Fine tuning Alzheimer's Disease (AD) treatment with Music-Based Interventions (MBI): An anatomical overview

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Abstract

Music is as universal as language itself across human culture. Music processing in the human brain is a dynamic and complex interplay of sensory, cognitive, and emotional functions that promotes healthy amounts of brain activity. The use of music as a nonpharmacological treatment is actively being researched for its potential in treating and managing symptoms associated with neurological disorders Parkinson's disease (PD), Alzheimer's disease (AD), and Alzheimer's disease-related dementias (ADRD), or sudden brain injury such as a stroke. This paper will discuss the anatomical hallmarks of music processing, which sets the foundation for discussing the dynamic activation of other brain regions notably affected by Alzheimer's disease. We will discuss the imaging studies that engaged multiple brain regions that allowed researchers to conclude how Music-Based Interventions (MBIs) potentially contribute to the enhancement of networks and pathways involved in sensory and motor processes and AD patient psychopathological outcomes.

Music Processing in the Brain

Music, a ubiquitous aspect of the human experience, can transport us through a multitude of physical sensations in milliseconds, yet it begins as something we can't see, touch or smell: tiny vibrations that swirl through the air. Those unique vibrations form notes, which merge into something more complex. It starts as a tune, then a melody, and before you know it, you're humming along to a song you first listened to at a cafe one afternoon many years ago. But your brain is tricked into thinking it's back in that moment once again, reanimating the neurons that sparked vividly while the song kept playing, even giving you the same goosebumps that had emerged on your skin back then. Music processing begins its journey in the inner ears, where acoustic data transforms into an electric signal via the cochlea. This signal travels through the auditory nerve to the brain stem, specifically to the inferior colliculus– the main area where fundamental sound features like periodicity and intensity undergo initial processing. Then, auditory information is sent to the thalamus, where all sensory information is relayed except smell, to finally arrive at the auditory cortex (AC). The AC directly projects to limbic structures, i.e., amygdala and medial orbitofrontal cortex (LeDoux, 2000). The primary AC also interacts with the superior temporal areas which further analyze acoustic cues, frequency, pitch, sound level, tempo changes, motion, and spatial locations. The left AC is more attuned to process temporal information, while the right AC in spectral resolution, contributing to the lateralization of speech in the left hemisphere and music right hemisphere (Hall et al., 2003). These fundamental structures of the auditory cortex work are what make the most basic sound processing possible.

However, music processing and further perception involves regions that go a bit beyond basic sound processing. Neuroimaging, primarily fMRI studies, have shown that music engages a larger network of cortical regions including the inferior and medial prefrontal cortex, premotor cortex, anterior and posterior parts of the superior temporal gyrus, and the inferior parietal lobe (Janata et al., 2002) (Patel, 2003).

An emotion-inducing piece of music also activates the regions deep in the limbic system–such as the midbrain, the basal ganglia (primarily the nucleus accumbens of the striatum), the amygdala, and the aforementioned hippocampus and cingulate cortex which are also involved in the processing of memory. The group of researchers led by Blood et al. in 2001, were the first to publish results that showed evidence of music producing intense pleasure via PET scans. The scans showed increased blood flow to the areas ventral striatum, midbrain, amygdala, orbitofrontal cortex, and ventral medial prefrontal cortex (also involved in music memory), which were previously known to be activated during in response to "euphoria-inducing stimuli" (Blood et al., 2001). Moreover, the perception of music rhythm, synchronized movement to its beat, and music production via singing or playing an instrument engage the sensory-motor networks of the brain (Grahn et al. 2009). These encompass regions in the cerebellum, basal ganglia, and the motor and somatosensory cortices (Zatorre et al., 2007).

Based on comprehensive imaging data, researchers have developed an anatomical delineation of pivotal brain regions implicated in music processing, as illustrated in Figure 1. This foundational knowledge is crucial to know in order to grasp the potential therapeutic advantages and outcomes of Music-Based Interventions.

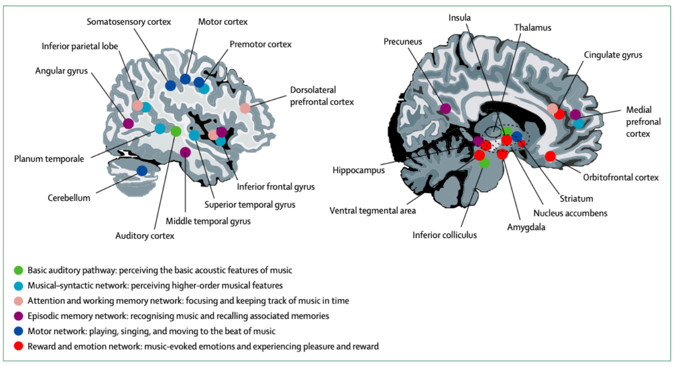

Figure 1. Key brain areas associated with music processing. Adapted from Särkämö and colleagues (Sihvonen et al., 2017)

Structures Affected by Alzheimer’s Disease

As we delve into the complexities of Alzheimer's Disease (AD), it's important to keep in mind our ultimate focus: understanding how Music-Based Interventions (MBIs) can offer new pathways in AD treatment. The progression of AD, marked by distinct neuropathological stages, sheds light on why and how MBIs might be uniquely poised to mitigate some of the cognitive and emotional deficits caused by this disease. Alzheimer's disease (AD) unfolds in distinctive neuropathological stages which start with the early accumulation of beta-amyloid plaques and the formation of tau tangles within the cell. In the mild cognitive impairment (MCI) stage, cognitive decline becomes noticeable, signaling dysfunction at the neuronal level. Progressing to the moderate stage, tau pathology spreads, which eventually impacts deep limbic and cortical regions involved in memory processing, ensuing widespread neuronal cell death (Ardent, 2009). At this point of AD, major deficits in memory, behavior, and emotions are noticeable and the major cause of decline in not just overall health but also quality of life (Alzheimer’s Association, 2023). With modern imaging techniques, researchers are now able to accurately map the structures of the brain that are affected by AD– which can aid the further development of therapeutic treatment options that can target these areas.

