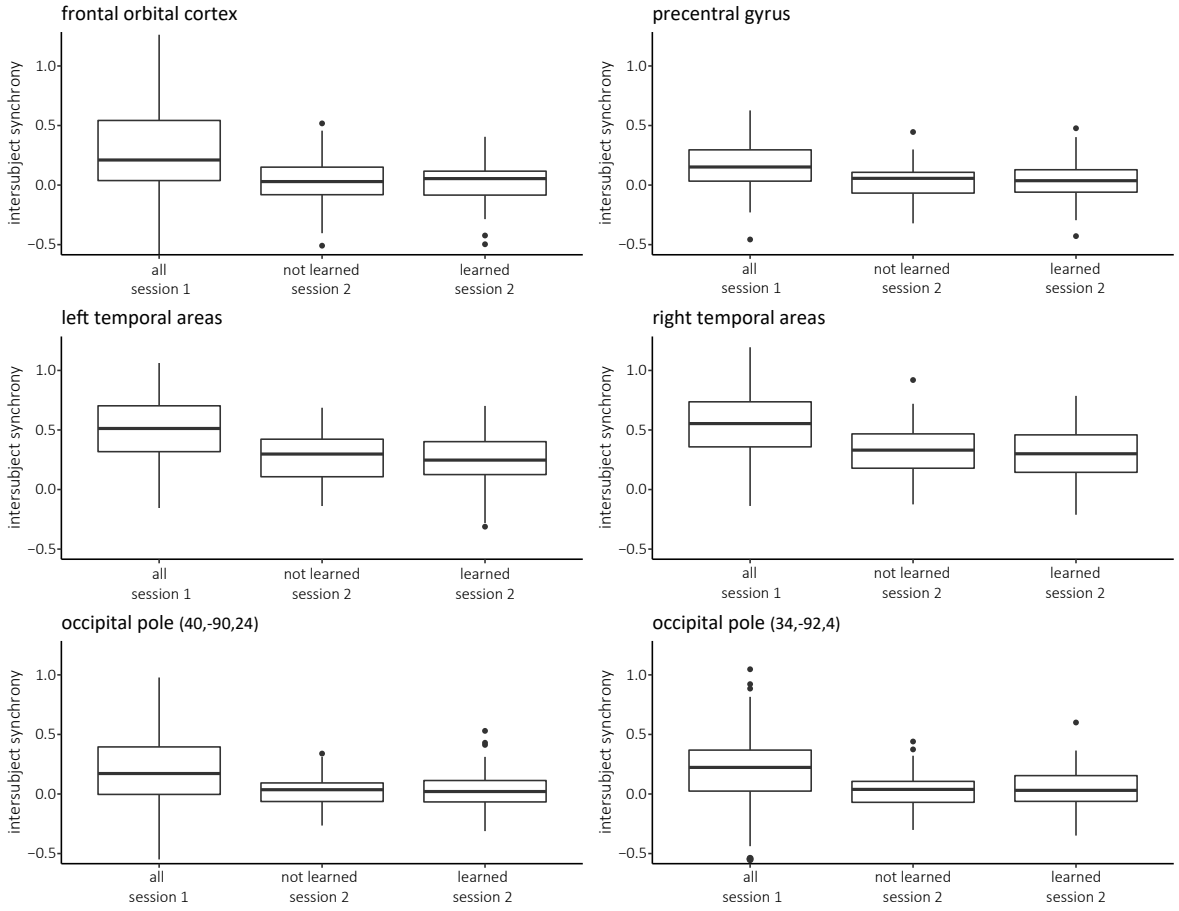


Figure 2. Synchrony values plotted for each of the six clusters for each of the learning conditions. The 'within session 1' and 'within session 2' synchrony values are shown here. Boxplots show the median value and contain values from the 25th to 75th percentile within each box. Whiskers represent 95% confidence intervals with outliers depicted as individual points.

The one-way ANOVA probing whether there were differences in synchrony between the first and second half of the first session showed a significant main effect of 'half' in the left and right temporal regions. There was significantly more intersubject synchrony in the second half of session 1 than in the first half (see Figure 3 and Table 2, row 5 for full statistics). This effect of session 'half' occured in the opposite direction as the differences between sessions from the 2(session 1/session 2) x 2(trained/not trained stimuli) ANOVA, where there was more synchrony to session 1 than to session 2.

Finally, the 'within session 2' synchrony values for all learned stimuli in each cluster were correlated with each individual's average score on the lyric modification and melody

memory tasks. The *p*-values were FWE corrected across all clusters. There were no significant correlations between the synchrony values and the behavioural scores.

Table 2. All statistical tests performed on the 'within session 1' and the 'within session 2' synchrony values. *p<.001

Statistical tests		**Frontal orbital cortex**	**Precentral**	**Left Temporal**	**Right Temporal**	**Occipital (40, -90, 24)**	**Occipital (34, -92,4)**
one-way ANOVA (all session 1 / session 2 not learned / session 2 learned)	main effect learning $F(2,317)$	25.52* η^2=.14	24.84* η^2=.14	45.91* η^2=.22	40.53* η^2=.20	24.79* η^2=.14	21.66* η^2=0.12
Tukey post-hoc tests	session 2 not learned / session 2 learned	-	-	-	-	-	-
	session 1 / session 2 learned	*	*	*	*	*	*
	session 1 / session 2 not learned	*	*	*	*	*	*
one-way ANOVA (session 1 first half / session 1 second half	main effect session 1 half $F(1,158)$	-	-	6.04 p=.01 η^2=.04	11.07 p=.001 η^2=.07	-	-

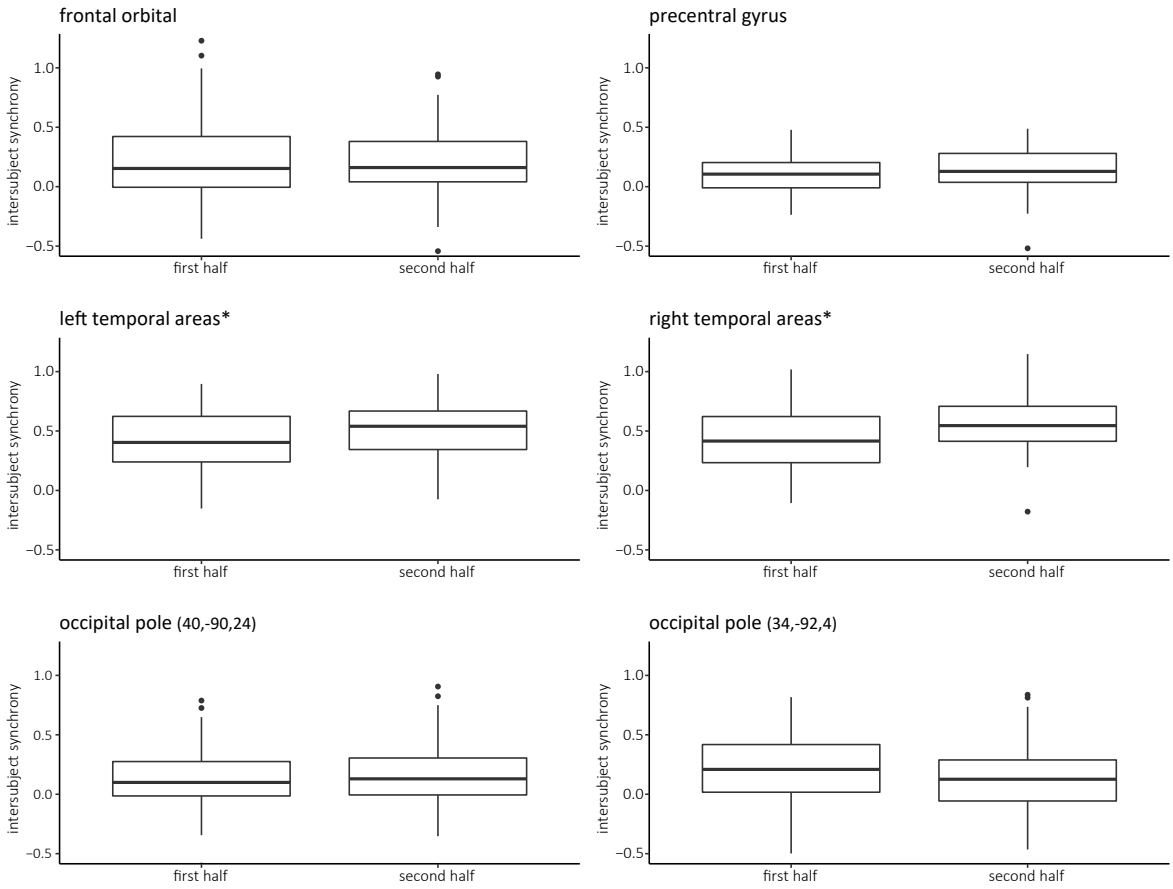


Figure 3. Synchrony values ('within session 1') from the first and second halves of the first scanning session plotted for each of the six clusters. Boxplots show the median value and contain values from the 25th to 75th percentile within each box. Whiskers represent 95% confidence intervals with outliers depicted as individual points.
* indicates a significant difference in synchrony between the two halves of session 1 (Table 2): 2nd half > 1st half.

Individual changes in synchrony

The one-way ANOVA using the 'individual changes' synchrony data to investigate synchrony differences between the session 2 learned and the session 2 not learned stimuli found no significant differences in synchrony in any of the clusters. This further indicates that the stimuli in the second session were processed in a similar way regardless of whether they had been trained on or not.

The 'individual changes' synchrony values were correlated with each individual's average score on the lyric modification and melody memory tasks. The *p*-values were FWE corrected across all clusters. There were no significant correlations between the synchrony values from the familiar stimuli and the behavioural scores.

Discussion

In the current study, we investigated whether intersubject synchrony to auditory stimuli was affected by previous exposure to the stimulus by asking participants to train on novel stimuli using a controlled training paradigm. Scores on the lyric modification task and the melodic memory task improved during the training period between the two fMRI scans, confirming that participants had, in fact, learned the stimuli over time. Moreover, an online follow-up study verified that the improvement required training and was not a result of repeated exposure to the task itself (Chapter 2; Sternin et al, 2021). The results from the two behavioural tasks indicated that the participants learned both the language and the musical components of the stimuli over the training period. The intersubject synchrony results indicated that there was an effect of exposure on synchrony, but this exposure effect was not related to training.

Contrary to our hypothesis, there was a decrease in synchrony between the two sessions regardless of whether the stimuli had been learned or not. When the 'within session 1' and the 'within session 2' values were compared across the whole brain, six clusters were identified as showing more synchrony in session 1 than in session 2 across bilateral temporal lobes, precentral gyrus, occipital areas, and frontal areas. This result suggests that even in the absence of behavioural evidence of learning (the online study detailed in Chapter 2 indicates that participants did not learn the stimuli they did not train on) there are persistent neural changes that occur as a result of stimulus exposure; even after not having heard the stimuli for three weeks participants showed a difference in synchrony. Some evidence of prolonged neural changes after exposure to auditory stimuli exists in the electroencephalography (EEG) and magnetoencephalography (MEG) literature. Early evoked responses, specifically the P200 event-related potential, have been used to study neural changes to auditory stimuli. The P200 is a positive deflection in neural activity approximately 200ms after the onset of a stimulus. The P200 has been shown to increase in amplitude with repeated exposure to auditory stimuli and this increase is thought to reflect enhanced auditory representations of the stimuli (Tremblay et al., 2001, 2009). When participants heard a stimulus four times (baseline, 24 hours later, one week later, up to one year later) the enhanced P200 (measured using EEG at the Cz electrode) persisted across the four sessions even when participants had not heard the stimuli for many months (Tremblay et al., 2010). The increased P200 amplitudes occurred as a result of repeated exposure, regardless of behavioural evidence of learning (Tremblay et al., 2014). Temporal lobe

areas, like those identified in the current study as showing synchrony differences between session, have been implicated as being the cortical sources of the increased P200 amplitude. Although these previous studies were performed using EEG and MEG rather than fMRI, the results suggest that persistent neural changes can be induced in similar bilateral temporal areas that showed differences in synchrony across sessions without behavioural evidence of learning in the current study. It is worth noting, however, that changes in ERP amplitudes are not directly related to synchrony measures. In fact, changes in the amplitude of neural activity that do not affect the pattern of fluctuations will have almost no effect on synchrony across individuals. However, intersubject synchrony is a fairly new analysis technique and not nearly as much research has been done to characterize synchrony changes as has been done to characterize changes to the strength of neural activation with auditory stimulation. Therefore, these results are presented here as evidence that neural changes in the absence of behavioural changes have been previously noted and support the idea that a single exposure to a stimulus may be enough to cause neural changes that are reflected in synchrony analyses even in the absence of learning.

Our results suggest that intersubject synchrony decreases following a single exposure to a stimulus followed by a plateau in the level of synchrony. Although we did not scan participants after each stimulus exposure, if synchrony steadily decreased in relation to the number of exposures to a stimulus, then we would have seen synchrony differences between the learned (heard many times) and not learned stimuli (heard once before) in the second session. We did not find any differences between the learned and not learned stimuli in session 2, indicating that the differences across the sessions were unlikely to be related to the number of times participants had heard the stimuli and suggesting that a significant reduction in synchrony occurred after a single exposure. This is in contrast to the research presented above regarding EEG and MEG measures of neural changes induced by repeated exposure to auditory stimuli that show *progressive* increases in P200 amplitudes with increased stimulus exposure. However, the P200 amplitudes are a very fast neural response to auditory stimuli and may be a more sensitive measure of identifying neural changes as a result of stimulus exposure than intersubject synchrony. The goal of the current experiment was to understand the effects of repetition on intersubject synchrony and our results suggest that there is a significant reduction in synchrony after a single exposure.

Strong intersubject synchrony is driven by similar neural responses across a group of individuals; higher similarity results in stronger synchrony. As individuals deviate from the group average and become less similar, the strength of the correlations is reduced. If participants each learned the stimuli to a different level of expertise or developed personal associations when listening to the stimuli over time, then they may have developed idiosyncratic responses to each learned stimulus. Such idiosyncrasies could have reduced the degree of synchrony across participants in the second session. For example, in the first session all stimuli were equally unfamiliar and synchrony was likely driven by the experience of hearing the stimulus for the first time. In the second session, each participant's experience of the learned stimuli will have been slightly different. For example, one participant may have learned 100% of the lyrics after just a few exposures while another may only have known 75% of the lyrics by the end of training. Although we did not collect data regarding the percentage of the lyrics each participant learned, there is literature that speaks to differences in how individuals memorize music. This research suggests that the ease with which music is memorized depends greatly on participants' preferred learning style, learning strategies, and musical abilities (Korenman & Peynircioglu, 2007; Mishra, 2011). Although it is possible that individual differences in level of knowledge contributed to the idiosyncrasies in the second scanning session, there was a lack of correlation between the behavioural memory scores and the second session synchrony scores. This null result indicates either that the reduction in synchrony was unrelated to differing levels of knowledge with the stimuli, or that our behavioural tasks were not sensitive enough to detect the subtle differences in familiarity across participants. The participants may also have listened to the songs while doing different activities, developing different associations that were recalled during scanning. Data regarding personal associations participants may have made with each of the stimuli by the end of the training period were not collected and therefore we can not speak to whether this was indeed a factor at play within this dataset. The differing levels of knowledge and personal associations created unique listening experiences in the second session for each participant and likely contributed to the reduction in synchrony across sessions.

It is possible that attentional differences between sessions reduced synchrony in the second session. Synchrony is affected by attention (Regev et al., 2019) with synchrony decreasing as participants are distracted. Therefore, the session effects could be a reflection of the participants' overall ability to pay attention. For example, if participants attended more to the

novel stimuli, this may have resulted in more synchrony within the first session. However, it is unlikely that the decreased second session synchrony is due solely to less attention to the stimuli themselves, as synchrony decreased similarly to both the 'learned' and 'not learned' stimuli. Considering that participants did not train on the 'not learned' stimuli, and some participants reported not recognizing the 'not learned' stimuli in the second session, these stimuli may reasonably be considered as novel as they were in the first session. This result disputes the idea that the differences in synchrony across sessions were due to participants paying more attention to novel stimuli. Changes in attention could also have resulted from familiarization with the scanner environment. To investigate this possibility, we compared synchrony in the first and second halves of session 1 (using the 'within session 1' synchrony values). If the reduction in synchrony across sessions was related to the time spent in the scanner, then there should have been less synchrony in the second than the first half of the session. However, only the left and right temporal clusters showed an effect of 'half' and in both clusters this difference was in the opposite direction: more synchrony in the second than the first half. Therefore, the synchrony reduction across sessions does not appear to be related to familiarity with the scanner environment. Additionally, the reduction in synchrony across sessions was not due to any systematic changes in the testing environments between the two sessions as the data were collected serially over a 12-month period; many participants completed both of their scanning sessions before others had completed their first session. Given that attention was likely not different as a result of familiarity with the stimuli or familiarity with the scanner environment, we can rule out attention differences as the driving force behind the decrease in synchrony across the two scanning sessions.

If all participants processed the stimuli equally differently in the second session in comparison to the first, it would be possible for synchrony, calculated 'within session 2', to not differ from the synchrony calculated 'within session 1' while the synchrony calculated by comparing an individual's second session data with their own first session data would be reduced. In other words, all participants could deviate from their first session 'baseline' synchrony by the same amount in the same direction resulting in individual changes across sessions but similar levels of synchrony within session 1 and session 2. Therefore, to capture individual changes in synchrony, we calculated the 'individual changes' synchrony values to determine whether there were changes in how an individual processed the stimuli that may have

been missed when synchrony was calculated using the average participant data within session 2. Comparing the synchrony values for the learned and not learned stimuli using the 'individual changes' synchrony values indicated that there was no difference in synchrony based on learning at the individual level; participants processed the stimuli in the second session differently than the way those same stimuli were processed in the first session regardless of whether the stimuli were learned or not. The lack of difference between the second session stimuli further confirms our conclusion that, at both the individual and group level, a single exposure to a stimulus caused a reduction in synchrony.

The present study aimed to examine how exposure to a stimulus influenced intersubject synchrony by asking participants to train on highly controlled novel stimuli. We expected that synchrony would decrease as exposure to the stimuli increased. However, rather than an effect of stimulus training, we found a 'single-listen' effect where there was reduced synchrony in the second session compared to the first regardless of whether the stimuli had been learned or not. This reduction may be related to an increase in idiosyncratic responses after exposure to a stimulus but does not seem to be related to how well the stimuli are learned or differences in attention. To further characterize how synchrony changes with repeated exposure, this result should be replicated in future studies using different types of stimuli (e.g. movies and stories) and measures of attention, engagement, and personal associations should be collected. The consistent reduction in synchrony after a single exposure has implications for studies using intersubject synchrony measures. If, for example, participants' degree of exposure to a stimulus systematically varies with the experimental conditions, this could complicate interpretation of the results. It will be important to further investigate this 'single-listen' effect by collecting synchrony data after each stimulus exposure to characterize the reduction and subsequent plateau in synchrony. Until the effects of repeated exposure on synchrony are fully understood, future studies using intersubject synchrony, where the novelty of the stimuli can not be guaranteed, may consider exposing all of their participants to the stimuli once before data are collected to mitigate the effects of any systematic differences in stimulus exposure.

Bibliography

Abrams, D. A., Ryali, S., Chen, T., Chordia, P., Khouzam, A., Levitin, D. J., & Menon, V. (2013). Inter-subject synchronization of brain responses during natural music listening. *European Journal of Neuroscience*, *37*(9), 1458–1469. https://doi.org/10.1111/ejn.12173

Aly, M., Chen, J., Turk-Browne, N. B., & Hasson, U. (2017). Learning Naturalistic Temporal Structure in the Posterior Medial Network. *BioRxiv*. https://doi.org/10.1101/196287

Aly, M., Chen, J., Turk-Browne, N. B., & Hasson, U. (2018). Learning Naturalistic Temporal Structure in the Posterior Medial Network. *Journal of Cognitive Neuroscience*, *30*(9), 1345–1365. https://doi.org/10.1162/jocn_a_01308

Anderson, J. S., Nielsen, J. A., Ferguson, M. A., Burback, M. C., Cox, E. T., Dai, L., Gerig, G., Edgin, J. O., & Korenberg, J. R. (2013). Abnormal brain synchrony in Down Syndrome. *NeuroImage: Clinical*, *2*, 703–715. https://doi.org/10.1016/j.nicl.2013.05.006

Audacity Team. (2020). *Audacity(R): Free Audio Editor and Recorder*. https://audacityteam.org/

Brett, M., Anton, J.-L., Valabrègue, R., & Poline, J. B. (2002, June 2). *Region of interest analysis using an SPM toolbox* [Abstract]. 8th International Conference on Functional Mapping of the Human Brain, Sendai, Japan.

Calhoun, V. D., Adali, T., Pearlson, G. D., & Pekar, J. J. (2001). A method for making group inferences from functional MRI data using independent component analysis. *Human Brain Mapping*, *14*(3), 140–151.

Cusack, R., Vicente-Grabovetsky, A., Mitchell, D. J., Wild, C. J., Auer, T., Linke, A. C., & Peelle, J. E. (2015). Automatic analysis (aa): Efficient neuroimaging workflows and parallel processing using Matlab and XML. *Frontiers in Neuroinformatics*, *8*. https://doi.org/10.3389/fninf.2014.00090

Dmochowski, J. P., Sajda, P., Dias, J., & Parra, L. C. (2012). Correlated Components of Ongoing EEG Point to Emotionally Laden Attention – A Possible Marker of Engagement? *Frontiers in Human Neuroscience*, *6*(May), 1–9. https://doi.org/10.3389/fnhum.2012.00112

Friston, K. J., Mechelli, A., Turner, R., & Price, C. J. (2000). Nonlinear Responses in fMRI: The Balloon Model, Volterra Kernels, and Other Hemodynamics. *NeuroImage*, *12*(4), 466–477. https://doi.org/10.1006/nimg.2000.0630

Furman, O., Dorfman, N., Hasson, U., Davachi, L., & Dudai, Y. (2007). They saw a movie: Long-term memory for an extended audiovisual narrative. *Learning & Memory*, *14*(6), 457–467. https://doi.org/10.1101/lm.550407

Hasson, U., Avidan, G., Gelbard, H., Vallines, I., Harel, M., Minshew, N., & Behrmann, M. (2009). Shared and idiosyncratic cortical activation patterns in autism revealed under continuous real-life viewing conditions. *Autism Research*, *2*(4), 220–231. https://doi.org/10.1002/aur.89

Hasson, U., Furman, O., Clark, D., Dudai, Y., & Davachi, L. (2008). Enhanced Intersubject Correlations during Movie Viewing Correlate with Successful Episodic Encoding. *Neuron*, *57*(3), 452–462. https://doi.org/10.1016/j.neuron.2007.12.009

Hasson, U., Malach, R., & Heeger, D. J. (2010). Reliability of cortical activity during natural stimulation. *Trends in Cognitive Sciences*, *14*(1), 40–48. https://doi.org/10.1016/j.tics.2009.10.011

Hasson, U., Nir, Y., Levy, I., Fuhrmann, G., & Malach, R. (2004). Intersubject Synchronization of Cortical Activity DuringNatural Vision. *Science*, *303*(5664), 1634–1640. https://doi.org/10.1126/science.1089506

Ki, J. J., Kelly, S. P., & Parra, L. C. (2016). Attention Strongly Modulates Reliability of Neural Responses to Naturalistic Narrative Stimuli. *Journal of Neuroscience*, *36*(10). https://doi.org/10.1523/JNEUROSCI.2942-15.2016

Korenman, L., & Peynircioglu, Z. (2007). versus Visual Presentation Individual Differences in Learning and Remembering Music: Auditory. *Journal of Research in Music Education*, *55*. https://doi.org/10.1177/002242940705500105

Lyons, K. M., Stevenson, R. A., Owen, A. M., & Stojanoski, B. (2020). Examining the relationship between measures of autistic traits and neural synchrony during movies in children with and without autism. *NeuroImage: Clinical*, *28*, 102477. https://doi.org/10.1016/j.nicl.2020.102477

Mishra, J. (2011). Influence of strategy on memorization efficiency. *Music Performance Research*, *4*, 60–71.

Müllensiefen, D., Gingras, B., Musil, J., & Stewart, L. (2014). The Musicality of Non-Musicians: An Index for Assessing Musical Sophistication in the General Population. *PLoS ONE*, *9*(2). https://doi.org/10.1371/journal.pone.0089642

Naci, L., Sinai, L., & Owen, A. M. (2017). Detecting and interpreting conscious experiences in behaviorally non-responsive patients. *NeuroImage*, *145*, 304–313. https://doi.org/10.1016/j.neuroimage.2015.11.059

R Core Team. (2013). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing.

