

# Harnessing Music Therapy to Alleviate Alzheimer's Disease Symptoms: A Review of Current Evidence

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Alzheimer's disease (AD) is a progressive brain disorder that causes memory loss and other cognitive decline. AD is the most common cause of dementia and usually affects people over 65 years. While there is currently no cure, there are pharmacological and non-pharmacological treatments that can alleviate the effects of AD. Several drugs have been approved for the treatment of AD and more drugs are being studied as potential therapies. Memory issues are a key feature of AD and typically worsen as the condition progresses. However, musical memory is partially preserved in patients with AD. Can a non-pharmacological intervention such as music play a role in AD treatment? This research aimed to identify the effects of music therapy as a non-pharmacological therapeutic intervention applied to AD. A literature review was conducted to compare pharmacological therapy to music therapy. Music therapy can reduce agitation and induce relaxation in individuals with AD. Music that has had significant influence in the individual's youth and early life is significantly more beneficial. Music therapy has the ability to alleviate some symptoms of AD and permits remarkable responses to be elicited in individuals. Future research should focus more on personalized approaches. This personalization might be supported by advanced technologies, such as AI-driven analysis of patients' responses to different types of music.

## Introduction

### Prevalence of Alzheimer's

Alzheimer's Disease (AD) is the most common neurodegenerative disorder characterized by progressive cognitive impairment and neuropsychiatric symptoms<sup>1,2</sup>. AD is currently ranked as the seventh leading cause of death in the United States and is the most common cause of dementia among older adults<sup>3</sup>. While there is currently no cure, there are pharmacological and non-pharmacological treatments that can alleviate the effects of AD. Several drugs have been approved for the treatment of AD and a larger number are being studied as possible therapies. However, current drug treatments have only symptomatic effects, and disease-modifying treatments are not yet available<sup>3</sup>. AD is an irreversible, progressive neurodegenerative disease associated with cognitive decline. According to Alzheimer's Association, nearly 7 million Americans are living with AD<sup>3</sup>. The number of people living with the disease doubles every 5 years beyond age 65, and this number could grow to 13.8 million by 2060<sup>4</sup>. Official death certificates recorded 121,499 deaths from AD in 2019, and AD was officially listed as the sixth-leading cause of death in the United States<sup>5</sup>. AD is the most prevalent type of dementia; it accounts for 60 – 80% of dementia cases. This is a disease that progresses, memory problems are typically among the first signs of cognitive impairment in AD, and it potentially ends with loss of ability to respond to surroundings.

### Potential relationship between music and AD

Significant episodes of our lives are accompanied by music. The brain can store memories and emotions during an event with music. Afterwards, retrieving memories can be prompted by the music associated with the memories. This effect can be useful to help individuals with loss of autobiographical memory. In AD patients, music can be used as an effective cue to recall autobiographical memories and elicit strong emotions, often offering a meaningful way to connect with themselves and their loved ones<sup>4</sup>. Anatomical areas in music perception and social cognition may be from the same area of the brain. Both music perception and social cognition utilize the same neurobiological circuits in frontotemporal dementia. Functional magnetic resonance imaging studies have been conducted to try to clarify how music affects cognition and behavior in AD. Previous studies propose music perception and social cognition use the same neurobiological circuits that are affected in AD. Brain imaging studies show neuronal circuits showing atrophy in AD patients are also functionally involved in music perception and social cognition<sup>6</sup>.

### Current Pharmacological Interventions

Although diagnostic technology to confirm the disease is improving, there are still no cures or treatment to halt or reverse the progression of AD. However, there are pharmacological and non-pharmacological interventions to treat cognitive and

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behavioral symptoms of the disease. There are currently six FDA-approved drugs for pharmacological treatment of the symptoms of AD as summarized in Table 1. These drugs may temporarily improve symptoms to a moderate degree, but they all have side effects, and their clinical impact remains modest and controversial<sup>7</sup>.

