Music Therapy and its Effects on Alzheimer's Disease

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Received November 09, 2024
Accepted March 13, 2025
Electronic access April 30, 2025

Alzheimer's disease (AD) is a common form of dementia that results in cognitive decline, memory loss, and behavioral changes. Symptoms of AD are results of beta-amyloid plaque accumulation, neurofibrillary tangles, and neuronal loss. These effects pose challenges for patients as they lead to behavioral issues such as memory loss, cognitive difficulties, and more. Recent studies suggested music therapy as a multifaceted approach to address these challenges in AD patients. This literary review examined the impact of music therapy on Behavioral and Psychological Symptoms of Dementia (BPSD), neuroplasticity, and neurotransmitter regulation in AD patients, highlighting the potential benefactors of using music therapy as a treatment of AD patients. Evidence shows that music therapy reduces aggression, agitation, and anxiety, significantly improving BPSD symptoms. It also enhances neuroplasticity by stimulating dopaminergic regions, facilitating social interactions, cognitive improvements, and better emotional expression. Functional MRI studies further revealed increased neural connectivity and efficiency in patients undergoing music therapy. Moreover, music therapy regulates key neurotransmitters such as dopamine and serotonin, which are crucial for mood and cognitive functions. This paper reviews multiple dimensions of how music therapy affects AD and delved into the underlying mechanisms that explain the effects of music therapy. It also offers insight into how future studies can be improved to discover more about the pathology of music therapy. However, the full effects of music therapy on AD are still unclear and whether it can be used as an ongoing intervention still needs to be evaluated. Overall, music therapy offers a promising non-pharmacological intervention for improving the cognition and behavior of AD patients.

Keywords: Alzheimer's disease, music therapy, dementia, neuroplasticity, neurotransmitters, BPSD, non-pharmacological interventions, fMRI

Introduction

Alzheimer's disease (AD) is one of the most common forms of dementia that results in the neurodegeneration of the brain, causing the decline of cognitive function, memory, and changes in behavior and action[1]. This neurodegenerative disorder arises from various factors including the accumulation of beta-amyloid plaques and neurofibrillary tangles[2,3], which leads to the decrease in function of neurons and synapses[4]. These factors contribute to the hallmark symptoms of AD, such as behavioral and psychological symptoms of dementia (BPSD), reduced neuroplasticity, and imbalances in inhibitory and excitatory neurotransmitters. The complex nature of AD pathology poses a significant challenge for developing effective therapeutic strategies. Despite extensive research, safe and effective treatments for all have yet to be discovered. For instance, lecanemab is an immunotherapy prescribed for the early stages of AD, which targets the protein beta-amyloid to help reduce beta-amyloid plaques, slowing down the neurodegenerative process of AD. Nevertheless, lecanemab can cause amyloid-related imaging abnormalities (ARIA), a condition that causes brain bleeding and brain swelling[5], leading to issues as severe as death or disability[6,7]. Side effects of AD drugs also include vomiting, headaches, confusion, and tiredness[8].

Additionally, patients with histories of seizures, cerebral amyloid angiopathy-related inflammation (CAA-ri), or amyloid beta-related angiitis (ABRA) are unable to receive treatment due to higher risk for ARIA and limited research performed on these patients[9]. Lastly, AD drug efficacy is also reduced with age, and it may lose effectiveness over time, serving as a short-term treatment rather than long-term[10,11]. Due to the complications that arise with the use of drug therapies, researchers have begun to consider non-pharmacological interventions that can be given in addition to or in place of pharmacological treatments as a more effective and stable form of treatment.

Recent research indicates that non-pharmacological multifaceted therapeutic interventions, which target multiple pathological pathways, has shown promising results in improving this disease[12]. For instance, lifestyle modifications, including diet, exercise, and cognitive stimulation have contributed positively to AD management[13]. One such multifaceted intervention is music therapy, which has gained increasing popularity as a non-pharmacological intervention for AD. Music therapy has been effectively used to treat various conditions like high blood pressure, anxiety, and depression due to its ability to alleviate stress and improve mood[14]. Music

therapy, with its potential to be a stable form of treatment, offers a sense of security and ease in the often-turbulent landscape of AD treatment.

Music therapy engages multiple cognitive functions and stimulates the release of critical neurotransmitters such as dopamine and serotonin. These neurotransmitters play vital roles in regulating mood, cognition, and reward pathways, which are often disrupted in AD patients[15]. Research demonstrates that music therapy is a way to improve AD symptoms and potentially slow disease progression. Music therapy also enhances neuroplasticity by engaging the brain's auditory and emotional processing centers, thereby promoting its ability to reorganize and form new neural connections[16]. Moreover, music therapy has been shown to influence underlying biological mechanisms associated with AD. A study conducted by Kanduri et al. has shown that music therapy can boost the expression of genes such as SNCA, RTN4, KLF4, and CD24, which are involved in neurodevelopment and neural growth[17]. These genetic changes provide strong evidence that music therapy could serve as a long-term therapeutic strategy for AD patients, promoting brain health and resilience against neurodegenerative processes.

