

REVIEW

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# Music therapy for Alzheimer's disease management: a narrative review

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## Abstract

Alzheimer's disease (AD), the most prevalent neurodegenerative disorder, is escalating globally. Characterized by cognitive decline, emotional instability, and neuropsychiatric symptoms, AD presents a growing challenge for effective management. Current pharmaceutical treatments, primarily acetylcholinesterase inhibitors and memantine, offer symptomatic relief but fail to halt disease progression or significantly address psychiatric manifestations. Consequently, non-pharmacological interventions, particularly music therapy, have garnered attention as potential adjunctive treatments. Musical memory is regarded as completely distinct from other memory processes, and patients with AD retain some musical recall despite the significant cognitive decline. In addition, music therapy is well-tolerated by the vast majority of patients and easy to administer. Herein, the mechanisms of music as a memory enhancer, how musical memory is preserved in AD, active and passive music therapy methods and their effects on each function, and factors affecting the efficacy of music therapy, such as music selection and genre, are discussed. Additional research is required to determine the optimal duration of music therapy sessions for patients to experience long-term benefits. In addition, as patients in severe stages cannot participate fully in music therapy sessions due to their disability, additional research finding a solution to this issue would be helpful.

**Keywords** Alzheimer's disease, Cognitive function, Dementia, Depressive symptom, Music therapy, Non-pharmacological interventions

## Introduction

Alzheimer's disease (AD) is the most common form of neurodegenerative disorders globally, affecting approximately fifty million people [1]. Worldwide, the frequency of AD and dementia is quickly increasing; by 2050, over

152 million individuals are estimated to have the disease [2]. Reduced cognitive functioning, emotional instability, and neuropsychiatric manifestations are all disease symptoms [3]. Verbal or physical aggressiveness and irritability are other behavioral and psychological indicators of dementia, as are psychosis, disorientation, emotional discomfort, and passivity [2].

Alzheimer's disease unfolds through a protracted course, initially marked by imperceptible pathophysiological alterations that precede symptomatic manifestation. This silent phase is characterized by the accumulation of amyloid- $\beta$  and tau proteins, which are precursors to neurodegeneration. During this period, some individuals may not exhibit symptoms, while others may begin to show signs of memory decline or broader cognitive impairment [4]. The National Institute on Aging and Alzheimer's Association has stratified AD into several stages, commencing with a preclinical phase

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devoid of symptoms, advancing to mild cognitive impairment (symptomatic predementia), and culminating in profound dementia [5–7]. In the preclinical stage, the detection of biomarkers, such as amyloid- $\beta$  and tau proteins in biological fluids can signal the onset of AD, facilitating early intervention [4]. This stage can be extended for around 15–20 years and preceded by a prodromal interval that may last for 3–6 years [8]. Mild cognitive impairment is discernible by a significant yet non-debilitating cognitive decline, with further categorization based on the domain of cognitive dysfunction. Nonetheless, the absence of neuropathological confirmation in mild cognitive impairment diagnosis may lead to an inaccurate attribution of AD, highlighting the necessity for an inclusive diagnostic framework that integrates biomarker analysis [4].

Advances in Alzheimer's disease (AD) diagnostics have introduced biomarkers like A $\beta$  and tau proteins, detectable in cerebrospinal fluid and via positron emission tomography (PET) scans, aiding early AD detection. However, their use is limited by invasiveness and practicality. The development of anti-A $\beta$  monoclonal antibodies offers a new therapeutic approach, slowing the progression of AD symptoms. Despite this progress, optimizing their effectiveness and accessibility remains a priority within a comprehensive AD management plan that includes lifestyle adjustments and supportive care [9].

Commonly, pharmaceutical treatments such as acetylcholinesterase inhibitors alleviate cognitive impairment without altering the progression of the disease. Memantine and cholinesterase inhibitors such as rivastigmine, donepezil, and galantamine are the preferred therapeutic approaches for managing AD. Still, none of them can delay or prevent neuronal degeneration, death, or the progression of the disease [10]. Regrettably, these treatments have little impact on reducing dementia's psychiatric symptoms [11]. As a result, more effective therapies must be evaluated, and non-pharmacological treatments, among others, have received tremendous attention as adjunct therapies to pharmacological agents for AD [10].

Non-pharmacological treatment options include psychosocial and cognitive therapies provided to individuals and groups, as well as physical or sensory practices like listening to music, receiving therapeutic touch, or being exposed to multimodal stimuli [12–14]. Music therapy is considered beneficial because the brain can retain memories and feelings from experiences accompanied by music. Several studies revealed that even though people with dementia might not be able to speak, they react to music and enjoy it [15–17]. Music has been utilized as a cognitive tool for integrating data and events over time. Many essential life developments are linked to music through song usage [8].

