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Review Article,

Music Therapy As A Low-Cost Treatment for Alzheimer's disease

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Abstract:

Introduction
Alzheimer's disease affects over 55 million people globally, projected to double by 2030 and triple by 2050. It ranks among the top 10 causes of death, necessitating urgent treatment and cures. Music therapy positively impacts brain development and plasticity, particularly in the medial temporal lobe. It shows promise as a therapeutic approach for enhancing neuroplasticity in the hippocampus, benefiting individuals with Alzheimer's disease.

Materials and Methods
This review explores music therapy as a cost-effective and side-effect-free avenue for patients to alleviate neurodegenerative symptoms based on the analysis of 21 other articles published by renowned authors.

Discussion
Alzheimer's disease causes hippocampal abnormalities and cognitive decline. Music, with musical mnemonics and enhanced working memory, shows promise for memory improvement. Music therapy induces neuroplasticity, potentially treating hippocampal neuron loss. Vocal training improves psychomotor speed and reduces dementia symptoms. Further exploration of music therapy may offer novel strategies for alleviating Alzheimer's symptoms and benefiting neurological disorders. Mechanisms underlying therapeutic benefits require further investigation. Music therapy holds inherent potential for Alzheimer's and related neurodegenerative diseases.

Conclusion
Empirical evidence shows musical training enhances hippocampal plasticity and gray matter volume, suggesting music therapy may treat hippocampal neuron loss in Alzheimer's disease, improving working memory. It holds promise for Alzheimer's and related neurodegenerative disorders by enhancing hippocampal function, but further research on underlying mechanisms is needed.

Keywords: Alzheimer disease, music therapy, hippocampal plasticity, neuroplasticity, working memory, neurogenerative disorders

Introduction:

Alzheimer's disease (AD) is the most critical neurodegenerative disorder and a common form of dementia, impacting people over 65. Some leading risk factors include age, family history, genetics, and lifestyle, which can significantly affect its pathogenesis. AD is characterized by amyloid plaques, neurofibrillary tau protein tangles, and hippocampal synapse loss (1). It is characterized by prominent neurodegeneration in the hippocampal CA1 region (2). CA1 neurons are crucial in forming and retrieving episodic and declarative memories, often impaired in AD. As the disease progresses, CA1 neurons develop neurofibrillary tangles, abnormal tau protein accumulations, and amyloid plaques, aggregates of beta-amyloid protein. These pathological changes lead to synaptic dysfunction, impaired neuronal communication, and neuronal loss in the CA1 region. The degeneration of CA1 neurons contributes significantly to profound memory impairment in individuals with AD. Anxiety, agitation, hallucinations, and apathy are commonly observed psychological symptoms in individuals with AD. However, the most prevalent symptom is memory loss. The prevention or reversal of hippocampal damage can benefit individuals with AD. Music therapy can potentially enhance hippocampal plasticity in AD, helping the brain's cognitive processes.

Music can affect brain function by stimulating interconnected brain regions, leading to various effects such as reduced stress levels, and increased emotional arousal (3, 4). Music engages multiple neural processes, influencing memory, learning, and emotional responses significantly (5). The brain receives music as sound waves through the ear (6). These sound waves travel through the external auditory canal, striking the tympanic membrane (eardrum) and causing vibrations. These vibrations pass through the middle ear's ossicles (malleus, incus, and stapes) and reach the oval (vestibular) window, which separates the middle ear from the fluid-filled cochlea. The cochlea, resembling a spiral-shaped snail shell, contains auditory receptor cells (hair cells) responsible for auditory processing. Within the cochlea, sound vibrations displace the basilar membrane, housing the organ of Corti. The organ of Corti comprises inner and outer hair cells, supported by specialized cells called supporting cells. The primary role of converting mechanical vibrations into electrical signals that the auditory system can process lies with the inner hair cells. Equipped with stereocilia, tiny hair-like structures, the hair cells respond to the movements of the basilar membrane, bending in response to sound-induced vibrations. As the stereocilia sway, mechanoelectrical transduction channels are activated, allowing ions to flow and neurotransmitters to be released. These neurotransmitters transmit auditory signals from the hair cells to the auditory nerve fibers, which comprise the vestibulocochlear nerve. The auditory nerve fibers carry the neural signals from the cochlea to the brainstem, specifically the cochlear nucleus. From there, the signs are relayed to the superior olivary complex, the lateral lemniscus, and ultimately reach the thalamus's inferior colliculus and medial geniculate nucleus. Finally, the primary auditory cortex in the temporal lobe receives the information, where complex auditory processing and perception occur. The flow of acoustic data from the primary auditory cortex to other brain regions, including the hippocampus, contributes to the formation of auditory memories. This intricate processing pathway allows for the perception, interpretation, and storage of music and other auditory stimuli in the human brain.