Regev, M., Simony, E., Lee, K., Tan, K. M., Chen, J., & Hasson, U. (2019). Propagation of information along the cortical hierarchy as a function of attention while reading and listening to stories. *Cerebral Cortex*, *29*(10), 291526. https://doi.org/10.1093/cercor/bhy282

Roiser, J. P., Linden, D. E., Gorno-Tempinin, M. L., Moran, R. J., Dickerson, B. C., & Grafton, S. T. (2016). Minimum statistical standards for submissions to Neuroimage: Clinical. *NeuroImage : Clinical*, *12*, 1045–1047. https://doi.org/10.1016/j.nicl.2016.08.002

Simony, E., Honey, C. J., Chen, J., Lositsky, O., Yeshurun, Y., Wiesel, A., & Hasson, U. (2016). Dynamic reconfiguration of the default mode network during narrative comprehension. *Nature Communications*, *7*(May 2015). https://doi.org/10.1038/ncomms12141

Tremblay, K. L., Inoue, K., McClannahan, K., & Ross, B. (2010). Repeated Stimulus Exposure Alters the Way Sound Is Encoded in the Human Brain. *PLoS ONE*, *5*(4), e10283. https://doi.org/10.1371/journal.pone.0010283

Tremblay, K. L., Kraus, N., McGee, T., Ponton, C., & Otis, and B. (2001). Central Auditory Plasticity: Changes in the N1-P2 Complex after Speech-Sound Training. *Ear and Hearing*, *22*(2), 79–90.

Tremblay, K. L., Ross, B., Inoue, K., McClannahan, K., & Collet, G. (2014). Is the auditory evoked P2 response a biomarker of learning? *Frontiers in Systems Neuroscience*, *8*. https://doi.org/10.3389/fnsys.2014.00028

Tremblay, K. L., Shahin, A. J., Picton, T., & Ross, B. (2009). Auditory training alters the physiological detection of stimulus-specific cues in humans. *Clinical Neurophysiology*, *120*(1), 128–135. https://doi.org/10.1016/j.clinph.2008.10.005

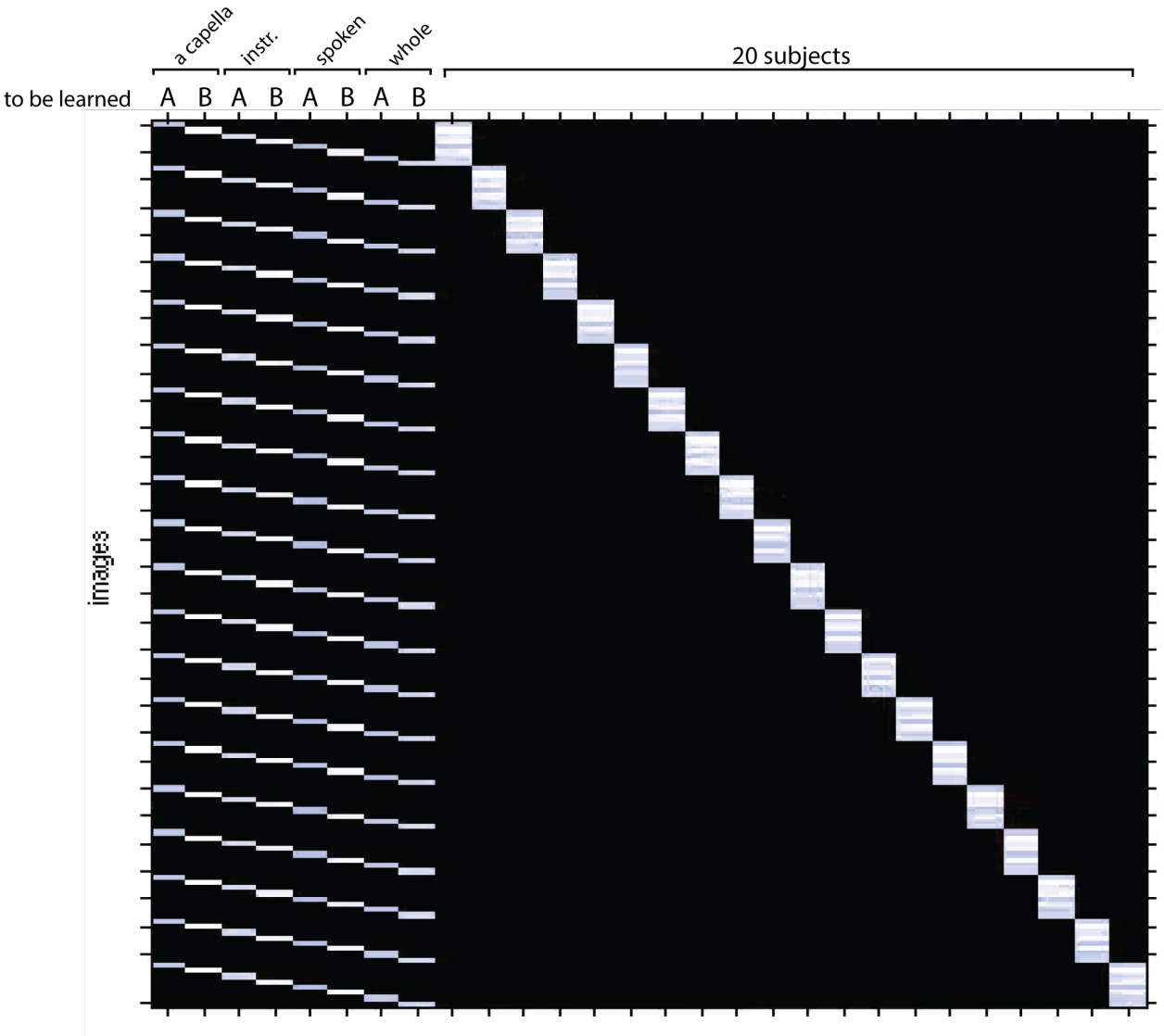
Trost, W., Frühholz, S., Cochrane, T., Cojan, Y., & Vuilleumier, P. (2015). Temporal dynamics of musical emotions examined through intersubject synchrony of brain activity. *Social Cognitive and Affective Neuroscience*, *10*(12), 1705–1721. https://doi.org/10.1093/scan/nsv060

Wilson, S. M., Molnar-Szakacs, I., & Iacoboni, M. (2008). Beyond Superior Temporal Cortex: Intersubject Correlations in Narrative Speech Comprehension. *Cerebral Cortex*, *18*(1), 230–242. https://doi.org/10.1093/cercor/bhm049

Supplementary Figure 1

The SPM12 second-level flexible factorial model of the synchrony data for session 1 (calculated 'within session 1') used to look for differences between the stimuli learned by participants in Group A and Group B.

No differences between the Group A and Group B stimuli were found.



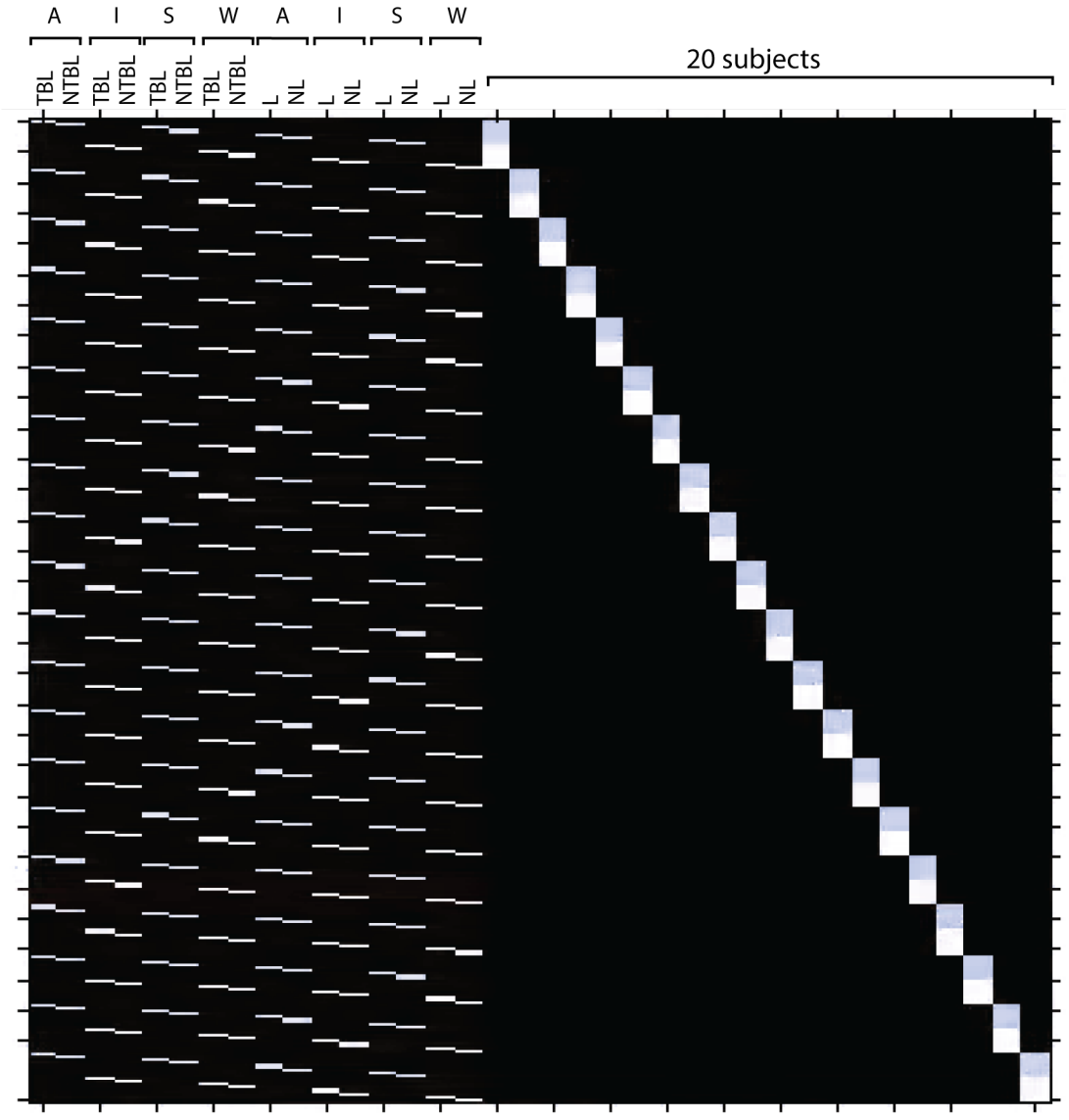
Supplementary Figure 2

The SPM12 second-level flexible factorial model of the synchrony data for session 1 and session 2 (calculated 'within session 1' and 'within session 2'. This model labeled stimulus type (two stimuli for each of the four types), learning condition (4 to be learned stimuli in session 1, 4 not to be learned stimuli in session 1, 4 learned stimuli in session 2, 4 not learned stimuli in session 2), and took subject effects into account

A = a capella, I = instrumental, S = spoken, W = whole

TBL = to be learned (session 1), NTBL = not to be learned (session 1)

L = learned (session 2), NL = not learned (session 2)



4 The effects of language and age on intersubject synchrony

Introduction

As discussed in the introduction to Chapter 3, the use of naturalistic stimuli to understand how the brain functions in the 'real world' is increasing. As the prevalence of the intersubject synchrony technique grows and is used to study both functional and dysfunctional brain activity, it is important to understand how stimulus characteristics (such as the presence of music and language) and participant characteristics (such as familiarity with the stimulus and age) affect intersubject synchrony. Synchrony is induced in different brain areas by different types of stimuli, although these differences have not been systematically investigated. For example, audio-only movie sequences (Naci et al., 2017) or audiobook excerpts (Regev et al., 2019; Simony et al., 2016) have successfully induced intersubject synchrony in fronto-temporal networks, while instrumental music (e.g. theme-songs from movies) has produced intersubject synchrony in auditory processing areas (Naci et al., 2017). To our knowledge, only two studies have compared synchrony across age groups (Campbell et al., 2015; Geerligs et al., 2018). These data showed that when older and younger adults watched the same movie while being scanned, the brains of the young adults were more synchronized in their responses than the older adults, who were more individualized in their responses. No studies have explored how aging affects synchrony across different types of stimuli. Given the evidence that memory for music is preserved in some neurodegenerative disorders associated with aging (Baird & Samson, 2009; Jacobsen et al., 2015), musical stimuli may be processed differently in the aging brain than stimuli without music.

The current study aimed to characterize how synchrony is affected by music and language stimuli and also to characterize how synchrony to music and language stimuli is affected by healthy aging. To address the first aim, we created stimuli that varied in music and

language content. Three conditions were generated from existing songs: (1) whole music (music and words together in a fully intact version of a song), (2) instrumental music without words (all vocal parts were removed, leaving just the non-vocal instrumentation), and (3) spoken words (the lyrics of each song were rerecorded in spoken form by the original lead singer to have a similar length, tempo, and emotional intonation as their original song counterparts). Unlike previous chapters, the a capella stimuli (sung leading and backing vocals without instrumental music) were not included. This stimulus condition was removed from the experiments involving older adults to reduce the burden on participants by shortening the scanning session. A detailed description of which stimuli were included in each experiment can be found in Appendix C. As shown in Chapter 3, repeated presentation of a stimulus reduces synchrony. To avoid any effects of repetition across stimulus conditions, each stimulus was created from a different original song. To address the second aim, we recruited two groups of participants: young and older adults. All participants were exposed to identical stimuli allowing us to investigate whether there is an age-related reduction in synchrony to music and language stimuli.

We calculated intersubject synchrony in two ways to answer two distinct questions. First, we calculated synchrony within the young and older adult groups separately. By correlating an individual's data with the average of their age-matched peers we can investigate how similarly individuals process stimuli to their peers across the lifespan. However, these synchrony values do not tell us anything about how similar older and young adults are to each other. For example, young and older adults could be equally highly synchronized within their age groups and we would see no group differences when statistically comparing these synchrony values but, the timecourse of the data within each of the age groups could look very different. Therefore, to compare how the stimuli were processed across age groups we used a second method of synchrony calculation. We correlated individual older adult data with the average of the *young adult* participants. If older adults were processing the stimuli differently than the young adults, we would expect weak correlations with the average young adult group and therefore, group differences when these weak correlations were statistically compared to the young adult synchrony values (calculated within young adults only). In contrast, if older adults were processing the stimuli in the same way as the young adults, we would expect equivalent synchrony values across the two groups of participants and, therefore, no group differences. Combining the results from both synchrony calculation methods tells us whether any differences

in synchrony across age groups are a result of age-related changes across all older adults, or idiosyncrasies within individuals.

We also used GLM analyses to examine BOLD responses to short stimulus clips to understand how the different stimuli recruited different brain areas across the two groups of participants. We were interested in comparing the brain areas identified by the GLM analysis to those identified by the synchrony analysis to understand whether the areas involved in processing different stimuli follow similar activation patterns across age groups. If similar areas are identified by both the GLM and synchrony analyses as differentiating between age groups, this may suggest that similar mechanisms of change (e.g. grey matter atrophy or increased functional connectivity) affect both age-related changes in the levels of BOLD activation across individuals and the timecourse of that activation.

When comparing synchrony values across music and language stimuli, we expected more synchrony to the whole stimuli (music and lyrics together) than to either the instrumental or spoken stimuli alone, as there were more aspects of the complex stimulus with which brain responses could synchronize. We also expected that the spoken stimuli would induce more synchrony than the instrumental stimuli (Sinai, 2015). Based on previous work (Campbell et al., 2015) we expected less synchrony in older adults than young adults both when synchrony was calculated within each age group separately (more idiosyncrasies in older adults) and when calculated by comparing the older adult data to the average young adult data (different activation time courses in older adults).

Methods

Ethics

Ethics approval for this project was granted by the Health Sciences Research Ethics Board at The University of Western Ontario (#100606).

Participants

Young adults

Twenty-six neurologically healthy, English-speaking participants (14 female) aged 18-39 (mean=24 years) were recruited at The University of Western Ontario. All participants had completed at least some post-secondary education and nine participants had completed some post-graduate education. According to the Goldsmith's Musical Sophistication Index (Müllensiefen et al., 2014), 17 participants reported having formal musical training (1-10yrs, mean=4.5yrs), but at the time of testing only nine of them played instruments regularly. Seven participants were fluent in a second language. All participants reported listening to music regularly in their daily lives (average 1.5 hours per day) via a phone, computer, or car radio.

Older adults

Fifteen neurologically normal, English-speaking participants (9 female) aged 64-74 (mean=70 years) were recruited in London, Ontario. All participants had completed at least some post-secondary education and four participants had completed some post-graduate education. Using the Goldsmith's Musical Sophistication Index (Müllensiefen et al., 2014), 11 participants reported having formal musical training (1-61yrs, mean=20.8yrs), but at the time of testing only three of them played instruments regularly. Five participants were familiar with a second language but did not rate themselves as fluent in those languages.

Stimuli

Twelve stimuli were created from the lyrics and music of different songs written and recorded by a member of the research team between 1997 and 2006 for an amateur rock band based in Cambridge, UK. Thus, all stimuli were completely novel to the Canadian participants. The original songs were all written in a similar style and instrumentation included a lead singer, bass, drums, guitar, string instruments, and backing vocals, each recorded on separate tracks. All stimuli were recorded using the exact same equipment directly to digital hard drive using the Sonar software (by Cakewalk) and a ShureSM58 microphone.

Three conditions were created by modifying the original twelve songs to include or exclude only certain tracks: (1) whole music (music and words together in a fully intact version

of each song), (2) instrumental music without words (all vocal parts were removed, leaving just the non-vocal instrumentation), and (3) spoken words (the lyrics of each song were rerecorded in spoken form by the original lead singer to have a similar length, tempo, and emotional intonation as their original song counterparts). There were four different stimuli for each condition, and none of the original songs were used for more than one condition (see Table 1).

Six of the stimuli (two per condition) were used in the GLM experiment. These six stimuli varied in length from 3:00-4:03 minutes, but during the fMRI experiment participants heard ten-second non-overlapping clips taken from each stimulus (see *fMRI acquisition and analysis* for details). The other six stimuli were used for the intersubject synchrony experiment. The stimuli were modified (e.g., lengthened by adding additional repetitions of the chorus) to each be five minutes long. During the synchrony portion of the fMRI scan sessions, participants heard each stimulus in its entirety (see *fMRI acquisition and analysis* for details). All stimuli were normalized to equate their perceived loudness using the *Audacity* software (Audacity Team, 2020). All stimuli are available in the supplementary materials (Appendix C).

Table 1. Visual representation of how the 12 different stimuli were divided between three conditions and two fMRI experiments. The numbers 1-4 refer to the individual stimuli in each condition.

Stimulus conditions	**Whole music**	**Instrumental music**	**Spoken words**
GLM experiment 10-s excerpts of 3-4min stimuli	Whole 1 Whole 2	Instrumental 1 Instrumental 2	Spoken 1 Spoken 2
Intersubject synchrony experiment 5-min stimuli	Whole 3 Whole 4	Instrumental 3 Instrumental 4	Spoken 3 Spoken 4

fMRI acquisition and analyses

Imaging was conducted at the Robarts Research Institute on a Siemens Magnetom 7 Tesla scanner with a 32-channel head coil. Functional scans were acquired with 54 slices per volume (TR = 1.25 s; TE = 20 ms; flip angle = 35°; FOV = 220 x 220 mm; voxel size = 2.5 mm^3). The scan session included two 12-minute functional runs for the GLM experiment and six 5-minute functional runs for the intersubject synchrony experiment. During the 12-minute runs, participants heard ten 10-second clips from each of the 6 stimuli (60 clips total) that were randomized across the two runs (30 clips in each run). During each of the six 5-minute runs, participants passively listened to one stimulus in its entirety. Stimulus order was randomized for

each participant. Between functional runs, a whole-head anatomical scan was acquired (TR = 6s; TE = 2.69 ms; FOV = 240 x 240 mm; voxel size = .75 mm^3; 208 slices). Both young and older adults underwent the same scanning procedures.

GLM experiment

BOLD data collected during the 12-minute runs were processed using SPM12. Three 'dummy' scans were excluded from the beginning of every run to allow stabilization of the signal. Images were realigned to the first image in the first run using six motion parameters (x, y, z, translation and rotation). Data were normalized to MNI space and smoothing was done with a Gaussian kernel of 8 mm FWHM. Subject-specific first-level models combined data from the two 12-minute runs and included epochs representing each of the 10-second stimulus clips (six regressors) convolved by the canonical hemodynamic response function. Six motion parameters (x, y, z, translation and rotation) were included as covariates of no interest. Serial correlations were accounted for using a first-order autoregressive model and low-frequency noise was removed with a high-pass filter of 128s. Contrast images estimated from single-participant models were created for each of the six stimuli vs rest resulting in a total of six contrast images per subject. The six contrasts were then entered into a second-level flexible-factorial model for group-level analysis. This model labeled stimulus type (two stimuli for each of the three types), group (young and older adults), and took subject effects into account. The cluster-forming threshold was specified at FWE $p<.0001$ uncorrected (Roiser et al., 2016). All data from within the clusters are reported at a corrected FWE $p<.05$. A 2(young/older adults) x 3(stimulus type) ANOVA was run to investigate where brain activity differed as a result of stimulus type and age group. Post-hoc tests included two t-contrasts to compare brain activity in the young and older adults, collapsing across stimulus type (young > older adults; older > young adults).

To replicate the pattern of stimulus differences seen in the young adult data in Chapter 2 (Sternin et al., 2021), a one-way ANOVA was run in the older adult participants alone to determine areas where brain activity differed as a result of the three stimulus types. As no studies have investigated how older adult brains respond to different musical stimuli, this analysis allowed us to fully characterize BOLD activation levels to different stimulus types in older adults. Post-hoc tests included six *t*-contrasts to investigate all pairwise comparisons between the three stimulus types.

Intersubject synchrony

Data from the six 5-minute runs were processed using automatic analysis (version 4.1 (Cusack et al., 2015): a MATLAB based processing and analysis pipeline that integrates with Statistical Parametric Mapping (SPM12). Three 'dummy' scans were excluded from the beginning of every data run to allow stabilization of the signal. Images were realigned to the first image in the first run using six motion parameters (x,y,z, translation and rotation). Data were normalized to MNI space and smoothing was done with a Gaussian kernel of 10mm FWHM. Low-frequency noise (e.g., drift) was removed with a high-pass filter of 128s. Data were denoised using cerebrospinal fluid, white matter signals, motion parameters, their lag-3 2nd-order Volterra expansion (Friston et al., 2000), and "spikes" (>3 standard deviations based on mean signal variance across volumes) as nuisance regressors. The data were then further cleaned by running a group ICA (Calhoun et al., 2001) within each stimulus and removing 1-2 components that spatially correlated with a mask of the ventricles to remove non-brain related activity.

The degree of intersubject synchrony across the whole brain was calculated separately within each of the groups of young and older adult participants. These data allow us to investigate whether individuals were similarly synchronized to age-matched peers across the lifespan, or if they become more idiosyncratic with age. Within each age group, synchrony was calculated separately for each stimulus using a leave-one-out approach. Synchrony was only ever calculated between identical stimuli. For each stimulus, the timecourse of every voxel in each participant was correlated (Pearson and then Fisher z-transformed) with the mean timecourse of every corresponding voxel from the rest of the participants' age group, minus that participant (N-1). This process created an *r*-value for each voxel, for each participant, that described the correlation between that participant's voxel and the same voxel in the other participants within their age group.

Each individual's correlation values for the six stimuli were entered into a group level flexible-factorial model using SPM12. This model labeled stimulus type (two stimuli for each of the three types), group (young and older adults), and took subject effects into account. A 2(age group) x 3(stimulus type) ANOVA was run to examine the main effects of age, stimulus type, and the age by stimulus type interaction. Post-hoc tests included two t-contrasts to compare brain

activity in the young and older adults, collapsing across stimulus type (young > older adults; older > young adults). Post-hoc tests following a significant main effect of stimulus type were conducted using an ROI approach. The cluster-forming threshold was specified at FWE $p<.0001$ uncorrected (Roiser et al., 2016) and clusters identified by the main effect of stimulus type were specified at a corrected FWE $p<.05$. Synchrony data, averaged across all voxels within each of the significant clusters identified by the ANOVA, were extracted using MarsBAR (Brett et al., 2002) and pairwise comparisons between the stimulus types were run using R (R Core Team, 2013).

Intersubject synchrony between age groups

The synchrony analysis described above provides insight into whether young and older adults process stimuli similarly to their age-matched peers but does not provide information about how similarly young and older adults process stimuli to each other. Therefore, to understand whether older and young adults processed the stimuli in a similar way, we compared the timecourse of the activation produced by stimulus processing in older and younger adults by calculating a second set of synchrony values for the older adults. These synchrony values were calculated within each of the clusters defined by a main effect of age group in the 2(age group) x 3(stimulus type) ANOVA above. The cluster-forming threshold was specified at FWE $p<.0001$ uncorrected (Roiser et al., 2016) and clusters identified by the main effect of age group were specified at a corrected FWE $p<.05$.