Using quantitative in vivo MRI techniques comparing healthy and AD brains, researchers noted initial structural changes in the medial temporal lobe, specifically the entorhinal cortex (deToledo, 2000). Further MRI studies combined with a series of linear regression showed that dysfunction in the entorhinal cortex disrupts communication between hippocampus and the prefrontal cortex (PFC) of the medial temporal lobe, which leads to more noticeable loss of function in memory, behavior, and emotional regulation (Killany et al., 2002). Connecting what we know about the areas uniquely activated by music processing and the areas affected in the progression of AD, the use of MBI’s has potential to more directly stimulate areas deep within the cortex. More recent evidence also points to the limbic system regions–which include the amygdala, ventral striatum, and insular cortex–as playing a crucial role in the development of loss of memory and emotional regulation (Peck, 2016). The amygdala, a crucial structure for emotional processing in the medial temporal lobe, is affected even in the early stages of AD according to Poulin et al. in 2011. Previous research shows that music can evoke a strong emotional response because it activates these areas of the limbic system as well. There are major overlaps between structures affected in AD and structures that involve music processing– this simple observation is what has propelled the development of MBIs as a plausible form of therapeutic intervention for patients affected by AD and other dementias.

Music Based Interventions

Music Based Interventions (MBI’s) were first developed in a series of workshops sponsored by the NIH in 2022 and have since published the NIH Music Based Intervention Toolkit (Edwards et al. 2023) which is a comprehensive paper delineating the main pillars of MBI’s and how to best integrate it as a non-pharmacological treatment for AD and other neurologic disorders. There is no current standard definition of an MBI because they are unique to each patient in regard to the music style, listening mode, cultural background, and personal significance.

It is also important to recognize the current model of care for dementia and where MBI’s fit into the current “standard”. According to the Alzheimer's Association in 2018, there are a set of recommendations for each category of patient centered treatment models. The integration of MBI’s would be most appropriate under Care of Behavioral and Psychological Symptoms of Dementia (BPSD), more specifically under the second recommendation of care developed by Scales et al. in 2018, which states to “implement nonpharmacological practices that are person-centered, evidence-based, and feasible in the care setting” (Fazio et al., 2018)

Despite the novelty of MBIs, there is research from the past decade that has already explored the potential therapeutic effect of music that provides insight on the efficacy of MBIs. Särkämö et al. completed three different studies over the course of 2014-2016 regarding music listening versus music singing compared to standard care for dementia and AD. Both music listening and singing groups showed improvements in behavioral disturbances and physical signs compared to the control group. While these effects weren't sustained after 6 months, singing notably enhanced working memory in mild dementia and maintained executive function and orientation in young people with dementia. Music listening supported general cognition, working memory, and quality of life, particularly in moderate dementia without Alzheimer’s in institutional care. Both interventions alleviated depression, regardless of musical background. Music listening improved mood, general orientation, episodic memory, attention, executive functions, overall cognitive performance, and quality of life.This was a decently sized, single blind study with a total of 83 participants. A slightly larger study (n=100) investigated the effects of group music therapy versus standard care alone, and these results showed group music therapy not only decreased depression but also delayed the deterioration of cognitive functions, especially recall. More importantly, these effects persisted 1 month after they stopped the intervention (Chu et al., 2014). Interestingly, music familiar to the listener distinctly activates the anterior cingulate and medial prefrontal cortex in a healthy brain, indicating their significance in musical memory (Jacobsen et al., 2015). In AD individuals, the medial prefrontal cortex experiences a slower degeneration compared to other cortical areas. Moreover, the regions responsible for encoding musical memory exhibit minimal atrophy or decline in glucose metabolism, despite similar amyloid-β deposition when compared to other cortical regions. These findings potentially explain why Alzheimer's patients can still recognize and emotionally respond to familiar songs, even in advanced stages of the disease (Jacobsen et al., 2015).

Conclusion

Music, in its simplest form, dynamically engages sensory, cognitive, and emotional functions in the human brain. Understanding the neurological pathways of music processing in the brain is one of many facets that involve the further development of Music-Based Interventions as a nonpharmacological treatment for neurological disorders. MBIs show promise in enhancing networks crucial for sensory, motor processes, emotions, and memory. While there are still major improvements to be made in terms of further data collection process and understanding of the molecular dynamics of music processing in the human brain, the current exploration of music's therapeutic benefits represents a progressive shift toward addressing the complexities of brain disorders associated with different types of dementia. Other limitations of MBIs that could be addressed pertain to the duration of the effects of treatment and the factors that most influence the effects of the treatments to be sustained. Overall, MBIs emerge as an accessible and non-invasive treatment option in addition to traditional therapies, offering potential improvements in AD patient outcomes.

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