Music therapists can earn the Music Therapy Board Certification (MT-BC) credential by completing an accredited program, clinical training, an internship, and passing the Certification Board for Music Therapists (CBMT) exam [18]. They utilize elements like harmony, melody, tempo, and acoustics in therapy sessions. People involved can merely listen to music or actively perform by singing and playing instruments [19]. Depending on the participant's preferences, personalized music is utilized during active music therapy for rehabilitation [3]. Music therapy has been shown to significantly impact behavior, mood, and memory by modifying brain physiology and enhancing cognitive abilities in areas, such as speaking, comprehension, concentration, and recall [11]. Music can also stimulate the limbic and emotional reward systems, resulting in feelings of well-being and satisfaction [20]. Despite the mixed results of the studies, many pieces of evidence suggest the inclusion of music therapy in the AD treatment plan [3].

This review aims to summarize the role of music therapy as an adjunct treatment for patients with AD and the underlying mechanisms mediating its effects. We reviewed the effectiveness of active and passive music therapy separately in improving cognitive, behavioral, and psychological symptoms in patients with AD. Lastly, we outlined future research directions that will facilitate the use of music therapy in clinical settings to treat AD patients.

### **How does music therapy affect individuals with Alzheimer's disease?**

While the exact process by which music therapy benefits individuals with AD is not fully understood, there is evidence and theoretical support for its effectiveness. Research indicates that music therapy engages various brain regions, involving cortical regions such as the medial prefrontal cortex and orbitofrontal cortex as well as subcortical regions such as the basal ganglia, nucleus accumbens, ventral tegmental area, hypothalamus, and cerebellum. These regions are less affected by AD than the medial temporal lobe, suggesting that music therapy may be more effective at enhancing memory function than speech therapy [19]. Hence, the perception of discovering and recalling music is remarkably maintained in patients with AD [1].

### **The beneficial effects of music therapy on AD Cognitive function**

Alzheimer's disease is a neurodegenerative disorder that causes mental impairment and gradually impairs the capacity to do daily life activities. Memory deterioration seems to be the most frequent and prevalent cognitive deficiency in AD. However, impairments in other

aspects of cognition (speaking, executive function, and visual–spatial abilities) are also noticeable [19]. Recently, studies have shown that music therapy can enhance several cognitive abilities in patients with AD [21]. The MMSE (mini-mental state examination) was mostly used to assess the cognitive function of the participants. It comprises several cognitive function domains, such as orientation, recognition, attention, computation, remembering, language, and practice [19, 22].

#### **Passive music therapy effects on cognition**

Several investigations have assessed the effects of passive music therapy on cognition [19, 22–25]. According to Johnson and colleagues after hearing a section of a Mozart piano concerto, the AD twin significantly improved on the spatial–temporal challenge [26]. Hearing Pachelbel's Canon and Mozart's concerto via headphones was a technique used by Li and colleagues for patients with mild AD. They found possibly little change in discernment while investigating subcategories of cognitive tests. The findings indicated that MMSE and CASI (Cognitive Abilities Screening Instrument) total scores were less reduced after 6 months of treatment than in the comparison group. However, the difference was not statistically significant, but the music therapy group performed significantly better in understanding an abstract concept [25]. According to Bruer and colleagues and other researchers, listening to music can improve AD patients' overall cognition [27, 28]. The Mozart effect is a method of enhancing cognition through classical music. This phenomenon has been linked to intense arousal brought on by the pleasure of hearing music, not because of the potential of classical songs to improve cognition outside of the music-listening session [29]. Listening to music (perhaps with a strong beat and in the dominant mode) can transiently improve mental function in older people by provoking positive impact and increased arousal. Music-induced improvements in motor function, pace, verbal proficiency, and autobiographical memory recall have been noted in studies that compare the short-term impacts of musical accompaniments versus no music in elderly persons [30–32]. In direct opposition, one study found that music in the background seemed to have a distracting impact on mental efficiency in an individual patient's visual, intuitive recall test [33].