Within each cluster, for each stimulus, the timecourse of every voxel in each older adult participant was correlated (Pearson and then Fisher z-transformed) with the mean timecourse of every corresponding voxel from the young adult participants. This process created an *r*-value for each voxel, for each older adult participant, that described the correlation between that participant's voxel and the same voxel in the young adults. Synchrony data, averaged across all voxels within each of the regions of interest, were extracted using MarsBAR (Brett et al., 2002). This second set of synchrony values for the older adult participants could be statistically compared to the synchrony values calculated within the young adult participants (calculated within the young adult group as described in the previous section). Two *t*-tests comparing synchrony values in young and older adults were run using R (R Core Team, 2013): young > older adults; older > young adults. If older adults were processing the stimuli differently than the

young adults, we would expect weak correlations with the average young adult group and therefore, group differences when these weak correlations were statistically compared to the young adult synchrony values. In contrast, if older adults were processing the stimuli similarly to the young adults, we would expect equivalent synchrony values across the two groups of participants and, therefore, no group differences.

Results

Participants

Young adults

Two individuals withdrew from the study following the scan session and one individual's data from one of the 12-minute runs was lost. Therefore, fMRI data from 23 individuals were included in the analysis.

Older adults

The data from one individual was removed because of excessive movement in the scanner (>2mm displacement in z) and one participant withdrew from the study. Therefore, fMRI data from 13 older adults were included in the analysis.

FMRI results

GLM experiment

The 2(young/older adults) x 3(stimulus conditions) ANOVA revealed a significant main effect of age group in large clusters across the brain (see Table 2 and Figure 1). There was no significant main effect of stimulus type and no significant interaction between age group and stimulus type.

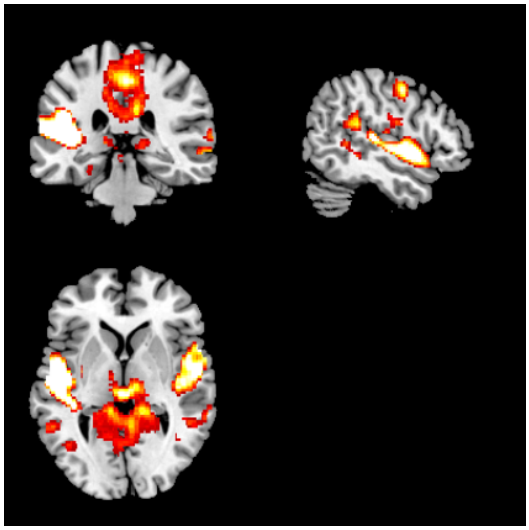


Figure 1. Brain regions where a significant main effect of age group was found in the 2(age group) x 3(stimulus conditions) ANOVA. The extent threshold was set to the FWEc value (=47). Hotter colours represent larger levels of activation. Displayed slices are at x= 50, y=-31, z=2.

Table 2. Peak voxels for cluster locations (depicted in Figure 1) from the GLM experiment *F*-contrast describing the main effect of age group. The extent threshold was set to the FWEc value (=47). $p<.05$ FWE. Reported peaks are >8.0mm apart. *All reported *F*-values are significant at $p<.001$.

extent = 47 peaks >8.0mm apart		*F*-value *
Planum temporale	-42, -30, 8	414.61
Parietal operculum	-50, -26, 12	381.62
Planum polare	-48, -8, 2	232.51
Planum temporale	58, -26, 8	174.31
Planum polare	44, -14, -2	162.25
Central opercular cortex	46, -2, -2	159.90
Temporal occipital fusiform cortex	36, -54, -20	115.68
Precuneous cortex	18, -48, 18	104.55
Thalamus	0, -26, 2	103.78
Central opercular cortex	54, -16, 12	95.64
Central opercular cortex	54, -12, 20	52.95
Parietal operculum cortex	62, -20, 18	33.42
Precentral gyrus	50, -4, 44	89.87
Supramarginal gyrus (posterior div.)	54, -38, 18	89.79
Insular cortex	32, -26, 18	86.27
Putamen	32, -12, 10	77.15
Central opercular cortex	36, -14, 20	54.80
Left ventricle	-2, 6, 16	65.74
Right ventricle	8, 8, 16	59.31
Cerebral white matter	20, -4, 18	45.25
IFG – pars opercularis	42, 16, 22	60.17
MTG – temporooccipital	-58, -52, 0	58.83
MTG – temporooccipital	-46, -48, 4	25.70
Paracingulate gyrus	-10, 26, 38	54.01
Precentral gyrus	-58, 0, 18	48.24
Putamen	-32, -8, 2	45.88
Putamen	-30, -6, -10	44.91
Insular cortex	-30, 6, -14	34.66
Lateral occipital cortex (inferior div.)	-42, -64, 2	38.94
Angular gyrus	-46, -60, 16	36.56
Lateral occipital cortex (inferior div.)	-42, -70, 8	31.80
Precentral gyrus	-42, -14, 42	38.66
Precentral gyrus	-54, -12, 48	36.63

The two post-hoc *t*-tests exploring the differences in activation levels based on age group revealed that young adults produced more activity in large, bilateral temporal areas than older adults, while older adults produced more activity in subcortical regions than did younger adults (see Figure 2 and Table 3).

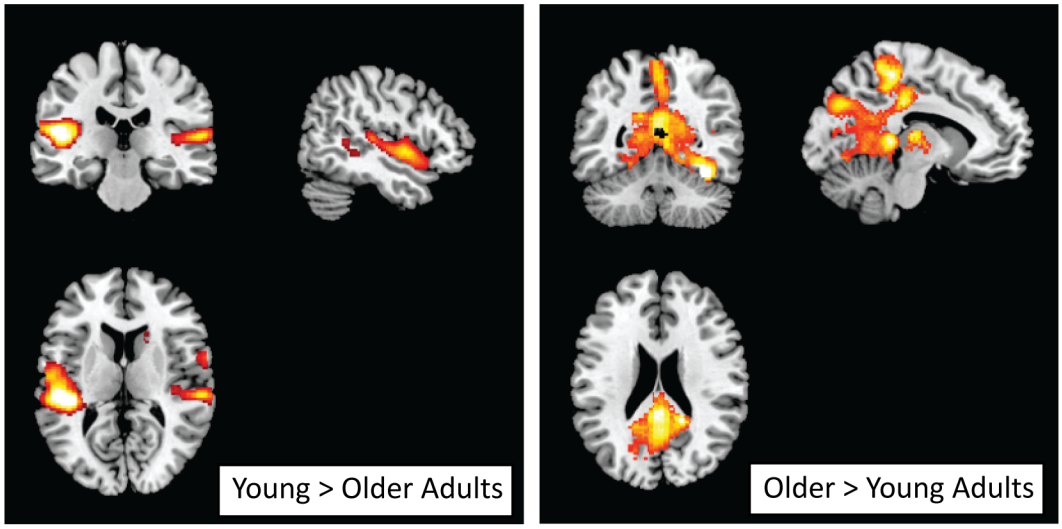


Figure 2. Left: Areas in which young adults showed more activation than older adults. Displayed slices are at x=48, y=-25, z=11, FWEc=95. Right: Areas in which older adults showed more activation than young adults. Displayed slices are at x=-9, y=-53, z=23, FWEc=52. Hotter colours represent larger levels of activation.

Table 3. Cluster coordinates from the GLM experiment for two *t*-contrasts comparing BOLD activation across age groups: young > older adults and older > young adults. The extent threshold was set to the FWEc value separately for each contrast and clusters were defined at $p<.05$ FWE. *All reported *t*-values are significant at $p<.001$.

Young > Older Adults extent = 95 peaks >4.0mm apart		**t-value***	**Older > Young Adults** extent = 52 peaks >8.0mm apart		**t-value***
Planum temporale	-42, -30, 8	20.36	Temporal occipital fusiform	36, -54, -20	10.76
Planum temporale	-48, -28, 10	19.66	Precuneous cortex	18, -48, 18	10.22
Parietal operculum	-54, -30, 14	19.44	Thalamus	0, -26, 2	10.19
Planum polare	-48, -8, 2	15.25	Central opercular cortex	54, -16, 12	9.78
Temporal pole	-46, 6, -10	15.17	Central opercular cortex	54, -12, 20	7.28
Insular cortex	-44, -10, -2	14.40	Parietal operculum cortex	62, -20, 18	5.78
Heschl's gyrus	-52, -18, 2	14.23	Precentral Gyrus	50, -4, 44	9.48
MTG – temporooccipital	-58, -52, 0	7.67	Supramarginal gyrus (posterior div.)	54, -38, 18	9.48
MTG – temporooccipital	-46, -48, 4	5.07	Insular cortex	32, -26, 18	9.29
Planum temporale	58, -26, 8	13.20	Putamen	32, -12, 10	8.78
Planum polare	44, -14, -2	12.74	Central opercular cortex	36, -14, 20	7.40
Insular cortex	46, -2, -2	12.64	IFG – pars opercularis	42, 16, 22	7.76
Heschl's gyrus	54, -10, 0	12.60	Precentral gyrus	-58, 0, 18	6.95
Planum temporale	50, -26, 8	10.92	Putamen	-32, -8, 2	6.77
Temporal pole	46, 8, -12	10.62	Putamen	-30, -6, -10	6.70
Central opercular cortex	62, 2, 6	10.25	Insular cortex	-30, 6, -14	5.89
Inferior frontal gyrus (operc.)	58, 10, 4	9.81	Insular cortex	-26, 16, -6	6.52
Heschl's gyrus	42, -20, 4,	9.13	Insular cortex	-30, 20, 0	4.90
Heschl's gyrus	42, -24, 6	8.88	Cerebral cortex	2, 6, 2	6.35
MTG – posterior	60, -32, -4	7.66	Caudate	-8, 0, 10	5.50
MTG – posterior	66, -36, 0	7.44	Lateral occipital cortex (inferior div.)	-42, -64, 2	6.234
MTG – posterior	66, -32, -2	7.43	Angular gyrus	-46, -60, 16	6.05
MTG – temporooccipital	64, -40, 0	7.28	Lateral occipital cortex (inferior div.)	-42, -70, 8	5.40
MTG – temporooccipital	50, -46, 4	6.72	Precentral gyrus	-42, -14, 42	6.22
MTG – posterior	50, -38, -6	6.55	Postcentral gyrus	-54, -12, 48	6.05
Left ventricle	-2, 6, 16	8.11	Postcentral gyrus	-42, -24, 38	4.83
Caudate	8, 8, 16	7.70			
Caudate	20, -4, 18	6.73			
Caudate	18, 6, 16	6.64			
Caudate	14, 10, 20	6.15			
Caudate	18, 14, 16	6.11			
Caudate	18, 20, 12	5.66			
Caudate	16, -2, 26	5.39			

A one-way ANOVA investigating differences in activation based on the three stimulus types in the older adult participants alone revealed a main effect of stimulus type in the older adults in right temporal areas (extent = 167; see Figure 3 and Table 4). Pairwise comparisons between all stimulus types showed that there was significantly more activity to spoken stimuli than to either the whole or instrumental stimuli and significantly more activity to whole stimuli than to instrumental stimuli replicating the results seen in the young adult data in Chapter 2. No other pairwise comparisons showed significant differences between stimulus types (see Table 5).

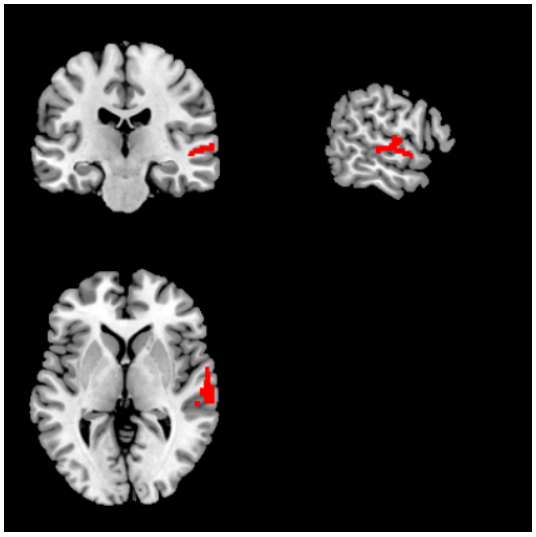


Figure 3. Areas in which BOLD activation differed across the three stimulus types in older adult participants only. FWEc = 167. Displayed slices are at x=60, y=-21, z=2.

Table 4. Cluster coordinates from the GLM experiment where activation differed based on the three stimulus types in older adults. The extent threshold was set to the FWEc value =167. Clusters were defined at $p<.05$ FWE.

extent = 167 peaks >4.0mm apart		***F*-value**	***p*-value FWE corr.**
Posterior STG	56, -22, 2	49.29	.001
Posterior STG	60, -18, 0	44.02	.001
Posterior STG	62, -14, 0	43.48	.001
Posterior STG	52, -32, 6	32.90	.002
Planum temporale	64, -8, 6	48.51	.002

Table 5. Significant clusters from binary contrasts between all stimulus categories in the older adults only. Missing results indicate no significant clusters were found. Coordinates for the peaks within each cluster and the corresponding t-values are listed. Reported peaks are >4.0mm apart.

Contrast	region	extent	*p* FWE corrected	Coordinates (x, y, z)	t-value
Instrumental > spoken	-	-	-	-	-
Instrumental > whole	-	-	-	-	-
Spoken > instrumental	Posterior STG	79	<.001	52, -22, -4	10.69
	Posterior STG		<.001	58, -4, -6	8.88
	Posterior STG		<.001	66, -28, 2	6.73
	Posterior STG		<.001	60, -12, -2	6.52
	Central opercular cortex		<.001	52, -34, 6	10.46
	Posterior MTG		<.001	-58, -32, 0	7.84
Spoken > whole	MTG – temporooccipital part	84	.001	50, -36, 4	6.46
	Posterior STG		.001	48, -26, -4	6.45
Whole > instrumental	Posterior STG	212	<.001	56, -22, -2	7.02
	Planum temporale		<.001	64, -8, 6	6.96
	Anterior STG		<.001	60, -6, -4	6.78
	Posterior STG		.001	60, -18, 0	6.63
	Posterior STG		.001	62, -14, 0	6.59
	Posterior STG		.028	52, -32, 6	5.74
Whole > spoken	-	-	-	-	-

Intersubject synchrony experiment

A 2(young/older adult) x 3(stimulus type) ANOVA (using young and older adult synchrony values calculated separately within each age group) identified 10 significant clusters in bilateral temporal, frontal, and occipital regions where synchrony differed based on age group, and five significant clusters in bilateral temporal lobes, precentral gyrus and occipital regions where synchrony differed based on stimulus category (see Table 6). There were no areas where a significant age by stimulus type interaction was identified. The 15 clusters can be seen in Figure 4.

Table 6. Cluster coordinates from two main effect *F*-contrasts from a 2(age group) x 3(stimulus type) ANOVA probing areas where synchrony differed based on age group and stimulus type. The extent threshold was set to the FWEc value for each contrast separately and clusters were defined at $p<.05$ FWE corrected. Three local maxima more than 8mm apart in each cluster are listed. * $p<.001$ (FWE corr)

ME of age group extent = 42	(x,y,z) coordinates	*F* value	ME of stimulus type extent = 49	(x,y,z) coordinates	*F* value
IFG triangularis	-42, 26, 10	48.58*	Anterior STG	-60, -12, 0	136.54*
IFG triangularis	-28, 34, 10	43.20*	Posterior STG	-66, -30, 6	136.51*
Frontal pole	-38, 42, 16	31.78*	Posterior STG	-66, -22, 2	135.37*
Middle frontal gyrus	-44, 4, 54	46.77*	Posterior STG	62, -14, -2	107.96*
Middle frontal gyrus	-30, 6, 58	22.49*	Posterior STG	72, -24, 6	53.53*
Middle frontal gyrus	-32, -14, 58	19.86 p=.001	Insular cortex	30, -24, 14	21.04*
MTG temporooccipital part	-50, -50, 6	34.13*	Precentral gyrus	-48, 0, 52	26.43 p=.002
MTG temporooccipital part	-66, -44, -2	27.03*	Occipital fusiform	-28, -78, -16	23.17 p=.020
Posterior MTG	-60, -38, -6	18.72 p=.003	Lateral occipital cortex (inferior div.)	-48, -76, 4	24.13 p=.012
Frontal orbital cortex	-16, 14, -22	22.55*			
Frontal orbital cortex	-24, 20, -28	16.22 p=.024			
Subcallosal cortex	-10, 8, -18	16.14 p=.026			
Anterior cingulate gyrus	-4, -16, 32	22.00*			
Anterior cingulate gyrus	-10, -10, 34	15.96 p=.030			
Posterior parahippocampal gyrus	36, -32, -6	21.17*			
Fusiform cortex	38, -38, -12	15.77 p=.036			
Frontal orbital cortex	14, 10, -20	20.38 p=.001			
Postcentral gyrus	-64, -18, 16	19.84 p=.001			
Postcentral gyrus	-64, -8, 10	19.29 p=.002			
Central opercular cortex	-56, -16, 20	18.15 p=.005			
Temporal pole	-44, 26, -22	16.80 p=.015			
Lateral occipital cortex (inferior div.)	-44, -74, 2	16.71 p=.016			

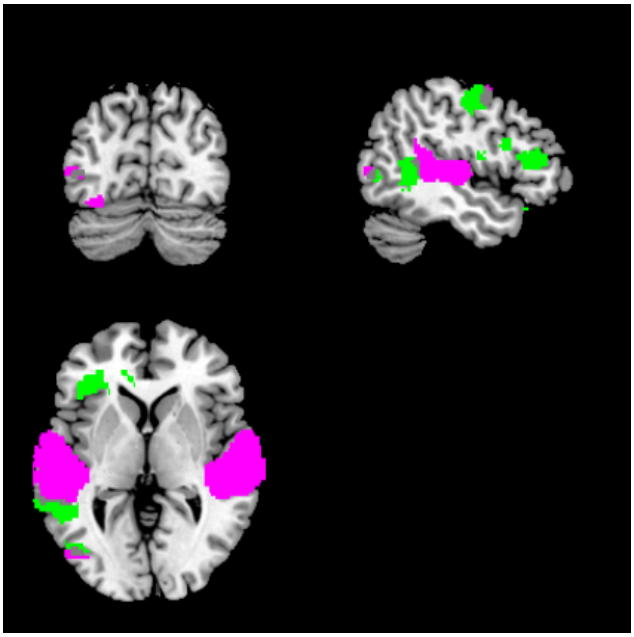


Figure 4. The 15 clusters identified by the main effects from a 2(age group) x 3(stimulus types) ANOVA are shown here. The 10 clusters where a main effect of age group was found are shown in green. The 5 clusters where a main effect of stimulus type was found are shown in purple. The two right-sided clusters identified by the main effect of age can not be seen in in the slices displayed here. Displayed slices are at: x= -48, y= -76, z= 2.

Two *t*-contrasts were performed to identify areas where synchrony differed based on age group. Young adults had more synchrony than older adults in three areas on the left: middle temporal lobe, temporal pole, and frontal orbital cortex (see Figure 5 and Table 7). Older adults had more synchrony than young adults in three areas on the left and one areas on the right: left IFG, left precentral gyrus, left central opercular cortex, and right parahippocampal gyrus (see Figure 5 and Table 7).

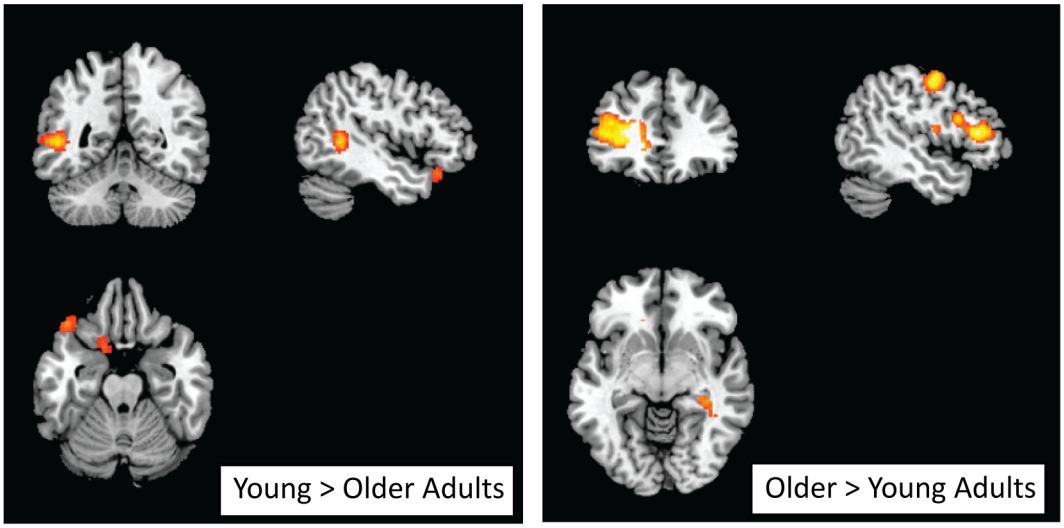


Figure 5. Left: Areas in which young adults showed more synchrony than older adults. Displayed slices are at x=-46, y=-51, z=-22, FWEc=95. Right: Areas in which older adults showed more synchrony than young adults. Displayed slices are at x=-48, y=35, z=-7, FWEc=52. Hotter colours represent larger levels of synchrony.

Table 7. Cluster coordinates for two t-contrasts comparing synchrony across age groups: young > older adults and older > young adults. The extent threshold was set to the FWEc value separately for each contrast and clusters were defined at $p<.05$ FWE. * $p<.001$ (FWE corr.).

Young > Older Adults extent = 71 local maxima >8.0mm apart		***t*-value**	**Older > Young Adults** extent = 63 local maxima >8.0mm apart		***t*-value**
MTG temporooccipital part	-50, -50, 6	9.01*	IFG pars triangularis	-42, 26, 10	12.07*
MTG temporooccipital	-68, -44, 0	8.38*	IFG pars triangularis	-28, 34, 10	10.88*
MTG posterior	-60, -38, -6,	7.32*	Frontal pole	-38, 42, 16	9.75*
Temporal pole	-44, 26, -22	7.00*	Precentral gyrus	-44, -4, 54	11.63*
Frontal orbital cortex	-14, 10, -22	6.36*	Precentral gyrus	-32, -14, 58	7.60*
Frontal orbital cortex	-24, 22, -30	5.93 p=.001	Middle frontal gyrus	-30, 6, 58	6.78*
			Central opercular cortex	-64, -18, 14	7.65*
			Postcentral gyrus	-64, -8, 10	7.20*
			Central opercular cortex	-50, -6, 16	6.80*
			Parahippocampal gyrus (posterior div.)	34, -34, -6	7.09*
			Fusiform cortex	38, -38, -12	6.64*
			Parahippocampal gyrus (posterior div.)	34, -26, -12	5.62 p=.005

Pairwise comparisons between stimulus conditions on the synchrony values extracted from the five clusters identified by the main effect of stimulus type showed that in all five regions, as expected, spoken stimuli induced more synchrony than the instrumental stimuli (see Figure 6 and Table 8) and whole stimuli induced more synchrony than instrumental stimuli in three areas: bilateral STG and precentral gyrus. However, contrary to our hypotheses, spoken stimuli induced more synchrony than whole stimuli in three areas: left posterior STG, occipital

fusiform, and lateral occipital cortex (inferior division). No other pairwise comparisons showed significant differences in any of the five regions.

Table 8. Pairwise comparisons between stimulus types performed in the five ROIs identified by a main effect of stimulus type. All reported *p*-values are FWE corrected within each region. Missing results indicate no significant results were found. Superscripts denote the labels used in Figure 6. *$p < .001$.

