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The effectiveness of music therapy for the treatment of Alzheimer's disease - A Review

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1. ABSTRACT

Introduction: Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most prevalent cause of dementia. It is caused by the degeneration of brain cells due to the accumulation of intracellular hyperphosphorylated tau - containing neurofibrillary tangles and extracellular plaques of amyloid-beta peptide. While pharmacotherapy remains the main form of treatment (including cholinesterase inhibitors and antagonists to NMDA), various non-pharmacological therapy modalities have gained increasing attention as complementary treatment options, such as music therapy.

Purpose of the study: This review examines the role of music therapy as an important complement to baseline therapy for AD patients, focusing on indications, methods, and the

prospect of music therapy.

Materials and methods: A comprehensive literature review was conducted, analyzing 48 studies from the PubMed database (English-language, up to November 2024) that assess the efficacy, methods, and prospect of music therapy as an adjunctive therapy in Alzheimer's disease.

Conclusions: Music therapy is an established and effective supportive treatment for AD patients. It has demonstrated clinical success over many years as a tool for engaging multiple motor and sensory areas, shaping emotions, and evoking memories. This may be due to activating limbic and paralimbic structures, enhancing neuroplasticity, and modulating neurotransmitter systems. Despite the observable benefits of music therapy, the methodological limitations of existing studies highlight the need for further long-term research to standardize treatment approaches.

Keywords: Alzheimer's disease, Music Therapy, Non-pharmacological treatment, New Therapy

2. INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most prevalent cause of dementia [1]. Nearly 55 million people suffer from AD [2] and the number is predicted to triple by 2050, due to the aging of the population. Both prevalence and mortality rates are higher among women than men [3].

The disease is caused by the degeneration of brain cells, as a result of the accumulation of plaques of amyloid-beta peptide (Aβ) [1] and hyperphosphorylated tau (p-tau) that form neurofibrillary tangles (NFTs). These proteins are perceived as a foreign body, which stimulates the response of the immune system and leads to inflammation. That process disrupts the connection between nerve cells, affecting synaptic transmission, axonal transport, and signal transduction, leading eventually to cell death and loss of brain tissue [4]. The pathogenesis is influenced by various factors, but the most important risk factor is age [5].

Plaque deposition occurs much earlier than symptoms; they can be detected up to 15 years before manifestation insert [6]. AD usually presents with cognitive decline, with short-term memory difficulty being the most common symptom. Other manifestations include aphasia, apraxia, or agnosia [1].

The diagnostic process is complex and it includes neurological examination, magnetic resonance imaging (MRI) for neurons, and laboratory examinations such as vitamin B12 levels [1]. Clinically AD can be divided into 6 stages: asymptomatic with deterministic gene; asymptomatic with biomarker evidence only; transitional decline: mild detectable change, but minimal impact on daily function; cognitive impairment with early functional impact; dementia with mild functional impairment; dementia with moderate functional impairment; dementia with severe functional impairment. Biologically we can distinguish four stages A-D, staged by amyloid and tau uptake in positron emission tomography (PET) or with a combination of T1 fluid markers and tau PET [6].

The treatment of Alzheimer's disease relies currently on two drugs: cholinesterase inhibitors, such as donepezil, rivastigmine, or galantamine, and antagonists to N-methyl d-aspartate (NMDA), including memantine [1]. While drug therapy is a base form of treatment, various non-pharmacological therapy modalities have gained increasing attention as complementary treatment options, including cognitive training and music therapy [7].

Music therapy is a clinical- and evidence-based usage of music interventions to accomplish individualized goals by a credentialed professional. It includes both active and receptive techniques [8]. Music therapy can influence mood, cognitive functions, memory, and sense of personal identity, which could significantly help in the management of symptoms of dementia. Various evidence suggests that it could be a useful therapy form in AD patients [7], as it seems to be a safe and adjunctive therapy to alleviate symptoms of the disease [9].