#### **Active music therapy effects on cognition**

Increasingly more studies are being conducted using music therapy, which includes music and various activities involving vocalization, rhythmic movement, and playing instruments, and so on [21]. For instance, Särkämö and colleagues classified mild and moderate AD individuals into three categories: a group for

rhythmically moving while singing, a team for concentrating on memories while listening, and a control group. Following a 10-week treatment, both the performing and listening teams' feelings and cognitions were enhanced [34]. Gómez Gallego and colleagues requested 42 people with mild or moderate AD to greet, dance, and play musical instruments. Their 6-week study showed that combining music with other tasks helped enhance cognitive status [1]. Simmons-Stern and colleagues looked at how well AD individuals could recognize verbal and written lyrics when compared to spoken language. They discovered that music would improve the brain's ability to encode verbal information [35]. Palisson and colleagues examined the verbal content's cognitive impacts and their data revealed that songs were more easily remembered [36]. Kim and colleagues found that multi-domain intellectual engagement, such as music therapy, might increase word-list recognition and memory test results [37]. Lyu and colleagues found that music therapy improves instant and delayed word recall in patients with mild AD. This finding can be justified by stimulating the brain areas involved in music comprehension by singing, improving memory function, and focusing capability. These areas may be underutilized by people living with AD. Unfortunately, this effect did not last for more than 3 months after treatment was finished. This finding suggests that long-term music therapy for AD patients may be beneficial [19].

#### **Psychobehavioral function**

Early psychological alterations in patients with AD include apathy, sadness, anxiety, and aggressiveness. All these symptoms may readily be neglected, resulting in the disease's steady worsening [38]. Also, people with AD frequently have behavioral issues [19]. Despite the severity of the patient's condition, music therapy has been proven to alleviate aggressiveness, anxiety, and activity disruptions in AD patients [39]. Neuropsychiatric symptoms and caregiver distress in AD patients were mostly assessed using the NPI (Neuropsychiatric Inventory). It investigates ten possible factors contributing to behavioral issues. These elements can cause a wide range of mental and behavioral disturbances, including delusions, apathy, anxiety, aggression, irritability, agitation, euphoria, hallucinations, dysphoria, disinhibition, and abnormal motor activity [19, 38, 40].

#### **Passive music therapy effects on psychobehavioral function**

Listening to music can have a considerable positive impact on several different topics. One of the most significant findings was that participants were less irritated in the presence of music than the control group [41]. The results of MOSES (the Multidimensional Observation

Scale for Elderly Subjects) indicate that music therapy can reduce irritability in AD patients by significantly lowering the irritation score [38]. The latest meta-analysis showed that passive music treatments could be more beneficial than active techniques in decreasing stress, irritability, and other attitudinal symptoms [1]. Guetins' investigation revealed that music could reduce stress and depression in individuals with mild to moderate AD [23]. Japanese research showed that emotional and psychological symptoms of people with severe AD were found to be significantly reduced through music therapy [42]. Svansdottir and colleagues used music therapy with participants with moderate to severe AD. They discovered that the music therapy group's aggressiveness and anxiety significantly decreased, and 4 weeks after the final session, the effects of music therapy faded [43].

#### **Active music therapy effects on psychobehavioral function**

Sakamoto and colleagues found that active and passive music interventions have soothing effects via autonomic nervous system activation in moderate and severe AD. Nevertheless, active music treatment resulted in a substantial decrease in behavioral issues. They evaluated psychosocial outcome indicators and discovered early advancement in anxiousness, affective disturbance, aggressive behavior, psychosis, and activity disruption [42]. Consequently, Raglio and colleagues reported greater impacts of active music treatments than listening to music on behavioral manifestations, like: depression, anxiety, stress, and sleeping disorders, even though the findings were unable to reach statistical validity [44]. Music therapy was shown to help manage psychological and behavioral symptoms in individuals with severe AD as well as alleviate caregiver anxiety [19]. Gómez Gallego and colleagues showed that combining music with other tasks helped to alleviate neuropsychiatric manifestations [1]. They also found that music therapy lowered anxiety in mild AD patients, while it resolved delirium, hallucinations, restlessness, aggressiveness, and linguistic difficulties in moderate cases [45].

Of late, A.M. Matziorinis and colleagues conducted a 12-month randomized pilot trial examining the effects of both active and passive music therapy on patients with mild to moderate AD. After the study, neuropsychological tests such as the MMSE and GDS (Geriatric Depression scale) were administered. The results indicated that the music therapy protocol was not feasible exclusively for patients with mild-to-moderate AD due to reasons for withdrawal such as accelerating AD symptoms and progression, inability to contact participants for follow-up tests, caregiver inability to continue, other illnesses (such as cancer diagnosis and broken hip), living far away, and being unable to attend sessions regularly. As a result,

the music therapy study protocol should be expanded to include individuals in the prodromal and preclinical stages [46]. Table 1 provides a detailed summary of various music therapy studies, encompassing their scope and results (Table 1).

