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Harmonious Healing: A Review of Music Therapy, a Humanities-Based Approach to Alzheimer's Disease Treatment

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Cover Page Footnote

Figure 1 was adapted from "Histopathological Features of Parkinson's Disease and Alzheimer's Disease", by BioRender.com (2023). Retrieved from https://app.biorender.com/biorender-templates. Figure 2 was adapted from "Synapse with Astrocyte and Pathway (Layout)", by BioRender.com (2023). Retrieved from https://app.biorender.com/biorender-templates

Erratum

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Abstract

Alzheimer's Disease (AD) is a progressive neurodegenerative disease often characterized by memory loss, confusion, and overall cognitive decline. The aging global population has, in recent years, highlighted the fundamental lack of pharmacological treatments for individuals facing an AD diagnosis. In response, a growing body of research has shifted focus to non-pharmacological humanities-based interventions. One such intervention has been music therapy (MT). Music-focused measures have shown great promise as a method of slowing cognitive decline, but mixed results in the literature warrant the need for further investigation. Often, socioeconomic barriers can limit an individual's access to drug-related treatments, but the affordable and straightforward nature of music therapy circumvents these issues and further establishes the prospect for widespread use. In particular, these measures have been shown to rescue episodic and semantic memory, and due to their non-invasive nature, can be utilized as a proactive treatment strategy for young individuals at a higher risk for cognitive decline. This review aims to showcase the efficacy of music therapy as a novel humanities-based approach to AD management and indirect mechanism for improving emotional well-being.

Keywords: Alzheimer's Disease, Music Therapy, Cognitive Decline, Health Humanities

Author's Profile

Rohan Desai is currently a junior at the University of Kentucky (expected to graduate in May 2025) and is actively involved in the Lewis Honors College and the Chellgren Fellowship Program. He will receive a Bachelor of Science degree and plans to pursue a career in medicine as an Interventional Radiologist or Neuroradiologist. Rohan states "minimally invasive procedures have improved outcomes and patient recovery timelines considerably over the past few decades," and he hopes to contribute to more of that success as a physician.

As someone who grew up in a medically underserved rural area of Christian County, Kentucky, Rohan was exposed to the harsh reality of healthcare from a young age. One-to-two-hour drives to doctor's appointments were a staple of his childhood and the principal catalyst behind his motivation to pursue a career in medicine. As someone who has experienced how overwhelming the healthcare system can be, he hopes to make people feel like they have a voice—not just any voice, but specifically, a voice that is heard.

Rohan was specifically interested in publishing research with a humanities intersection because "numerous STEM disciplines, particularly medical research, are on the receiving end of billions of dollars in funding and grants aimed at addressing issues related to all aspects of our lives. The mistake most people make, however, is assuming the causes, and by extension, the solutions, for these issues are confined to the STEM world as well." Desai continues that "understanding how to find intersections between different ways of life and fields of study has proven difficult, but when successful, the results speak for themselves. This piece is just one example of how fruitful the relationship between the hard sciences and the humanities can be if given the chance to live up to its true potential."

Introduction

Alzheimer's Disease (AD) is the most common form of age-related dementia, with current projections estimating that over 153 million people will live with the disease by 2050. Clinical symptoms of AD include memory loss, impaired judgement, emotional instability, communication disability, and more. Pharmacological interventions have had limited success in treating AD, leading professionals to explore the efficacy of alternative management strategies. In particular, humanities-based methods, such as music therapy (MT), have become increasingly common in AD management plans. In this review, the existing literature on music interventions involving individuals with AD is examined to assess the impact of such measures on cognition and behavior.