Table 1. FDA approved drugs for Alzheimer's Disease<sup>8</sup>

### Non-pharmacologic Interventions

Can a non-pharmacological intervention such as music play a role in AD treatment? Music interventions have been widely adopted as a potential non-pharmacological therapy with a long history of use for patients with AD to treat behavior, cognitive, and psychological symptoms of the disease<sup>4</sup>. In recent years, there has been focus and growing interest in non-pharmacological interventions for people with AD. Non-pharmacological interventions are easily implemented, versatile, and potentially cost-effective for people suffering from AD. It has the potential to improve and maintain cognitive performance, quality of life, and psychosocial aspects in mild to severe cognitive impairment, and fewer side effects makes them a favorable option also for preventive strategies<sup>9</sup>. Commonly used non-pharmacological interventions are cognitive therapy, physical activity, light therapy, music therapy, aromatherapy, animal-assisted therapy, etc. to improve symptoms of dementia<sup>10</sup>.

### Methodology

A literature review was conducted using the following search terms in the National Library of Medicine's PubMed database: music, therapy, and Alzheimer. This returned 149 results in the last 5 years. The following inclusion and exclusion criteria were used to assess which research was included in this study: full text available and type of articles: clinical trials, randomized controlled trials, meta-analysis. This yielded 11 studies. Of the 11 studies, 5 were excluded since music therapy was not the focus of the study. For 2 of the excluded studies exercise or music was combined with art and cognitive therapy. For the 2 other excluded studies, one study was a meta-analysis and other were focused on pain study. The last excluded study was a description of the neurobiological basis of dementia and music perception. Data were gathered and synthesized for the 6 remaining studies which 5 were randomized clinical studies and one quasi-experimental study.

### Analysis and Summary of Literature Review

Study No. 1 was cluster randomized quasi-experimental study with nursing home residents diagnosed with AD. The study of 90 AD patients were from nursing homes. The study

found that active music intervention improved symptoms of 3 clinical domains of AD, cognition, behavior, and functional state. Specifically, there was improvement in autobiographical memory. Adding music intervention for mild to moderate AD residents showed improvements<sup>11</sup>. Study No. 2 included 26 women and 6 men. In the randomized clinical trial (RCT), a singing based music therapy intervention improved feelings, positive emotions, and social engagement significantly more so than the comparison condition. The music therapy intervention resulted in significant positive effects on feelings, emotions, and social engagement, particularly for those with moderate dementia. The study provides empirical support for the use of music therapy to improve psychosocial well-being. Participants reported they felt better and demonstrated more pleasure in response to music therapy when compared to verbal discussion<sup>12</sup>. Study No. 3 included 24 females and 9 male, 82 % black, 18% white participants. In the RCT, the efficacy of music therapy on sleep disturbance was examined. Groups improved on objective sleep outcomes of sleep latency and wake sleep after onset. Tailored music intervention was based on the musical preferences of persons with dementia. Tailored music is an innovative and widely available approach that can be used to target sleep disturbances among older adults. In addition, the study had a positive effect of increasing total sleep duration<sup>13</sup>. Study No. 4 was a large study of 432 participants- 55% male 45% female. The RCT used home-based caregiver-delivered music intervention for people living with dementia to evaluate the effectiveness of a 12-week music intervention. There was no statistical or clinically important difference in the change between caregiver-delivered music, reading and usual care alone at 90-days. The study compared music, reading and standard care. Two-hour home-based session with a qualified music therapist instructed caregivers on receptive (music listening) and active (singing, movement to music, instrument playing) music methods. Instruction was provided on targeted use of music to regulate arousal and to stimulate autobiographical memories. Subgroup analyses suggest that people with moderate to severe dementia were more responsive to the music interventions than those with no or mild cognitive impairment but was not statistically significant. This supports previous research findings where people with moderate to severe dementia had larger enduring symptom reductions in response to music compared with those with milder symptoms. The study showed that neither music or reading interventions delivered by trained family caregivers, were beneficial in managing lasting behavioral and psychological symptoms or other health outcomes<sup>14</sup>. Study No.5 included 229 participants with 69 % (229) being female. The RCT studied beneficial effects from recreational choir singing. This study examined the two active music interventions: group music therapy and recreational choir singing. Subgroup analyses suggested group music therapy to be more beneficial in later-stage dementia than in earlier stages. In residents with