3.STATE OF KNOWLEDGE

3.1.Music-evoked memories and emotions

Music is omnipresent and an integral part of human nature. Activities related to listening to music can be tools for engaging and causing changes in multi-sensory and motor networks [10]. Music can evoke strong emotions and affect mood [11]. Furthermore is often associated with important life events for a given individual. The brain can store memories and emotions experienced during such an event, and then recall them when listening to music associated with them [12]. This effect is used in work with people who have lost autobiographical (episodic) memory - this group includes patients suffering from Alzheimer's disease (AD). For patients with AD, music can be an effective signal to recall autobiographical memories and experience strong emotions. This can enable them to establish

contact with loved ones and themselves, influencing a sense of connection, and improving mood and cognitive functions [11].

Music therapy has been used for many years as a support in combating the symptoms of dementia [13,14]. Studies have shown that this method can alleviate the effects of dementia – patients who underwent music therapy improved the fluency of categorical vocabulary and autobiographical memory [15,16]. Autobiographical memory is a long-term memory of life experiences, mainly episodic. It refers to memories related to spatial and temporal contexts [17]. Emotions are also a component of autobiographical memory. Emotional memories are much easier to recall compared to memories without an emotional element [18,19].

Patients suffering from AD, despite impaired autobiographical memory, have an intact ability to recognize familiar melodies [20]. On this basis, there have been suggestions that music-evoked autobiographical memories (MEAM) are preserved in Alzheimer's disease. MEAM can be very detailed and can evoke immediate emotional reactions [21].

In 2012, El Haj et al. conducted a study of the MEAM in healthy patients and patients with a clinical diagnosis of probable AD. The patients were asked to recall autobiographical memories in different conditions with music of their choice and silence. Memories recalled with music were more detailed, emotional, and recalled faster. The study also showed that these memories engaged fewer executive processes. All these features of autobiographical memories, as well as the fact that they were activated by a perceptual cue (i.e., music), allow them to be classified as involuntary memories [22].

In 2020, Alaine E Reschke-Hernández et al. conducted a study involving 20 patients with AD and 19 healthy individuals. Participants were played 4.5-minute blocks of music of their choice to induce sadness or happiness. Both groups reported negative emotions after listening to sad music and positive emotions after listening to happy music. Negative and positive feelings lasted about 20 minutes after induction. The study concludes that music can affect emotions in people with AD [23]. Moreover, it has been shown that even music unfamiliar to a patient with AD can improve their episodic memory.

In 2006, Muireann Irish et al. conducted a study in which patients with mild AD were asked to recall important life situations from the past. The study was conducted in two variants - once without music, and once with Vivaldi's "Spring" from The Four Seasons playing in the background [15]. Patients with AD recalled memories much more easily when music was playing in the background. However, studies show that memories and accompanying emotions are stronger when the music is chosen by the patient [23].

In 2018, Jihui Lyu et al. conducted a similar topic study in which music therapy was used in patients with mild, moderate, and severe AD. The study included 298 patients. The patients were randomly assigned to three groups (singing, reading lyrics, and control) for 3 months. The studies were conducted first after 3 months and then after 6 months. The results showed that singing has a better effect on improving verbal fluency and reducing psychiatric symptoms than reading lyrics. In addition, active music therapy has a positive effect on improving memory, especially in immediate and delayed recall. However, these effects were not maintained after 3 months after the end of the study. The results suggest that music therapy may be useful in speech training and in controlling psychiatric and behavioral symptoms. In addition, group music interventions may help improve social interactions in patients with AD. The authors of the study suggest that continuous use of music therapy may have a positive effect on patients with AD in both the short and long term [24].

The ability of music to evoke memories strongly correlates with the ability to evoke emotions. Functional neuroimaging studies of emotions and music have indicated hippocampus activity changes [25]. This suggests that the hippocampus whose function is known in autobiographical memory, is also involved in music-induced emotions. The co-localization of music-induced emotions and memory functions may explain why episodic memory recall may be easier with music. However, further research is needed. Currently, few studies focus on music therapy in patients with AD, most of the studies concern dementia in a broad sense. However, it is known that the hippocampus is not the only structure involved in this correlation, which is promising in the fight against AD symptoms. A more detailed pathophysiology will be discussed later.