Background

Functional Impact of AD

While the impact of AD on cognitive function has been well-documented, the clinical presentations of AD patients are modified by the presence of non-AD pathologies. Many patients report disturbances in sleep cycles, citing excessive sleep fragmentation and a greater tendency for daytime sleep. While such changes occur in normal aging, heightened severity often signals a worsening in dementia symptoms (Lucey 2). AD also frequently co-occurs with speech and language disorders, most notably aphasia and apraxia (Wang et al. 4808). Aphasia refers to the loss of ability to understand or express speech, often caused by damage to language centers in the brain. Logopenic/phonological progressive aphasia (LPA) is the form typically associated with AD and is characterized by difficulties in single-word retrieval, phrase repetition, and phonologic errors (Kirshner 709). Apraxia is defined as a disorder of skilled movements in which individuals fail to perform motor tasks when asked. Despite its use as a diagnostic criterion for AD, apraxia is seldom considered in reviews, although recent research has shifted away from this lack of focus (Lesourd et al. 234). Aphasia and apraxia often occur concurrently, which hinders an individual's ability to communicate and carry out coordinated gestures, effectively cutting them off from the outside world. As a result, depression and anxiety also plague many AD patients.

Pathology of AD

The pathological features of AD have also been well-documented. Extracellular senile plaques of amyloid beta (Aβ) protein as well as hyperphosphorylated tau protein neurofibrillary tangles are characteristic features of AD. More recently, transactive response DNA binding protein 43 (TDP-43) has been identified as another driver of cognitive decline. TDP-43 cytoplasmic inclusions are intracellular, a key difference from many Aβ plaques. AD patients with TDP-43 pathology show increased levels of cognitive decline, positioning the protein as a vital component of dementia pathogenesis. New evidence has also suggested that these three proteins colocalize and interact (Meneses et al. 5). As a whole, these pathologies

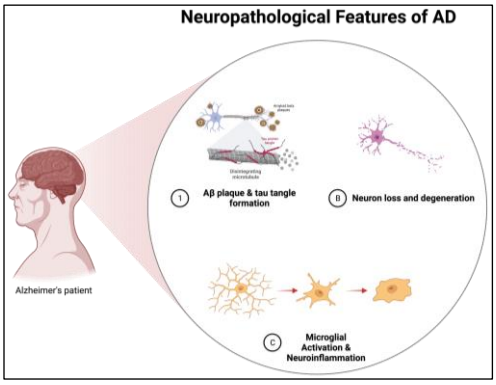

Figure 1: Pathological Features of AD

collect in and around neurons, impacting cellular functions, driving neuroinflammation, and even leading to cellular death (see Figure 1).

Another key component of AD pathology is mitochondrial dysfunction. Changes in the shape and size of mitochondria directly impair their metabolomic function. Moreover, the release of reactive oxygen species (ROS) as a result of impaired metabolism can result in inflammation and even cell death. Aβ plaques can also localize to mitochondria, which highlights the complex chain of events that lead to AD (Bhatia et al. 679).

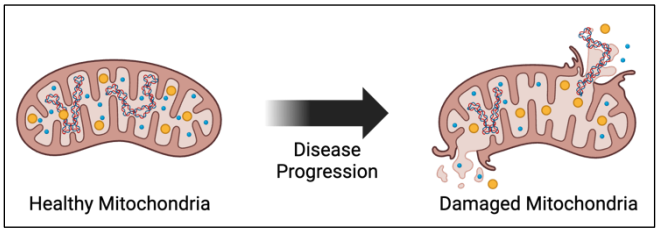

Figure 2: Mitochondrial Damage

Traditional Medical Interventions with AD

In recent years, many researchers have focused on developing novel therapeutics that can target the specific neurons that experience aberrant protein aggregation. Cholinergic neurons, involved in the production of the neurotransmitter, acetylcholine, are one such target. Levels of acetylcholine are markedly low in AD patients, supporting the notion that these neurons are lost or rendered non-functional by the pathological features listed above (Chen et al. 2). Studies have shown that acetylcholinesterase & cholinesterase inhibitors can increase the amount of acetylcholine in the brain by inhibiting its breakdown. Several drugs, namely Donepezil, Rivastigmine, and Galantamine have earned FDA approval by targeting this pathway (Yang et al. 4). See Figure 2 for the mechanism of action for these drugs. Although they hold promise, conflicting results have intensified the call for clinical trials with larger sample sizes to determine the true efficacy of these medications (Hsu et al. 8).