	Spoken > Instrumental[a]	Whole > instrumental[b]	Spoken > whole[c]
R anterior STG	*	*	-
L posterior STG	*	*	p=.01
Precentral gyrus	*	*	-
Occipital fusiform	p=.005	-	*
Lateral occipital Inferior division	p=.009	-	*

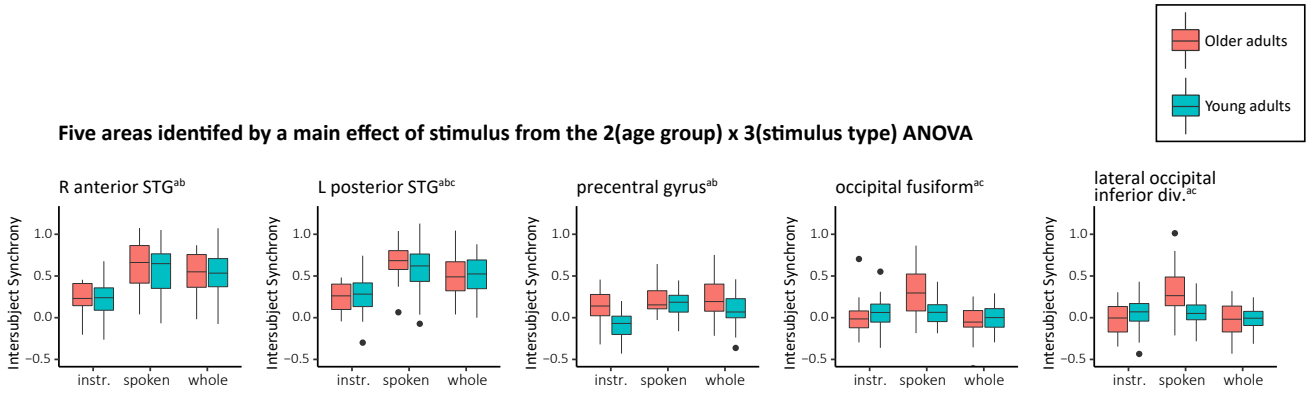


Figure 6. Synchrony values plotted for each of the 5 regions identified by a main effect of stimulus type in a 2(age group) x 3(stimulus type) ANOVA for each condition and for each group. Boxplots show the median value and contain values from the 25th to 75th percentile within each box. Whiskers represent 95% confidence intervals with outliers depicted as individual points. The following superscripts denote the significant pairwise comparisons listed in Table 7: a = spoken > instrumental, b = whole > instrumental, c= spoken > whole,

Intersubject synchrony between age groups

Two t-contrasts comparing synchrony in the young adults (calculated within the group of young adults) to synchrony in the older adults (calculated by comparing each individual older adult to the average young adult data) were run in each of the 10 clusters identified by a main effect of age group (see Table 6 and Figure 4). These t-contrasts identified four areas where synchrony differed between the two age groups. Young adults were significantly more synchronized than older adults ($p<.01$) in three areas: the middle temporal gyrus (temporooccipital part), anterior cingulate gyrus, and the temporal pole indicating that individual young adults were more synchronized to the rest of the group of young adults than any of the individual older adults. This can be interpreted as the timecourse of the activation in older adults following a different pattern than that of the young adults and is likely reflective of age-related changes in temporal cortex. In contrast, older adults were significantly more synchronized than young adults ($p=.007$) in only the posterior parahippocampal gyrus indicating that individual older adults were more synchronized to the group of young adults than any of the individual young adults. There were no differences between the two age groups in the six other areas: the IFG, middle frontal gyrus, left and right frontal orbital cortex, postcentral gyrus, and lateral occipital cortex (inferior division). In these six areas, individual older adults were just as synchronized to the average of the young adult group as the individual young adults indicating no age-related changes in stimulus processing.

Discussion

In the current study, we investigated neural activation differences based on stimulus contents and participant age using a traditional fMRI GLM analysis and an intersubject synchrony analysis. We were interested in comparing the brain areas identified by the GLM analysis to those identified by the synchrony analysis to understand whether the areas involved in processing different stimuli follow similar activation patterns across age groups. We were also interested in whether stimuli that include both music and language induce more synchrony than stimuli that include either component on its own.

GLM experiment

First, we examined age differences in the brain areas involved in the processing of music and language. The GLM experiment results indicated that there were differences in how the stimuli were processed based on participants' age and follow-up tests showed that young adults had more activation in auditory processing areas in the temporal cortex than the older adults, while older adults had more activation in subcortical and occipital regions. This pattern of results is in keeping with a frequent observation in fMRI studies of aging that young adults show greater activation in task-related areas (auditory regions in the current experiment), while older adults show increased activity in regions not activated in the younger population (the subcortical and occipital regions; Grady, 2000; Sikka et al., 2015). In addition, the areas identified as showing differences in activation between the two age groups are in keeping with previous literature that showed less activity in cortical regions in older adults compared to young adults (Cardin, 2016). This is true in both passive listening tasks (Cliff et al., 2013) and tasks that require participant responses (Kuchinsky et al., 2012; Peelle et al., 2010; Tyler et al., 2010). The differences in recruitment of areas between the young and older adults may be related to the compensatory mechanisms that develop to support auditory processing with age (Peelle, 2019; Wingfield & Grossman, 2006). For example, both increasing age and decreasing intelligibility were related to increased activation in occipital cortex during an auditory word recognition task (Kuchinsky et al., 2012). These activation changes were seen in occipital areas similar to those identified in the current study as being more active in older than young adults (inferior lateral occipital cortex and angular gyrus; Table 3). Similarly, older adults showed additional recruitment of frontal areas like the inferior frontal gyrus during sentence comprehension tasks (Peelle et al., 2010; Tyler et al., 2010). This same frontal area also showed more activity in older than young adults in the current experiment (Table 3). In a passive listening task, like the task in the current experiment, young adults showed significantly more activation within bilateral superior and middle temporal gyri than in older adults (Cliff et al., 2013). The current results showed more activation in young adults than older adults in similar temporal areas.

As no studies have investigated how older adult brains respond to different musical stimuli, we performed pairwise comparisons between all stimulus types in the older adult data to fully characterize BOLD activation levels to different stimulus types in older adults. By

comparing the older adult results to those seen in young adults in Chapter 2, we could investigate whether the pattern of stimulus processing was maintained across the lifespan. We found that, like in the young adults, spoken stimuli resulted in more activity than either whole or instrumental stimuli and whole stimuli resulted in more activity than the instrumental stimuli. No other comparisons resulted in significant differences. When comparing the significant pairwise comparison results in older adults to those found in the young adults, we saw that there were some contrasts that elicited activation in young adults that did not have the same effect in the older adults (e.g., young adult brains activated more to whole than spoken stimuli in bilateral planum polare, but in older adults, activity to whole and spoken stimuli was similar).

There are a number of possible explanations for why the older adults showed fewer activation differences between stimulus types than did younger adults. First, 20 young adults were included in the analyses in Chapter 2 while only 13 older adults were included here (older adult data collection was put on hold due to the COVID-19 pandemic resulting in sample size discrepancies). In Chapter 2, young adults showed more activation to instrumental and whole stimuli than to spoken stimuli in bilateral auditory areas (Chapter 2, Table 5). In the current experiment, there were no significant differences between these stimuli in older adults. However, when the statistical thresholds in these two pairwise comparisons in older adults (instrumental > spoken; whole > spoken) were lowered to $p<.001$ without familywise error correction, similar bilateral auditory areas as seen in the young adults were identified. It is possible that with a larger group of older adults we may have seen activation differences similar to those seen in young adults between more pairs of stimuli.

The differences in BOLD activation to different stimuli in young and older adults may also be related to how language processing changes with age. When older adults hear language embedded in noise their brains show different patterns of activation than young adults and, specifically, decreasing activation in temporal auditory areas with decreasing language intelligibility (Eckert et al., 2008; Peelle, 2019). The older adult results in this experiment showed more activity to stimuli that included language than to the instrumental stimuli that did not (spoken > instrumental; whole > instrumental). Spoken stimuli also resulted in more activity than whole stimuli and, although both stimuli contained language information, the spoken stimuli contained only language while the whole stimuli contained both language and music. If the

language in the whole stimuli was processed similarly to how language is processed in a noisy environment, this could explain the pattern of results seen here; the most activation was seen to the most intelligible stimuli (spoken), the least activation was seen to the least intelligible stimuli (instrumental), with activation to the whole stimuli falling in between. Although we did not collect any measures of lyric comprehension in older adults, the participants did not report any issues in understanding the words that were present in the stimuli. To further understand whether the BOLD activation differences seen here in older adults are related to language comprehension, future studies should aim to collect information regarding lyric comprehension in musical stimuli.

Intersubject synchrony differences to language and music

We expected more synchrony to the whole stimuli (music and lyrics together) than to either the instrumental or spoken stimuli alone, as there was more information within the whole stimuli with which brain responses could synchronize. In line with our hypothesis, we found that whole stimuli induced more synchrony than instrumental stimuli in three regions (bilateral STG and precentral gyrus). However, contrary to our hypothesis we found that spoken stimuli resulted in significantly more synchrony than the whole stimuli in three ROIs (left posterior STG and the two occipital areas). None of the five regions of interest showed more synchrony to whole than to spoken stimuli; more information within a stimulus did not necessarily increase synchrony.

When comparing the spoken and the instrumental stimuli we found that spoken stimuli induced more synchrony than instrumental stimuli across all five regions. There were no regions where the instrumental stimuli induced more synchrony than the other two stimulus categories that contained language information. This result supports findings from previous work that suggest that language is a key component to driving synchrony across a group of listeners (Naci et al., 2017; Regev et al., 2019; Simony et al., 2016). However, differences in synchrony between the spoken stimuli and the other two conditions may be because of the physical characteristics of the stimuli themselves. Specifically, the spoken stimuli contained more silent periods (pauses between words and phrases) and therefore more onsets of sound from silence compared to the whole and instrumental stimuli, where the music was more continuous with few to no silent periods. The more frequent contrasts between sound and silence in the spoken stimuli could drive greater fluctuations in the BOLD signal, resulting in stronger synchrony across

participants. However, if the synchrony differences were driven solely by sound onsets, we would expect there to be no difference in synchrony between the more continuous whole and instrumental stimuli. Our results do not support this explanation as we do see synchrony differences between the whole and instrumental stimuli. Therefore, the differences in the number of sound onsets can not fully explain why we see stronger synchrony to the spoken stimuli.

When the synchrony results across stimulus types were compared to the results seen from the GLM experiments, the pattern of results was similar. In the GLM experiments, young and older adults showed more activation to stimuli that included language over stimuli that did not (spoken > instrumental; whole > instrumental) and showed more activation to spoken stimuli than to whole stimuli. This same pattern was seen in the synchrony results. In the GLM experiment, the differences in activation were discussed in the context of existing literature on how language is processed in the presence of noise. However, the differences in synchrony may be related to how the presence of language and music affect what aspects of the stimuli participants pay attention to.

Synchrony is affected by attention (Regev et al., 2019) with the degree of synchrony (as measured with fMRI) decreasing as participants are distracted. Synchrony also decreases when the stimulus does not include a coherent narrative for participants to attend to, compared to when the stimulus contains an intact storyline (Ki et al., 2016). Here, when participants heard the spoken stimuli, they processed a single language stream. Even if participants were not actively focusing on the words, there is an element of automatic processing that occurs for language (Fodor, 1983; Hartsuiker & Moors, 2016; Levelt, 1993). The consistency of the language processing likely resulted in strong synchrony. In contrast, when hearing instrumental stimuli, participants may have focused on different instruments, or mind-wandered and made personal associations with the music. These individual differences would have caused a less consistent neural response to the instrumental stimuli across the group. When stimuli contain multiple tracks, such as the whole stimuli that contained both music and language, the synchrony appears to fall between the levels induced by the spoken and instrumental stimuli. With whole stimuli, there is likely some directed synchrony, from the automatic processing of the clearly intelligible language, but the multiple instrumental tracks may cause inconsistencies across participants and reduce synchrony. Therefore, it is likely that a stimulus with music and language will be most

effective at inducing synchrony if there is an obvious portion to which all participants' attention is drawn (e.g. an audio story being told over background music). Multiple tracks in the whole stimuli may have caused each participant to attend to a different component (the music, rhythm, or lyrics) and reduced synchrony across the group.

Intersubject synchrony differences with age

To investigate whether music and language stimuli had the same effects on synchrony across different age groups, we compared intersubject synchrony between older and young adults. To our knowledge, only two previous studies have directly compared synchrony across age groups. These studies found that when watching a movie, older adults were less synchronized than younger adults (Campbell et al., 2015; Geerligs et al., 2018). However, if all of the older adults were processing the stimuli similarly to each other but differently than the young adults, it would be possible for the older adults to be highly synchronized with each other but have low synchrony with the young adults. In the current study, we calculated older adult synchrony in two ways. First, by comparing synchrony values calculated within age groups we investigated whether individuals maintain the same level of synchrony with their age-matched peers across the lifespan or whether they become more idiosyncratic with age. Second, by calculating synchrony in the older adults by correlating the individual older adult data with the average young adult data we investigated whether older adults process music and language stimuli in a similar way to young adults or whether there are age-related differences in the way music and language stimuli are processed.

The first method correlated individual older adult data with the average of the rest of the older adult data. When comparing these synchrony values to the young adult synchrony values (calculated within the young adult group) we found that young adults showed more synchrony than older adults in left temporal and frontal orbital clusters. Previous studies have shown that the reduction in synchrony in these frontal areas is correlated with reductions in cognitive functioning with age (Geerligs et al., 2018). We did not collect information on participants' cognitive function, and therefore are unable to say whether the reduction in synchrony with age seen in these regions is related to cognitive function.

Interestingly, in four clusters we did *not* see age-related decreases (in left inferior frontal gyrus, pre- and post-central gyrus, parahippocampal gyrus) and instead saw more synchrony

within older adults than young adults. The discrepancy in results between the previous study and the current results may have to do with how language processing changes with age. Many of the regions associated with language processing (e.g., inferior frontal gyrus, precentral gyrus; Borowsky et al., 2007; Pulvermuller et al., 2006) seemed resistant to age-related synchrony decreases (Geerligs et al., 2018). Older adults may recruit additional resources as a compensatory mechanism to make up for lost neural efficiency when processing language stimuli (Peelle, 2019; Wingfield & Grossman, 2006). Therefore, it is possible that, in our study, older adults were more synchronized than young adults within regions associated with language processing because they relied more heavily on these regions to process the music and language stimuli than did the young adults. In support of the idea that older adults may have relied more heavily on these language networks, the results from the GLM experiment show that in some of the same areas where we saw more synchrony in older adults, we also saw more BOLD activation to older than young adults (central opercular cortex, IFG, pre- and post-central gyrus; see Table 3 and Table 7). In addition, language regions have shown to be generally resilient against the effects of age, especially during passive listening tasks (Campbell et al., 2016; Davis et al., 2014). If young adults were not relying on these networks as heavily as the older adults, and older adults do not generally show age-related decline in these regions, it may be reasonable to expect more synchrony in older adults than younger adults within these networks.

Our investigation into whether individuals maintain synchronization with age-matched peers across the lifespan has shown that synchrony changes as a result of age, but a reduction in synchrony across all brain areas is not seen. The differences in synchrony across age groups may have to do with the contents of the stimuli and the way those contents interact with aging. The stimuli that were used in the previous two studies where synchrony was compared across age groups (Campbell et al., 2015; Geerligs et al., 2018) differed from the types of stimuli that were used in the current study. We used stimuli designed to manipulate the presence of language, while the previous studies used a movie stimulus that may not have required as much processing of language (i.e. parts of the story may have been conveyed visually instead of through words). If the movie stimulus did not recruit these language networks, older adults may not have relied on them as heavily, may not have been as synchronized and therefore, showed an age-related reduction in synchrony. Further characterization of age-related changes in synchrony should

consider comparing synchrony across different types of stimuli (e.g., language, music, movies, tactile stimuli, etc.).

The second method used to calculate synchrony in older adults correlated individual older adult data with the average of the young adult data within each of the 10 regions identified by a main effect of age group (see Table 6 and Figure 4). This method allowed us to assess whether older and young adults were processing a stimulus similarly. If older adults were processing the stimuli differently than the young adults, we would expect weak correlations between the older adult and the average young adult group and therefore, group differences when these weak correlations were compared to the within-group young adult synchrony values. In contrast, if older adults were consistently processing the stimuli similarly to the young adults, we would expect to see equivalent synchrony values across the two groups of participants and therefore, no group differences. In this analysis we found that, in most areas (6 out of 10), there were no group differences. This result indicates that in these areas of the brain there are no age-related differences in how music and language stimuli are processed; the BOLD fluctuations in response to the stimuli followed a similar pattern in both older and young adults.

Using the second method of synchrony calculation, we found that in the posterior parahippocampal gyrus the individual older adults were more synchronized to the average of the young adult groups than were the individual young adults. This is an interesting result because atrophy in parahippocampal gyrus is known to be involved in age-related memory decline (Burgmans et al., 2011; Thangavel et al., 2008). The older adult participants in this study did not report memory difficulties, therefore, if synchrony in older adults is related to the way young adults process a stimulus, perhaps studies aiming to characterize synchrony changes in clinical populations with degenerative memory disorders should include the parahippocampal gyrus in their analyses. Increasingly idiosyncratic responses in this region as a result of disease progression may provide insight into the neural mechanisms behind such disorders.

We found that young adult within-group synchrony was greater than the older adult synchrony (calculated by comparing older to young adults) in three regions. Individual young adults were more synchronized to the young adult group average than were the older adults in the middle temporal gyrus (temporooccipital part), the anterior cingulate gyrus, and the temporal pole. All three of these areas are known to undergo age-related increases in functional

connectivity (Cao et al., 2014; Hafkemeijer et al., 2013; Peelle et al., 2010) and reductions in grey matter volume (Mann et al., 2011; Pacheco et al., 2015; Saenger et al., 2012). Age-related structural and functional changes within these regions may have reorganized how stimuli are processed, requiring the older adults to process the stimuli differently than the young adults.

When the results from the two methods of investigating intersubject synchrony across age groups are combined, we can conclude that synchrony changes with age but, it is not always the case that there is a generalized synchrony reduction with age. In fact, in the posterior parahippocampal gyrus it seems that idiosyncrasies in older adults decrease (causing an increase in synchrony). Structural changes that occur with age like grey-matter atrophy (e.g., Giorgio et al., 2010; Walhovd et al., 2005) may be responsible for the regional differences in synchrony. Relating differences in grey-matter volume between the groups of young and older adults may be one way to investigate whether structural differences are responsible for synchrony differences. However, there is a significant age-related decline in grey matter volume in regions associated with language processing (Campbell et al., 2016; Giorgio et al., 2010) and our results showed that synchrony was not reduced in these areas. Although we might expect a reduction in grey matter to lead to a reduction in synchrony, this is an empirical question that should be tested in future studies.

Conclusions

The results of the current experiment indicate that both the areas recruited to process auditory stimuli and the degree of synchrony to these stimuli differ based on the presence of music and language. Stimuli that are simple and have a salient component that attracts the listener's attention appear the most reliable for inducing synchrony across a group. This may be why audiobook stories, or movies with a clear plot, are successfully used in studies probing intersubject synchrony. It is likely that movies with abstract visuals or less clear story lines would allow for greater variation in synchrony across a group of participants. Stimuli that allow for mind wandering or have different aspects to focus on will also reduce synchrony within the group. Future intersubject synchrony studies should take into consideration the contents of their stimuli to obtain greatest synchrony. A simple stimulus with a clear focal point will be the most effective at inducing synchrony across different age groups.

Finally, our results show that young and older adults recruit different brain areas to process the same music and language stimuli and that the degree of synchrony to these stimuli changes with age. We found that although some areas showed an age-related decrease other areas were more synchronized in older adults than in young adults. Future studies characterizing the effects of age on synchrony should compare different types of stimuli and correlate synchrony values with other factors such as cognitive measures or grey-matter volume to understand the factors driving age-related changes in synchrony.

Bibliography

Audacity Team. (2020). *Audacity(R): Free Audio Editor and Recorder*. https://audacityteam.org/

Baird, A., & Samson, S. (2009). Memory for music in Alzheimer's disease: Unforgettable? *Neuropsychology Review*, *19*(1), 85–101. https://doi.org/10.1007/s11065-009-9085-2

Borowsky, R., Esopenko, C., Cummine, J., & Sarty, G. E. (2007). Neural Representations of Visual Words and Objects: A Functional MRI Study on the Modularity of Reading and Object Processing. *Brain Topography*, *20*(2), 89–96. https://doi.org/10.1007/s10548-007-0034-1

Brett, M., Anton, J.-L., Valabrègue, R., & Poline, J. B. (2002, June 2). *Region of interest analysis using an SPM toolbox* [Abstract]. 8th International Conference on Functional Mapping of the Human Brain, Sendai, Japan.

Burgmans, S., van Boxtel, M. P. J., van den Berg, K. E. M., Gronenschild, E. H. B. M., Jacobs, H. I. L., Jolles, J., & Uylings, H. B. M. (2011). The posterior parahippocampal gyrus is preferentially affected in age-related memory decline. *Neurobiology of Aging*, *32*(9), 1572–1578. https://doi.org/10.1016/j.neurobiolaging.2009.09.008

Calhoun, V. D., Adali, T., Pearlson, G. D., & Pekar, J. J. (2001). A method for making group inferences from functional MRI data using independent component analysis. *Human Brain Mapping*, *14*(3), 140–151.

Campbell, K. L., Samu, D., Davis, S. W., Geerligs, L., Mustafa, A., & Tyler, L. K. (2016). Robust Resilience of the Frontotemporal Syntax System to Aging. *The Journal of Neuroscience*, *36*(19), 5214–5227. https://doi.org/10.1523/JNEUROSCI.4561-15.2016

Campbell, K. L., Shafto, M. A., Wright, P., Tsvetanov, K. A., Geerligs, L., Cusack, R., Tyler, L. K., Brayne, C., Bullmore, E., Calder, A., Dalgleish, T., Duncan, J., Henson, R., Matthews, F., Marslen-Wilson, W., Rowe, J., Cheung, T., Davis, S., Kievit, R., … Villis, L. (2015). Idiosyncratic responding during movie-watching predicted by age differences in attentional control. *Neurobiology of Aging*, *36*(11), 3045–3055. https://doi.org/10.1016/j.neurobiolaging.2015.07.028

Cao, W., Luo, C., Zhu, B., Zhang, D., Dong, L., Gong, J., Gong, D., He, H., Tu, S., Yin, W., Li, J., Chen, H., & Yao, D. (2014). Resting-state functional connectivity in anterior cingulate cortex in normal aging. *Frontiers in Aging Neuroscience*, *6*. https://doi.org/10.3389/fnagi.2014.00280

Cardin, V. (2016). Effects of Aging and Adult-Onset Hearing Loss on Cortical Auditory Regions. *Frontiers in Neuroscience*, *10*. https://doi.org/10.3389/fnins.2016.00199

Cliff, M., Joyce, D. W., Lamar, M., Dannhauser, T., Tracy, D. K., & Shergill, S. S. (2013). Aging effects on functional auditory and visual processing using fMRI with variable sensory loading. *Cortex*, *49*(5), 1304–1313. https://doi.org/10.1016/j.cortex.2012.04.003

Cusack, R., Vicente-Grabovetsky, A., Mitchell, D. J., Wild, C. J., Auer, T., Linke, A. C., & Peelle, J. E. (2015). Automatic analysis (aa): Efficient neuroimaging workflows and parallel processing using Matlab and XML. *Frontiers in Neuroinformatics*, *8*. https://doi.org/10.3389/fninf.2014.00090

Davis, S. W., Zhuang, J., Wright, P., & Tyler, L. K. (2014). Age-related sensitivity to task-related modulation of language-processing networks. *Neuropsychologia*, *63*, 107–115. https://doi.org/10.1016/j.neuropsychologia.2014.08.017

Eckert, M. A., Walczak, A., Ahlstrom, J., Denslow, S., Horwitz, A., & Dubno, J. R. (2008). Age-related Effects on Word Recognition: Reliance on Cognitive Control Systems with Structural Declines in Speech-responsive Cortex. *Journal of the Association for Research in Otolaryngology*, *9*(2). https://doi.org/10.1007/s10162-008-0113-3

Fodor, J., A. (1983). *The modularity of mind*. MIT Press.