### **The physiological basis for the enhancement of memory through music**

#### **Modulation of neuronal connections and functions**

Research has verified the link between steroids and cerebral plasticity in humans. Steroids from peripheral glands or neurosteroids that are made by nerve cells affect the nervous system. Both kinds of steroids are neuroactive, irrespective of their origin. They modulate essential processes such as reproductive activity, brain maturation, neuronal formation, neuronal preservation, cognitive function, and memory [47]. Musical exposure influenced the maturation and function of cranial nerves in human participants from the fetal to the adult stages, according to research. It revealed that musical stimuli affect neural activity and the number of cells [48]. There is a strong correlation between musical stimuli and steroid hormones [49, 50]. Moreover, Särkämö T and colleagues conducted a clinical study that demonstrated music listening could enhance neuronal regeneration and cognitive preservation in the early post-stroke phase [51]; as steroids influenced neuronal development, protection, and performance [47].

#### **Dopamine pathways**

The dopaminergic pathway regulates cognitive and behavioral functions. Dopamine appears to be a chemical messenger required for rewarding and motivating processes. It works with acetylcholine to improve memory retention and learning integration of newly learned information, as demonstrated in both behavioral and cellular domains [52, 53]. Concurrently, music has been shown to promote the release of a number of chemical messengers, including neuropeptides and other biochemical mediators such as endorphins, endocannabinoids, dopamine, and nitric oxide [54]. This implies that music plays a role in human reward, nervousness, arousal, immunity, and social connection systems [55].

#### **The autonomic system regulation**

Music has the ability to arouse strong emotional feelings and feedback, which generally results in physiological changes due to autonomic nervous system stimulation [56]. The level of arousal induced by music and its following effects on attention vary depending on the person's baseline physiological state [52]. Increased skin permeability, respiration, heart rate, blood pressure, and vigilance are indicators of sympathetic activation of the

**Table 1** Reported studies on the effect of music therapy on cognitive and psychobehavioral symptoms in AD patients

Authors and date	Sample size, #Pts	Type of music therapy	Duration and frequency of sessions	Inclusion/exclusion criteria	Assessment tools	Key conclusion
Lyu et al., 2018 [19]	298 A: 100 B: 99 C: 99	A: singing B: lyric reading C: control	3 months A, B: 2 sessions per day/30–40 min	Inclusion Criteria: • Age 65 years or older • Diagnosed with probable AD according to NINCDS–ADRDA criteria Exclusion Criteria: • Hearing difficulties, even with hearing aids • Significant communication difficulties • Any conditions that may interfere with assessments or interventions	NPI MMSE Barthel Index WHO–UCLA AVLT	Music therapy has been shown to improve memory and speech in mild dementia cases, alleviate psychiatric conditions in severe dementia, and lessen caregiver stress
Gómez-Gallego et al., 2021 [1]	42 Active music therapy: 28 Passive music therapy: 21	Active music therapy: keep rhythm by clapping hands, dancing, or music quiz Passive music therapy: listen to music played on a CD player	6 weeks 2 weekly sessions of 45 min	Inclusion Criteria: • Mild or moderate stage of dementia, as per Clinical Dementia Rating • Informed consent to participate in the study • Receiving pharmacological therapy and cognitive stimulation therapy at nursing home Exclusion Criteria: • Aphasia • Hearing impairment affecting participation	GDS Barthel Index MMSE NPI	Passive music therapy helped maintain neuropsychiatric symptoms, while active music therapy significantly improved both cognitive function and neuropsychiatric conditions, potentially offering greater cognitive stimulation than its passive counterpart
Li et al., 2015 [25]	41 Passive music therapy: 20 Control group: 21	Passive music therapy: Music listening with headphones	6 months 30 min daily in the morning and before sleep	Inclusion Criteria: • Diagnosed with AD as per DSM-IV • Mild stage of AD (clinical dementia rating score between 0.5 and 1) • Under Acetylcholinesterase Inhibitors treatment for at least 3 months • Capable of participating without severe hearing loss • Free from major psychiatric disorders • Stable health condition • Support from family or caregiver to follow the study protocol Exclusion Criteria: • Severe hearing loss, major psychiatric disorders, or unstable health status	CASI NPI MMSE CDR-SB	While music therapy did not significantly enhance overall cognitive function or daily activities in mild AD patients over 6 months, it did support additional cognitive benefits in attention span and short-term memory