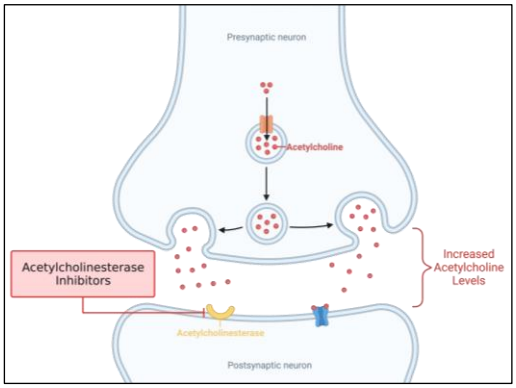

Figure 3: Mechanism of Action for Acetylcholinesterase Inhibitors

Another FDA-approved approach has utilized immunotherapies to target the Aβ plaques themselves instead of downstream effectors like neurotransmitters. The most well-known example is Lecanemab, a humanized IgG1 monoclonal antibody that binds to Aβ plaques in the brain. Clinical studies showed Lecanemab slowed the rate of cognitive decline and reduced amyloid levels in the brain over the course of the 18-month study (Van Dyek et al. 15). These results, while exciting, are limited due to the fact that clinical studies of Lecanemab have only been conducted in patients with early-stage Alzheimer's. Aducanumab, another immunotherapy that was granted accelerated FDA approval, faces similar calls for additional research.

Treatments do exist, however, for patients with moderate to severe Alzheimer's. Memantine, an N-methyl-D-aspartate (NMDA) antagonist, is a widely used example. Memantine works by regulating the levels of glutamate, an important neurotransmitter. Over-activation of glutamate receptors can have neurotoxic effects on the brain, which Memantine works to prevent. An additional benefit of Memantine is that its mechanism of action differs greatly from the drugs mentioned above, opening the door for simultaneous use with acetylcholinesterase inhibitors (Folch et. al 1224).

As a whole, pharmacological interventions are increasing in effectiveness every year, but the lack of universally accepted treatment plans has led many to turn to humanities-based methods of AD management.

Music Therapy

Music interventions, as an application of the health humanities, have grown exponentially in popularity to fill this void. To examine the effects of music therapy (MT), it is important to first define the features of the approach. MT is commonly defined as the "intentional use of music and musical experiences by a professional music therapist to enrich human life; alleviate human suffering; enhance physical, cognitive, emotional, and social functioning; and promote processes of normal development and self-actualization" (Aigen 2409). As the definition implies, music-based treatments involve more than simply playing music to patients. Active involvement of the patient in their care has been shown to provide the most benefits. This can include writing music, discussing components of a musical composition, and even singing in tandem with a song. The goal of this review is to establish the effectiveness of various music interventions on managing the clinical manifestations of AD and showcase the potential for further intersection between the humanities and healthcare.

Forms of Music Therapy

As referenced above, music therapy can take many forms, and these can be categorized into one of four domains: compositional, improvisation, receptive, and re-creative.

Compositional music therapy (CMT) is a form in which a therapist supports a client in creating their own lyrics or music. This strategy emphasizes creative processes with the hopes of specifically targeting problem-solving and organizational skills. Currently, CMT takes many forms, but the most common is *songwriting*. The widespread reach of music, via routes such as the radio and streaming services, make *songwriting* easy to implement and cost effective. Another distinct division of compositional therapy is *song-transformation*. Unlike *songwriting*, which tasks clients with creating something out of nothing, *song-transformation* involves taking an established piece of music and modifying specific aspects of the piece. As a collective, individuals that require music therapy, such as those with AD, are often dependent on others for care and need assistance to perform activities of daily living. To combat associated emotional impacts of this lifestyle, CMT promotes an internal locus of control and helps these clients verbalize their inner thoughts and emotions (Gardstrom and Sorel 122). Doing so can alleviate the symptoms of depression and isolation that may plague individuals with AD.