Friston, K. J., Mechelli, A., Turner, R., & Price, C. J. (2000). Nonlinear Responses in fMRI: The Balloon Model, Volterra Kernels, and Other Hemodynamics. *NeuroImage*, *12*(4), 466–477. https://doi.org/10.1006/nimg.2000.0630

Geerligs, L., Cam-CAN, & Campbell, K. L. (2018). Age-related differences in information processing during movie watching. *Neurobiology of Aging*, *72*, 106–120. https://doi.org/10.1016/j.neurobiolaging.2018.07.025

Giorgio, A., Santelli, L., Tomassini, V., Bosnell, R., Smith, S., De Stefano, N., & Johansen-Berg, H. (2010). Age-related changes in grey and white matter structure throughout adulthood. *NeuroImage*, *51*(3), 943–951. https://doi.org/10.1016/j.neuroimage.2010.03.004

Grady, C. L. (2000). Functional brain imaging and age-related changes in cognition. *Biological Psychology*, *54*(1–3), 259–281. https://doi.org/10.1016/S0301-0511(00)00059-4

Hafkemeijer, A., Altmann-Schneider, I., Oleksik, A. M., van de Wiel, L., Middelkoop, H. A. M., van Buchem, M. A., van der Grond, J., & Rombouts, S. A. R. B. (2013). Increased Functional Connectivity and Brain Atrophy in Elderly with Subjective Memory Complaints. *Brain Connectivity*, *3*(4), 353–362. https://doi.org/10.1089/brain.2013.0144

Hartsuiker, R., & Moors, A. (2016). On the automaticity of language processing. In *Entrenchment and the Psychology of Language Learning: How We Reorganize and Adapt Linguistic Knowledge*. https://doi.org/10.1515/9783110341423-010

Jacobsen, J., Fritz, T., Stelzer, J., & Turner, R. (2015). Why musical memory can be preserved in advanced Alzheimer's disease. *Brain: A Journal of Neurology*, 1–13. https://doi.org/10.1093/awv148

Ki, J. J., Kelly, S. P., & Parra, L. C. (2016). Attention Strongly Modulates Reliability of Neural Responses to Naturalistic Narrative Stimuli. *Journal of Neuroscience*, *36*(10). https://doi.org/10.1523/JNEUROSCI.2942-15.2016

Kuchinsky, S. E., Vaden, K. I., Jr, Keren, N. I., Harris, K. C., Ahlstrom, J. B., Dubno, J. R., & Eckert, M. A. (2012). Word Intelligibility and Age Predict Visual Cortex Activity during Word Listening. *Cerebral Cortex*, *22*(6), 1360–1371. https://doi.org/10.1093/cercor/bhr211

Levelt, W. J. M. (1993). *Speaking: From Intention to Articulation*. MIT Press.

Mann, S. L., Hazlett, E. A., Byne, W., Hof, P. R., Buchsbaum, M. S., Cohen, B. H., Goldstein, K. E., Haznedar, M. M., Mitsis, E. M., Siever, L. J., & Chu, K.-W. (2011). Anterior and Posterior Cingulate Cortex Volume in Healthy Adults: Effects of Aging and Gender Differences. *Brain Research*, *1401*, 18–29. https://doi.org/10.1016/j.brainres.2011.05.050

Müllensiefen, D., Gingras, B., Musil, J., & Stewart, L. (2014). The Musicality of Non-Musicians: An Index for Assessing Musical Sophistication in the General Population. *PLoS ONE*, *9*(2). https://doi.org/10.1371/journal.pone.0089642

Naci, L., Sinai, L., & Owen, A. M. (2017). Detecting and interpreting conscious experiences in behaviorally non-responsive patients. *NeuroImage*, *145*, 304–313. https://doi.org/10.1016/j.neuroimage.2015.11.059

Pacheco, J., Goh, J. O., Kraut, M. A., Ferrucci, L., & Resnick, S. M. (2015). Greater cortical thinning in normal older adults predicts later cognitive impairment. *Neurobiology of Aging*, *36*(2), 903–908. https://doi.org/10.1016/j.neurobiolaging.2014.08.031

Peelle, J. E. (2019). Language and aging. In G. De Zubicaray I. & N. O. Schiller (Eds.), *The Oxford Handbook of Neurolinguistics*. Oxford University Press.

Peelle, J. E., Troiani, V., Wingfield, A., & Grossman, M. (2010). Neural Processing during Older Adults' Comprehension of Spoken Sentences: Age Differences in Resource Allocation and Connectivity | Cerebral Cortex | Oxford Academic. *Cerebral Cortex*, *20*(4). https://academic.oup.com/cercor/article/20/4/773/303007

Pulvermuller, F., Huss, M., Kherif, F., Moscoso del Prado Martin, F., Hauk, O., & Shtyrov, Y. (2006). Motor cortex maps articulatory features of speech sounds. *Proceedings of the National Academy of Sciences*, *103*(20), 7865–7870. https://doi.org/10.1073/pnas.0509989103

R Core Team. (2013). *R: A language and environment for statistical computing*. R Foundation for Statistical Computing.

Regev, M., Simony, E., Lee, K., Tan, K. M., Chen, J., & Hasson, U. (2019). Propagation of information along the cortical hierarchy as a function of attention while reading and listening to stories. *Cerebral Cortex*, *29*(10), 291526. https://doi.org/10.1093/cercor/bhy282

Roiser, J. P., Linden, D. E., Gorno-Tempinin, M. L., Moran, R. J., Dickerson, B. C., & Grafton, S. T. (2016). Minimum statistical standards for submissions to Neuroimage: Clinical. *NeuroImage : Clinical*, *12*, 1045–1047. https://doi.org/10.1016/j.nicl.2016.08.002

Saenger, V. M., Barrios, F. A., Martínez-Gudiño, M. L., & Alcauter, S. (2012). Hemispheric asymmetries of functional connectivity and grey matter volume in the default mode network. *Neuropsychologia*, *50*(7), 1308–1315. https://doi.org/10.1016/j.neuropsychologia.2012.02.014

Sikka, R., Cuddy, L. L., Johnsrude, I. S., & Vanstone, A. D. (2015). An fMRI comparison of neural activity associated with recognition of familiar melodies in younger and older adults. *Frontiers in Neuroscience*, *9*(OCT), 1–10. https://doi.org/10.3389/fnins.2015.00356

Simony, E., Honey, C. J., Chen, J., Lositsky, O., Yeshurun, Y., Wiesel, A., & Hasson, U. (2016). Dynamic reconfiguration of the default mode network during narrative comprehension. *Nature Communications*, *7*(May 2015). https://doi.org/10.1038/ncomms12141

Sinai, L. (2015). *Naturalistic paradigms for neuroimaging and bedside measures of conscious awareness* [MSc]. University of Western Ontario.

Sternin, A., McGarry, L. M., Owen, A. M., & Grahn, J. A. (2021). The Effect of Familiarity on Neural Representations of Music and Language. *Journal of Cognitive Neuroscience*, 1–17. https://doi.org/10.1162/jocn_a_01737

Thangavel, R., Van Hoesen, G. W., & Zaheer, A. (2008). Posterior parahippocampal gyrus pathology in Alzheimer's disease. *Neuroscience*, *154*(2), 667–676. https://doi.org/10.1016/j.neuroscience.2008.03.077

Tyler, L. K., Shafto, M. A., Randall, B., Wright, P., Marslen-Wilson, W. D., & Stamatakis, E. A. (2010). Preserving Syntactic Processing across the Adult Life Span: The Modulation of the Frontotemporal Language System in the Context of Age-Related Atrophy. *Cerebral Cortex*, *20*(2), 352–364. https://doi.org/10.1093/cercor/bhp105

Walhovd, K. B., Fjell, A. M., Reinvang, I., Lundervold, A., Dale, A. M., Eilertsen, D. E., Quinn, B. T., Salat, D., Makris, N., & Fischl, B. (2005). Effects of age on volumes of cortex, white matter and subcortical structures. *Neurobiology of Aging*, *26*(9), 1261–1270. https://doi.org/10.1016/j.neurobiolaging.2005.05.020

Wingfield, A., & Grossman, M. (2006). Language and the Aging Brain: Patterns of Neural Compensation Revealed by Functional Brain Imaging. *Journal of Neurophysiology*, *96*(6), 2830–2839. https://doi.org/10.1152/jn.00628.2006

5 The effects of long-term knowledge on intersubject synchrony in older adults

Introduction

The degree of intersubject synchrony across individuals is affected by stimulus familiarity (learned vs. not learned stimuli – Chapter 3), stimulus contents (presence of music and/or language – Chapter 4), and the age of the participants (young vs. older adults – Chapter 4). In the previous studies, training young adult participants on novel stimuli allowed for careful control of acoustic factors (identical stimuli before and after training) and an objective measurement of the degree of familiarity (tracking the number of stimulus presentations during training). Although this training paradigm was successful in making participants familiar with the stimuli (see Chapter 2 – *Results – Behavioural familiarity tasks*), it did not replicate the way participants become familiar with music or language in the real world. Studies that use music or language to investigate memory in neurodegenerative disorders generally use stimuli that participants have learned over their lifetimes (Jacobsen et al., 2015; Sikka et al., 2015). With the increasing use of intersubject synchrony in studies of clinical populations it is important to understand the effects of long-term familiarity on synchrony. In this final study, we aimed to understand how synchrony is affected by long-term familiarity with a stimulus learned over the course of an individual's lifetime.

The synchrony data collected in young adults before and after the training paradigm (Chapter 3) largely replicated the pattern seen in the small number of previous studies that have explored the effect of repetition on intersubject synchrony. As in our study, previous investigations have shown that synchrony decreases with repeated exposure to a stimulus. For example, after six consecutive viewings of 90-second movie clips, synchrony (measured using fMRI) in the posterior medial network decreased from the first to the sixth viewing (Aly et al.,

2017, 2018). A similar study involved participants being presented with three short films that were each viewed twice (Dmochowski et al., 2012). The researchers found that synchrony (using EEG) decreased between the first and second viewings. In all of these studies, stimulus repetition occurred over a short time period. Similarly, in Chapter 3 we investigated how synchrony to music and language stimuli was affected by repeated exposure over a 3-week period which is a fairly short period relative to the longer time frames (years or decades) over which some music is remembered. No studies to our knowledge have investigated changes in synchrony related to long-term knowledge of a stimulus.

To probe the effects of long-term knowledge on intersubject synchrony, we presented older adults with two stimuli that they had known for more than 50 years. Although each participant may have heard these stimuli a different number of times over their lifetime, presenting participants with well-known stimuli from their past is a method used regularly in studies investigating the neural correlates of musical memory. Previous studies have used familiar music like widely known movie or tv theme songs, folksongs, children's songs, or popular songs chosen from the period of time when the participants were young (e.g., Agustus et al., 2018; Jacobsen et al., 2015; Sikka et al., 2015). Therefore, we presented participants with a familiar whole music song (*Hey Jude* by The Beatles) and a familiar spoken word poem (*'Twas the night before Christmas* by Clement Clarke Moore; see *Methods – Long-known stimuli* for details on participants' familiarity with the stimuli). For novel stimuli, the same spoken and whole novel stimuli used in the investigation of musical memory in young adults (Chapter 3) were used here. Unlike previous chapters, the a capella stimuli (sung leading and backing vocals without instrumental music) and the instrumental stimuli (instrumental music without lyrics) were not included. All of the older adult data presented in this thesis were collected during a single scanning session. The a capella and instrumental stimulus conditions were removed in our long-known stimulus comparisons to reduce the burden on participants by keeping the entire fMRI scanning session to less than two hours. A detailed description of which stimuli were included in each experiment can be found in Appendix C.

To our knowledge there are no studies that have investigated how stimulus characteristics, such as familiarity, affect synchrony within older adults specifically. As more studies use synchrony to investigate clinical populations with progressive diseases that appear

later in life (e.g. Alzheimer's disease; Huntley et al., In preparation), understanding how intersubject synchrony changes during healthy aging is important to create an age-matched baseline level of synchrony against which clinical populations can be compared. Therefore, the aim of this last study was to complement the previous intersubject synchrony results by providing a full picture of how synchrony is affected by listener age and previous knowledge of the stimulus using a more ecologically valid approach. In line with our previous results, we expect to find less intersubject synchrony to the long-known stimuli than to the novel stimuli.

Methods

Ethics

Ethics approval for this project was granted by the Health Sciences Research Ethics Board at The University of Western Ontario (#100606).

Participants

Fifteen neurologically normal, English-speaking participants (nine female) aged 64-74 (mean=70 years) were recruited in London, Ontario. All participants had completed at least some post-secondary education and four participants had completed some post-graduate education. Using the Goldsmith's Musical Sophistication Index (Müllensiefen et al., 2014), 11 participants reported having formal musical training (1-61yrs, mean=20.8yrs), but at the time of testing only three of them played instruments regularly. Five participants were familiar with a second language but did not rate themselves as fluent in those languages.

Long-known stimuli

Two well-known stimuli were selected: one whole stimulus and one spoken word stimulus. As the target age group was those over the age of 65, we chose 'Hey Jude' by The Beatles as our long-known whole stimulus. This song was popular when the group of participants would have been in their 20s (late 1960s-mid 1970s); 'Hey Jude' was the highest-ranking song on the Canadian billboard charts in 1968 ("The RPM 100 - Top Singles of 1968," 1969). It also maintained similar instrumentation to the novel stimuli (guitar, drums, voice), as

well as the accent of the lead singer. The long-known whole stimulus had a length of 3:33. The long-known spoken word stimulus was created in lab by asking the same lead singer of the novel stimuli to record the poem *'Twas the night before Christmas*. The long-known spoken stimulus had a length of 3:46. All participants reported being very familiar with both stimuli (see *Results – Stimulus Familiarity*).

Novel stimuli

The same four spoken and whole novel stimuli used in the investigation of musical memory in young adults (Chapter 3) were used here (see Appendix C for details on the exact stimuli used). The four stimuli were created from the lyrics and music of different songs written and recorded by a member of the research team between 1997 and 2006 for an amateur rock band based in Cambridge, UK. Thus, all stimuli were completely novel to the Canadian participants. The original songs were all written in a similar style and instrumentation included a lead singer, bass, drums, guitar, string instruments, and backing vocals, each recorded on separate tracks. All stimuli were recorded using the exact same equipment directly to digital hard drive using Sonar software (by Cakewalk) and a Shure SM58 microphone.

Two conditions were created by modifying the original four songs to include or exclude only certain tracks: (1) whole music (music and words together in a fully intact version of each song), and (2) spoken words (the lyrics of each song were rerecorded in spoken form by the original lead singer to have a similar length, tempo, and emotional intonation as their original song counterparts). There were two different stimuli for each condition, and none of the original songs were used for more than one condition. The stimuli were modified (e.g., lengthened by adding additional repetitions of the chorus) to each be five minutes long. During the fMRI scan session, participants heard the entire 5-minute stimuli. Each stimuli was normalized to equate perceived loudness using the *Audacity* software (Audacity Team, 2020). All stimuli are available in Appendix C.

fMRI acquisition and analyses

Imaging was conducted at the Robarts Research Institute on a Siemens Magnetom 7 Tesla scanner with a 32-channel head coil. Functional scans were acquired with 54 slices per

volume (TR = 1.25 s; TE = 20 ms; flip angle = 35°; FOV = 220 x 220 mm; voxel size = 2.5 mm^3). The scan session included six functional runs: 2 runs for each of the long-known stimuli (each less than 4-minutes) and four 5-minute runs for each of the novel stimuli. During each of the runs, participants passively listened to each of the stimuli in their entirety. Stimulus order was randomized for each participant. Between functional runs, a whole-head anatomical scan was acquired (TR = 6s; TE = 2.69 ms; FOV = 240 x 240 mm; voxel size = 0.75 mm^3; 208 slices).

Data from each of the functional runs were processed using automatic analysis (version 4.1; Aly et al., 2017, 2018; Cusack et al., 2015; Dmochowski et al., 2012): a MATLAB based processing and analysis pipeline that integrates with Statistical Parametric mapping (SPM12). Three 'dummy' scans were excluded from the beginning of every run to allow stabilization of the signal. Images were realigned to the first image in the first run using six motion parameters (x,y,z, translation and rotation). Data were normalized to MNI space and smoothing was done with a Gaussian kernel of 10mm FWHM. Low-frequency noise (e.g., drift) was removed with a high-pass filter of 128s. Data were denoised using cerebrospinal fluid, white matter signals, motion parameters, their lag-3 2nd-order Volterra expansion (Friston et al., 2000), and "spikes" (>3 standard deviations based on mean signal variance across volumes) as nuisance regressors. The data were then further cleaned by running a group ICA (Calhoun et al., 2001) within each stimulus and removing 1-2 components that spatially correlated with a mask of the ventricles to remove non-brain related activity.

Intersubject synchrony

The degree of intersubject synchrony across the whole brain during each of the six stimuli (2 long-known and 4 novel stimuli) was calculated using a leave-one-out approach. That is, for each stimulus, the time course of every voxel in each participant was correlated (Pearson and then Fisher z-transformed) with the mean time course of every corresponding voxel from the rest of the participants, minus that participant (N-1). This process created an *r*-value for each voxel, for each participant, that described the degree to which that participant's voxel was correlated with the rest of the participants while listening to that particular stimulus.

Each individual's synchrony values for the six stimuli were entered into a second-level flexible-factorial model using SPM12. This model labeled stimulus type (three stimuli each for spoken and whole music stimuli), familiarity (four novel and two long-known stimuli), and took subject effects into account. Two t-contrasts were conducted to investigate familiarity: novel > long-known; long-known > novel. Two t-contrasts were conducted to investigate whether the differences between the long-known spoken and the long-known whole stimuli were similar to the differences between the novel spoken and novel whole stimuli described in Chapter 4: long-known spoken > long-known whole; long-known whole > long-known spoken. Two interaction contrasts were also run to determine where synchrony differed based on familiarity and stimulus type ([novel spoken – novel whole] – [long-known spoken – long-known whole]; ([novel whole – novel spoken] – [long-known whole – long-known spoken]). The cluster-forming threshold in each contrast was specified at FWE p=.0001 uncorrected (Roiser et al., 2016). All cluster peaks are reported at a corrected FWE p=.05.

Behavioural tasks

Participants were asked to return to the lab for a behavioural testing session within a week of their fMRI scan session. During the behavioural testing session, participants completed demographic questionnaires, the Goldsmith's Musical Sophistication Index (Müllensiefen et al., 2014), and familiarity questionnaires that asked participants to listen to the stimuli they heard in the scanner and rate their level of familiarity on a scale of 1 (not familiar – *I had never heard this stimulus before my scan session*) – 5 (extremely familiar – *I have heard it more than 10 times*).

Results

Participants

One participant did not complete the scan session due to technical difficulties and data from the long-known stimuli were not collected. A second participant withdrew from the study. A third participant was excluded because of excessive movement in the scanner (>2mm displacement in z). Therefore, fMRI data from 12 individuals were included in the analysis.

Stimulus familiarity

Participants reported being much more familiar with the familiar stimuli than the novel stimuli ($p<.001$). The average familiarity score for the two long-known stimuli was 4.9 ($SD=.06$) and the average familiarity score for the four novel stimuli was 1.3 ($SD=.13$). Participants also reported having heard the long-known whole stimulus (*Hey Jude* by The Beatles) for the first time when they were an average age of 18.5 years ($SD=2.9$) and having heard the long-known spoken stimulus (*'Twas the Night Before Christmas*) for the first time when they were an average age of 6 years ($SD=2.2$). Therefore, all participants had known each of the long-known stimuli for more than 50 years.

FMRI results

The two *t*-contrasts investigating the differences in synchrony induced by the novel and long-known stimuli showed that there was significantly more synchrony to novel than long-known stimuli in bilateral temporal areas (clusters at FWE $p<.05$; see Figure 1). There were no regions with more synchrony to long-known than novel stimuli. Figure 1 presents the overlap in the brain areas where synchrony differed based on familiarity that were identified by the *t*-contrast in the older adult data (novel > long-known) and by the main effect of session *F*-contrast in young adults from Chapter 3, Figure 1. The peak values from the older adult clusters can be found in Table 1 alongside the peak values from the young adult clusters reprinted from Chapter 3, Table 1.

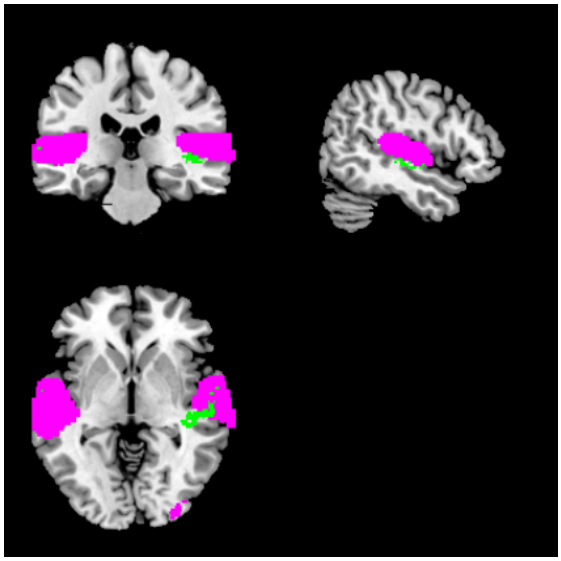


Figure 1. Overlap between the brain regions in which intersubject synchrony differed based on familiarity in the older and young adult data. All clusters were defined at $p<.05$ FWE. Green: Older adult novel > long-known t-contrast. The extent threshold was set to the FWEc value = 64. Magenta: The main effect of session F-contrast from the 2(session) x 2(training) ANOVA conducted in young adults (reprinted from Chapter 3, Figure 1). The extent threshold was set to the FWEc value = 40. Displayed slices are at x=47, y=-26, z=-2.

Table 1. The left column contains the coordinates of peak values from the significant clusters identified in the Older Adult novel > long-known t-contrast. The right column reprints the Young Adult cluster peak values from Chapter 3, Table 1 for comparison. The extent threshold FWEc values for each contrast are listed. The clusters were defined at $p<0.05$ FWE. Peak values > 4mm apart are listed.

Older Adults novel > long-known *t*-contrast extent = 64		Young Adults* Main effect of session *F*-contrast extent = 43	
Posterior STG	-66, -18, 8	Planum temporale	-52,-20, 0
Posterior STG	-60, -22, 2	Planum temporale	-62, -34, 8
Anterior STG	-66, -8, 0	Posterior STG	-58, -36, 10
		Posterior STG	-68, -22, 2
Posterior MTG	44, -26, -4		
Planum polare	54, -4, -6	Planum temporale	56, -20, 6
Planum polare	42, -22, -4	Planum temporale	60, -18, 6
Planum polare	40, -18, -8	Posterior STG	68, -28, 6
Planum polare	44, -14, -8	Posterior STG	66, -24, 8
Planum polare	48, -14, -6	Heschl's gyrus	38, -26, 10
Heschl's gyrus	40, -28, 0	Temporal pole	62, 8, -10
Anterior STG	64, -4, 0	Anterior STG	62, 4, -8
Posterior STG	56, -22, -4		
Posterior STG	50, -22, -4	Frontal orbital cortex	-12, 6, -22
Posterior STG	60, -20, -2	Frontal orbital cortex	-12, 14, -20
Posterior STG	56, -16, -4	Parahippocampal gyrus (anterior div.)	-14, 0, -26
Posterior MTG	42, -32, -2	Frontal orbital cortex	-16, 12, -24
Posterior MTG	46, -22, -6	Subcallosal cortex	-12, 22, -18
		Parahippocampal gyrus (anterior div.)	-14, -4, -28
		Precentral gyrus	58, 4, 46
		Occipital pole	40, -90, 24
		Lateral occipital cortex (inferior div.)	46, -84, 18
		Occipital pole	34, -92, 4
		Occipital pole	32, -96, 6
		* reprinted from Chapter 3, Table 1	

The two *t*-contrasts showed that there were no significant differences between the long-known spoken and the long-known whole stimuli in either contrast. This is contrary to the results from the novel stimuli in Chapter 4 that showed more synchrony to the novel spoken stimuli than to the novel whole stimuli in right temporal areas in older adults. The two familiarity by stimulus type interaction *t*-contrasts also found no significant differences in synchrony in any areas of the brain.

Discussion

In the current study, we set out to understand how intersubject synchrony is affected by long-term knowledge of a stimulus. We found a similar effect of familiarity on synchrony as was seen in the young adults (Chapter 3): greater synchrony to novel than to long-known stimuli. In older adults, these differences were present in bilateral temporal regions. Although the regions in the older adults were spatially smaller than the areas that differed between learned and not learned stimuli in young adults, there was overlap in the posterior STG on the left and Heschl's gyrus and posterior STG on the right. As was the case in young adults, the older adults did not synchronize more to the familiar than the novel stimuli in any brain regions. The results from both the older and young adult studies investigating the effects of familiarity on synchrony indicate that novel stimuli induce greater intersubject synchrony than stimuli that have been known for either short (3 weeks) or very long (50 years) periods of time.