Table 1. FDA approved drugs for Alzheimer's Disease<sup>8</sup>

Active Name	Proprietary Name	Strength	Dosage Form	Mechanism of Action	Approval Date
Moderate to severe Alzheimer's Disease					
Memantine Hydrochloride	Namenda®	5 mg, 10 mg, 14 mg, 21 mg, 28 mg	Tablet, Capsule ER1	Reduction of chemical glutamate amount in brain	2003
Mild to moderate Alzheimer's Disease					
Galantamine Hydrobromide	Razadyne®	5 mg, 10 mg, 15 mg	Tablet DR2	Cholinesterase inhibitors, which boost brain levels of acetylcholine	2005
		8 mg, 16 mg, 24 mg	Capsule ER		
		4 mg/mL	Solution		
Rivastigmine	Exelon®	1.5 mg, 3 mg, 4.5 mg, 6 mg	Capsule		2000
		Transdermal 4.6 mg/24 HR, 9.5 mg /24 HR, 13.3 mg/24 HR	Film ER		
		2 mg/mL	Solution		
Donepezil Hydrochloride	Aricept®	5 mg, 10 mg, 23 mg	Tablet		1996
		5 mg/5 mL	Solution		
Donanemab	Kisunla®	350 mg/20 mL	Injection	Removal of brain amyloid, protein builds up in brain	2024
Lecanemab	Lequemi®	500 mg/5 mL	Injection		2023
1 Extended Release 2 Delayed Release					

Table 2. Summary of six studies on music therapy and AD

Study No.	Type of Study	Average Age	Number of Participants	Positive Outcome
1	Randomized quasi-experimental Study	84	90	Yes
2	Randomized Clinical Trial (RCT)	65	32	Yes
3	RCT	72	33	Yes
4	RCT	77	432	No
5	RCT	86	330	Yes
6	RCT	84	31	No

moderate to severe dementia, both group music therapy and recreational choir singing were beneficial in reducing depression at 3 months and recreational choir singing was also effective at 6 months. The study showed that recreational choir singing was beneficial for older care home residents with dementia and depressive symptoms. In addition, group singing led to clinically important improvements in depression, as well as neuropsychiatric symptoms and generic quality of life<sup>15</sup>. Study

No. 6 included 2 % (13) female and 58% (18) male participants who were 77 % white, 6.5 % black, and 12 % Hispanic. The RCT compared effects of chair yoga, compared to music intervention and chair-based exercise in this population. The chair yoga group improved significantly in quality of life compared to the music intervention group. No significant differences were observed in physical function, behavioral, or psychological symptoms including anxiety. There were no significant group differences among the 3 intervention groups for agitation level or sleep quality. Quality of life improved more in participants in the combined chair yoga and music intervention groups after the 12-week intervention than those in the music intervention group; both exercise groups showed improvement over time, while a decline was seen for the only music intervention group<sup>16</sup>. In addition, real-world relevance from case studies shows promising results. In one multiple case study, Improvements in cognitive functioning were observed for participants after music therapy<sup>17</sup>. In another case study report, a patient with AD showed reduction in social isolation and improvement in mood and prevention of cognitive decline when exposed to non-pharmacological interventions including music therapy<sup>18</sup>.