Improvisation music therapy is similar to compositional therapy in that it involves the creation of new musical pieces. However, several factors differentiate this strategy from the former. The obvious factor is its spontaneous nature, whereas compositional therapies are more structured. Likewise, improvisation music therapy often involves listening to music while spontaneously dancing. This helps patients organize their movements in space, which holds specific efficacy for disorders affecting conscious motion, such as Parkinson's Disease (Gardstrom and Sorel 122).

While the first two domains of MT involve the creation of novel ideas and compositions, receptive music therapy does quite the opposite. In this form, patients listen and respond to music, which can either be live or pre-recorded. Responses to the music can vary, with many patients preferring to write about their experience while others engage in verbal conversation. However, the goal of receptive music therapy, independent of the medium of expression, is not to confine individuals into a single, one-size-fits-all form. Enhancing mood, relieving anxiety, and encouraging relaxation are the primary goals of receptive therapy, and because of that, the best

approach is to individualize the treatment plan in question. *Song discussion* is a commonly used form that allows a group of people to listen to music and discuss their thoughts and feelings. By doing so, clients often report a decreased sense of isolation and more meaningful connections with their peers (Gardstrom and Sorel 117). Most importantly for this review, however, is the fact that receptive music therapy has documented benefits on memory, making it a well-studied avenue for AD management.

The final domain of music therapy is re-creative therapy. This style takes the key components of the first three and blends them together into one. Re-creative interventions involve reproducing music that has already been created. This can involve playing a well-known symphony on the piano or even singing karaoke. In essence, patients are tasked with interpreting a known composition and using that knowledge to perform it independently. While this may not stress creativity as explicitly as compositional or improvisational methods, re-creative styles have still been shown to affect cognitive function. Attention, sensorimotor skills, spatial orientation, and sociability all benefit from re-creative music therapy (Gardstrom and Sorel 124). An interesting aspect of this method is also its potential to exclusively target one side of the body. Studies have shown that music therapy, including re-creative methods, improves mobility and cognitive function in stroke patients. Arm movements associated with the weakened side of the body and even overall gait have shown improvements. The hypothesized mechanism of action for these effects is the rhythmic pattern that provides patients with a continuous cadence from which to map their conscious movements (Thaut and McIntosh 108). A similar strategy can be used to help organize memories, which will be explored in a later section.

Measures of Cognitive Function

To evaluate the efficacy of treatments, many different assessments can be administered to evaluate cognitive function and emotional state. The most common methods used to evaluate music therapy by the studies referenced in this review are listed below:

Mini-Mental State Examination (MMSE): Evaluates overall cognitive status on a scale of 0 to 30. Specific components include orientation, memory, attention, and language-motor skills (Arevalo et al. 9).

Neuropsychiatric Inventory (NPI): Examines 10 domains of behavior. These include elation, anxiety, irritability, disinhibition, apathy, aberrant motor disturbances, hallucinations, agitation, irritability, and delusions (Cummings 73). An updated 12-item exam adds sleep and appetite changes to the list of domains. Each of these symptoms is scored from 0-4 with respect to frequency, while severity is scaled from 0-3 (Gomez 302).

The Geriatric Depression Scale (GDS): 30-item (Long-Form) or 15-item (Short-Form) questionnaire comprised of Yes or No questions that reference how a patient felt over the last week. For Long-Form GDS, scoring is as follows: 0-9 is normal, 10-19 is mild depression, 20-30 is severe depressive state. Short-Form GDS follows a similar pattern: 0-4 is normal, 5-8 is mild depression, 9-11 is moderate depression, and 12-15 indicates severe depressive state (Kurlowicz and Greenberg 1).

Hamilton Rating Scale for Depression (HRSD): 17 to 29-item assessment to test for common symptoms of depression. Each question is scored on a 3-point or 5-point scale. For the 17-item version, which is the most commonly used, a score of 0-7 is considered normal, 8-13 signals subthreshold depression, 14-18 is mild, 19-22 is moderate, and scores above 22 are severe and warrant clinical intervention (Porter et al. 17).