2.1. Methods of music therapy

Music Therapy (MT) is a specialized intervention based on the therapeutic use of music, administered by qualified music therapists who employ music to achieve clinical goals within a therapeutic relationship. MT involves interactions among the patient, the therapist, and the music itself. Regarding music in MT, misconceptions often arise, such as the belief that certain musical genres are inherently beneficial or that specific genres are likely to negatively impact health. However, the music preferred by each individual is typically the most effective and therapeutic, regardless of genre or lyrical content. The use of live, preferred music during interactive MT can also foster a stronger therapeutic alliance and result in improved

therapeutic outcomes [26].

Within music therapy, various techniques are applied, including music listening, singing, music-based interventions, background music, music integrated with activities, and multisensory stimulation [27].

- **Music Listening**

In 2015, Li CH et al. implemented a listening intervention involving Mozart's Sonata (KV 448) and Pachelbel's Canon through headphones for patients with mild Alzheimer's disease (AD). Results indicated that MT had a positive effect on supporting cognitive functions, specifically abstraction [28]. A study in 2013 by Arroyo-Anlló EM et al. found that listening to familiar Spanish songs stabilized or improved self-awareness (SC) in patients with mild to moderate AD. The AD group exposed to familiar songs performed better on the MMSE and Frontal Assessment Short (FAS) tests compared to the group exposed to unfamiliar songs [29].

- **Singing**

In a 2015 study by Satoh et al., 10 patients participated in MT sessions incorporating singing training once a week for six months. Another 10 AD patients were recruited as a control group. In the MT group, the time required to complete the Japanese Raven's Colored Progressive Matrices was significantly reduced, and caregiver interviews revealed a notable reduction in Neuropsychiatric Inventory scores and an increase in patient sleep duration. fMRI analysis showed increased activity in the right angular gyrus and left lingual gyrus when comparing pre-MT and post-MT interventions [30].

- **Music-based Interventions**

In 2015, Palisson et al. conducted a study where 12 patients with mild AD and 15 healthy controls learned texts presented with either a musical (sung) or a nonmusical association (spoken associated to a silent movie sequence) or without association (spoken alone). Immediate and delayed recall (following a 5-minute delay) was measured. Key findings indicated that musical association during encoding facilitated learning and recall in AD, and this benefit appeared to be specific to music [31].

- **Background Music**

In a 2006 study by Irish et al., notable improvement was observed in autobiographical memory recall on the Autobiographical Memory Interview for AD patients in the music condition, with an interaction effect for condition by group. A significant reduction in state anxiety was identified on the State-Trait Anxiety Inventory in the music condition ($p < 0.001$), suggesting that anxiety reduction may be an underlying mechanism enhancing the effect of music on autobiographical memory recall [32].

- **Music with Activities**

MT increasingly explores incorporating music alongside other activities, such as singing, dancing, playing instruments, and rhythmic movements [27]. In 2017 Gómez Gallego M and colleagues engaged 42 individuals with mild or moderate AD in an intervention combining music with various activities, including greetings, dancing, and instrumental play. The 6-week intervention demonstrated that music, when combined with other activities, could simultaneously improve cognitive status and alleviate neuropsychiatric symptoms in AD patients [33].

- **Multisensory Stimulation**

Beyond pharmacotherapy for dementia, there is a growing trend toward interventions combining multiple cognitive stimuli, referred to as multisensory stimulation [27]. A study conducted by Hee-Jin Kim et al. in 2017 reported that a 6-month cognitive multisensory stimulation program - encompassing art, music, exercise, memory activities, and gardening therapy - improved memory test scores and social functioning in AD patients [34].

In a 2016 study by Spina et al., MT showed a beneficial effect on cognitive functions. At the program's end, improvements were observed in tests assessing frontal lobe functions (cognitive flexibility, processing speed, attention, and working memory), suggesting that MT may enhance frontal functions, acting as a training ground for these cognitive skills. Memory improvements were also observed. These results align with previous research describing MT’s beneficial impact on frontal function and memory in individuals with brain injuries, mild cognitive impairment, and dementia [35,36]. Unfortunately, no significant differences from baseline were noted six months post-program, indicating that MT’s beneficial effect on cognitive abilities tends to diminish after treatment ends [37].

