Music Therapy as a Transformative Remedy in Alzheimer's Care

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Alzheimer's disease (AD) is a progressive neurodegenerative disorder and a leading cause of death among the elderly, marked by cognitive decline and emotional disturbances. AD does not manifest symptoms immediately and is a complex disease with no definitive cure available. Nevertheless, music therapy, a non-invasive and increasingly recognized therapeutic intervention, has emerged as a promising approach to mitigating cognitive and emotional deterioration in AD patients. This review examines the effects of music therapy on AD patients across three cognitive domains: (i) memory retention and recall, (ii) awareness and attention, and (iii) emotional regulation and engagement.While music therapy does not cure AD, it plays a significant role in enhancing cognitive function and emotional well-being. This review investigates the neurological and psychological implications of music therapy in AD treatment and underscores the need for further research to optimize its applications. .

Keywords: Behavioral and Social Sciences; Neuroscience; Alzheimer's Disease (AD); Music Therapy; Memory; Awareness; Mood .

1 Introduction

Categorized as the most predominant brain disorder within the spectrum of dementia, Alzheimer's disease (AD) is a serious neurodegenerative health condition. In 2021, over 50 million people were diagnosed with dementia worldwide, and this number is expected to rise to 152 million by 2050[1,2]. Within the United States, AD ranks as the seventh leading cause of death and the most common cause of death among the elderly[3]. In addition to the prevalence of this ailing disease, it is estimated that less than 25% of AD cases are diagnosed, while only two-thirds are treated[4].

AD is characterized by the loss of cognitive memory and thinking skills along with the struggle to carry out everyday tasks. Its etiology begins at the entorhinal cortex and hippocampus, which are regions critical for memory formation. As the disease advances, pathological changes spread to the thalamus, parietal and temporal lobes, and eventually the cerebral cortex, impairing functions like attention, judgment, and language[5]. AD can be characterized by two neuropathological hallmarks: extracellular deposition of amyloid-beta (Aβ) plaques and intracellular neurofibrillary tangles composed of hyperphosphorylated tau proteins. Microscopic examinations in blood vessels reveal that our brains are often exposed to Aβ plaques, which disrupt synaptic signaling and induce neuroinflammation, explaining the increased neuropathic burdens associated with symptoms including forgetfulness, misjudgment of items, and mood changes[6]. Neurofibrillary tangles, composed of hyperphosphorylated tau protein, normally bind to and stabilize microtubules; however, in AD, tau detaches from microtubules and sticks to other tau molecules, forming tangles that ultimately lead to synaptic failure and neuronal death7. These structural changes, visualized in Figure 1, highlight the accumulation of tau tangles and Aβ plaques alongside associated brain atrophy and synaptic loss. Supportive glial cells, including astrocytes and microglia, also contribute to disease progression by responding to neuronal injury and modulating inflammatory pathways.

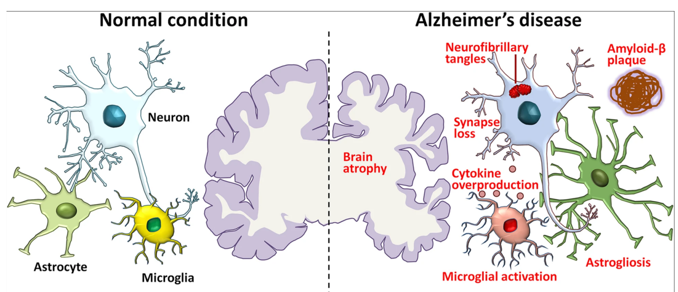

Fig. 1 Key pathological features of Alzheimer's disease, including amyloid-beta plaques, neurofibrillary tangles, synapse loss, and brain atrophy. Also shown are associated cells such as neurons, astrocytes, and microglia[7].

Doctors often categorize Alzheimer's disease into early onset or late onset. Early-onset occurs before age 65 and is often familial, while late-onset AD, the more prevalent form, typically develops after age 65 and is associated with multifactorial risks including aging, the ApoE4 genotype, and lifestyle habits[7,8]. The progression of AD can be precluded through pharmaceutical interventions such as prescribed antipsychotics or anti-cholinesterase drugs; however, the effectiveness of these treatment methods is still limited[9]. As an alternative approach, music therapy has emerged as a promising intervention for individuals with AD.

Music therapy is defined as the use of music interventions to address the physical, emotional, cognitive, and social needs of individuals[10]. Music therapy can be classified into two forms: active and receptive therapy. In active music therapy, patients are involved in first-hand music such as music composition and instrument playing. Receptive music therapy involves patients listening to music, whether it is performed live or through a recording[11]. The notion of music therapy has been extant throughout humanity since ancient times. For example, the ancient Greeks considered music a remedy for heavy alcohol consumption. Similarly, Native Americans incorporated music into their healing practices after battles with European colonizers[12]. Ever since the late 20th century, however, substantial advancements in brain-imaging equipment have allowed clinicians to postulate biological mechanisms behind the neurological interpretation of music. For example, our temporal lobes process and differentiate melodies while the limbic region of the brain provides the emotional context of music[13]. Additionally, the cerebellum and frontier lobe motor cortex play crucial roles in regulating mood and emotional reactions[14]. Music is a multifaceted form of auditory art; its melodies abound with tones, timbres, rhythms, melodies, harmonies, and pulses. Our brain, known for its malleability and proclivity to appreciate music, possesses the ability to respond to unique musical stimuli in ways that can enhance cognitive functioning, emotional well-being, and overall quality of life.