In summary, AD presents a severe challenge to the medical field due to its complex pathology and intricate pathways. Multifaceted therapeutic approaches, such as music therapy, offer a promising route to alleviating symptoms and potentially slowing disease progression. By enhancing neuroplasticity, regulating neurotransmitter levels, and alleviating BPSD symptoms, music therapy presents a promising intervention that requires further exploration and integration into AD treatment regimens.

Music therapy effects on BPSD

BPSD is considered one of the most challenging aspects of AD. BPSD symptoms encompass a wide range of behavior and emotional disturbances, including agitation, anxiety, depression, delusions, hallucinations, and apathy[18]. However, BPSD in AD patients are not merely random occurrences. Instead, they are meaningful expressions that allow them to express their emotions and communicate their needs[19]. Even then, addressing these symptoms is crucial for improving of quality life for AD patients. Music therapy helps alleviate the stress of BPSD in many ways, as it can engage areas of the brain that remain intact despite the progression of dementia. First, music therapy has been found to reduce cortisol levels, a biomarker of stress in AD patients. The reduction of cortisol contributes to the decrease of agitation in AD patients and slows the progression of BPSD symptoms[20]. Second, as music memory often lasts longer than other types of memories, it can facilitate reminiscence, thereby triggering specific memories and creating a sense of familiarity and comfort in the environment[21,22] . This familiarity can significantly reduce anxiety and improve emotional well-being in AD patients.

Numerous studies have demonstrated promising effects of music therapy on BPSD. For instance, Whear et al. investigated the impact of music therapy administered during mealtimes on patients with BPSD. This study analyzed eleven comparative studies to identify improvements and correlation between music therapy and BPSD symptoms. The interventions included in the study were those conducted in care home settings that provided comparative data on mealtime interventions specifically designed to alleviate dementia-related behaviors. Participants were patients aged 65 years or older with dementia. The results of this meta-analysis showed that listening to music during meals significantly decreased physical and verbal aggression and non-aggressive disruptive behaviors, signifying a decrease in BPSD[23]. A limitation in this study is the fact that most results only come from observations, and the underlying mechanisms of exactly how music therapy benefits BPSD needs to be further studied. Additionally, Chang et al. performed a meta-analysis of randomized trials that evaluated effects of music therapy on disruptive behaviors, anxiety levels, and depressive mood. The analysis found that music playing significantly reduced disruptive behaviors and anxiety levels in patients with dementia, thereby emphasizing the positive outcomes of implementing music therapy into daily routines of AD patients[24].

Often, BPSD causes stress and anxiety in patients with dementia[18]. Music has been observed to help alleviate this stress by activating the parasympathetic nervous system (PSNS), which, when activated, reduces stress, anxiety, and improves mood[25]. Compared to healthy individuals, the PSNS is significantly reduced in AD patients, causing sympathetic dominance and sympathovagal imbalance[26]. Sympathetic dominance and sympathovagal imbalances can lead to chronic stress and social anxiety, the most common states of BPSD[27]. To discover the effects of music therapy on the PSNS, Sakamoto et al. gathered thirty-nine patients with severe AD and separated them into a no-music control group, a passive music group, and an interactive music group. The findings indicated that short-term PSNS dominance was present after moderate passive and interactive music activity. BPSD reduction was found in both the interactive and passive music groups while symptoms increased in the control group. However, three-weeks after the cessation of music therapy, BPSD symptoms increased across all three groups, indicating that music therapy would only be a plausible solution if treatment was served as a long-term intervention[28]. Although this study indicated positive results, further research needs to be done with more standardized procedures.

Additionally, music therapy's efficacy is not only limited to independent applications; it can be effectively combined with other therapeutics. For instance, when paired with physical activity, music therapy can help reduce restlessness, anxiety,

irritability, and aggression in patients with dementia[29]. Studies have highlighted that combining music therapy with physical activity not only prevents motor dysfunction and improves cognition, but also increases attention span, improves memory, and reduces agitation in patients with BPSD[30–32]. Music therapy can also enhance the effectiveness of pharmacological treatments. Giovagnoli et al. examined the combined impacts of passive music therapy and memantine (M) on BPSD on forty-five AD patients. The study formed two groups: one receiving M and active music therapy (M-AMT) and another, the control group, receiving only M. The patients were all on stable doses of acetylcholine inhibitors (AchEI). Groups were compared to evaluate whether or not combining music therapy with M would improve depressive symptoms and communication among AD patients. The results indicated that the M-AMT group experienced a greater reduction in depression and anxiety compared to the control group. Additionally, the M-AMT group showed increased motor activity and euphoria after 24 weeks of treatment. Even though positive results were shown, the groups did not exhibit statistically significant differences for all examined samples. These findings suggest that music therapy paired with drug treatment can enhance the management of BPSD, particularly in alleviating anxiety and depression in AD patients[33].