**Table 1** (continued)

Authors and date	Sample size, #Pts	Type of music therapy	Duration and frequency of sessions	Inclusion/exclusion criteria	Assessment tools	Key conclusion
Lin et al., 2011 [70]	104 Music therapy: 49 Control: 51	group music intervention (Combined active and passive music therapy) • Active Elements: Rhythmic activities, singing, instrument playing (glockenspiel) • Passive Elements: Listening to selected music based on patient preferences	6 weeks twice a week/30 min	Inclusion Criteria: • Diagnosed with dementia by a physician according to DSM-IV-TR • Age 65 years or older Exclusion criteria: N/A	MMSE C-CMAI	Following the group music therapy sessions, improvements were observed in the elderly with dementia, evidenced by a decrease in overall agitation, non-aggressive behaviors, and aggression. Notably, a decline in verbal aggression became apparent after six sessions. The therapy effectively mitigated agitation among these individuals
Arroyo-Anlló et al., 2013 [24]	40 A: 20 B: 20	A: Listening to a familiar song, in a passive (no singing along/ no movements) B: Listening to a non-familiar song	3 months 3 sessions per week/2–4 min at each session	Inclusion Criteria: • Hachinski Ischemic Scale score < 5 • Mild–moderate AD according to clinical dementia rating and Mini-Mental State (MMS) • Verbal comprehension (assessed by MMS three-stage command) ≥ 2 • History of progressive intellectual decline without motor or sensory features • Brain CT scan showing mild cortical and central atrophy only Exclusion Criteria: • Other pathologies or possible causes of dementia identified on Brain CT scan • Previous musical education or standard musical experiences (choirs, dance groups) • Hearing impairments	MMSE FAS self-consciousness questionnaire	Familiar music can enhance self-consciousness in AD patients, with varying effects across different aspects of self-consciousness. Implementing such music interventions at home and in geriatric institutions can evoke positive responses and emotional expression, reducing symptoms like agitation and depression. Moreover, these interventions can improve the quality of life for patients and their families by fostering emotional connections

**Table 1** (continued)

Authors and date	Sample size, #Pts	Type of music therapy	Duration and frequency of sessions	Inclusion/exclusion criteria	Assessment tools	Key conclusion
Guétin et al., 2009 [23]	30 Passive music therapy: 15 Control group: 15	Individual passive music therapy based on patient's personal preferences (determined through interviews/questionnaires)	18 months once a week/20 min sessions	<p><b>Inclusion Criteria:</b></p> <ul style="list-style-type: none"> <li>Mild to moderate AD</li> <li>MMSE score between 12 and 25</li> <li>Hamilton Anxiety Scale score <math>\geq</math> 12</li> <li>Age 70–95 years</li> <li>Adequate verbal/written expression, visual and hearing abilities (without hearing aids)</li> <li>Stable anticholinergic treatment for 6 months</li> </ul> <p><b>Exclusion Criteria:</b></p> <ul style="list-style-type: none"> <li>High likelihood of non-compliance or dropping out</li> <li>Life-threatening illness during the study period</li> <li>Other neurological disorders (stroke, Parkinson's disease, epilepsy)</li> <li>Lewy body dementia (presence of extrapyramidal symptoms, hallucinations, confusion)</li> <li>Dementia of possible vascular origin (modified Hachinski ischemia score <math>&gt;</math> 4)</li> <li>Frontal dementia (frontal score <math>&gt;</math> 3)</li> <li>Psychiatric disorders (schizophrenia, bipolar disorders, depression as per DSM-IV)</li> </ul>	<p>Hamilton Anxiety Scale</p> <p>GDS score</p> <p>MMSE</p>	<p>Music therapy is a beneficial and straightforward approach that supports the treatment of anxiety and depression in AD patients. It works by engaging various aspects of the disease, including sensory and cognitive functions. Passive music therapy is particularly effective in stimulating memory recall</p>