While studies show that degenerative AD yields brain atrophy in our body's coherent cerebral systems, patients who engage in music therapy have demonstrated notable changes in their daily patterns of living[15]. The impact of music therapy can be defined by separating patient cognitive outcomes into three subcategories: i) memory retention and recall; ii) awareness and attention; and iii) mood and stress. Through a comprehensive examination of clinical trials and studies, this review will evaluate and discuss the clinical applications of music therapy while assessing its effectiveness in influencing physiological responses.

2 Method

This review employs a narrative synthesis approach through a comprehensive literature search of the National Library of Medicine's PubMed database and JSTOR, using search terms "music therapy" and "Alzheimer's disease"; this search yielded 42 studies published from 2000 to 2025. Only clinical trials, randomized controlled trials, and meta-analyses with full-text availability were chosen. Additionally, studies were excluded if they did not focus primarily on music therapy for AD patients, employed music therapy in conjunction with other interventions or employed pain relief as their outcome measure rather than cognitive or emotional outcomes. This resulted in 23 eligible studies, and after further. Primary details extracted from each study included trial design, type of music therapy used, experimental setup, duration and frequency of sessions, patient population (age, phase of cognitive decline, gender, and race), description of control group, and clinical outcomes. Findings were synthesized to evaluate the impact of music therapy on memory retention and recall, awareness, and attention, and mood and stress regulation in AD patients. While no formal scoring system was used, preference was given to RCTs with neuroimaging data and larger sample sizes to ensure methodological rigor. As a narrative review, potential selection bias is acknowledged due to the lack of systematic protocol registration and manual screening. However, it allowed heterogeneous evidence to be included in a flexible manner to anchor the effect of music therapy on neurocognitive outcome in AD.

3 Results

3.1 Memory Retention and Recall

Loss of memory is often associated with being the most common and easily recognized prognosis symptom reported by patients suffering from AD[16]. This symptom can be attributed to the gradual, yet harmful, atrophy of the brain's hippocampal volume. Found in the medial temporal lobe of both hemispheres of the brain, the hippocampus of the human brain is correlated with the body's ability to recall information. Greater hippocampal gray matter volume, for example, indicates better performance in memory tasks. A study analyzing AD patients' hippocampal volume over a 4-year time period showed a decrease in gray matter volume by 12 percent a year[16]. Annual follow-up sessions conducted on the patients indicated poorer performance in terms of measures of episodic memory[16]. If hippocampal plasticity can be improved, AD patients suffering from hippocampal damage may demonstrate improved memory recall. Therefore, further research on the mechanisms of hippocampal repair is vital to the development of more effective treatments for AD. Fortunately, interventions in music therapy have shown promises that yield better memory results.

To quantify the neuroplastic effects of music therapy in AD patients, researchers have employed a range of neuroimaging and computational tools. These include voxel-based morphometry to examine gray matter volume, diffusion tensor imaging and fiber tractography to assess white matter integrity, and resting-state functional connectivity to evaluate changes in brain network interactions. In addition, the BrainAGE algorithm, a machine learning interface for the prediction of biological brain age, has been used to track deviations from normal aging processes.

A study by Groussard et al. examined the structural brain differences associated with long-term musical practice using voxel-based morphometry to assess gray matter volume in healthy adults[17]. Participants included amateur and professional musicians compared to non-musicians, with age, gender, and education level controlled across groups. Importantly, individuals with neurological or psychiatric diseases were not included, hence any differences that were ascertained were not confounded by pathologies. Results indicated that musicians had significantly greater gray matter volume in the right hippocampus, a region implicated in memory consolidation and spatial navigation. While this study did not involve AD patients directly, it demonstrates a correlation between sustained musical engagement and hippocampal plasticity. It must be observed, however, that the cross-sectional design limits causal interpretation, and previous or inherent anatomical differences cannot be ruled out. Furthermore, no longitudinal follow-up was performed to examine whether music-induced structural changes correlate with improvements over time. Nevertheless, the current study offers strong neuroimaging evidence for the notion that musical training is correlated with memory-related adaptations in brain structure.

To build on these findings, a randomized controlled trial was designed to evaluate the cognitive and neural effects of music therapy in patients with AD[18]. Participants were randomized into three groups: a music therapy group (weekly singing exercise, choir, and home practice), an exercise group, and a passive control condition with no intervention. The study enrolled patients with mild-to-moderate AD or prodromal symptoms but not patients with non-AD dementias. Over a 12-month period, the subjects received MRI imaging (structural, DTI, fMRI) and neuropsychological evaluation of memory, executive functions, mood, and brain aging (via BrainAGE scoring). Episodic and verbal memory recall, two areas that become impaired early in AD and are particularly linked to the hippocampus, improved most in the music therapy group. Episodic memory allows individuals to relive the past in rich detail, while verbal recall is essential for day-to-day communication and linguistic fluidity. These cognitive enhancements are thought to be mediated by enhanced hippocampal neuroplasticity, as demonstrated by preserved gray matter volume and fiber tract integrity on MRI. Moreover, music's engagement of a broader memory-relevant brain network—a network that comprises the auditory cortex, prefrontal cortex (working memory and attention), and mesolimbic reward system (emotional salience)—likely contributes to this effect by enhancing synaptic efficacy and promoting the survival of neurons involved in memory trace consolidation, particularly in hippocampal circuits[19]. Such effects suggest the possibility that music plays a role in slowing neurodegeneration of the hippocampus in AD patients.