Cohen-Mansfield Agitation Inventory (CMAI): A scale that examines agitation, a measure of emotional state. 29 agitated behaviors are scored on a 7-point scale of frequency. 1 corresponds

to least frequent, while a 7 means the behavior manifests multiple times per hour. A total score summed up to yield a range from 29-203, greater than 45 signals clinically significant agitation (Panca et al. 3).

Hospital Anxiety and Depression Scale (HADS): A 14-item questionnaire split into two subsections (anxiety and depression) with 7 questions each. Each item is scored on a 4-point Likert scale (0-3) that quantifies frequency, bringing the total possible score for each section to 21. Scores between 11-21 in either section signal abnormal levels of anxiety or depression (Michopoulos et al. 2).

The Montreal Cognitive Assessment (MoCA): 30-point test to detect mild cognitive impairment (MCI) in patients. Tested domains include visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation. Scores above 26 are considered normal, but those under this threshold signal MCI (Hobson 764).

Methods

Inclusion/Exclusion Criteria

For this review, studies published in the last 15 years (2008-2023) were assessed. The interventions used in each study must have been clearly defined as MT, through either individualized or non-individualized means. Moreover, a music therapist must have administered the treatments. Approaches tested without a music therapist, referred to as generalized therapies, were verified to have been conducted in controlled settings. The studies analyzed in this review were also exclusive to patients with AD. Other forms of dementia, including mixed dementia or Lewy body dementia, were not examined.

Search Strategy

The electronic databases, PubMed and ScienceDirect, were searched using varying combinations of the following key terms: “AD”, “music therapy”, “music intervention”, and “cognitive decline”. The results from these searches were then examined to see if they met the aforementioned inclusion and exclusion criteria.

Results

Search Results

Initial screening using the key terms listed above yielded 49 results. After removing repeat articles and enforcing the remaining search criteria, six studies were identified as viable candidates for review (See Table 1).

Table 1

Study	Measures Used	Participants	Key Outcomes
Wang et al. (2017) *International Journal of Clinical and Experimental Medicine*	MMSE, MoCA, & NPI	60 patients with mild AD symptoms	Music therapy helped improve cognitive function and decrease behavioral symptoms, such as depression, in mild AD.
Gallego and García (2017) *Neurología (English Edition)*	MMSE & NPI	42 patients with mild to moderate AD symptoms	Cognitive scores improved significantly following music therapy, but no appreciable impact on depressive symptoms was observed.
De la Rubia et al. (2018) *Journal of Alternative and Complementary Medicine*	Enzyme-Linked Immunosorbent Assay (ELISA)	25 patients with mild AD symptoms	Music therapy helped significantly decrease symptoms of depression and anxiety as measured by salivary cortisol levels.
Guétin et al. (2009) *Dementia and Geriatric Cognitive Disorders*	HRSD & GDS	30 patients with mild to moderate AD symptoms	Music therapy reduced depression and anxiety levels. Notably, this decrease was sustained 8 weeks after interventions were stopped.
Fukui et al. (2012) *International Journal of Alzheimer's Disease*	Salivary 17 β-estradiol and testosterone tests	6 female AD patients with mild symptoms	Music therapy increased levels of 17 β-estradiol and testosterone, which are hormones thought to have protective effects on the AD brain.
Sakamoto et al. (2013) *International Psychogeriatrics*	Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD)	39 individuals with severe AD symptoms	Individualized music therapy provided greater benefits for emotional state of the patient than generalized interventions.

Effects of Music Therapy on Cognitive Function and Emotional State

Using the measures outlined previously, several studies have quantified the effects of music therapy on cognitive function and emotional state. One study examined the compound effect of music therapy when used in tandem with traditional drug therapies. Sixty patients with

mild AD were chosen for participation and divided into two groups: observational and control. The control group was treated with a drug therapy, while the observational group received both drug and music therapy concurrently. Songs that were familiar to the age group of the observational group were chosen, and the patients were asked to sing along with the therapist. Three measures of cognitive function were used: MMSE, MoCA, and NPI. The study found no initial changes in MMSE scores, but three months following the study's conclusion, the observational group scored much higher on the MMSE. MoCA and NPI scores also improved in this group. These results demonstrate the impact music therapy can have on both cognitive function and behavior (Wang et al. 4813).