**Table 1** (continued)

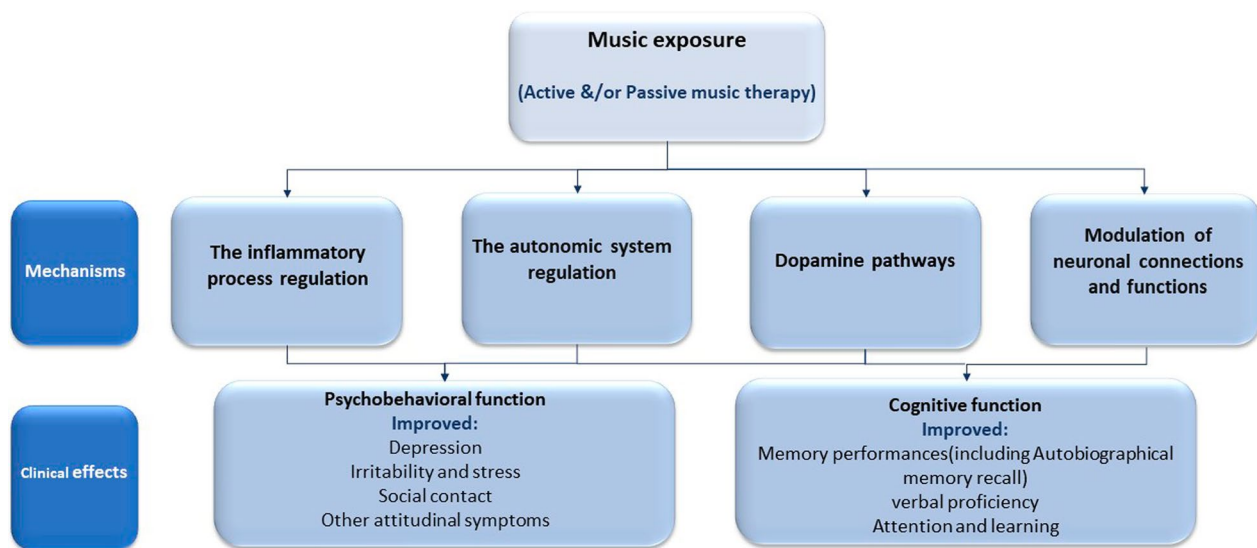
Authors and date	Sample size, #Pts	Type of music therapy	Duration and frequency of sessions	Inclusion/exclusion criteria	Assessment tools	Key conclusion
Sakamoto et al., 2013 [42]	39 Control group: 13 Passive therapy group: 13 Active music therapy group: 13	Active music therapy: Listen to music played on a CD player and clap, sing, or dance Passive music therapy: Participants listen to music played on a CD player	10 weeks once a week/30 min	Inclusion Criteria: • Diagnosed with Alzheimer's-type dementia as per DSM-IV • Severe dementia (Level 3) on the Clinical Dementia Rating Scale • No hearing impairments affecting music listening • No musical instrument playing experience • Age 65 years or older Exclusion Criteria: • History of heart disease, hypertension, or diabetes • Conditions affecting the autonomic nervous system	MMSE BEHAVE-AD Faces Scale	Music interventions, both passive and interactive, are effective in calming and reducing stress in severe dementia patients. Notably, these interventions led to a noticeable decrease in behavioral and psychological symptoms 2 weeks post-intervention, with the interactive method showing greater benefits. However, the positive effects diminished after 3 weeks. Interactive music therapy seems to aid in enhancing cognitive and emotional functions, which could improve social interactions for those with severe dementia
Gómez Gallego et al., 2017 [45]	42	Passive music therapy: Listening to music played on a high-quality stereo Active music therapy: singing, moving arms and hands, or guessing the name of it, rhythmic accompaniment activities with clapping and with musical instruments (triangles, tambourines, and maracas)	6 weeks 2 weekly/45 min	Inclusion Criteria: • Fulfillment of the criteria for probable AD as NINCDS-ADRDA criteria • Mild or moderate stage of Alzheimer's Disease according to the Clinical Dementia Rating Exclusion Criteria: • Presence of aphasia that impedes activity comprehension • Hearing impairment	MMSE HAD NPI Barthel Index	Music therapy positively impacted cognitive, psychological, and behavioral aspects in AD patients. Future research could explore the potential benefits of integrating music with dance therapy to enhance motor skills and functional abilities
Belenchia et al., 2023 [66]	21	individualized music listening with headphone for low agitation level/without headphone for high agitation level	Over 10 weeks 30 min	Inclusion Criteria: • Patients diagnosed with dementia • Admitted to the medical-surgical unit for inpatient care • Patients of any age, sex, and race Exclusion Criteria: • Family refusal • Medically unstable patients • Patients with severe hearing impairment or complete hearing loss	PAS	Custom music listening effectively calms dementia patients in hospitals, enhancing their stay and health results. This approach, which is non-medical and focuses on the individual, should be the initial option for treating dementia's behavioral and psychological issues, enriching scientific insights into high-quality, safe patient care