Another prominent example is offered by the ALMUTH music therapy trial a 12-month randomized controlled study assessing both behavioral and neural outcomes of music-based interventions in individuals with mild-to-moderate Alzheimer's disease[20]. Participants were randomized into a music therapy group, an active physical exercise group, and a passive control group, while individuals with other forms of dementia, including frontotemporal dementia, Lewy body dementia, and mixed dementia, were particularly excluded. Outcome measurements included episodic memory (Rey Auditory Verbal Learning Test, Logical Memory), working memory (Digit Span), executive function (Trail Making Test), verbal fluency (category and letter fluency), and mood (Geriatric Depression Scale, Neuropsychiatric Inventory). Neuroimaging was performed with structural MRI, diffusion tensor imaging, and fMRI, and analysis of the BrainAGE biomarker to quantify aberrations in brain aging. The study found that music therapy was associated with significantly enhanced episodic and verbal memory preservation, as well as lessened increments in brain aging compared to controls.

However, in both studies, the observed cognitive and emotional benefits of music therapy were not sustained three months after the intervention ended, indicating short-term effects. Additionally, the lack of standardization in music-based interventions, due to varying musical content, modes of delivery, and individual preferences, makes it difficult to define consistent protocols and apply uniform dosages across participants. In fact, a 2013 study showed that AD patients who underwent familiar music interventions showed improvements in memory questionnaires, but those who underwent unfamiliar music interventions showed signs of deterioration[21]. Thus, while singing and music-listening interventions demonstrated efficacy in enhancing episodic memory amongst AD patients, it cannot be concluded that all forms of music render positive patient outcomes. These issues, including the contrast between short-term and long-term efficacy, as well as cultural and personal variability in music selection, will be further addressed in the discussion section.

A neurobiological understanding of how music enhances memory functions in Alzheimer's patients is provided by Koelsch and colleagues, who investigated the common and distinct neural correlates of music and memory processes using meta-analytic neuroimaging techniques[22]. Their analysis revealed significant overlap in brain areas activated during musical engagement and memory tasks, notably the hippocampus, prefrontal cortex, and anterior cingulate cortex, all of which are regions that are crucial for episodic memory and emotion processing. This activation stimulates adult neurogenesis, particularly in the dentate gyrus, decelerating the typical atrophy seen in AD and preserving memory-related function[23]. Moreover, music-induced modulation of the autonomic nervous system—such as reductions in heart rate and blood pressure—and alterations in neuroendocrine responses—such as decreased cortisol levels—can reduce chronic stress and inflammation. By mitigating these physiological stressors, music helps maintain the neural environment necessary for effective memory consolidation and retrieval.

Several mechanisms depict music as a stimulus that can influence one's memory; some of these mechanisms are well-supported by empirical studies, while others remain theoretical Firstly, music may support sequence learning by acting as a temporary scaffolding, providing a driving formation of an internal rhythm in cortical networks involved in memory[24]. On top of that, the pulsating beats and rhythms of music are hypothesized to facilitate the processing and interpretation of multi-modal and sequential information in the environment. The more complicated a piece, the easier our brains retrieve information; the temporal structures in our brain form a one-to-one correspondence between music and information acquisition (Figure 2A). In other words, simple rhythms and tones beget memory performance[25]. Furthermore, music, in general, has been shown to direct our brain's attention toward relevant points in time, yielding better performance in both perceptual and memory tasks[26]. Other links between emotion and mood have also been shown to enhance memory. For example, neuropsychological studies have found that emotion valences, such as reward, and arousal, such as enjoyment, engage in neural mechanisms during memory encoding and the consolidation process to trigger an enhanced memory outcome[27]. Dopaminergic activity, which naturally declines with aging, is further diminished in AD patients[28]. Music-induced activation of the mesolimbic reward system is a well-established pathway, known to elevate dopamine levels and re-engage reward pathways that promote memory retention. The ventral tegmental area of the brain increases our body's dopamine levels and projects to various brain regions, including the locus coeruleus. From there, the locus coeruleus secretes norepinephrine, the neurotransmitter most strongly associated with arousal[29]. Dopamine levels also cause the amygdala, hippocampus, and medial prefrontal cortex to engage in a circuitry underlying reward process, including hedonic impact, reward learning, and motivation. In parallel, studies show that music modulates the autonomic and neuroendocrine systems by reducing sympathetic arousal and stress hormone release[30]. This process includes lowering cortisol levels and inflammatory cytokines, both of which have been shown to inhibit adult neurogenesis in the dentate gyrus and promote synaptic loss in the hippocampus[31]. By dampening these stress-related biological responses, music helps preserve the neural substrates essential for memory encoding and long-term consolidation. Although there is no comprehensive model that combines these mechanisms, it is hypothesized that stimuli allow these processes to orchestrate simultaneously, as shown in Figure 2B. That these links mutually reinforce each other underscores the importance of our body's mechanisms to facilitate musical engagement and neurological responses.