The hippocampus, situated in the medial temporal lobe, possesses a seahorse-like shape and is bilateral. It comprises distinct subregions, including cornu ammonis (CA), dentate gyrus (DG), and subiculum. The CA region, resembling rams' horns, further divides into CA1, CA2, CA3, and CA4, each playing specific roles within the limbic system. The entorhinal cortex (EC) acts as a gateway in the medial temporal lobe system, facilitating the integration of sensory information between the neocortex and the hippocampus (7, 8). The neocortex, especially the anterior temporal neocortex, processes auditory information by analyzing the acoustic features of different objects and instruments, contributing to auditory object processing (9). While the connectivity between the auditory cortex and the hippocampus is still being studied, evidence suggests a direct projection from the auditory cortex to the parahippocampal cortex, which then connects to the posterior hippocampus (10). These neural connections provide a pathway for music and music therapy to influence hippocampal function potentially. Understanding the intricate relationship between auditory processing pathways and the hippocampus sheds light on how music may positively impact memory formation and cognitive processes.

The hippocampus plays a vital role in two primary circuits: the trisynaptic circuit and the monosynaptic circuit, both facilitating the transmission of information from the EC to the hippocampus. These circuits differ in the type of information they convey. The perforant path facilitates data communication from the entorhinal cortex (EC) to the trisynaptic circuit's dentate gyrus (DG). Signals continue their transmission within the trisynaptic course, connecting the dentate gyrus (DG) to CA1, involving intermediate pathways like the mossy fibers and Schaffer collaterals. On the other hand, the monosynaptic circuit allows for direct transmission of information from the EC to CA1, bypassing intermediate regions. Studies by Basu and Siegelbaum in 2015 discovered a slight delay of approximately 15-20 milliseconds between transmitting information in the trisynaptic and monosynaptic circuits (11). Additionally, research has shown that CA1, within the trisynaptic course, integrates spatial and nonspatial sensory details. The function of CA1 in comparing spatial sensory inputs with stored mnemonic information implies its role in forming episodic memories, encompassing recollections of past events and personal experiences.

The hippocampus can be impaired in forming new declarative memories due to damage or degeneration. The phenomenon has been extensively researched on individuals like Henry Molaison, who had temporal lobe-related seizures. Molaison underwent bilateral temporal lobe resection to alleviate his seizures, removing a significant portion of his hippocampus and adjacent temporal lobe structures. As a result, Molaison experienced a profound inability to form new episodic memories. Individuals with similar hippocampal damage also exhibit severe impairment in long-term memory formation, while other cognitive functions, including short-term memory, remain relatively intact (12). The research on Henry Molaison resulted in the recognition of anterograde amnesia, a condition observed not only in Alzheimer's disease cases but also in individuals with traumatic brain injury and various neurological disorders. Detailed investigations of such cases have established a strong association between AD and the significant deterioration of memory functions due to hippocampal degeneration.

The auditory cortex's connection with the hippocampus facilitates music therapy's impact on hippocampal function. This process involves encoding pitch patterns and timbre memories through synaptic plasticity in the hippocampus's primary circuits. As a result, individuals can recall previously heard songs and musical compositions, regardless of their musical background. The auditory cortex processes auditory inputs like pitch, tone, and duration, contributing to memory formation in the hippocampus. This process activates other brain structures like the nucleus acumens and amygdala, linked to retrospective processing and emotional responses (13). Considering AD's impact on the CA1 region of the hippocampus, music therapy holds promise as a therapeutic intervention to mitigate hippocampal damage (14).

Materials and methods:

This article is a comprehensive overview analyzing 21 articles by authors published in renowned scientific publications and peer-reviewed journals. It provides insights into the neurological aspects of Alzheimer's disease and highlights music therapy as a therapeutic approach. The information gathered from these sources was meticulously examined, analyzed, and systematized to present a fully completed scientific work that characterizes the potential of music therapy as a treatment for Alzheimer's disease.