**Table 1** (continued)

Authors and date	Sample size, #Pts	Type of music therapy	Duration and frequency of sessions	Inclusion/exclusion criteria	Assessment tools	Key conclusion
Matziorinis et al., 2023 [46]	18 Active Music therapy: 6 Physical activity: 6 Control: 6	Physical activity: Warm-up, individual and group-based Physical activity, cool-down, indoor and outdoor training Nordic walking Music therapy: weekly singing lessons, Warm-up, vocal exercises, practice of choir songs, music listening Choir sessions	12 months 40 sessions once a week / up to 90 min	Inclusion Criteria: • First language: Norwegian • Diagnosis: Alzheimer's Disease • MMSE score: Above 10 (Moderate AD: 11–20, Mild AD: 21–30) • Residence: Living at home • Consent: Able to provide informed consent, with an accompanying caregiver's consent • MRI: Able to undergo MRI scanning Exclusion Criteria: • Psychiatric disorders: Severe cases like Major Depressive Disorder, Bipolar Disorder, Schizophrenia, Psychotic Symptoms • Brain injury: History of traumatic brain injury • Neurological disease: Conditions like Multiple Sclerosis, Epilepsy • Hearing: Severe auditory impairments • Mobility: Physical immobility • Vascular disorders: History of heart disease, heart attack, heart surgery, stroke • Other Dementia types: Lewy body dementia, Frontotemporal Dementia, Vascular Dementia • Claustrophobia • MRI compatibility: Ferromagnetic metal in soft tissue not compatible with MRI (pacemakers) • Residence: Living in a residential aged care facility	CERAD GDS MMSE FTT SPPB Mini-PROMS Stroop World list delayed recall sMRI fMRI DTI	The initial trial found the Alzheimer's and Music Therapy protocol unsuitable for mild-to-moderate Alzheimer's patients. In response, the study's scope has been widened to encompass individuals with early stage memory issues (pre-AD) and a more comprehensive set of cognitive tests

AD Alzheimer's disease, *AVLT* auditory verbal learning test, *BEHAVE-AD* behavior pathology in Alzheimer's Disease scores, *CASI* cognitive abilities screening instrument, *C-CMAI* Chinese version of the Cohen-Mansfield Agitation Inventory, *CDR* clinical dementia rating, *CDR-SB* Clinical Dementia Rating Scale with Sum of Box Scores, *CERAD* Consortium to Establish a Registry for Alzheimer's Disease, *CMAI* Cohen-Mansfield Agitation Inventory, *DTI* diffusion tensor imaging, *FAS* frontal assessment short test, *FFT* finger tapping test, *fMRI* functional magnetic resonance imaging, *GDS* Geriatric Depression Scale, *HADS* Hospital Anxiety and Depression Scale, *Mini-PROMS* mini-version of the profile of music perception skills, *MRI* magnetic resonance imaging, *N/A* not applicable, *MINDCS-AD/RA* National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association, *NPi* neuropsychiatric inventory, *PAS* Pittsburgh Agitation Scale, *Pts* patients, *sMRI* structural magnetic resonance imaging, *SPPB* short physical performance battery



**Fig. 1** Visual depiction of the beneficial effects of music therapy on AD and mechanism of music as a memory enhancer

autonomic nervous system triggered by slightly elevated music (quicker tempo, primary mode, higher pitch) [56, 57]; In contrast, calming music (low tone, slower speed, classical) may cause parasympathetic activation of the autonomic nervous system, leading to decreased skin permeability, pulse rate, blood pressure, and respiration [58]. As a result, music may modulate autonomic function, which in turn helps influence attentional processes during the coding of new information [52]. Patients with AD have higher levels of agitation, which may indicate higher physiological arousal [59]. Considering that greater agitation and anxiety can adversely impact attentional processes, it is possible that reducing anxiety and agitation can improve attention at encoding and hence memory performance [60].

#### The inflammatory process regulation

Cognitive decline and the presence of two primary pathologies, amyloid plaques, and neurofibrillary tangles, are the hallmarks of AD. The third major pathology in AD is the presence of a prolonged immunological response in the brain. It has been shown that consistent activation of the brain's local macrophages (microglia) and other immune cells worsens both amyloid and tau pathology and may play a role in the etiology of the disorder [61]. In addition, Cortisol levels are significantly influenced by the music stimulus. Music can modify immune system function, for instance by influencing the secretion of cytokines and the neuroendocrine response to stress [62]. As a result, music's favorable effect on immune system function may also slow neurodegeneration [61].

Figure 1 summarizes the benefits of music therapy and the potential mechanisms underlying its effect on memory.