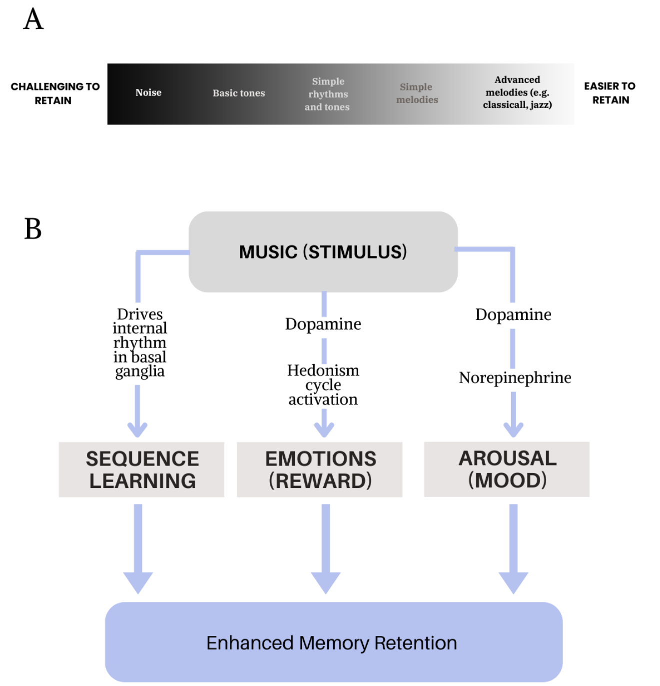

Fig. 2 (A) Retention spectrum of auditory stimuli that illustrateshow musical elements (e.g., rhythm, melody, familiarity) differ in their capacity to engage memory systems. (B) Model showing how music enhances memory retention through three primary pathways: sequence learning via internal rhythm entrainment in the basal ganglia, emotional activation through dopamine-driven reward circuits, and arousal modulation via dopamine and norepinephrine.

3.2 Awareness and Attention

The fundamental aspects of navigating through environments, maintaining focus on tasks, and making important decisions require adequate levels of awareness and attention. Unfortunately, AD patients have a short attention span, are easily distracted, and are sometimes unable to conduct simple tasks such as donning a set of clothes[32].

To better understand the effects of music therapy on a patient's physical and sensory awareness, Götell et al. examined post-therapy behaviors among 24 patients with severe dementia[33]. Participants were selected based on their diagnosis of advanced-stage dementia and required assistance with morning care; individuals with acute psychiatric symptoms or severe hearing loss were excluded. Patients were divided into three types of morning care sessions throughout an average observation period of 13 days. Conducted in a bathroom with an average duration of 14 minutes, the sessions included a typical morning care routine without any musical elements, morning care with familiar background music playing, and morning care in which caregivers sang to or with the patients. The latter two sessions were essentially receptive and active music therapy, respectively, while the former session served as the control. A qualitative content analysis using video recordings allowed researchers to examine physical and visual behavioral cues. However, the study had several limitations. First, it lacked randomized assignment, reducing its generalizability. Second, the short duration and highly individualized nature of the care sessions limit the replicability of findings. Finally, although video data provided rich qualitative insights, the absence of standardized quantitative outcome measures limits the strength of inferential conclusions.

In terms of visual awareness, patients who underwent the typical morning care session exhibited signs of impaired visual awareness by frequently looking down and slowly lifting their gaze, sometimes appearing unfocused or staring into blank space. These symptoms are indeed commonly observed in patients with mild to severe AD, as confirmed by prior research[30]. Patients who were given receptive and active music therapy, on the other hand, were bright-eyed and gazed around attentively, most of whom even had continuous eye contact with the caregiver. Moreover, in terms of physical behaviors, when caregivers sang to patients, patients exhibited upright posture, straighter shoulders, and moved harmoniously with vigilance, whereas patients engaged in sessions devoid of music therapy exhibited symptoms such as faltering gait and unsteady balance. It is important to note that the most significant improvements stemmed from active music therapy. That is, when caregivers sang to or with patients during morning care sessions, there was a noticeable improvement in physical behaviors and visual awareness compared to sessions without musical elements. Lastly, the researchers noted that the use of drugs such as haloperidol, a common antipsychotic used to alleviate AD, induces drowsiness and dizziness, thereby increasing the risk of falling[29]. Music therapy, the researchers concluded, provides a nonpharmacological adjunct to such drug treatments. Overall, the results of Götell et al. suggest that music can improve the sensory awareness of patients.

Building on the potential of applications of active music therapy, a 2012 study evaluated the musical ability and awareness of an amateur saxophonist, SZ[34]. SZ suffered from anterograde amnesia, a common symptom in AD that decreases functioning in processing speed, postictal disorientation, and attention[35,36]. MRI scans of SZ's medial temporal lobes, temporal poles, insular cortex, and hippocampus indicated severe bilateral damage. SZ's condition resulted from a different type of global cerebral dysfunction—namely, herpes simplex encephalitis. Nevertheless, SZ displayed a range of symptoms akin to cognitive deficits observed in AD. SZ participated in an orchestra and was tasked with learning 11 new songs. SZ practiced for a total of 30 hours, engaging in biweekly rehearsals over a period of 3 months. A professional saxophonist, unaware of the practice period, SZ rated each performance session during two testing sessions 100 days apart: one before and one after three months of practice. Intonation, sound quality, rhythmic and note awareness, and overall sight-reading accuracy were rated on a 10-point scale.