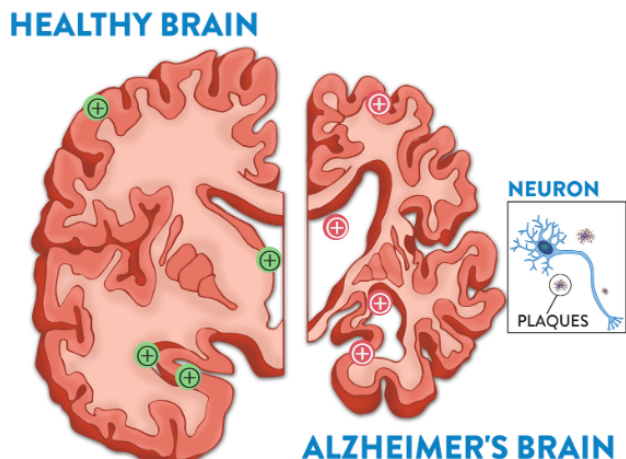


Fig. 1 The Healthy Brain vs. Alzheimer's Brain<sup>19</sup>

## Discussion

### The Brain with Alzheimer's Disease

The healthy brain does not lose a significant number of its neurons as it ages. However, many neurons stop functioning properly in AD, lose their connections with other neurons, and eventually die. Compared to a healthy person, the brain of an Alzheimer's patient is noticeably smaller. In fact, as the disease worsens, the brain can shrink to just one-third of its original size as shown in Figure 1. The brain shrinks as a result of neuronal deterioration and breakdown; the progressive loss of neurons (brain cells) and synapses (connections between neurons) in various regions of the brain, particularly those involved in memory, cognition, and decision-making<sup>3</sup>. As neurons die, the brain tissue shrinks.

Grey matter, a major component of the central nervous system, is vital for the functions of an individual's memory skills, "when diminished, it slows down every process which involves the use of the brain"<sup>20</sup>. Beta-amyloid plaques are abnormal clumps of protein fragments that build up between nerve cells in the brain. In AD, beta-amyloid plaques form which are tested to be toxic, "a disruption of balance between production and clearance of amyloid precursor protein leads to formation of amyloid- $\beta$  plaques, development of neurofibrillary tangles, neural dysfunction, regional atrophy and finally dementia"<sup>21</sup>. The imbalance of these plaques and clusters of them will disrupt cell function<sup>3</sup>. Neurofibrillary tangles are abnormal structures, bundles of twisted filament made up of abnormally formed protein, that form inside neurons in the brain. Both beta-amyloid plaques and neurofibrillary tangles are defining features of AD. In addition, neurofibrillary tangles accumulate, forming threads and tangles within neurons, causing the

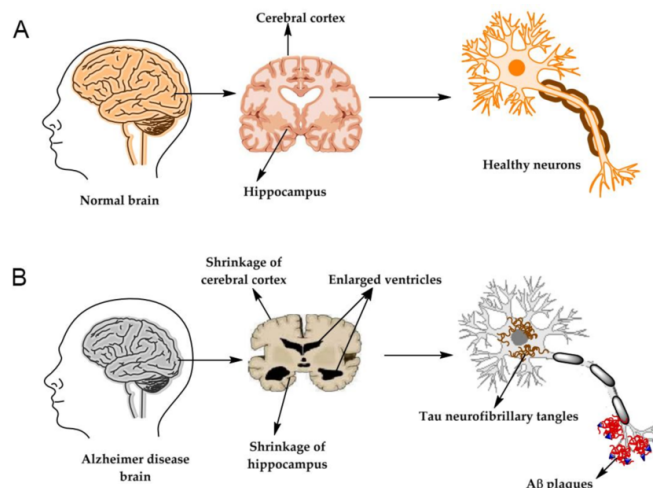


Fig. 2 The physiological structure of the brain and neurons in (a) healthy brain and (b) Alzheimer's Disease brain<sup>23</sup>

blockage of transportation of these vital cells and harm to the communication between them<sup>22</sup>. The decay of all this matter will also lead to brain atrophy and shrinkage of the volume of the brain, limiting space for transmissions of neurons and lacking cognitive functions. Some of these effects cause damage to the neurons, neurotransmitters, and decay of gray matter within the prefrontal cortex, cerebral cortex, and the hippocampus (Figure 2)<sup>3</sup>. These parts of the brain are responsible for memory and communication. Damages and decay in these areas will inevitably decrease the functionality and motor functions of the patient and lower the quality of life for them, specifically involving memory and communication.