#### Music selection affecting the effectiveness of music therapy

##### Individualized and non-individualized music

Music listening methodologies imply a music therapist creating a music playlist for the patient, which can be personalized or selected by the therapist. Generalized music approaches entail the use of music without the assistance of a music therapist to improve the participant's well-being. These techniques can also be considered active or passive protocols [44]. Individualized playlists seem to result in better cognitive and behavioral functioning in most active and passive music treatments [23, 24, 42, 45]. In addition, according to recent research, individualized music is more helpful in AD by improving autobiographical memory [52, 63–65]. Arroyo-Anlló and colleagues studied groups of people that listened to familiar and generalized music and discovered that the group listening to familiar music showed increased self-awareness and overall cognition [24]. Gómez Gallego and colleagues utilized personalized music and discovered benefits in the mental abilities of orientation, linguistics, and remembering, as well as improvements in anxiety and sadness [45]. Sakamoto and colleagues also found improvement in anxiety, emotional disturbance, aggressiveness, psychosis, and behavioral disruptions [42]. A recent investigation by Elizabeth J. Belenchia and her colleagues revealed that individualized music listening effectively reduces agitation in dementia patients in acute care

hospitals. This intervention improves the patient's experience, decreases fear during hospitalization, and leads to better outcomes. The most significant reduction in agitation was observed in motor agitation, followed by aberrant vocalization, resistance to care, and aggressiveness [66].

### Music genre and emotionality

Another implementation component that needs to be investigated further is whether the genre of music affects the results. Only the practical study by Meilán Garca and colleagues conducted this assessment among the articles. They discovered that "sad" music improved memory [65]. Emotional music also seemed to impact autobiographical memory more than non-emotional music. This is consistent with investigations of healthy people demonstrating the advantages of "sad" or "passionate" music, for example, in memorizing new faces, verbal memory, and phonemic fluency evaluation [30, 67, 68]. It is unclear whether this is because "sad" music creates an environment that is more beneficial to memory formation and retrieval or if it is because the emotional stimulation level is helpful for cognitive performance [67]. Sad music is advantageous to cognition, but this may be compensated by adverse effects on mood and health. Patients with severe depression may be more vulnerable since studies have indicated an increase in adverse facial expressions in this population when listening to sad music. Consequently, future research should assess if the negative consequences of specific music-based interventions exceed any potential advantages [67, 69].

### Future directions

This review provides some useful recommendations for subsequent research. First, the majority of studies have only examined the short-term effects of music therapy on AD, so more research is required to fully comprehend the long-term effects of music therapy. Second, further research is needed to determine how long music therapy sessions should continue. Third, it is necessary to determine the optimal time to initiate music therapy based on the progression of the disease. Fourth, the effects of music therapy in severe cases need further investigation, as most patients with mild to moderate AD were included in the previous trial, and the most severe cases were unable to participate due to their disability, especially in active approaches. These investigations should investigate potential solutions that can enable music therapy use in patients with severe AD. Fifth, given the controversial findings regarding the effects of active and passive music therapy, more research is required to determine

which method is more advantageous in improving each domain for different subgroups of patients. Sixth, more trials are needed to assess the genre-specific pros and cons of music selection in patients with AD.

### Conclusions

We reviewed the effects of music therapy on the management of AD. Previous studies suggest that music therapy can be a beneficial non-pharmacological treatment as an adjunct. Notably, music memory is preserved in AD as it is partially separate from other memory processes, and patients with AD still retain some of their musical recall while having significant cognitive deterioration. Music therapy may help AD patients via four mechanisms, including activation of neurogenesis and neuroplasticity, activation of dopamine release, modulating the autonomic system, and modulating the inflammatory process. Music therapy proved to be an effective treatment for cognitive abilities such as episodic memory and autobiographical memory, which were enhanced in most studies. It also proved to be effective, especially in alleviating psychiatric and behavioral symptoms. It was shown to reduce anxiety and depression and improve the social bonding of patients. The major limitation of the relevant studies is that AD patients in moderate to severe stages cannot participate in music therapy because of their disability, especially active music therapy approaches. Moreover, further investigations are needed to evaluate the long-term effects of music therapy, as most studies had a short follow-up period, while the recent long-term follow-up study revealed impractical results.

### Abbreviations

AD	Alzheimer's disease
CASI	Cognitive abilities screening instrument
GDS	Geriatric depression scale
MMSE	Mini-mental state examination
NPI	Neuropsychiatric inventory
MOSES	The multidimensional observation scale for elderly subjects
PET	Positron emission tomography
CBMT	The certification board for music therapists
MT-BC	The music therapy board certification

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SNB: conceptualization, investigation, writing—original draft, writing—review and editing, SM: conceptualization, investigation, writing—review and editing, NR: conceptualization, writing—review and editing, supervision.

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### Availability of data and materials

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## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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