SZ's musical awareness demonstrated a significant improvement after prolonged practice. The median score for note awareness increased from 7 to 9 ($p = 0.016$), while the median score for overall sight-reading accuracy improved from 7 to 8 over the same period of 3 months. Despite the promising results of this study, increases in rhythmic awareness, intonation, and sound quality were modest (intonation and sound quality stayed the same while rhythmic awareness increased by 1), especially when compared to note awareness; the limited progress in these areas is likely due to multiple factors. Skills like acquiring shrewd sound quality and pitch require extensive practice, and a mere 30 hours of practice would not suffice. Furthermore, SZ's practice environment differed significantly from his testing environment: during practice sessions, visual and auditory cues were given by the conductor—a customary conducting method during rehearsals—but these were absent during the testing sessions. These limitations thus indicate why some factors underwent marginal improvements. Lastly, there were no significant differences in the difficulty of the songs that showed improvement versus those that did not. This highlights that variations in song complexity did not affect the results. The study's findings, however, are constrained by its single-subject design, and cannot be generalized to other amnesic patients or musicians with differing levels of musical background.

Both Götell et al. and Cavaco et al. showed the impact of music therapy on perceptual-motor functioning and awareness through quantitative methodologies. However, quantifying changes in awareness and perceptual functioning is inherently challenging as they are multifaceted and complex constructs that do not always translate neatly into imaging metrics or standardized scores. Nevertheless, different brain regions have been shown to play a role in participants' perceptual-motor aspects of music. For example, structural MRI data shows the proliferation of gray volume in the prefrontal cortex and anterior cingulate cortex of the brain; both regions are crucial for carrying out executive functions and sustaining attention, and the formation of neurons and synapses from increased gray matter volume enhances neural connectivity, further strengthening cognitive resilience[32,33]. Moreover, in regard to Cavaco's experiment, playing a musical instrument by sight-reading has been found to activate the superior parietal cortex, both in professional and novice individuals, after training[36]. Indeed, high-resolution MRI images indicate that the superior parietal cortex, the basal ganglia, and parts of the anterior position of the insular cortex are not damaged, suggesting that music therapy may be contributing to his improved musical performance on perceptual-motor aspects of learning[37]. These findings indicate that patients with neurological deficits like AD would most likely experience enhanced visual and physical awareness.

3.3 Mood and stress

At least 90% of patients with AD experience behavioral symptoms, including agitation, apathy, restlessness, and aggressiveness[38]. Persistent emotional distress can occur at any disease stage and represents a management challenge for caregivers and clinicians, as shown to increase both self-injury and injury to others[35]. A closer look at the brain's neural mechanisms that contribute to these behavioral manifestations may generate crucial, innovative interventions. Already, scientists have discovered that music intervention significantly ameliorates many of the underlying factors in the brain that contribute to the symptoms.

Agitation, for example, is a sign of dysphoria that is often precipitated by several factors such as low-lighted environments, hospitalization, admission to nursing residences, and lack of human interaction. Fittingly, AD patients have a poor ability to adapt while entering these circumstances. The brain's hippocampal region plays an important role in regulating cortisol, which inhibits the hypothalamic-pituitary-adrenal axis, a regulator of cortisol production[35]. However, AD affects the hippocampus, resulting in unstable cortisol output and high cortisol variability. Elevated cortisol levels affect age-related cognitive and brain changes, possibly contributing to impaired episodic memory and further hippocampal atrophy.

A clinical study has shown that music therapy markedly decreases cortisol levels through the endogenous opioid system (EOS)[39]. The EOS is a system whereby the body produces endorphins by stimulating the pituitary gland and hypothalamus. These hormones act as the body's natural analgesic and also serve to protect the body from stressful conditions. As music triggers the brain's EOS, the study found that given the strong role of opioid receptor activation in analgesia, the connection between pain and music is generally regarded as convincing evidence of the role of opioid activation.

Besides the role of hormonal abnormalities in AD, the noradrenergic system also seems to be directly involved. The compensatory overactivity of noradrenaline resulting from the progressive loss of noradrenergic neurons in the locus coeruleus may influence dopaminergic transmission, particularly in the prefrontal cortex, thereby contributing to symptoms such as agitation in frontotemporal dementia. In search of conclusive evidence, a study by Bowling et al. found a positive correlation between pupil dilation and rhythm perception[40]. Upon analyzing electrophysiological methods in rhesus macaques from another study, the researchers also found that activity in the LC is closely correlated with pupil dilation in spontaneous and stimulus-driven (musical) contexts[41]. Both studies, therefore, suggest that high levels of the groove may activate the LC, which would increase the release of noradrenalin (norepinephrine) at multiple sites of the brain. These projections have been known to stimulate cortisol production and facilitate motor and coordination planning.

Music therapy's practical ability to remove undesirable irregularities in our bodily systems has been proven to be an efficacious treatment for AD patients. A study in Valencia, Spain examined 25 patients, aged 65 and over, who were diagnosed with mild AD[42]. The participants were recruited from a local Alzheimer's care facility and met specific inclusion criteria, including a Mini-Mental State Examination (MMSE) score between 18 and 23. Patients who did not meet this cognitive threshold or who were unwilling to engage in music therapy were excluded. There was no control in the study, however; only pre- and post-intervention comparisons within subjects were analyzed. After a 60-minute music therapy session, researchers measured cortisol levels, quantified by the Enzyme-Linked ImmunoSorbent Assay, by taking saliva samples. These samples were collected in sterile tubes at 9:30 a.m. before and after the session to ensure consistency and avoid diurnal variation in cortisol. The Hospital Anxiety and Depression Scale tests were administered concurrently to provide insight into patients' emotional states. The test score range was between 0 and 21, with higher scores indicating more severe anxiety or depression. The results showed that music therapy significantly reduced anxiety and depression levels. Before music therapy, the average depression score was 7.55 ± 5.04, which decreased significantly to 3 ± 2.95 after therapy. Similarly, the average anxiety score dropped from 8.64 ± 3.47 to 1.63 ± 1.79. Finally, the average cortisol level before therapy was 4.59 ± 1.95 ηgr/mL, which decreased to 4.17 ± 2.15 ηgr/mL after therapy. The authors found a linear correlation between cortisol reduction and decreased depression. These results support the hypothesis that decreased cortisol levels are consistent with positive emotional and physiological behaviors. In AD, where LC degeneration disrupts this balance, music may act as a compensatory mechanism by transiently enhancing noradrenaline signaling pathways. Reduced amygdala activity dampens the hypothalamic-pituitary-adrenal (HPA) axis, thereby lowering cortisol secretion. Simultaneously, music-induced activation of the mesolimbic dopaminergic system can enhance feelings of pleasure and reduce stress reactivity[43].