Discussion:

Hippocampal abnormalities can lead to impaired cognitive abilities and reduced quality of life. Neurodegenerative disorders like AD involve hippocampal neuron loss, leading to investigations into neurogenesis as a potential therapy. Neuropeptide growth factors have also demonstrated their ability to aid neurogenesis. However, the slower rate of neurogenesis compared to hippocampal volume reduction in moderate to severe cases poses a challenge for AD treatment (15). Enhancing hippocampal plasticity offers a potential way to improve the well-being of individuals with hippocampal damage. Additional extensive studies on hippocampal repair are paramount in devising interventions for AD.

Alzheimer's disease (AD) profoundly impacts memory, cognitive functions, and thinking abilities. The atrophy of the hippocampus in AD patients often results in memory loss and difficulty retaining new memories over extended periods. In a study by Simmons-Stern et al., Alzheimer's patients were examined to assess their response to different auditory stimuli, specifically different lyrics formats (16). The findings showed that AD patients exhibited higher accuracy in recognizing songs when presented in a sung format than in said form. This suggests that musical mnemonics, which use melodic patterns for memorization, may assist individuals with AD in acquiring new information.

Additionally, investigations have examined the relationship between musical training and working memory (WM). It involves the short-term retention of a limited amount of information for brief durations. It plays a vital role in appreciating musical experiences and enabling predictions of upcoming events. Studies have indicated that musicians have enhanced WM abilities compared to non-musicians, and the evidence suggests that musical training improves auditory memory encoding in neuronal networks. (17, 18). These findings suggest that music could help improve memory functions in AD patients.

The impaired capacity to form memories in individuals with Alzheimer's disease (AD) also directly correlates with the loss of gray matter volume in the hippocampus. A study conducted by Groussard et al. in 2014 demonstrated that musical training could increase gray matter volumes in various brain regions among musicians. During music therapy, the researchers observed progressive changes in the hippocampus, temporal lobe, and motor cortex (19). Shortly after engaging in musical therapy, neuroplasticity was observed in the left side of the hippocampus and the region of the superior frontal cortices. Although the results were promising, further studies are required to assess the impact of musical training on distinct brain regions and neural circuits and to determine whether music therapy can mitigate or lessen Alzheimer's-induced brain atrophy.

Music therapy's potential for Alzheimer's disease treatment:

Researchers delved into music therapy as a potential therapeutic approach for Alzheimer's disease, recognizing its ability to enhance neurological functions in specific brain regions. Satoh et al. (2015) investigated vocal training's impact on individuals with mild to moderate AD, with weekly sessions for six months and home singing practice three times a week. Satoh and colleagues reported significant improvements in psychomotor speed and reduced dementia symptoms among patients in the experimental group after the 6-month vocal training program (20). Another comprehensive literature review conducted in 2017 also supported the positive effects of music therapy on attention, memory, and executive functions in individuals with AD (21). The available research suggests a correlation between musical training and increased plasticity in motor and administrative brain regions, along with alleviating dementia symptoms.

Previous studies on the impact of Music on Alzheimer's disease have predominantly focused on music-related interventions. However, the potential benefits and effectiveness of instrumental and vocal training as treatment approaches have yet to be thoroughly explored. Considering the mounting evidence suggesting that music therapy enhances hippocampal plasticity and improves cognitive functions impaired in AD, it is proposed to systematically investigate the application of formal vocal and instrumental music training as a therapeutic approach to address hippocampal degeneration caused by Alzheimer's. By incorporating a wide range of instruments and implementing tailored training programs, this research avenue holds excellent promise in uncovering novel strategies to alleviate AD symptoms and potentially benefit individuals with other neurological disorders. Ultimately, such investigations may have far-reaching implications for the large population affected by AD.

Conclusion:

Empirical evidence supports that musical training can enhance hippocampal plasticity and increase gray matter volume, specifically in the hippocampus. These neuroplastic changes suggest that music therapy could be used to treat the hippocampal neuron loss seen in Alzheimer's disease. Particularly noteworthy are the observed improvements in working memory, highlighting the therapeutic potential of musical training for conditions that impact hippocampal function. This therapeutic approach could benefit Alzheimer's disease patients, who often experience memory and hippocampal integrity deficits. Although studies have shown symptom alleviation in Alzheimer's disease through music therapy, further research is needed to understand the mechanisms underlying these therapeutic benefits. Given its inherent potential, music therapy shows promise as a therapeutic intervention for Alzheimer's disease and related neurodegenerative disorders.

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