Despite the small areas of overlap (see Figure 1), both young and older adults showed a decrease in synchrony as a result of familiarity in primary and secondary auditory areas. BOLD activity is known to increase after training on auditory tasks in Heschl's gyrus (Bermudez et al., 2009; Gaab et al., 2006; Schneider et al., 2002), posterior STG, planum polare, and planum temporale (Brown & Penhune, 2018). The connection between increased BOLD activity and neural synchrony has been previously investigated in dorsolateral prefrontal cortex (dlPFC) using a voluntary forgetting task while recording simultaneous EEG and fMRI (Hanslmayr et al., 2012). It was found that increased BOLD activity in dlPFC was correlated with a decrease in neural phase synchrony measured using EEG. Although the task used was not an auditory task, this research may relate to the synchrony reduction seen in the current experiment. It is possible that increased BOLD activity in temporal areas to the long-known stimuli in older adults is responsible for the reduction of synchrony within these areas (Heschl's gyrus and posterior STG). Unfortunately, our fMRI paradigm used in older adults was not designed to investigate similarities between BOLD and synchrony activity to long-known stimuli. However, the young adult data discussed in previous chapters may provide some insight. If decreased synchrony is driven by increased BOLD activity, then we should have seen BOLD activity differences as a result of training in the same areas where we saw synchrony differences. In Chapter 2 we saw no differences in BOLD activity as a result of repeated exposure to the stimuli, but in Chapter 3 we

did see a synchrony reduction. This synchrony reduction occurred regardless of whether stimuli had been heard once or heard multiple times before and was likely not related to how well the stimuli were learned. Therefore, it is possible that the discrepancy between BOLD and synchrony activity in young adults may indicate that although there were behavioural changes in learning in young adults (recognition of words and melodies), the stimuli were not learned enough to cause neural changes that affected the level of BOLD activity. The behavioural tasks used to measure learning in the young adults asked participants to recognize the correct lyric or melodies. Although scores on the behavioural tasks were not at ceiling (average 79% correct on the lyric task; see Chapter 2 – Results), we may have seen even lower levels of learning if we had used more difficult tasks that required participants to freely recall the words or melodies of the stimuli. Therefore, it is possible that participants did not learn the stimuli well enough and the synchrony reduction was due to other factors like the amount of attention paid to the stimuli (synchrony is known to decrease with decreased attention; Regev et al., 2019). A follow-up study should compare long-known stimuli (rather than stimuli learned over 3 weeks) to novel stimuli to see if the synchrony reduction to long-known stimuli seen in older adults is related to increased BOLD activity in similar brain areas. Such an experiment would help to tease apart whether synchrony reduction is due to knowledge of a stimulus (as indexed by increased BOLD activity) or whether the synchrony reduction as a result of repeated exposure should be investigated by focusing on other factors like attention.

In contrast to the results of Chapter 4 where the novel spoken stimuli induced more synchrony than the novel whole stimuli, we found no differences in synchrony between the long-known spoken and long-known whole stimuli. This lack of difference could be due to a number of reasons. First, this comparison was between only two stimuli, rather than four stimuli as in the comparisons of the novel stimuli. It is possible that using only one stimulus per category was not enough to see differences between the spoken and whole stimulus categories. When the pairwise comparisons between the two long-known stimuli were investigated with a lower statistical threshold ($p<.001$ uncorrected) there were some large areas that showed differences between the stimulus types but they were not obviously similar to the areas identified when comparing the novel stimuli. Therefore, the lack of difference between the stimulus types may not be due to a lack of power and may be a result of other factors. For example, unlike the novel spoken stimuli,

'*Twas the night before Christmas* was written to be experienced as a poem and was not a modified set of lyrics taken from a whole song. In Chapter 2, we hypothesized that one of the reasons there were differences in BOLD activation based on stimulus contents in the group of young adults was a result of differences in attention across stimulus types because of the way the stimuli were designed (modified whole songs rather than stimuli chosen from the particular genre categories). It is possible that because both the long-known stimuli were heard as they were meant to be experienced, they engaged participants similarly and therefore induced similar amounts of synchrony within the group of older adults. Finally, both stimuli were very familiar to the participants. As was shown in Chapter 3 with the young adult data and in the older adult data presented here, synchrony decreases with familiarity. Therefore, it is possible that the synchrony induced by both of the highly familiar stimuli was equally low resulting in no stimulus differences between the two long-known stimuli.

When a group of individuals is repeatedly exposed to a stimulus (whether it is a musical stimulus, an audio book excerpt, or a movie), their experiences of the stimulus will be the most similar the first time they are exposed to it. With every repeated exposure each individual may have a slightly different experience of the stimulus as they learn the words to the song or know what to expect in the next scene of the movie. Additionally, each exposure to the stimulus may create a slightly different memory, unique to that individual. These idiosyncratic experiences may diversify individuals' neural responses, reducing synchrony across the group. If synchrony steadily decreased in relation to the number of exposures to a stimulus, then we would have seen synchrony differences in the young adult data between the learned and not learned stimuli in the second session (Chapter 3). We do not see such differences and concluded from that experiment that a single listen may be enough to cause a persistent reduction in synchrony. In the current experiment, we did not ask older adults to train on novel stimuli to reduce the burden of participation on the older adults and therefore could not directly compare the degree of synchrony between short-term (3 weeks) and long-term (50 years) knowledge of a stimulus without introducing the confound of age differences. However, an EEG study into the effects of repeated exposure to auditory stimuli on event-related potentials (ERP) showed that ERP amplitudes increased with stimulus repetition and this increase persisted over long-periods of time even if the participants had not heard the stimuli for many months (Tremblay et al., 2010).

Therefore, it is possible that the reduction in synchrony as a result of repeated exposure to our musical and language stimuli is maintained over long periods of time and that the synchrony differences seen between novel and familiar stimuli at 3 weeks would persist. A future longitudinal study during which participants are asked to train on novel stimuli and measures intersubject synchrony over short and long periods of time (e.g., at baseline, after 1 month, and again after 1 year) would better be able to characterize how synchrony changes as a result of long-term familiarity with a stimulus.

The final set of results presented here complete our investigations into how intersubject synchrony is affected by a listener's age and previous knowledge of the stimulus. We found that older adults, like young adults, show a reduction in synchrony to familiar stimuli. However, given the design of the experiment we can not say whether the reduction to long-known stimuli seen in older adults is greater than the reduction in stimuli in recently learned stimuli in young adults. Until the effects of repeated stimulus exposure are more clearly characterized, future studies that wish to maximize intersubject synchrony measures across participants should use novel stimuli.

Bibliography

Agustus, J. L., Golden, H. L., Callaghan, M. F., Bond, R. L., Benhamou, E., Hailstone, J. C., Weiskopf, N., & Warren, J. D. (2018). Melody Processing Characterizes Functional Neuroanatomy in the Aging Brain. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00815

Aly, M., Chen, J., Turk-Browne, N. B., & Hasson, U. (2017). Learning Naturalistic Temporal Structure in the Posterior Medial Network. *BioRxiv*. https://doi.org/10.1101/196287

Aly, M., Chen, J., Turk-Browne, N. B., & Hasson, U. (2018). Learning Naturalistic Temporal Structure in the Posterior Medial Network. *Journal of Cognitive Neuroscience*, *30*(9), 1345–1365. https://doi.org/10.1162/jocn_a_01308

Audacity Team. (2020). *Audacity(R): Free Audio Editor and Recorder*. https://audacityteam.org/

Bermudez, P., Lerch, J. P., Evans, A. C., & Zatorre, R. J. (2009). Neuroanatomical correlates of musicianship as revealed by cortical thickness and voxel-based morphometry. *Cerebral Cortex*, *19*(7), 1583–1596.

Brown, R. M., & Penhune, V. B. (2018). Efficacy of Auditory versus Motor Learning for Skilled and Novice Performers. *Journal of Cognitive Neuroscience*, *30*(11), 1657–1682. https://doi.org/10.1162/jocn_a_01309

Calhoun, V. D., Adali, T., Pearlson, G. D., & Pekar, J. J. (2001). A method for making group inferences from functional MRI data using independent component analysis. *Human Brain Mapping*, *14*(3), 140–151.

Cusack, R., Vicente-Grabovetsky, A., Mitchell, D. J., Wild, C. J., Auer, T., Linke, A. C., & Peelle, J. E. (2015). Automatic analysis (aa): Efficient neuroimaging workflows and parallel processing using Matlab and XML. *Frontiers in Neuroinformatics*, *8*. https://doi.org/10.3389/fninf.2014.00090

Dmochowski, J. P., Sajda, P., Dias, J., & Parra, L. C. (2012). Correlated Components of Ongoing EEG Point to Emotionally Laden Attention – A Possible Marker of Engagement? *Frontiers in Human Neuroscience*, *6*(May), 1–9. https://doi.org/10.3389/fnhum.2012.00112

Friston, K. J., Mechelli, A., Turner, R., & Price, C. J. (2000). Nonlinear Responses in fMRI: The Balloon Model, Volterra Kernels, and Other Hemodynamics. *NeuroImage*, *12*(4), 466–477. https://doi.org/10.1006/nimg.2000.0630

Gaab, N., Gaser, C., & Schlaug, G. (2006). Improvement-related functional plasticity following pitch memory training. *NeuroImage*, *31*(1), 255–263. https://doi.org/10.1016/j.neuroimage.2005.11.046

Hanslmayr, S., Volberg, G., Wimber, M., Oehler, N., Staudigl, T., Hartmann, T., Raabe, M., Greenlee, M. W., & Bauml, K.-H. T. (2012). Prefrontally Driven Downregulation of Neural Synchrony Mediates Goal-Directed Forgetting. *Journal of Neuroscience*, *32*(42), 14742–14751. https://doi.org/10.1523/JNEUROSCI.1777-12.2012

Huntley, J., Bor, D., Fleming, S. M., Mancuso, M., Mediano, P., Naci, L., Owen, A. M., Rocci, L., Sternin, A., & Howard, R. (In preparation). *Assessing awareness in severe Alzheimer's disease*.

Jacobsen, J., Fritz, T., Stelzer, J., & Turner, R. (2015). Why musical memory can be preserved in advanced Alzheimer's disease. *Brain: A Journal of Neurology*, 1–13. https://doi.org/10.1093/awv148

Müllensiefen, D., Gingras, B., Musil, J., & Stewart, L. (2014). The Musicality of Non-Musicians: An Index for Assessing Musical Sophistication in the General Population. *PLoS ONE*, *9*(2). https://doi.org/10.1371/journal.pone.0089642

Regev, M., Simony, E., Lee, K., Tan, K. M., Chen, J., & Hasson, U. (2019). Propagation of information along the cortical hierarchy as a function of attention while reading and listening to stories. *Cerebral Cortex*, *29*(10), 291526. https://doi.org/10.1093/cercor/bhy282

Roiser, J. P., Linden, D. E., Gorno-Tempinin, M. L., Moran, R. J., Dickerson, B. C., & Grafton, S. T. (2016). Minimum statistical standards for submissions to Neuroimage: Clinical. *NeuroImage : Clinical*, *12*, 1045–1047. https://doi.org/10.1016/j.nicl.2016.08.002

Schneider, P., Scherg, M., Dosch, H., Specht, H., Gutschalk, A., & Rupp, A. (2002). Morphology of Heschl's gyrus reflects enhanced activation in the auditory cortex of musicians. *Nature Neuroscience*, *5*, 688–694. https://doi.org/10.1038/nn871

Sikka, R., Cuddy, L. L., Johnsrude, I. S., & Vanstone, A. D. (2015). An fMRI comparison of neural activity associated with recognition of familiar melodies in younger and older adults. *Frontiers in Neuroscience*, *9*(OCT), 1–10. https://doi.org/10.3389/fnins.2015.00356

The RPM 100—Top Singles of 1968. (1969, January 6). *RPM Music Weekly*, *10*(19).

Tremblay, K. L., Inoue, K., McClannahan, K., & Ross, B. (2010). Repeated Stimulus Exposure Alters the Way Sound Is Encoded in the Human Brain. *PLoS ONE*, *5*(4), e10283. https://doi.org/10.1371/journal.pone.0010283

6 General Discussion

In the preceding four chapters I have identified and addressed discrepancies in the literature regarding the neural networks associated with musical memory. I used a training paradigm that included musical and language stimuli to compare stimulus conditions that were identical except for the subject's level of familiarity. The highly controlled nature of this paradigm fills a crucial gap in decades of musical memory research where inconsistencies in stimulus type and the definition of familiar music are widespread. The results from this experimental manipulation revealed that the areas previously identified as responsible for musical memory may in fact be related to autobiographical memories or emotional involvement with the stimuli rather than memory for the music itself. Intersubject synchrony analyses further revealed that neural activity becomes more idiosyncratic across individuals after a single exposure to a stimulus and does not significantly change with further stimulus exposures. This unexpected finding has significant implications for the design of future studies that use intersubject synchrony; without controlling for stimulus familiarity across conditions, researchers run the risk of confounding their results with a stimulus exposure effect. For example, a study using data from the Child Mind Institute Healthy Brain Network databank that includes fMRI data from hundreds of children in the New York area watching a 10-minute clip from the children's movie '*Despicable Me'* but does not include information on whether participants had seen the movie prior to the experiment (Alexander et al., 2017), may find synchrony differences between children from different neighbourhoods. The researchers may claim that these differences are related to factors that are available within the databank (such as socioeconomic status or parental education) when in fact the differences may be related to the children's access to the film. Finally, by exploring how intersubject synchrony changes with age, I identified areas that do not show age-related synchrony reductions and instead show increased synchrony in older adult participants. Follow-up research that characterizes what is driving the fluctuations in synchrony within these areas may shed light on why memories for music are better preserved

than other types of memories in the presence of neurodegenerative disorders. In the discussion that follows, I will consider the results and limitations of each of the experimental chapters in more detail. I will also discuss how the results from these experiments could affect the use of intersubject synchrony in future studies. Lastly, I will summarize the conclusions that can be drawn from the presented studies and their implications on future musical memory research.

Neural correlates of music familiarity

The GLM experiment investigating the neural markers of music and language memory in young adults (Chapter 2) found no differences in the neural networks responsible for processing the learned and not learned stimuli using univariate or multivariate analyses. The null result sheds some light on the inconsistencies that exist across the musical memory literature. Previous studies that have investigated how the brain processes familiar music have used stimuli such as folksongs (e.g., Alonso et al., 2016; Herholz et al., 2012; Saito et al., 2012; Schaal et al., 2015), popular music from the radio charts (e.g., Jacobsen et al., 2015; Pereira et al., 2011), or classical music excerpts (e.g., Agustus et al., 2018; Groussard et al., 2010). These types of stimuli are learned over a person's lifetime and, as a result, the level of familiarity likely varies across people. The inconsistencies that exist in the literature regarding the neural correlates of musical memory (e.g. Freitas et al., 2018; Halpern & Zatorre, 1999; Herholz et al., 2012) may be related to these differences in familiarity as using well-known music does not control for the amount of exposure or the personal associations participants may have with the stimuli. The lack of activation differences between the learned and not learned stimuli when stimulus exposure was tightly controlled suggests that the neural correlates of musical memory are affected by factors other than exposure alone such as autobiographical memories and the degree of emotional engagement.

As noted in Chapter 2, the areas that are associated with musical memory overlap with those areas associated with autobiographical memories (Groussard et al., 2009; Janata, 2009; Klostermann et al., 2009; Plailly et al., 2007). A meta-analysis found that the left superior frontal gyrus (SFG), the ventral lateral nucleus of the left thalamus and the left inferior frontal gyrus (IFG) were the three areas most likely to be activated by familiar music across 10 studies (Freitas et al., 2018). Autobiographical memories evoked using non-musical stimuli (e.g. photos, sentences containing episodic information) have been found to activate a wide-spread left

lateralized network of regions that include the SFG and IFG as well as temporal areas (medial temporal lobe, temporal pole, insula, superior and inferior lateral temporal lobe), prefrontal cortex, the hippocampus, the amygdala, and occipital areas (Cabeza & St Jacques, 2007; Fink et al., 1996; for a review see: Svoboda et al., 2006). These same SFG and IFG regions were positively correlated with the degree of autobiographical salience of a memory evoked by a piece of music in a study specifically investigating the overlap between familiar music and autobiographical memories (Janata, 2009). Music is known to evoke vivid autobiographical memories (Belfi et al., 2015) and approximately 30% of excerpts from popular music were shown to evoke such memories (Janata et al., 2007). It is possible that the lack of a consistent musical memory network in the literature has to do with musical memories being confounded with autobiographical memories. Rather than identifying neural correlates of musical memory, previous studies may have reported areas that were activated as a result of autobiographical memories.

To my knowledge, no studies investigating musical memory using well-known music have taken into account whether autobiographical memories are triggered by the stimuli. For example, 5 of the 10 studies included in the Freitas, et al. (2018) meta-analysis investigating the neural correlates of musical memory used well-known stimuli from participants' past. None of these studies controlled for autobiographical memory (Groussard et al., 2010; Jacobsen et al., 2015; Pereira et al., 2011; Plailly et al., 2007; Sikka et al., 2015). The other five studies were either specifically interested in the relationship between musical familiarity and autobiographical memory (Janata, 2009), or used a training and retrieval paradigm with short novel musical phrases (Altenmüller et al., 2014; Klostermann et al., 2009; Nan et al., 2008; Watanabe et al., 2008). Other studies (not included in the meta-analysis) chose their well-known stimuli by excluding music the researchers decided were likely to evoke autobiographical memories (e.g. "Wedding March") but details regarding how they decided which stimuli would evoke such memories and which would not are lacking (Platel, 2005; Slattery et al., 2019). In contrast to previous studies, the experiments presented in this thesis used a controlled training paradigm that asked participants to learn novel stimuli. Although participants could have incorporated the stimuli into their daily lives (e.g., listening while cooking or driving), few participants reported having done so. Instead, participants reported listening to the stimuli while sitting in front of their computers which likely lowered the number of autobiographical memories associated with

the stimuli. This lack of autobiographical memory may be the reason there were no differences in the activated brain areas between the novel and the learned stimuli. However, the interpretation of whether the lack of neural differences between the learned and not learned stimuli was related to a lack of autobiographical memories is limited. Participants were not asked to share whether, at the end of training, the learned stimuli reminded them of more memories from the previous three weeks than the not learned stimuli. Had there been no difference in the number of recollected memories between the learned and not learned stimuli alongside no neural differences, the role of autobiographical memories in driving the neural differences seen in previous studies investigating musical memory would have been more definitively characterized.

If previous investigations into the neural correlates of musical memory that use well-known stimuli are confounded by autobiographical memories, then perhaps the studies that use training/retrieval paradigms with novel stimuli more 'purely' identify musical memory correlates. However, there are discrepancies in the design of these studies as well. For example, one study compared culturally familiar to culturally unfamiliar music (Western vs. Chinese music; Nan et al., 2008), while three others asked participants to listen to unfamiliar instrumental excerpts and then complete an old vs. new task. However, the definition of an 'unfamiliar' piece of music differed across the three studies: one used excerpts from little-known film scores (Altenmüller et al., 2014), the second used excerpts from novel compositions that did not adhere to traditional rules of musical structure (Klostermann et al., 2009), and the third used short tonal compositions that were created in lab (Watanabe et al., 2008). The range in types of stimuli should be taken into account when comparing results across these studies as there is behavioural evidence to suggest that simple melodies involving a single stream of information (e.g. tonal compositions) are remembered better than more complex, polyphonic music that contains multiple streams of information (Demorest et al., 2016). In addition, the brain areas identified as being activated by the learned stimuli within these studies may be responsible for processing learned auditory information, but there may be different mechanisms involved when learning a novel stimulus to perform well on an old vs new task within a single lab session and when remembering a piece of music over a lifetime.

Besides a probable lack of autobiographical memories associated with the stimuli, participants indicated via their preference ratings that they did not like listening to the stimuli. If the lack of preference for the stimuli is interpreted as an absence of emotional involvement, then

this may be another reason for the lack of difference between the neural networks involved in processing the familiar and unfamiliar stimuli in young adults. Besides evoking autobiographical memories (Janata et al., 2007), music also can evoke strong emotions (Juslin & Sloboda, 2010) and it is well established that emotional memories are better remembered than neutral events (Dolcos et al., 2004). The lack of emotional engagement in the current experiments may have reduced participants' memory for the stimuli and resulted in no neural differences between the learned and not learned stimuli.

The connections between musical memory and emotional engagement may be key to understanding what makes memory for music so unique and robust in the presence of neurodegenerative disorders such as Alzheimer's disease. Emotional networks are largely found within the limbic system (Catani et al., 2013) and some dementias like Alzheimer's disease specifically affect the limbic system (Hopper & Vogel, 1976; Li et al., 2016). However, there is evidence that emotional arousal can enhance the formation of long-term declarative memories in patients with dementia (Hamann et al., 2000; Satler et al., 2007) and can enhance the recollection of personal autobiographical memories (El Haj et al., 2012). When investigating the effects of music on memory in patients with dementia, researchers may want to take into account participants' preferences and the level of engagement that participants have with a stimulus.

Intersubject synchrony to familiar stimuli

Across the experiments presented in this thesis, there was no effect of familiarity on intersubject synchrony. Instead, regardless of whether a stimulus was heard once or multiple times, the degree of synchrony across individuals was reduced after a single exposure (Chapter 3). Although individuals were not scanned after each stimulus exposure, had synchrony been directly related to the number of exposures there would have been a difference in the second session between the learned (heard multiple times) and not learned stimuli (heard once before in the first session) in the young adult intersubject synchrony experiment. Given that there was no such difference it is likely that training on stimuli had no effect on synchrony beyond a 'single-listen' effect. However, because all stimuli in the second session showed reduced synchrony, it is possible that session specific differences other than stimulus exposure drove the reduction. To investigate whether the reduction in synchrony related to familiarity with the scanning environment, I compared synchrony between the first four and the last four stimuli in session

one. If synchrony reduction was related to participants becoming more comfortable in or familiar with the scanner, synchrony might have differed between these two sets of stimuli. There were no differences between the first four and last four stimuli in session one. Therefore, either familiarity with the scanner environment was not entirely responsible for the synchrony reduction, or it may take longer than a half hour for the novelty to wear off. To further support the conclusion that familiarity with the scanning environment was not driving the synchrony reduction, there was lower synchrony to long-known stimuli than novel stimuli in older adults (Chapter 5). The long-known stimuli were presented to older adults in the same scanning session as the novel stimuli. The results from both of these experiments suggest that synchrony reduction is related to previous stimulus exposure rather than familiarity with the scanner environment.

Interpretation of the synchrony reduction seen between the novel and long-known stimuli in older adults is limited because older adult participants did not train on novel stimuli. I chose not to implement a training paradigm with the older adult participants to keep their burden of participation low. As a result, I could not directly compare the degree of synchrony to stimuli known for 3 weeks to stimuli known over 50 years. Ideally, a future study will ask participants to train on novel stimuli to compare intersubject synchrony between novel stimuli, stimuli known for a short period of time, and stimuli known for a long period of time within the same group of participants. Understanding how intersubject synchrony changes as a function of familiarity with a stimulus is important for the design of future intersubject synchrony studies. If the level of familiarity of a stimulus differs systematically with the experimental manipulation within a study, then the interpretation of the results could be influenced by a familiarity confound. Without fully understanding how familiarity affects synchrony, researchers run the risk of confounding their results with a familiarity induced reduction.

To understand the cause behind the single exposure effect on synchrony reduction, we can turn to the auditory memory literature where mere exposure to sounds has been shown to improve performance on subsequent recognition tasks (Clarke & Garrett, 2004; Szpunar et al., 2004). For example, when participants were asked to listen to 12 30s-long novel melodies and then identify them in an old vs. new recognition task a week later, they were easily able to identify which melodies had been previously heard (Schellenberg & Habashi, 2015). This result indicates that after a single listen participants had incorporated a representation of the auditory information into their musical lexicon (Peretz et al., 2009). The musical lexicon refers to the

perceptual representation system for melodies against which incoming acoustic signals are compared to make judgements about whether the sounds have been heard before or not. Key for this discussion on intersubject synchrony is the fact that the musical lexicon does not exist in isolation, but rather interacts with a number of different processing systems including the phonological lexicon, association memories, emotional expression analysis, and motor planning networks. If music can be incorporated into the musical lexicon after a single exposure, and interacts with these other processing systems, it may be no surprise that synchrony to musical stimuli reduces after a single exposure. Each individual's stored representation of the initially novel stimulus will be unique because of the associations created with their specific memories and emotions. The triggering of this unique representation of the stimulus with subsequent exposures results in idiosyncratic neural responses to the stimulus and therefore a reduction in intersubject synchrony. Each individual's unique experience of the stimulus likely only further diversifies with repeated exposure as additional associations are made. However, once the level of synchrony reaches a floor there will be no more reduction. The results shown in Chapter 3, Figure 2 suggest that after a single listen to the stimulus participants became very diverse in their processing of the stimulus and had very low levels of synchrony. Therefore, repeated exposure had no further effects on reducing synchrony. On one hand, future studies using intersubject synchrony where the novelty of the stimuli can not be guaranteed could consider exposing all of their participants to the stimuli once before data collection to mitigate the effects of any systematic differences in stimulus exposure that could affect subsequent interpretation of their results. However, this may greatly reduce the degree of synchrony and impact the ability to see any differences in synchrony across their experimental manipulations. Therefore, using novel stimuli may be the most effective way of maximizing intersubject synchrony within a group of participants.