Another international randomized controlled trial assessed whether music interventions delivered by trained family caregivers could alleviate behavioral and psychological symptoms of dementia in community-dwelling patients[44]. The study recruited 432 dyads across five countries and assigned them to one of three groups: music, reading, or usual care (UC). Caregivers in the intervention arms received three online training sessions and were asked to conduct music or reading sessions at least twice weekly for 90 days. Participants were required to have a dementia diagnosis, live in the community with a cohabiting caregiver, and score $\geq$6 on the Neuropsychiatric Inventory Questionnaire (NPI-Q); those who did not meet these standards were excluded. To ensure methodological integrity, interventions were drawn from a standardized manual, and the therapists were supervised on a regular basis for fidelity. Difference in NPI-Q severity scores at 90 days was the main outcome and was not significantly different from the music group (0.15) and UC. Masking was maintained with regard to assessors and statisticians, though not possible to blind the participants due to intervention nature. Secondary measures of depression, cognition, and caregiver distress did not differ significantly. Subgroup analysis did suggest some responsiveness in patients with more severe symptoms or vascular dementia but the findings were not statistically significant.

Discussion

There is currently a vast collection of studies that highlight music therapy's ability to elicit positive outcomes across psychological, cognitive, and biological domains. The mechanisms behind each neural adaptation of the brain, enabling improvements in memory, cognition, and mood, are dissected into rudimentary perceptual features. Ultimately, this review offers frameworks between the three domains for understanding how music orchestrates the manifold processes within the brain of AD patients.

A comparative analysis of the studies reviewed reveals both compelling points of convergence and divergence (Table 1). To start with, a consistent pattern that emerges across all studies is the preferential benefit of active, structured, and professionally delivered music intervention, such as choir participation, instrument playing, or caregiver singing, over passive listening. For instance, both the ALMUTH study and the Götell et al. study show considerable improvements in outcomes through active engagement: the former showed improved episodic and verbal memory alongside preserved hippocampal structure, while the latter found enhanced posture and attention during caregiver-sung sessions compared to background music or no music at all[18,33]. These findings are corroborated by the case report of Cavaco et al., where repeated instrumental rehearsal strengthened note awareness and sight-reading in a person with severe anterograde amnesia, suggesting that improvements in cognition and motor are optimal when patients are active participants in multi-sensory, dynamic musical activities, perhaps due to greater network activation in memory, attention, and motor planning neural networks[34]

Moreover, with respect to hippocampal neuroplasticity, the ALMUTH and the Groussard et al. studies, though differing methodologically, both demonstrate that increased hippocampal volume through musical training or therapy and that music activity may reverse or delay neurodegeneration[17,18]. A second common theme is music's role in mood stabilization and stress management. The de la Rubia Ortí et al. cortisol study found reductions in anxiety, depression, and cortisol levels after music therapy sessions[42]. This finding aligns with the neurobiological mechanisms discussed in Koelsch et al., such as the activation of the endogenous opioid system and the modulation of the HPA axis[18,42]. These biochemistry processes are consistently cited as central to music's therapeutic impact in numerous studies. Simultaneously, studies like Bowling et al. and studies of LC activation by rhythm perception suggest a noradrenergic mode of control and pupil-related arousal through musical grooves that may yield improvement of attention and control of behavior[40,41].

For example, García-Casal et al.'s multinational trial was unable to identify significant benefits for neuropsychiatric symptoms with caregiver-led music sessions, compared to the therapist-led, highly structured interventions of the ALMUTH study.[18,42] The divergence here implies heterogeneity of intervention fidelity, individualization, and participant retention that may undermine efficacy in large, heterogeneous samples. Divergence also occurs because of the disease stage. Matziorinis et al. cited that their intervention was more feasible and potentially more effective in preclinical cohorts, whereas studies with severe dementia documented increased behavioral compared to cognitive improvement[20].

Methodologically, several patterns and limitations recur. First, small sample sizes limit statistical power and generalizability. Second, heterogeneity in outcome measures—ranging from high-resolution neuroimaging to observational behavioral coding—makes cross-comparison difficult. Third, the lack of control groups in some studies and the absence of long-term follow-up in many studies limit conclusions about sustained efficacy. That said, there is a growing methodological pattern of integrating biological (e.g., MRI, cortisol levels), behavioral, and psychological measures to holistically assess music's impact, as seen in ALMUTH and de la Rubia Ortí studies[18,42]. Finally, a critical limitation across studies is the variable reporting or exclusion of non-AD dementias, affecting sample specificity and replicability.