### Music and Memory

Despite severe memory problems, patients with AD can remember music, and music can stimulate the formation of new nerve cells in the brain and facilitate recall of episodic memories<sup>6</sup>. Although music is one of the most abstract art forms, music has the ability to elicit palpable and actual physiological processes in the brain. Music therapy is a versatile therapeutic approach that can provide benefits for individuals with AD. Music therapy introduces a reliable and effective alternative, hence various music therapy techniques have been developed. When music is intercepted in the brain, both hemispheres of the brain are involved to interpret it. Music can stimulate feelings and memories even in individuals with advanced AD. Music possesses a special power to access memories, even in those with severe cognitive impairment. Through centuries of research, it is evident that music for memory can remain intact for persons with AD, even while experiencing rapid cognitive decline<sup>24</sup>. Cognitive and physical processes, including learning, mobility, and communication,

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have all been enhanced by music. Researchers found that “piano practice and music education can slow and even reverse the brain’s atrophy in certain parts of the brain, mediating cognitive decline in healthy older adults.”<sup>25</sup>. The study shows that patients recalled the words to songs dramatically better than they recalled spoken words. Furthermore, with consistent practice, some patients apparently are capable of learning a new song, even when they do not seem able to recall new spoken material; most who retain some self-care skills may be able to apprehend and react to music even when they cannot master learning the words<sup>26</sup>. Music therapy and music-based interventions have been proven to have great influence and effects on the brain. Although the idea may seem abstract, ideologies of music as medicine and the inextricable linkage between music and the brain have been utilized and researched in the ancient times<sup>27</sup>. “They equated the study of music with the power to balance the core faculties of the brain, harmonize the soul and achieve emotional catharsis. While our methodology and technology have evolved since then, the core search remains the same”<sup>27</sup>. In an experiment conducted by Petr Janata, selected subjects were exposed to historically popular excerpts of music where autobiographical memories were evoked<sup>28</sup>. In addition, individuals also evoked strong emotions related to these core memories, related to the music. This experiment essentially explains the correlation between emotions aroused by music related to specific events enhanced by memory<sup>29</sup>. Outside of emotional connections, music-based interventions can increase and improve the functionality and structure of the brain, showing evident improvements in the prefrontal cortex<sup>27</sup>. All of these benefits and effects of music on the brain and an individual’s cognitive processes can be applied to an individual with AD.

The negative effects on cognition in Alzheimer’s patients can be improved through music. AD involves the deterioration of cognitive functions in the brain that can be improved by the effects of music-based interventions. Although patients with Alzheimer’s do suffer from the disturbance of high cortical functions, specifically memory, they can still remember the tune or recite the lyrics of a song which was remembered and went through the processes mentioned before in their youth. An experiment focusing on the property of musical memory and its preservation found that, “Amyloid- $\beta$  deposition was predominantly found in the medial and orbital prefrontal cortex, precuneus and posterior cingulate. The primary sensorimotor cortex, occipital cortex, thalamus, and medial temporal lobe were relatively spared.”<sup>21</sup>. Rather than being stored in the hippocampus with ordinary memories, music is stored within the supplementary motor cortex which region is somewhat spared while the disease takes place. In areas where ordinary memories are stored and parts of the brain where other cognitive functions take place, they are targeted by the disease and amyloid plaques, causing much more deterioration and negative effects. On the other hand, the supplementary motor cortex and other spared

parts of the brain remain intact and preserved throughout AD. This allows music memory to be stored independently and also remain intact in a patient with AD, allowing music therapy to ensure its effects and benefits.