The effects of music and language on neural activation across age groups

In the GLM experiments in Chapters 2 and 4, there were higher levels of BOLD activation to stimuli with language than without. However, some brain areas differed based on stimulus type in young adults but not in older adults. For example, in bilateral planum polare, young adult brains showed more activation to whole, instrumental, and a capella stimuli than to spoken stimuli, but planum polare activity in the older adults did not differ between stimulus types. The planum polare plays a role in processing language and musical syntax, with increasing

stimulus complexity resulting in more activation (Bookheimer, 2002; Brown et al., 2006; Constable et al., 2004; Griffiths et al., 1998; Merrill et al., 2012). In addition, the planum polare responds more to stimuli with melodic pitch information than without pitch information (Merrill et al., 2012). These previous results are in line with the current study's young adult activation differences, but the differences between the two age groups may be related to language processing changes with age. When older adults hear language in the presence of noise, their brains show lower temporal auditory activation than young adult brains as language intelligibility reduces (Eckert et al., 2008; Peelle, 2019). In the current study, the lower planum polare activity in older adults may be related to how older adults process stimuli in noise. If the language in the whole stimuli was processed similarly to language in noisy environments, then the most intelligible stimuli (spoken) would result in the most temporal activation, the least intelligible stimuli (instrumental) would result in the least activation, with activation levels to the whole stimuli falling in between. Despite differences in the brain areas that were activated in the young and older adults, the presence of language was key to increased BOLD activation levels across both groups.

The intersubject synchrony experiment in Chapter 4 investigated whether more synchrony was induced to stimuli that contained music and language together than to either stimulus type on its own in young and older adults. Across both age groups synchrony was affected by stimulus contents in five significant clusters: bilateral temporal cortex, precentral gyrus, occipital fusiform cortex, and the lateral occipital cortex. The occipital fusiform and the lateral occipital cortex have been previously identified as involved in processing musical stimuli that contain language information (Saito et al., 2012) and the temporal cortices and precentral gyrus are known to be involved in both language and music processing (e.g., Schön et al., 2010). I expected to see more synchrony to complex whole stimuli (containing both music and language) than to either the spoken or instrumental stimuli. Contrary to this hypothesis, more information within a stimulus did not increase synchrony. However, I did find that the whole stimuli induced more synchrony than the instrumental stimuli in bilateral temporal cortex and precentral gyrus, but in no areas did the whole stimuli induce more synchrony than the spoken stimuli. Spoken stimuli induced significantly more synchrony than the instrumental stimuli in all five clusters and induced more synchrony than the whole stimuli in three of those clusters (left posterior STG, occipital fusiform cortex and the lateral occipital cortex). These results are

contrary to those reported by Naci et al (2017) where complex movie stimuli induced more synchrony than popular tv-show theme songs. The discrepancy in the results likely has to do with the type of stimuli used. The stimuli in the current study were audio-only, while the previous study compared levels of synchrony between audio-visual stimuli (movies) and audio-only stimuli (theme songs) suggesting that more synchrony is induced when more senses are involved (sight and hearing vs hearing along). Areas processing visual information are involved during audio-visual stimuli that are not involved when processing audio-only information. Participants may also have enjoyed the audio-visual stimuli in Naci et al. (2017) more than the current audio-only stimuli. Although the hypothesis about whole stimuli inducing the most synchrony was incorrect, I did find that the contents of the audio-only stimuli affected the level of intersubject synchrony.

Similar to the results from the GLM experiments, the presence of language was integral to inducing intersubject synchrony. Stimuli containing language induced more synchrony than stimuli without language, and this result supports findings from previous work that suggest that language is a key component to driving synchrony across a group of listeners (Laforge et al., 2020; Naci et al., 2017; Regev et al., 2019; Simony et al., 2016). When the stimuli had a single, attention-grabbing component that could not be ignored (the language in the spoken stimuli), these stimuli induced the strongest amount of synchrony within the group compared to stimuli that included other options for participants to pay attention to (like the instrumental tracks in the whole music). This was true regardless of age. Previous research has shown that synchrony is affected by attention (Regev et al., 2019) and synchrony decreases as participants are distracted. There is also less synchrony across a group when the presented stimulus does not include a coherent narrative for participants to attend to compared to when the stimulus contains an intact storyline (Ki et al., 2016). It is possible, then, that when participants listened to stimuli that contained ‘too much’ information, like the whole music stimuli, each participant focused on a different component of the stimulus (the music, rhythm, or lyrics) which reduced synchrony across the group. Although stimuli that rely on multiple senses may induce higher levels of intersubject synchrony, when choosing stimuli for synchrony studies in clinical populations that may have impaired vision, audio stimuli with language should be used to induce the strongest synchronization results.

The stimuli containing language resulted in both higher levels of BOLD activation and stronger synchrony than stimuli that did not contain language. These results could have implications for the design of future studies in which aspects of auditory stimulus processing (e.g., attention, memory, etc.) are manipulated and the effects of those manipulations are investigated using GLM or synchrony analyses. For example, understanding how differences in attention affect intersubject synchrony to musical stimuli may provide insight into whether the differences seen in previous studies of attention on synchrony to short stories (Regev et al., 2019) also exist with musical stimuli. However, using musical stimuli that contain language may increase the ability of researchers to see subtle changes in synchrony. By maximizing baseline activation levels, any effects of manipulations of other factors will be easier to detect than if baseline levels are at a floor. It is important to note that the level of BOLD activation and the degree of synchrony are not directly related to one another. In the current experiments participants could have been equally idiosyncratic in the timecourse of their activation across stimulus types while showing differences in the amplitudes of that activation. This would have resulted in no differences in synchrony across stimulus types but significant differences in BOLD activation. Given that both the GLM and the synchrony analyses showed differences in neural activation as a result of the presence of language, researchers should use stimuli containing language if they wish to maximize BOLD responses and synchrony in future studies.

The effect of age on intersubject synchrony

In Chapter 4 I investigated how synchrony to identical music and language stimuli differed between groups of young and older adults. Age-related differences in synchrony have been described in only two other studies (Campbell et al., 2015; Geerligs et al., 2018). The researchers found that when older and young adults watched the same movie there were brain areas that showed an age-related reduction in synchrony, while in other areas there was preservation of synchrony with age. In the current experiments, there was an age-related reduction in synchrony in the middle temporal gyrus (temporooccipital part), frontal orbital cortex, and the temporal pole (more synchrony within the group of younger adults than within the group of older adults). Interestingly, none of these areas were previously identified as showing an age-related reduction in synchrony to the movie stimuli. In fact, the left and right middle temporal gyrus were previously identified as showing *preservation* of synchrony with age (Geerligs et al., 2018) contrary to the effect found in the current experiments. I also investigated

age-related synchrony reductions in older adults by comparing the individual older adult data with the average of the young adult group. Older adults were less synchronized to the young adult group in the middle temporal gyrus (temporooccipital part), anterior cingulate gyrus, and the temporal pole. This can be interpreted as an age-related reduction in synchrony; older adults were not as similar to the young adults as the individual young adults were to each other. This result is again in contrast to the previous study as these areas were previously identified as showing preservation of synchrony with age to the movie stimuli (Geerligs et al., 2018). The older adults were also significantly *more* synchronized than young adults in the posterior parahippocampal gyrus. This is in contrast to results from the previous study (Geerligs et al., 2018) as the parahippocampal gyrus was specifically identified as showing an age-related reduction; the opposite effect was found in the current experiments. The plot of the audio-visual movie stimulus used by Geerligs et al. (2018) is largely driven by visual information while the stimuli in the current experiments were audio only and participants had to rely on the language or music information. The discrepancy in results between the previous study (Geerligs et al., 2018) and the current results may also have to do with the role of language in the stimuli and how language is processed with age.

Many of the regions where there was no age-related decline are known to be involved in language processing (e.g., inferior frontal gyrus, precentral gyrus, lateral occipital cortex; Borowsky et al., 2007; Pulvermuller et al., 2006). Language regions have been shown to be generally resilient against the effects of age, especially during passive listening tasks (Campbell et al., 2016; Davis et al., 2014) and also may be resistant to age-related synchrony decline (Geerligs et al., 2018). In addition, older adults may recruit additional resources as a compensatory mechanism to make up for lost neural efficiency when processing language stimuli (Peelle, 2019; Wingfield & Grossman, 2006). For example, increasing age was related to increased activation in occipital cortex during an auditory word recognition task (Kuchinsky et al., 2012) and additional recruitment of frontal areas like the inferior frontal gyrus during sentence comprehension tasks (Peelle et al., 2010; Tyler et al., 2010). This same frontal area was more synchronized within the group of older adults than within the group of younger adults in the current experiments. Therefore, it is possible that in the current study older adults were more synchronized than young adults within regions associated with language processing because they relied more heavily on these regions to process the music and language stimuli than did the

young adults. If young adults were not relying on these networks as heavily as the older adults, and older adults do not generally show age-related decline in these regions, it may be reasonable to expect more synchrony in older adults than younger adults within these networks.

Age-related structural changes like grey- and white-matter atrophy that occur with healthy aging (Giorgio et al., 2010; Walhovd et al., 2005), may be related to the synchrony differences seen here across age groups. Future studies should investigate whether differences in synchrony are related to changes in brain structure. The relationship between synchrony and structural changes was not investigated within the current set of experiments as the primary goal of this thesis was to elucidate the neural correlates of musical memory. However, focusing future synchrony studies specifically on areas with and without age- or disorder-related structural changes may provide further insight into whether areas that have undergone structural changes process stimuli in a similar way to corresponding areas in brains without such structural changes. Intersubject synchrony may provide a further avenue for asking questions about functional changes in the brain across the lifespan and may help to understand how aging brains compensate for various structural changes and how those changes affect musical memory.

Considerations for the future use of intersubject synchrony measures

As the popularity of the intersubject synchrony technique has grown, it has been used to study attention (Ki et al., 2016), memory (Furman et al., 2007; Hasson et al., 2008), emotion (Trost et al., 2015), speech processing (Wilson et al., 2008), music perception (Abrams et al., 2013), and brain function in clinical populations (Anderson et al., 2013; Hasson et al., 2009; Lyons et al., 2020). Synchrony has also been used to study consciousness by interpreting the level of synchrony in fronto-parietal networks as a proxy for the shared experience of a stimulus. For example, when the brain activity of a patient diagnosed as being in a vegetative state was highly synchronized with the brain activity of a group of healthy controls, that result was interpreted as suggesting that the patient experienced the stimulus similarly to the controls (Naci et al., 2014). Given the way that intersubject synchrony is calculated there are some limitations to the types of conclusions that can be drawn from intersubject synchrony results.

Intersubject synchrony captures the *shared* experience between two individuals (or an individual and a group) rather than the idiosyncrasies that make up each individual's unique experience of the world. Synchrony is calculated as a correlation between two sets of data and

the calculated values provide information about how similar the two datasets are. To use intersubject synchrony to characterize the conscious experience of individuals such as, for example, patients with dementia (Huntley et al., In preparation), it is important to recognize that additional tools are required to understand what might be driving differences in synchrony across experimental groups. For example, collecting data from a sustained attention response task (SART; Naci et al., 2014), galvanic skin response (GSR; Sinai, 2015) or heart rate while a participant is exposed to a stimulus can provide additional information about the meaning of the brain's fluctuations in response to that stimulus. If synchrony decreases during a period of increased performance on a SART and increases during a period of decreased performance on a SART the claim could be made that the fluctuations in synchrony are related to how much attention is being paid to the stimulus (Naci et al., 2014). Alternatively, if synchrony fluctuations are related to changes in skin conductivity as measured using GSR or changes in heart rate, then the claim could be made that synchrony is related to the emotional state of the individual (Sharma et al., 2016). Combining techniques allows researchers to not only understand how individuals from clinical groups of interest compare to controls in the way they process stimuli but will also shed some light on what the causes of the similarities or differences might be.

An important limitation to consider when using synchrony measures to assess patient populations lies in the comparison group. When calculating synchrony in clinical populations, it is not obvious who should make up the comparison group. Patients with Alzheimer's disease have altered emotional perception (Lavenu & Pasquier, 2005), visuospatial perception (Mandal et al., 2012), and attention (Parasuraman & Greenwood, 1998). Therefore, correlating the brain activity from a patient with severe Alzheimer's with a group of healthy controls will likely show low levels of synchrony. Such a result will only indicate that the experience of a patient is different from that of the controls. A similar approach was taken in Chapter 4 when individual older adult data was correlated with the average young adult data to understand whether there were age related changes in synchrony to the different stimulus types. In most areas where synchrony differentiated between age groups, young and older adults did not differ statistically in how synchronized they were (older adults were processing the stimuli within these regions in a similar way to the young adults). However, the areas where they did differ (middle temporal gyrus, anterior cingulate gyrus temporal pole, parahippocampal gyrus) are known to undergo age-related changes in functional connectivity and grey matter volume (Giorgio et al., 2010;

Walhovd et al., 2005) and may be of interest in future investigations of whether age-related structural differences are responsible for age-related differences in synchrony. Another option for calculating synchrony is to correlate the brain data from a single patient with that of a group of patients. However, each patient's disease progresses differently and differences in synchrony across patients will only indicate that individual disease progression results in individualized experiences of the environment. However, corroboration with other tools (e.g., SART or GSR as mentioned above) could be used to further understand a patient's individual experience. A third option is to correlate a patient's brain activity with their own activity at a different point in time (similar to what was done in Chapter 3 when an individual's data after the training period was correlated with their own data before the training period). A reduction in synchrony over time might be indicative of disease progression. Regardless of how the comparison group is chosen, it will be important for researchers to address their choice to ensure that the way synchrony is calculated is consistent with the research question and the conclusions drawn.

Conclusions

The series of experiments presented in this thesis have uncovered a number of important results. First, contrary to the musical memory literature I did not see a specific neural network for musical memory when using a highly controlled training paradigm. This was true regardless of whether the stimuli contained language information or not. Therefore, the discrepancies in the neural networks identified in the previous literature may stem from differences in the paradigms used across studies that result in differences in the type of previous experiences participants have had with the stimuli. Specifically, considering the autobiographical memories or emotional engagement that individuals have with the musical stimuli may be key to understanding what makes memory for music so unique in the presence of neurodegenerative disorders such as Alzheimer's disease. Second, I showed that previous exposure to a stimulus reduces the degree of intersubject synchrony. This was true in young adults when comparing synchrony between stimuli that had been heard once and those heard multiple times, and in older adults when comparing synchrony between novel stimuli and stimuli with lifelong familiarity. However, this reduction effect seems to be a result of a 'single listen' rather than a result of learning. To further characterize how synchrony changes as a function of repetition it will be important to collect data at more time points to solidify whether the synchrony decrease after a single-listen changes over longer periods of time or more stimulus repetitions. Third, I found that intersubject

synchrony was stronger to stimuli that contain language information than those that do not, and strongest to the language stimuli without additional musical features. This was true in both young and older adults despite differences in synchrony across the age groups. These results have implications for how researchers design future intersubject synchrony studies as stimuli that contain language may maximize synchrony. Finally, I also found that some areas showed an age-related decline in synchrony while other areas showed the opposite (more synchrony in older adults than young adults). Further characterizing the brain regions that do not show age-related reductions in synchrony, and understanding what is driving synchrony within those regions, could provide an additional avenue for investigating why musical memories are more resilient than other types of memories in the presence of neurodegenerative disorders.

Bibliography

Abrams, D. a., Ryali, S., Chen, T., Chordia, P., Khouzam, A., Levitin, D. J., & Menon, V. (2013). Inter-subject synchronization of brain responses during natural music listening. *European Journal of Neuroscience*, *37*(9), 1458–1469. https://doi.org/10.1111/ejn.12173

Agustus, J. L., Golden, H. L., Callaghan, M. F., Bond, R. L., Benhamou, E., Hailstone, J. C., Weiskopf, N., & Warren, J. D. (2018). Melody Processing Characterizes Functional Neuroanatomy in the Aging Brain. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00815

Alexander, L. M., Escalera, J., Ai, L., Andreotti, C., Febre, K., Mangone, A., Potler, N. V., Langer, N., Alexander, A., Kovacs, M., Litke, S., O'Hagan, B., Andersen, J., Bronstein, B., Bui, A., Bushey, M., Butler, H., Castagna, V., Camacho, N., … Milham, M. P. (2017). An open resource for transdiagnostic research in pediatric mental health and learning disorders. *BioRxiv*, 149369. https://doi.org/10.1101/149369

Alonso, I., Davachi, L., Valabrègue, R., Lambrecq, V., Dupont, S., & Samson, S. (2016). Neural correlates of binding lyrics and melodies for the encoding of new songs. *NeuroImage*, *127*, 333–345. https://doi.org/10.1016/j.neuroimage.2015.12.018

Altenmüller, E., Siggel, S., Mohammadi, B., Samii, A., & Münte, T. F. (2014). Play it again, Sam: Brain correlates of emotional music recognition. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/fpsyg.2014.00114

Anderson, J. S., Nielsen, J. A., Ferguson, M. A., Burback, M. C., Cox, E. T., Dai, L., Gerig, G., Edgin, J. O., & Korenberg, J. R. (2013). Abnormal brain synchrony in Down Syndrome. *NeuroImage: Clinical*, *2*, 703–715. https://doi.org/10.1016/j.nicl.2013.05.006

Belfi, A. M., Karlan, B., & Tranel, D. (2015). Music evokes vivid autobiographical memories. *Memory*, *August 2015*, 1–11. https://doi.org/10.1080/09658211.2015.1061012

Bookheimer, S. (2002). Functional MRI of Language: New Approaches to Understanding the Cortical Organization of Semantic Processing. *Annual Review of Neuroscience*, *25*(1), 151–188. https://doi.org/10.1146/annurev.neuro.25.112701.142946

Borowsky, R., Esopenko, C., Cummine, J., & Sarty, G. E. (2007). Neural Representations of Visual Words and Objects: A Functional MRI Study on the Modularity of Reading and Object Processing. *Brain Topography*, *20*(2), 89–96. https://doi.org/10.1007/s10548-007-0034-1

Brown, S., Martinez, M. J., & Parsons, L. M. (2006). Music and language side by side in the brain: A PET study of the generation of melodies and sentences. *European Journal of Neuroscience*, *23*(10), 2791–2803. https://doi.org/10.1111/j.1460-9568.2006.04785.x

Cabeza, R., & St Jacques, P. (2007). Functional neuroimaging of autobiographical memory. *Trends in Cognitive Sciences*, *11*(4), 219–227.

Campbell, K. L., Samu, D., Davis, S. W., Geerligs, L., Mustafa, A., & Tyler, L. K. (2016). Robust Resilience of the Frontotemporal Syntax System to Aging. *The Journal of Neuroscience*, *36*(19), 5214–5227. https://doi.org/10.1523/JNEUROSCI.4561-15.2016

Campbell, K. L., Shafto, M. A., Wright, P., Tsvetanov, K. A., Geerligs, L., Cusack, R., Tyler, L. K., Brayne, C., Bullmore, E., Calder, A., Dalgleish, T., Duncan, J., Henson, R., Matthews, F., Marslen-Wilson, W., Rowe, J., Cheung, T., Davis, S., Kievit, R., … Villis, L. (2015). Idiosyncratic responding during movie-watching predicted by age differences in attentional control. *Neurobiology of Aging*, *36*(11), 3045–3055. https://doi.org/10.1016/j.neurobiolaging.2015.07.028

Catani, M., Dell'Acqua, F., & Thiebaut de Schotten, M. (2013). A revised limbic system model for memory, emotion and behaviour. *Neuroscience & Biobehavioral Reviews*, *37*(8), 1724–1737. https://doi.org/10.1016/j.neubiorev.2013.07.001

Clarke, C. M., & Garrett, M. F. (2004). Rapid adaptation to foreign-accented English. *The Journal of the Acoustical Society of America*, *116*(6), 3647–3658. https://doi.org/10.1121/1.1815131

Constable, R. T., Pugh, K. R., Berroya, E., Mencl, W. E., Westerveld, M., Ni, W., & Shankweiler, D. (2004). Sentence complexity and input modality effects in sentence comprehension: An fMRI study. *NeuroImage*, *22*(1), 11–21. https://doi.org/10.1016/j.neuroimage.2004.01.001

Davis, S. W., Zhuang, J., Wright, P., & Tyler, L. K. (2014). Age-related sensitivity to task-related modulation of language-processing networks. *Neuropsychologia*, *63*, 107–115. https://doi.org/10.1016/j.neuropsychologia.2014.08.017

Dolcos, F., LaBar, K. S., & Cabeza, R. (2004). Interaction between the amygdala and the medial temporal lobe memory system predicts better memory for emotional events. *Neuron*, *42*(5), 855–863.

Eckert, M. A., Walczak, A., Ahlstrom, J., Denslow, S., Horwitz, A., & Dubno, J. R. (2008). Age-related Effects on Word Recognition: Reliance on Cognitive Control Systems with Structural Declines in Speech-responsive Cortex. *Journal of the Association for Research in Otolaryngology*, *9*(2). https://doi.org/10.1007/s10162-008-0113-3

El Haj, M., Fasotti, L., & Allain, P. (2012). The involuntary nature of music-evoked autobiographical memories in Alzheimer's disease. *Consciousness and Cognition*, *21*(1), 238–246. https://doi.org/10.1016/j.concog.2011.12.005

Fink, G. R., Markowitsch, H. J., Reinkemeier, M., Bruckbauer, T., Kessler, J., & Heiss, W.-D. (1996). Cerebral Representation of One's Own Past: Neural Networks Involved in Autobiographical Memory. *The Journal of Neuroscience*, *16*(13), 4275–4282. https://doi.org/10.1523/JNEUROSCI.16-13-04275.1996

Freitas, C., Manzato, E., Burini, A., Taylor, M. J., Lerch, J. P., & Anagnostou, E. (2018). Neural Correlates of Familiarity in Music Listening: A Systematic Review and a Neuroimaging Meta-Analysis. *Frontiers in Neuroscience*, *12*. https://doi.org/10.3389/fnins.2018.00686

Furman, O., Dorfman, N., Hasson, U., Davachi, L., & Dudai, Y. (2007). They saw a movie: Long-term memory for an extended audiovisual narrative. *Learning & Memory*, *14*(6), 457–467. https://doi.org/10.1101/lm.550407

Geerligs, L., Cam-CAN, & Campbell, K. L. (2018). Age-related differences in information processing during movie watching. *Neurobiology of Aging*, *72*, 106–120. https://doi.org/10.1016/j.neurobiolaging.2018.07.025

Giorgio, A., Santelli, L., Tomassini, V., Bosnell, R., Smith, S., De Stefano, N., & Johansen-Berg, H. (2010). Age-related changes in grey and white matter structure throughout adulthood. *NeuroImage*, *51*(3), 943–951. https://doi.org/10.1016/j.neuroimage.2010.03.004

Griffiths, T. D., Büchel, C., Frackowiak, R. S. J., & Patterson, R. D. (1998). Analysis of temporal structure in sound by the human brain. *Nature Neuroscience*, *1*(5), 422–427. https://doi.org/10.1038/1637

Groussard, M., Rauchs, G., Landeau, B., Viader, F., Desgranges, B., Eustache, F., & Platel, H. (2010). The neural substrates of musical memory revealed by fMRI and two semantic tasks. *NeuroImage*, *53*(4), 1301–1309. https://doi.org/10.1016/j.neuroimage.2010.07.013

Groussard, M., Viader, F., Landeau, B., Desgranges, B., Eustache, F., & Platel, H. (2009). Neural Correlates Underlying Musical Semantic Memory. *Annals of the New York Academy of Sciences*, *1169*(1), 278–281. https://doi.org/10.1111/j.1749-6632.2009.04784.x

Halpern, A. R., & Zatorre, R. J. (1999). When That Tune Runs Through Your Head: A PET Investigation of Auditory Imagery for Familiar Melodies. *Cerebral Cortex*, *9*(7), 697–704. https://doi.org/10.1093/cercor/9.7.697

Hamann, S., Monarch, E., & Goldstein, F. (2000). Memory enhancement for emotional stimuli is impaired in early Alzheimer's disease. *Neuropsychology*, *14*, 82–92. https://doi.org/10.1037//0894-4105.14.1.82

Hasson, U., Avidan, G., Gelbard, H., Vallines, I., Harel, M., Minshew, N., & Behrmann, M. (2009). Shared and idiosyncratic cortical activation patterns in autism revealed under continuous real-life viewing conditions. *Autism Research*, *2*(4), 220–231. https://doi.org/10.1002/aur.89

Hasson, U., Furman, O., Clark, D., Dudai, Y., & Davachi, L. (2008). Enhanced Intersubject Correlations during Movie Viewing Correlate with Successful Episodic Encoding. *Neuron*, *57*(3), 452–462. https://doi.org/10.1016/j.neuron.2007.12.009

Herholz, S., Halpern, A., & Zatorre, R. (2012). Neuronal correlates of perception, imagery, and memory for familiar tunes. *Journal of Cognitive Neuroscience*, *24*(6), 1382–1397. https://doi.org/10.1162/jocn_a_00216

Hopper, M. W., & Vogel, F. S. (1976). The limbic system in Alzheimer's disease. A neuropathologic investigation. *The American Journal of Pathology*, *85*(1), 1–20.