In summary, the evidence reveals an orderly sequence of discovery of cluster types: organized, multimodal, and active music interventions work best, particularly when they are done earlier in the disease course and as adjuncts to physiologic monitoring. Yet, the divergence in findings also underlines the need for methodological standardization—especially regarding outcome metrics, control conditions, and staging criteria. Future studies should adopt rigorous, multimodal designs with stratified samples to further clarify music therapy's mechanisms and optimize its clinical application for diverse dementia populations.

3.4 Long-term and short-term effects:

The conclusion that music therapy serves as a beneficial therapeutic intervention, however, is tenuous in the long term. For example, the study by Clément et al. showed that emotional improvements such as facial expressiveness, positivity of speech,

Study	Design	Sample Size	AD Stage	Intervention Type and Duration	Outcome Measures	Key Findings	Limitations
Groussard et al. (2014)	Cross-sectional, voxel-based morphometry study	44 (15 non-musicians, 15 amateur, 14 professionals)	Not AD (healthy adults)	Active music therapy; Long-term musical practice (>10 years)	Gray matter volume via structural MRI (VBM)	Musicians showed increased right hippocampal volume; supports music-memory neuroplasticity link	No AD patients; cross-sectional design; no causality or longitudinal data
Koelsch & Matziorinis (2022) – AL-MUTH Study	3-arm RCT (open-label, ongoing)	Not specified	Mild-to-moderate AD (initially); now includes MCI and SCD	Active music therapy; 12 months; weekly singing, choir, daily practice	BrainAGE, fMRI, DTI, MMSE, FC-SRT, IADL/PADL, GDS, CERAD, CWIT	Improved verbal and episodic memory; preserved hippocampal volume; increased neuroplasticity	No blinding; mixed cognitive stages; sample size not reported
Matziorinis et al. (2023)	12-month RCT (3-arm: Music, PA, Control)	18 (6 per group)	Mild-to-moderate AD	Music: weekly choir; PA: weekly exercise; Control: none	Neuropsychological tests, MRI (sMRI, DTI, fMRI); feasibility metrics	Music group showed higher engagement; protocol revised to target earlier stages (MCI, SCD)	Small sample; 50% attrition; caregiver burden; generalizability limited
Götell et al. (2018)	Crossover observational study	24	Advanced-stage dementia	13-day observation; 3 conditions: no music, background music, caregiver singing	Video-recorded behavioral cues	Active music therapy improved attention and coordination; receptive music had moderate effects	Small sample; no long-term follow-up; single setting
Cavaco et al. (2012)	Case study (longitudinal)	1 patient with herpes encephalitis-induced amnesia	Not AD (similar symptoms)	Active music therapy; 3 months; biweekly rehearsals (30 hours total)	Expert ratings on musical skills	Improved sight-reading and note awareness; no improvement in intonation	Single subject; not AD; short duration; not generalizable
de la Rubia Ortí et al. (2017)	Quasi-experimental (no control)	25	Mild AD	One 60-minute group music therapy session	HADS (anxiety, depression), salivary cortisol	Decrease in anxiety, depression, and cortisol levels	No control group; short-term; homogenous sample
Baker et al. (2023)	Multi-site, 3-arm RCT	495 caregiver–patient dyads	Various dementias incl. AD	3 online sessions; 90-day music or reading sessions (2/week)	NPI-Q (primary); caregiver distress, depression, cognition (secondary)	No significant change in NPI-Q; subgroup effects non-significant	Unblinded; mixed dementia types; limited effect in mild/moderate cases

Table 1 Summary of Seven Studies on Music Therapy and Alzheimer's Disease

and mood increased significantly during and immediately after eight sessions[45]. However, most of these effects faded soon after, suggesting only short-term benefits. While mood improvements lasted up to four weeks post-intervention, discourse positivity dissipated after two weeks, and facial expression benefits disappeared entirely. Similarly, in another study on memory, the addition of music had no significant impact on either immediate or delayed recall performance[46]. Instead, it was the retrieval learning strategy—not the music—that drove statistically significant improvements in both the short and long term. Collectively, these results suggest that whereas music potentially increases mood or interest temporarily, its independent therapeutic effect might be minimal in the absence of reinforcement or other cognitive strategies. A likely explanation for the discrepancy is that music primarily acts as a transient stimulus rather than a durable cognitive enhancer for long periods of time. For instance, music therapy temporarily lowers cortisol levels, but once sessions stop, cortisol levels often rise again in response to renewed, chronic stressors[47]. In the case of AD, physiological stress resulting from disorientation, behavioral symptoms, and prolonged cognitive decline is the causes that not only elevate cortisol but also exacerbate neurodegeneration, especially in hippocampal regions involved in memory[47].

While music therapy should not be dismissed as a mere placebo, current evidence suggests that its short-term benefits often resemble those of a general mood-enhancing intervention, especially when not paired with sustained engagement or structured strategies. Without active components like emotional reflection, improvisation, or goal-oriented participation, music therapy may function more as a passive distraction, offering temporary relief that fades once the sessions end. This is especially problematic in conditions like AD, where stress and cognitive decline are persistent, sometimes lasting up to 20 years[48]. Therefore, momentary mood boosts without reinforcement hold limited clinical value. To disentangle genuine therapeutic impact from temporary distraction, studies must include long-term follow-up. This would mean tracking participants' emotional, cognitive, or behavioral outcomes weeks or months after therapy ends. Additionally, using active control groups—such as white noise, reading, or other non-musical activities—can help isolate the specific effects of music. Incorporating biological or neural markers, like cortisol levels or brain activity patterns, would further clarify whether observed changes reflect deep therapeutic engagement or short-lived emotional responses. Only through these methods can we determine whether music therapy produces lasting clinical benefits or simply offers a temporary emotional reset.