2.2. Brain mechanisms responsible for the effects of music therapy

This section delineates the primary neural pathways and processes through which music therapy affects AD, supported by contemporary research findings.

- **Activation of Limbic and Paralimbic Structures**

The limbic system, encompassing structures such as the amygdala, hippocampus, and anterior cingulate cortex, plays a pivotal role in emotion regulation and memory processing. Music therapy engages these regions, thereby enhancing emotional responses and facilitating memory recall. Notably, the hippocampus, which is crucial for the formation of new memories, remains relatively preserved in the early to moderate stages of AD. Studies have demonstrated that familiar and preferred music can activate the hippocampus and amygdala, leading to improved emotional well-being and reduced agitation in AD patients [38].

- **Enhancement of Neuroplasticity and Functional Connectivity**

Neuroplasticity refers to the brain's ability to reorganize itself by forming new neural connections. Music therapy promotes neuroplasticity by strengthening functional connectivity between disparate brain regions, including the auditory cortex, prefrontal cortex, and hippocampus. This enhanced connectivity supports cognitive functions such as attention, executive function, and memory. Research in 2003 by Gaser and Schlaug indicates that musical training induces structural changes in the brain, suggesting that music therapy could similarly foster neural resilience in AD [39].

- **Modulation of Neurotransmitter Systems**

Music therapy influences the dopaminergic and serotonergic systems, which are integral to mood regulation and cognitive processes. Listening to music stimulates the release of dopamine in the mesolimbic pathway, enhancing mood and motivation while mitigating symptoms of depression and anxiety commonly observed in AD patients. Additionally, music-induced serotonin release contributes to improved mood stability and reduced aggression, thereby enhancing overall quality of life [40].

- **Hemispheric Synchronization and Bilateral Brain Engagement**

Engaging with music involves the simultaneous activation of both hemispheres of the brain, promoting hemispheric synchronization. This bilateral engagement enhances interhemispheric communication, which is often compromised in AD. Rhythmic and melodic elements of music facilitate the coordination between the left and right hemispheres, thereby improving cognitive processing speed and memory retention. Studies have shown that musical activities can lead to increased connectivity and synchronization across hemispheric networks, supporting cognitive functions that are otherwise deteriorating in AD [41].

- **Reduction of Stress and Neuroinflammation**

Chronic stress and associated neuroinflammation are significant contributors to the progression of AD. Music therapy has been shown to lower cortisol levels, thereby reducing physiological stress responses. By mitigating stress, music therapy can decrease neuroinflammatory markers, which are implicated in neuronal damage and cognitive decline. Furthermore, the relaxation response elicited by music promotes parasympathetic nervous system activity, fostering a state of calm and reducing the overall stress burden on the brain [42].

- **Enhancement of Sensory Integration and Social Connectivity**

Music therapy facilitates sensory integration by engaging multiple sensory modalities simultaneously, including auditory, visual, and motor systems. This multisensory engagement can enhance cognitive functions and promote neural network efficiency. Additionally, group music therapy sessions foster social interaction and emotional bonds among participants, reducing feelings of isolation and enhancing social cognition. Enhanced social connectivity not only improves emotional well-being but also stimulates cognitive engagement, which is beneficial in slowing the progression of AD symptoms [43].

- **Preservation of Musical Memory and Procedural Memory**

Interestingly, musical memory and procedural memory often remain intact longer than declarative memory in AD patients. Music therapy leverages this preserved memory system to facilitate cognitive and emotional engagement. Familiar tunes and rhythms can evoke autobiographical memories and support the retrieval of personal histories, thereby reinforcing a sense of identity and continuity in individuals with AD. This phenomenon underscores the

unique ability of music to tap into deeply ingrained memory networks that are resilient to AD pathology [5].