Huntley, J., Bor, D., Fleming, S. M., Mancuso, M., Mediano, P., Naci, L., Owen, A. M., Rocci, L., Sternin, A., & Howard, R. (In preparation). *Assessing awareness in severe Alzheimer's disease*.

Jacobsen, J., Fritz, T., Stelzer, J., & Turner, R. (2015). Why musical memory can be preserved in advanced Alzheimer's disease. *Brain: A Journal of Neurology*, 1–13. https://doi.org/10.1093/awv148

Janata, P. (2009). The neural architecture of music-evoked autobiographical memories. *Cerebral Cortex*, *19*(11), 2579–2594. https://doi.org/10.1093/cercor/bhp008

Janata, P., Tomic, S. T., & Rakowski, S. K. (2007). Characterisation of music-evoked autobiographical memories. *Memory*, *15*(8), 845–860. https://doi.org/10.1080/09658210701734593

Juslin, P. N., & Sloboda, J. A. (2010). *The past, present, and future of music and emotion research* (p. 955). Oxford University Press.

Ki, J. J., Kelly, S. P., & Parra, L. C. (2016). Attention Strongly Modulates Reliability of Neural Responses to Naturalistic Narrative Stimuli. *Journal of Neuroscience*, *36*(10). https://doi.org/10.1523/JNEUROSCI.2942-15.2016

Klostermann, E. C., Loui, P., & Shimamura, A. P. (2009). Activation of right parietal cortex during memory retrieval of nonlinguistic auditory stimuli. *Cognitive, Affective, & Behavioral Neuroscience*, *9*(3), 242–248. https://doi.org/10.3758/CABN.9.3.242

Kuchinsky, S. E., Vaden, K. I., Jr, Keren, N. I., Harris, K. C., Ahlstrom, J. B., Dubno, J. R., & Eckert, M. A. (2012). Word Intelligibility and Age Predict Visual Cortex Activity during Word Listening. *Cerebral Cortex*, *22*(6), 1360–1371. https://doi.org/10.1093/cercor/bhr211

Laforge, G., Incio Serra, N., Blain-Moraes, S., Stojanoski, B., & Owen, A. M. (2020). A Comparison of English and French Naturalistic Listening Paradigms for the Assessment of Consciousness in Unresponsive Individuals. *2020 IEEE International Conference on Systems, Man, and Cybernetics (SMC)*, 526–533. https://doi.org/10.1109/SMC42975.2020.9283263

Lavenu, I., & Pasquier, F. (2005). Perception of Emotion in Frontotemporal Dementia and Alzheimer Disease: A longitudinal study. *Dementia and Geriatric Cognitive Disorders*, *19*(1), 37–41. https://doi.org/10.1097/00002093-199904000-00007

Li, X., Wang, H., Tian, Y., Zhou, S., Li, X., Wang, K., & Yu, Y. (2016). Impaired White Matter Connections of the Limbic System Networks Associated with Impaired Emotional Memory in Alzheimer's Disease. *Frontiers in Aging Neuroscience*, *8*. https://doi.org/10.3389/fnagi.2016.00250

Lyons, K. M., Stevenson, R. A., Owen, A. M., & Stojanoski, B. (2020). Examining the relationship between measures of autistic traits and neural synchrony during movies in children with and without autism. *NeuroImage: Clinical*, *28*, 102477. https://doi.org/10.1016/j.nicl.2020.102477

Mandal, P., Joshi, J., & Saharan, S. (2012). Visuospatial Perception: An Emerging Biomarker for Alzheimer's Disease. *Journal of Alzheimer's Disease : JAD*, *31*, S117-35. https://doi.org/10.3233/JAD-2012-120901

Merrill, J., Sammler, D., Bangert, M., Goldhahn, D., Lohmann, G., Turner, R., & Friederici, A. D. (2012). Perception of Words and Pitch Patterns in Song and Speech. *Frontiers in Psychology*, *3*. https://doi.org/10.3389/fpsyg.2012.00076

Naci, L., Cusack, R., Anello, M., & Owen, A. M. (2014). A common neural code for similar conscious experiences in different individuals. *Proceedings of the National Academy of Sciences of the United States of America*, *111*(39), 14277–14282. https://doi.org/10.1073/pnas.1407007111

Naci, L., Sinai, L., & Owen, A. M. (2017). Detecting and interpreting conscious experiences in behaviorally non-responsive patients. *NeuroImage*, *145*, 304–313. https://doi.org/10.1016/j.neuroimage.2015.11.059

Nan, Y., Knösche, T. R., Zysset, S., & Friederici, A. D. (2008). Cross-cultural music phrase processing: An fMRI study. *Human Brain Mapping*, *29*(3), 312–328.

Parasuraman, R., & Greenwood, P. M. (1998). Selective attention in aging and dementia. In *The attentive brain* (pp. 461–487). The MIT Press.

Peelle, J. E. (2019). Language and aging. In G. De Zubicaray I. & N. O. Schiller (Eds.), *The Oxford Handbook of Neurolinguistics*. Oxford University Press.

Peelle, J. E., Troiani, V., Wingfield, A., & Grossman, M. (2010). Neural Processing during Older Adults' Comprehension of Spoken Sentences: Age Differences in Resource Allocation and Connectivity | Cerebral Cortex | Oxford Academic. *Cerebral Cortex*, *20*(4). https://academic.oup.com/cercor/article/20/4/773/303007

Pereira, C. S., Teixeira, J., Figueiredo, P., Xavier, J., Castro, S. L., & Brattico, E. (2011). Music and Emotions in the Brain: Familiarity Matters. *PLoS ONE*, *6*(11). https://doi.org/10.1371/journal.pone.0027241

Peretz, I., Gosselin, N., Belin, P., Zatorre, R. J., Plailly, J., & Tillmann, B. (2009). Music lexical networks: The cortical organization of music recognition. *Annals of the New York Academy of Sciences*, *1169*, 256–265. https://doi.org/10.1111/j.1749-6632.2009.04557.x

Plailly, J., Tillmann, B., & Royet, J.-P. (2007). The Feeling of Familiarity of Music and Odors: The Same Neural Signature? *Cerebral Cortex*, *17*(11), 2650–2658. https://doi.org/10.1093/cercor/bhl173

Platel, H. (2005). Functional neuroimaging of semantic and episodic musical memory. *Annals of the New York Academy of Sciences*, *1060*(January 2006), 136–147. https://doi.org/10.1196/annals.1360.010

Pulvermuller, F., Huss, M., Kherif, F., Moscoso del Prado Martin, F., Hauk, O., & Shtyrov, Y. (2006). Motor cortex maps articulatory features of speech sounds. *Proceedings of the National Academy of Sciences*, *103*(20), 7865–7870. https://doi.org/10.1073/pnas.0509989103

Regev, M., Simony, E., Lee, K., Tan, K. M., Chen, J., & Hasson, U. (2019). Propagation of information along the cortical hierarchy as a function of attention while reading and listening to stories. *Cerebral Cortex*, *29*(10), 291526. https://doi.org/10.1093/cercor/bhy282

Saito, Y., Ishii, K., Sakuma, N., Kawasaki, K., Oda, K., & Mizusawa, H. (2012). Neural Substrates for Semantic Memory of Familiar Songs: Is There an Interface between Lyrics and Melodies? *PLoS ONE*, *7*(9). https://doi.org/10.1371/journal.pone.0046354

Satler, C., Garrido, L. M., Sarmiento, E. P., Leme, S., Conde, C., & Tomaz, C. (2007). Emotional arousal enhances declarative memory in patients with Alzheimer's disease. *Acta Neurologica Scandinavica*, *116*(6), 355–360. https://doi.org/10.1111/j.1600-0404.2007.00897.x

Schaal, N. K., Javadi, A.-H., Halpern, A. R., Pollok, B., & Banissy, M. J. (2015). Right parietal cortex mediates recognition memory for melodies. *European Journal of Neuroscience*, *42*(February), n/a-n/a. https://doi.org/10.1111/ejn.12943

Schellenberg, E. G., & Habashi, P. (2015). Remembering the melody and timbre, forgetting the key and tempo. *Memory & Cognition*, *43*(7), 1021–1031. https://doi.org/10.3758/s13421-015-0519-1

Schön, D., Gordon, R., Campagne, A., Magne, C., Astésano, C., Anton, J.-L., & Besson, M. (2010). Similar cerebral networks in language, music and song perception. *NeuroImage*, *51*(1), 450–461. https://doi.org/10.1016/j.neuroimage.2010.02.023

Sharma, M., Kacker, S., & Sharma, M. (2016). A Brief Introduction and Review on Galvanic Skin Response. *International Journal of Medical Research Professionals*, *2*. https://doi.org/10.21276/ijmrp.2016.2.6.003

Sikka, R., Cuddy, L. L., Johnsrude, I. S., & Vanstone, A. D. (2015). An fMRI comparison of neural activity associated with recognition of familiar melodies in younger and older adults. *Frontiers in Neuroscience*, *9*(OCT), 1–10. https://doi.org/10.3389/fnins.2015.00356

Simony, E., Honey, C. J., Chen, J., Lositsky, O., Yeshurun, Y., Wiesel, A., & Hasson, U. (2016). Dynamic reconfiguration of the default mode network during narrative comprehension. *Nature Communications*, *7*(May 2015). https://doi.org/10.1038/ncomms12141

Sinai, L. (2015). *Naturalistic paradigms for neuroimaging and bedside measures of conscious awareness* [Master's Thesis]. University of Western Ontario.

Slattery, C. F., Agustus, J. L., Paterson, R. W., McCallion, O., Foulkes, A. J. M., Macpherson, K., Carton, A. M., Harding, E., Golden, H. L., Jaisin, K., Mummery, C. J., Schott, J. M., & Warren, J. D. (2019). The functional neuroanatomy of musical memory in Alzheimer's disease. *Cortex*, *115*, 357–370. https://doi.org/10.1016/j.cortex.2019.02.003

Svoboda, E., McKinnon, M. C., & Levine, B. (2006). The functional neuroanatomy of autobiographical memory: A meta-analysis. *Neuropsychologia*, *44*(12), 2189–2208. https://doi.org/10.1016/j.neuropsychologia.2006.05.023

Szpunar, K. K., Schellenberg, E. G., & Pliner, P. (2004). Liking and Memory for Musical Stimuli as a Function of Exposure. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *30*(2), 370–381. http://dx.doi.org.proxy1.lib.uwo.ca/10.1037/0278-7393.30.2.370

Trost, W., Frühholz, S., Cochrane, T., Cojan, Y., & Vuilleumier, P. (2015). Temporal dynamics of musical emotions examined through intersubject synchrony of brain activity. *Social Cognitive and Affective Neuroscience*, *10*(12), 1705–1721. https://doi.org/10.1093/scan/nsv060

Tyler, L. K., Shafto, M. A., Randall, B., Wright, P., Marslen-Wilson, W. D., & Stamatakis, E. A. (2010). Preserving Syntactic Processing across the Adult Life Span: The Modulation of the Frontotemporal Language System in the Context of Age-Related Atrophy. *Cerebral Cortex*, *20*(2), 352–364. https://doi.org/10.1093/cercor/bhp105

Walhovd, K. B., Fjell, A. M., Reinvang, I., Lundervold, A., Dale, A. M., Eilertsen, D. E., Quinn, B. T., Salat, D., Makris, N., & Fischl, B. (2005). Effects of age on volumes of cortex, white matter and subcortical structures. *Neurobiology of Aging*, *26*(9), 1261–1270. https://doi.org/10.1016/j.neurobiolaging.2005.05.020

Watanabe, T., Yagishita, S., & Kikyo, H. (2008). Memory of music: Roles of right hippocampus and left inferior frontal gyrus. *NeuroImage*, *39*(1), 483–491. https://doi.org/10.1016/j.neuroimage.2007.08.024

Wilson, S. M., Molnar-Szakacs, I., & Iacoboni, M. (2008). Beyond Superior Temporal Cortex: Intersubject Correlations in Narrative Speech Comprehension. *Cerebral Cortex*, *18*(1), 230–242. https://doi.org/10.1093/cercor/bhm049

Wingfield, A., & Grossman, M. (2006). Language and the Aging Brain: Patterns of Neural Compensation Revealed by Functional Brain Imaging. *Journal of Neurophysiology*, *96*(6), 2830–2839. https://doi.org/10.1152/jn.00628.2006

Appendix A

Western Research

Date: 8 March 2019

To: Jessica Grahn

Project ID: 100606

Study Title: Neural mechanisms of rhythm and music perception - 18067E

Application Type: HSREB Amendment Form

Review Type: Delegated

Full Board Reporting Date: 26March2019

Date Approval Issued: 08/Mar/2019 11:08

REB Approval Expiry Date: 06/Jun/2019

Dear Jessica Grahn ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
GrahnProtocol_OurBrainsCAN - clean	Protocol	05/Mar/2019	1
LOI_OurBrainsCAN - clean	Consent Form	05/Mar/2019	1
OlderAdultPoster-2-clean	Recruitment Materials	07/Mar/2019	2

REB members involved in the research project do not participate in the review, discussion or decision.

The Western University HSREB operates in compliance with, and is constituted in accordance with, the requirements of the TriCouncil Policy Statement: Ethical Conduct for Research Involving Humans (TCPS 2); the International Conference on Harmonisation Good Clinical Practice Consolidated Guideline (ICH GCP); Part C, Division 5 of the Food and Drug Regulations; Part 4 of the Natural Health Products Regulations; Part 3 of the Medical Devices Regulations and the provisions of the Ontario Personal Health Information Protection Act (PHIPA 2004) and its applicable regulations. The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Nicola Geoghegan-Morphet, Ethics Officer on behalf of Dr. Joseph Gilbert, HSREB Chair

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Appendix B

Western Research

Date: 27 June 2019

To: Dr. Adrian Owen

Project ID: 114263

Study Title: Behavioural study of musical memory

Application Type: NMREB Initial Application

Review Type: Delegated

Full Board Reporting Date: 05/Jul/2019

Date Approval Issued: 27/Jun/2019 11:41

REB Approval Expiry Date: 27/Jun/2020

Dear Dr. Adrian Owen

The Western University Non-Medical Research Ethics Board (NMREB) has reviewed and approved the WREM application form for the above mentioned study, as of the date noted above. NMREB approval for this study remains valid until the expiry date noted above, conditional to timely submission and acceptance of NMREB Continuing Ethics Review.

This research study is to be conducted by the investigator noted above. All other required institutional approvals must also be obtained prior to the conduct of the study.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
Compensation	Online Survey	26/Jun/2019	1
LOI_4	Implied Consent/Assent	26/Jun/2019	4
LOI_Scheduling_LOIBlocked	Online Survey	26/Jun/2019	1
Session1	Online Survey	26/Jun/2019	2
Session2A	Online Survey	26/Jun/2019	2
Session2B	Online Survey	26/Jun/2019	2
Session3-5A	Online Survey	26/Jun/2019	2
Session3-5B	Online Survey	26/Jun/2019	2
Session6	Online Survey	26/Jun/2019	2
SONAad	Recruitment Materials	10/Jun/2019	1
WebsiteAd_2	Recruitment Materials	20/Jun/2019	2

No deviations from, or changes to the protocol should be initiated without prior written approval from the NMREB, except when necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

The Western University NMREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the Ontario Personal Health Information Protection Act (PHIPA, 2004), and the applicable laws and regulations of Ontario. Members of the NMREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB. The NMREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000941.

Please do not hesitate to contact us if you have any questions.

Sincerely,

Katelyn Harris, Research Ethics Officer on behalf of Dr. Randal Graham, NMREB Chair

Note: This correspondence includes an electronic signature (validation and approval via an online system that is compliant with all regulations).

Appendix C

Below is a table describing the distribution of novel stimuli across the experiments detailed in Chapters 2-5.

All stimuli were created using the lyrics and music of songs written and recorded by Adrian M. Owen between 1997 and 2006 for an amateur rock band based in Cambridge, UK. The stimuli were therefore unknown to the Canadian participants in our studies.

The a capella stimuli used only the vocal tracks from the original songs. The instrumental stimuli used only the instrumental tracks from the original songs. The spoken stimuli were re-recorded by A.M.O. in spoken form to have a similar length, tempo, and emotional intonation as their original song counterparts. The whole stimuli were presented as intact versions of the original songs.

All stimuli can be found at https://owenlab.uwo.ca/research/research_tools.html

Analysis	**Original Song Titles**	**Training Group**	**Category**	**Chapter**				**Participants**	
				2	**3**	**4**	**5**	**young**	**older**
10-s clips for GLM	Big in the City	A	a capella	x				x	
	Stones in Your Pocket	B	a capella	x				x	
	Tonopah	A	instrumental	x				x	x
	Killing Time	B	instrumental	x				x	x
	Take Off Not Landing	A	spoken	x				x	x
	Yeah Yeah	B	spoken	x				x	x
	People Like You	A	whole	x				x	x
	Superman	B	whole	x				x	x
Intersubject synchrony	Lost in Notting Hill	A	a capella		x			x	
	Waving Not Drowning	B	a capella		x			x	
	Half Life	A	instrumental		x	x		x	x
	Fun Loving Angels	B	instrumental		x	x		x	x
	Sold	A	spoken		x	x	x	x	x
	Thinking About You	B	spoken		x	x	x	x	x
	20th Century	A	whole		x	x	x	x	x
	Americans	B	whole		x	x	x	x	x

Curriculum Vitae

Education

2021: PhD Psychology, University of Western Ontario, London, Ontario, Canada.
Advisors: Dr. Jessica A. Grahn & Dr. Adrian M. Owen

2016: MSc Psychology, University of Western Ontario, London, Ontario, Canada.
Advisors: Dr. Jessica A. Grahn & Dr. Adrian M. Owen

2014: BSc Neuroscience (Honours), Brock University, St.Catharines, Ontario, Canada.
Advisor: Dr. Sidney Segalowitz

Honours Awarded

2021: Psychology Department Donor Award $650
G. Keith Humphrey Memorial Award

2018: Trainee Travel Award, $350
Promoting Healthy Brain Aging and Preventing Dementia Conference

2018: CIFAR Women in Science Leadership Workshop, Kigali, Rwanda

2017: NSERC Postgraduate Scholarship - Doctoral, $63 000

2017: Award for Outstanding Teaching Assistant Contributions, $50
Council of Canadian Departments of Psychology

2016: Ontario Graduate Scholarship, $15 000

2015: NSERC Canada Graduate Scholarship - Master's $17 500

2015: Ontario Graduate Scholarship, $15 000 (declined)

2013: NSERC Undergraduate Student Research Award, $6000

2013: Writing Award - Department of Psychology, $100

2013: Dean's Award for Good Writing - Faculty of Social Sciences, $100

Peer-Reviewed Publications

2021: **Sternin, A**. McGarry, L.M., Stojanoski, B., Grahn, J.A., Owen, A.M. (2021). The effect of learning on intersubject synchrony.
In preparation for submission to Cortex.

2021: **Sternin, A**. McGarry, L.M., Owen, A.M., Grahn, J.A. (2021). The effect of familiarity on neural representations of music and language. *Journal of Cognitive Neuroscience*, 33(8), doi:10.1162/jocn_a_01737

2021: Huntley, J., Bor, D., Fleming, S.M., Mancuso, M., Mediano, P., Naci, L., Owen, A.M., Rocci, L., **Sternin, A**. Howard, R. Assessing awareness in severe Alzheimer's disease. *In preparation*

2019: **Sternin, A**., Burns, A., Owen, A.M. (2019). 35 Years of Computerized Cognitive Assessment of Aging — Where are we now? *Diagnostics*, 9(3). doi:10.3390/diagnostics9030114

2017: Segalowitz, S. J., **Sternin, A**., Lewis, T. L., Dywan, J., Maurer, D. (2017). Electrophysiological Evidence of Altered Visual Processing in Adults who Experienced Visual Deprivation During Infancy. *Developmental Psychobiology*, 59(3), 375-389. doi:10.1002/dev.21502

Book Chapters

2019: McGarry, L., **Sternin, A**., Grahn, J.A. (2019). Music and Movement. In Rentfrow, P.J. & Levitin, D.J. (Eds.), *Foundations in music psychology: Theory and research*.

2018: Stober, S. & **Sternin, A**. (2018). Decoding music perception and imagination using deep learning techniques. In Tanaka, T. & Arvaneh, M. (Eds.), *Signal processing and machine learning for Brain-Machine Interfaces*.

Other Publications

2015: Stober, S., **Sternin, A**., Owen, A.M., Grahn, J.A. (2016). Deep Feature Learning for EEG Recordings. In: *arXiv:1511.04306 2015*. (submitted as conference paper for ICLR 2016).

2015: Stober, S., **Sternin, A**., Owen, A.M., Grahn, J.A. (2015). Towards Music Imagery Information Retrieval: Introducing the OpenMIIR Dataset of EEG Recordings from Music Perception and Imagination. *Proceedings of the 16th International Society for Music Information Retrieval Conference*. Malaga, Spain.

2015: **Sternin, A**., Stober, S., Owen, A.M., Grahn, J.A. Tempo Estimation from the EEG signal during perception and imagination of music. *Proceedings of the 1st International Workshop on Brain-Computer Music Interfacing*. Plymouth, UK.

Oral Presentations

2021: Music and language affect strength of inter-subject synchrony in young and older adults
ICMPC, Online Conference

2018: Classifying music, speech, and rhythm perception and imagination using EEG
Invited Speaker
Decoding Mental States Using EEG, Montreal Neurological Insitute

2017: Classifying rhythm and speech from the EEG signal
Symposium on Timing and Rhythm, McMaster University

2015: Similarity and feature learning for EEG recordings of music perception and imagination
Fifth Annual Cognitive Based Music Informatics Research, Toronto, ON
Awarded the Best Paper Award

2015: Tempo Estimation from the EEG signal during perception and imagination of music
First international workshop on Brain-Computer Music Interfacing, Plymouth, UK

Poster Presentations

2018: Identifying the neural correlates of music familiarity using a strict training paradigm
Society for Neuroscience, San Diego, CA

2018: Fine tuning cognitive assessment in the elderly using an online test battery
Promoting Healthy Brain Aging and Preventing Dementia Conference, Banff, AB

2017: Identifying characteristics of perception and imagination of rhythms and speech in an EEG signal
Neuroscience and Music VI: Music, Sound and Health, Boston, MA

2015: Classifying Perception and Imagination of rhythms and speech from EEG
Inaugural Brain and Mind Symposium, London, ON

2015: Classifying Perception and Imagination of Music from EEG
Society for Music Perception and Cognition, Nashville, TN

2015: Differentiating Music Perception and Imagination Using EEG-processing
Lake Ontario Visionary Establishment 44th Annual Conference, Nashville, TN

2014: Electrophysiological evidence of altered visual processing in adults with blocked pattern vision during infancy
Society for Psychophysiological Research (SPR) 54th annual meeting, Atlanta, GA

2014: Electrophysiological evidence of altered visual processing in adults with blocked pattern vision during infancy
Compute Ontario Research Day, Waterloo, ON

2015: Electrophysiological evidence of altered visual processing in adults with blocked pattern vision during infancy
Southern Ontario Neuroscience Association, London, ON

Professional Experience

2019: Member of the MSc Grant Review Panel
Branch Out Research Foundation

2018: Interview for Music Science Podcast âĂŸSo StrangelyâĂŹ
Episode 7: Society for Neuroscience 2018 Music Science Review

2017-2019: Chair - Western Women in Neuroscience

2017-2019: Brain and Mind Institute - Move Team
Graduate Representatitve

2016-2019: Brain and Mind Institute - Steering Committee
Graduate Representative

2016: Co-Chair - Inspiring Young Women in STEM conference

2016: Undergraduate Outreach Symposium - Lead Organizer

2015-2019: Brain and Mind Institute - Tour and Research Demonstrations Organizer
TD Discovery Days, Musical Learning Across the Lifespan, Take Your Kids to Work Day, Canadian Association for Girls in Science

2015-2016: Executive - Psychology Graduate Students Association

2015: Member of the Graduate Student Teaching Awards Committee

2015: Program Support Team - Society for Music Perception and Cognition

2013-2014: Student Senator on the University Senate

2013-2014: Student Representative on the Student Appeals Board

2013-2014: Students' Union Academic Affairs Committee Member

Teaching Experience

2016-2021: Undergraduate Honours Thesis supervisor

- Jai Ravipati (2020/21) *co-supervised with Sarah Schwann*
- Ben Shapiro (2017/18) *co-supervised with Dr. Christina van den Bosch der Nederlanden*
- Neeraja Murali Dharan (2017/18) *co-supervised with Dr. Molly Henry*
- Garret Myles (2016/17)

2016: Cognitive Neuroscience of Music - 4 guest lectures

2014-2020: Graduate Teaching Assistant