3.5 Active and Receptive Music Therapy:

Both active and receptive forms of music therapy were utilized across the studies presented in this review (Table 1). Notably, active music therapy is proven to be more effective than receptive approaches. For example, long-term active engagement, as seen in Groussard et al. and the ALMUTH studies, was associated with hippocampal preservation, improved episodic and verbal memory, and broader neuroplastic effects [17,18]. These benefits are attributed to music's multisensory stimulation, emotional salience, and rhythmic structure, which are especially potent when individuals are actively engaged [21]. By contrast, receptive music therapy, such as passive listening or background music, showed more modest outcomes. Götell et al. found that background music improved mood and attentiveness in late-stage dementia patients, but to a lesser degree than caregiver singing, which constituted active therapy [33]. Similarly, in the HOME-SIDE trial, semi-structured caregiver-led music and reading sessions produced no significant improvements in behavioral symptoms across a large cohort, although some trends suggested potential benefit in subgroups with more severe symptoms [44].

Granted, receptive approaches are easy to implement and less taxing on a caregiver than active approaches but do perhaps not address the relational needs of AD patients in the same way as singing, dancing, or making music together do. Given that active approaches had better immediate effects in our study, future training programs should include explanations of the potential differences between implementing active and receptive approaches so that caregivers can make more informed choices of where and when to expend the extra effort involved in implementing active approaches.

Therapy duration emerged as another critical factor. Short-term interventions such as the single-session protocol in de la Rubia Ortí et al. yielded acute emotional and hormonal benefits, but lacked evidence of sustained cognitive change [42]. In contrast, longer interventions spanning several months to a year, such as in Cavaco et al., demonstrated meaningful cognitive improvements, including enhanced note awareness and preserved brain structure on imaging [34]. These findings suggest that longer durations are necessary to induce measurable changes in memory and neuroplasticity.

3.6 Familiar and Unfamiliar Music:

There is evidence that familiar music therapy intervention reduces forgetting in episodic memory and enhances autobiographical recall in patients with Alzheimer's disease. To start with, there is no evidence that suggests music genre significantly impacts physiological or emotional responses [49]. Rather, and more importantly, familiar songs consistently evoke stronger autobiographical memories and mood improvements compared to unfamiliar ones [21]. Moreover, studies using individualized playlists report better cognitive and behavioral outcomes than those using experimenter-selected music [21]. Previous studies have found that familiar music engages brain regions linked to emotion, memory, and movement such as the reward system, superior frontal gyri, left thalamus, and medial superior frontal gyrus [50]. In contrast, unfamiliar music tends to activate areas involved in novelty detection and music recognition, including the insula and anterior cingulate cortex [51]. Personalization is therefore likely important because familiar and preferred music stimulates dopaminergic and opioid activity in the ventral striatum more strongly than unfamiliar music, and in Alzheimer's patients, this reward-related activation is linked to enhanced connectivity across cortical and cerebellar networks [52].

Cultural familiarity also plays a key role as individuals process and recall music from their own cultural background more vividly, and emotional cues are interpreted more accurately when the music aligns with cultural expectations [52]. Despite this, most interventions lack a standardized approach for incorporating both personal musical biography and cultural relevance. To address this gap, scholars have proposed using multicultural assessment tools and culturally competent therapy guidelines to better match musical interventions to each patient's background and identity [53].

One widely used approach is the Individualized Music Preference Assessment or the Gerdner protocol, which gathers input from patients, caregivers, and family members to identify music tied to the person's past, culture, and emotional resonance [54]. Other surveys such as the Music Preference Questionnaire allow researchers to rank genres, artists, and listening habits, while also enabling correlation with emotional or physiological responses [54]. Another mechanism that researchers may use is artificial intelligence (AI). AI algorithms have already been developed in digital music streaming platforms; recommendation engines drive user engagement by analyzing listening patterns and contextual factors like time of day [55]. While no standardized AI-based protocol currently exists for music therapy in treating Alzheimer's disease, clinical settings can leverage similar personalization technologies to enhance therapeutic outcomes.

Despite the advantages of familiar music, unfamiliar music should not be dismissed entirely. In fact, unfamiliar music may offer marginal therapeutic benefits when it shares rhythmic, tonal, or structural similarities with music a patient is familiar with. One study, for example, showed that even without personal association, background classical music improved memory retrieval, likely by easing anxiety [56]. The tonal and rhythmic familiarity seems to be key: Alzheimer's patients retain the ability to appreciate the tonal structure of music and detect the "feel" of a genre. If the unfamiliar piece aligns with those preserved musical templates, it can be almost as effective in the moment as a known song in promoting engagement or calming the person [57]

Conclusion

While far from a panacea, music therapy is poised as an effective therapy in AD and other neurodegenerative diseases. AD patients, on average, exhibited positive responses to music therapy, many of whom experienced better management of symptoms compared to those in pre-therapy. However, key factors such as intervention duration, personalization, the distinction between active versus receptive modalities, and the familiarity of the music must be carefully considered to maximize efficacy. In summary, while music therapy's impact on memory, awareness, and mood is not universally effective across all populations, music therapy puts forth a non-invasive, patient-centered approach to enhancing the quality of life in individuals with AD. Further interdisciplinary research aimed at decoding other broader applications of music therapy beyond AD could potentially illuminate its benefits across more neurological and psychological conditions.

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