### **Familiar Music and Memory**

There is evidence that the music therapy intervention had a positive effect on reducing forgetting in episodic memory and evoking autobiographical memory. Episodic memory refers to the ability to recall specific events or episodes and involves remembering by re-experiencing; autobiographical memory encompasses more general knowledge about one’s life history and refers to information that directly involves the rememberer<sup>30</sup>. Patients with AD who listen to familiar songs have more enhanced autobiographical memory and mood than patients with AD who do not listen to familiar songs<sup>31</sup>. Studies which used individualized playlists resulted in improved outcomes for cognition and behavior in both active music therapy and music listening compared to methods that used experimenter chosen music<sup>31</sup>. Music therapist, caregivers, and /or healthcare professional work collaboratively to curate a playlist or music selection of approximately 15 – 30 songs based on each patient’s preferred music genres, favorite artists, and favorite songs. Music selection is often based on the personal preferences of the patient, including their past musical experiences, favorite genres, and familiar songs that can evoke positive memories or emotional responses<sup>32</sup>. In some protocols, the music is also chosen according to therapeutic goals, such as relaxation or stimulation, which may influence the type of music selected<sup>33</sup>. Sessions typically last between 20 to 60 minutes, depending on the patient’s condition and attention span. Shorter sessions may be employed for patients with more severe cognitive impairment, while longer sessions may be suitable for those who are able to focus for extended periods. The frequency of music therapy sessions can vary, but it is commonly held multiple times a week. Some studies suggest that more frequent sessions (1-3 times per week) are beneficial in maintaining patient engagement and enhancing therapeutic outcomes<sup>34</sup>. The individualized music which was related to special memories for each patient with AD to evoke positive emotions was selected. Rather than using general music or time periods far too early or late corresponding to the patient, music that has had major impacts in the patient’s youth and early life is much more beneficial. The study shows interventions involving individualized music associated with special memories reduced stress, induced laughter, evoked memories, and increased relaxation in individuals with severe dementia immediately after intervention, compared with participants in the no-music control condition<sup>35</sup>. Haj et al’s research data have shown that autobiographical memory of patients with mild AD in three conditions: (a) in Silence, (b) after being exposed to

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the Four Seasons music, and (c) after being exposed to their own Chosen music. Autobiographical recall was better in the Chosen condition than in the Four Seasons one, and both were better than Silence<sup>36</sup>. More emotional positive memories were obtained in the Chosen condition than in the Four Seasons one, and both were superior to Silence. These findings demonstrate the existence of emotional processes in music-evoked autobiographical memories. Researchers observed that, in contrast to memories recalled in quiet, memories produced in the presence of music had a greater emotional intensity and content, were recovered more quickly, and required fewer executive functions. The effect of individualized music on agitation with individuals with dementia has been studied. The music was carefully selected for specific meaningfulness to the person during his or her younger years<sup>37</sup>. The individualized music can stimulate memory for remote events, and elicitation of memories associated with positive feelings will have a soothing effect and will alleviate or decrease agitated behaviors<sup>37</sup>. It is evident that the mean agitation levels of individuals with dementia were significantly lower while and after listening to preferred music than before listening to the music<sup>38</sup>. There are gaps in the area of music therapy for AD. Is there a role for music therapy to improve not just episodic memory but working memory also in AD? Is the therapeutic benefit of music therapy more profound in early diagnosed AD vs later stage AD- in mild to moderate vs severe AD? Can digital health technology accelerate development of cost-effective treatments that leverage music therapy? Future research should also explore effect differences by race, gender, and culture.

## Conclusion

There is limitation of the previous research conducted. Retaining all study participants throughout the research study is challenging as well as controlling for confounding variables such as education level, prior exposure to music therapy, severity of AD when dealing with randomized clinical trial that had relatively small sample sizes. A major gap as pointed out below is the lack of long-term studies that follow AD research subjects over multiple years. Alzheimer's disease (AD) is major neurodegenerative disease in the United States. It is the most common form of dementia, characterized by a decline in cognitive abilities that interferes with daily life and activities. As AD advances, memory issues become worse and are usually one of the earliest indications of cognitive impairment. This paper explored the benefits of music therapy. It is a promising intervention to provide positive impact on cognitive functions in patients with AD. Music therapy has the ability to alleviate some symptoms of AD and permits remarkable responses to be elicited in individuals. It is evident that music intervention can reduce agitation and induce relaxation individual with AD. The studies show that rather than using general music, music that

has had major impacts in the individual's youth and early life is much more beneficial. Although music therapy offers significant benefits for patients with AD, it also comes with certain challenges. While some patients may respond positively to music therapy, others might not show the same level of engagement or benefit. It's crucial to pay attention to whether music elicits a favorable or negative response since some music may bring up upsetting memories or feelings. Also, it might be difficult to customize therapy to meet the needs and preferences of every patient. It can take some time to determine the patient's favorite music and necessitates working with caregivers to learn about the patient's past and current musical preferences. Future music therapy needs to focus more on personalized approaches. This personalization might be supported by advanced technologies, such as AI-driven analysis of patients' responses to different types of music.

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