Similar studies have shown increases in MMSE scores in AD patients following music therapy, specifically in three domains: orientation, language, and memory. Decreases in NPI scores were also observed across the board (Gallego and García 302). However, these same studies conflict in their assessments on depression. A study conducted in 42 patients with mild to moderate dementia found MMSE and NPI score improvements, but no significant improvement in depression was seen (Gallego and García 302). Another study with a sample of 25 AD patients experiencing mild cognitive decline found significant decreases in depression and anxiety through measurements of cortisol, a stress hormone, levels (De la Rubia Ortí et al. 1). Similarly, Stéphane Guétin et. al found sustainable improvements in anxiety and depression levels up to 8 weeks after stopping MT interventions (36). These measures were quantified using the HRSD and GDS scales. In short, most studies support the notion that music therapy does improve cognitive function and behavior. Further research, however, is needed to assess the impacts of MT on emotional well-being.

Additional studies have aimed to quantify the hormonal impacts that may explain the benefits music therapy in AD management. Six female AD patients were chosen for participation in one such project. The songs that were used were chosen to reflect the preferences outlined by each patient in a survey, signaling an individualized approach. By monitoring salivary hormone levels of 17 β-estradiol, the researchers were able to find a significant increase in these levels following music therapy. A smaller increase was seen in the group that simply listened to music and did not engage in therapy, supporting the notion that individualized therapy is the optimal approach. 17 β-estradiol is a hormone that is thought to have preventative effects in AD. The sharp increase in salivary hormone levels highlights a potential biological mechanism of action for these therapies (Fukui et al. 3).

Different MT strategies were also found to impact brain function in distinct manners. Specifically, therapy that utilized individualized music playlists, as opposed to a standardized set of music, found greater positive outcomes for patients similar to the study outlined above. Sakamoto et. al directly compared passive and interactive strategies, and the results showed a significant reduction in behavioral and emotional symptoms of AD following individualized music therapy (Sakamoto et al. 782). As a whole, music that is familiar to the individual has greater benefits than music the patient does not know.

Discussion and Future Directions

In this review, six studies met the established criteria and were chosen for analysis. As a whole, MT was found to improve memory, cognitive capabilities, and behavioral symptoms of AD. Significant improvements in MMSE, NPI, MoCA, and more were observed following music therapy. More research is needed to see if these beneficial effects are sustainable following the end of therapy and determine the exact effects of MT on depression and anxiety.

Much like studies have tested the cumulative effects of MT and drug treatments, other research has sought to unify MT with other humanities-based interventions. Dance therapy, commonly used for physical disabilities, could be an interesting avenue of research. Few studies, if any, have looked at the effects of concurrent MT and dance therapy. This could hold promise in improving both cognitive and physical symptoms that may manifest in neurodegenerative diseases like Parkinson's Disease and ALS.

Based on this review, it is also not possible to determine an optimal music type for patients with AD. The "Mozart Effect" has been shown to increase spatial intelligence, but most studies on this effect have focused on children rather than cognitively impaired adults. The strength of this review is further limited due to differences in participant characteristics across studies as well as varying intervention methods. The small number of studies available exclusively for AD management also place a limit on these findings. However, many current reviews of music therapy focus primarily on the cognitive and behavioral assessments, while this piece also incorporates physiological tests, such as salivary 17 β-estradiol levels. This multi-faceted approach yields gives greater weight to the conclusions in this paper.

Overall, MT is a promising non-pharmacological treatment strategy for individuals with mild to moderate AD. These therapies demonstrate the utility of the humanities in health-related fields and warrant further investigation.

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