The multifaceted brain mechanisms through which music therapy exerts its effects on Alzheimer's disease underscore its potential as a valuable adjunctive treatment. By activating limbic and paralimbic structures, enhancing neuroplasticity, modulating neurotransmitter systems, promoting hemispheric synchronization, reducing stress and neuroinflammation, enhancing sensory integration and social connectivity, and preserving musical and procedural memory, music therapy addresses both the cognitive and emotional dimensions of AD. Future research should continue to elucidate these mechanisms to optimize therapeutic protocols and maximize the benefits for individuals living with Alzheimer's disease.

2.3. The prospect of music therapy for Alzheimer’s disease

The findings of lots of results show that music therapy could have a positive impact on AD patients, especially on their cognitive functions. Music therapy seems to be a promising cognitive rehabilitation process. Improvements in memory, executive functions, or attention can enhance the quality of life of both the patients and their caregivers [44]. The early interventions have a greater chance for a deceleration of cognitive decline, and perhaps even preventing the onset of disease [45].

The music can facilitate the recall of episodic memories, even if the music is not related to the recalled events. It has been used as a therapeutic means to stimulate social bonding and preserve their sense of personal identity in AD patients [46].

One of the most significant outcomes of music therapy in Alzheimer's disease is its effect on quality of life (QoL). Several studies have reported that music therapy interventions lead to improved QoL measures, including enhanced social interaction, increased participation in daily activities, and reduced feelings of depression and isolation. A 2014 study by Särkämö et al. found that individuals with AD who participated in regular music therapy sessions demonstrated greater social engagement and a more positive effect compared to a control group.

Furthermore, music therapy can provide a meaningful and enjoyable activity for individuals with AD, promoting a sense of autonomy and self-expression, particularly as the disease progresses and verbal communication becomes more difficult. The rhythm and

melody inherent in music can evoke memories and feelings of connection, thus offering both patients and caregivers a form of non-verbal communication [47].

Music therapy has emerged as a promising and well-tolerated intervention for individuals with Alzheimer's dementia, offering a non-invasive approach to improve emotional well-being and manage behavioral symptoms. Research indicates that music therapy can effectively enhance emotional expression, foster social connections, and alleviate non-cognitive symptoms. It has been shown to reduce cortisol levels - a key marker of stress - thereby helping to mitigate symptoms of anxiety and depression. In addition, while the impact on behavioral symptoms, such as aggression, is less pronounced, music therapy still provides notable benefits in calming agitation and improving mood in patients with dementia.

Despite these positive outcomes, there are several methodological limitations in the existing literature, including variability in study designs, intervention protocols, and sample sizes. These factors contribute to inconsistencies in the reported results and highlight the need for further investigation. Larger-scale, longitudinal studies are essential to confirm the long-term efficacy of music therapy and to develop standardized treatment protocols that can optimize its benefits for Alzheimer's patients [48].

3. CONCLUSIONS

Non-pharmacological forms of treatment in AD are important complements to baseline therapy consisting of cholinesterase inhibitors and NMDA antagonists. The training of cognitive functions is proven to alleviate AD's symptoms and help maintain patients' social interactions which play a crucial role in positively influencing the prognosis of AD.

Music therapy is an established and effective supportive treatment for AD patients. It has demonstrated clinical success over many years as a tool for engaging multiple motor and sensory areas, shaping emotions, and evoking memories. A long list of brain mechanisms that are potentially responsible for the therapy's effects includes activating limbic and paralimbic structures, enhancing neuroplasticity, and modulating neurotransmitter systems.

Music therapy notably enhances autobiographical memory and fluency of categorical vocabulary by utilizing a range of techniques and multisensory activities. It also has a great influence on controlling psychiatric and behavioral symptoms. One of its most significant advantages is the marked improvement in quality of life as it effectively boosts mood, strengthens social interactions, and mitigates anxiety, depression, and isolation among

patients. Given the disappearance of the effects of therapy soon after its completion, it requires continuity and the introduction of its elements in various forms into patients' daily routines to maintain its beneficial aspects.

Despite the apparent effects of music therapy due to the many methodological limitations of the available sources, further long-term research is needed to help standardize treatment.

DISCLOSURE

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