Music therapy effects on neuroplasticity

Neuroplasticity is the ability of the brain to change neuronal pathways in response to internal and external stimuli, and it is severely impaired in patients with AD[34,35]. Listening to music have been found to increase cerebral blood flow and increase dopaminergic projection, both of which lead to increased neuroplasticity. Dopaminergic projections are crucial for motor learning and are found to be associated with cortical synaptic plasticity. Studies have shown that impairments in dopaminergic systems causes impaired motor skill acquisition as dopamine is crucial for learning and memory processing[36,37]. Diminished cerebral blood flow (CBF) in areas including the frontal cortex, nucleus accumbens, and temporal gyrus, has been a significant contributing factor to a continuous decrease of cognition in AD patients[4]. Music therapy has been revealed to increase CBF in the prefrontal cortex, which led to improved cognitive impairments in patients with mild cognitive impairment[4]. Moreover, PET scans have revealed increased CBF changes in dopaminergic regions like the ventral striatum and cingulate gyrus in response to passive music listening[38]. AD patients also experience neuronal energy deficits, disrupting neuroplasticity. Music can increase CBF by leading to secondary dilation of blood vessel, which can also better help the brain meet metabolic needs, bridging a connection between music and improvements in neuroplasticity[39]. Music induced improvements in neuroplasticity can be explored in five domains: Social, emotional, cognitive, speech and communication, and movement.

Music therapy serves as a way to increase social interactions between AD patients and their peers. AD patients are mostly withdrawn or refuse to interact with others, reducing social communication[40]. In contrast, increasing social interaction among AD patients presents memory and communication benefits. Through music therapy, therapists can encourage AD patients to interact with each other through instrument sharing or by singing together. When groups of people come together to make music, stress levels are reduced due to increased production of the adrenocorticotrophic hormone, positivity and endorphin levels are increased, all while negative emotions decreased[41–43]. Group singing, or other synchronized human activities, were also found to release endorphins, increase pain tolerance, and assist in social bonding[42,44]. Repeated social interaction through music therapy can establish new neuronal connections within the brain as neural pathways activated by music processing are closely related to pathways activated by social processing[45]. Through music induced bonding, AD patients are able to increase neuroplasticity and interact more with other patients. Furthermore, connecting music with dopaminergic pathways can build and improve upon connections associated with proper emotional expression while repressing improper emotional expression, such as aggression[46]. In the context of AD, music-based interventions involving synchronized group activities, have the potential to regulate hormonal and neuromodulator levels, providing a new path for increasing neuroplasticity in patients[46].

Communication requires language, memory, and cognition. Music listening and language production share certain interconnected properties. For instance, both linguistic and musical syntax share common synaptic processes that are executed by the same brain regions[3]. Studies have shown that language processing and melody analysis were correlated at regional and network levels, proving neuronal link between the two processes[47]. Musical stimuli were also found to facilitate word learning and long-term memory of learned words, further proving correlation between music, memory, and speech[48]. In the context of AD, music can serve as a beneficial therapeutic for memory and language impairment in patients. Not only can music improve neuroplasticity through passive music listening, it can also improve neuroplasticity in AD patients through movement. As music contains rhythm and beat, patients with mobility issues can often overcome the difficulty of moving by being in sync with the music. By associating music with walking, the increase in dopamine and neural synchrony stimulates the strengthening of cortical remapping and increases neuroplasticity[46].

Additionally, fMRI studies have shown changes in the brain after patients are treated with music therapy. The studies indicated that listening to music can uplift mood due to increased

connectivity between certain networks in the brain. Results also show that patients were able to carry out tasks like karaoke more easily using a smaller area of the brain after music therapy and singing interventions[49]. This is referred to as neuronal efficiency, in which the brain uses a smaller region to efficiently carry out a once complicated task[50]. For instance, neuronal efficiency is seen when individuals use a smaller region of their brain to complete a task whereas another might need to use a larger region of their brain[51], and this aids in better performances when repeating a task[52]. Although fMRI studies have repeatedly shown increased brain activity while listening to music, the correlation between the two in the context of AD are not yet supported by sufficient evidence. Future studies can seek to use fMRI on AD patients to discover a more specified correlation between brain activity and music.

Specifically, King et al. 2019 analyzed the effects of passive music listening on neural networks within AD patients using preferred music. Music listening tasks were given to 17 different patients. The tasks consisted of 24 blocks of 20 second random ordered selected music. The 24 blocks consisted of 8 blocks of the selected music played forward, 8 blocks reversed, and 8 blocks of silence. This procedure showed that both forward and reverse musical stimuli activated the bilateral auditory cortex, areas of left lateral frontal lobe, and cerebellum. To evaluate the functional improvements of music, 10-minute resting state fMRI acquisitions were performed, and functional connectivity was evaluated. Significantly higher functional connectivity was observed in the corticocortical and corticocerebellar networks of patients after the music tasks. However, due to the small sample size, no individual connections were significantly significant, leading to the inability to prove music therapy to other AD patients even though the mean functional connectivity was significantly higher after the trails. Further research with larger sample sizes should be taken into consideration for more accurate and reliable results. Moreover, musical memory in AD is generally spared from neurodegeneration, and recognizing famous music passages has been associated with preserved brain tissues in the anterior temporal lobe[53].

Neuroplasticity is severely impacted in AD, leading to neuronal network damage and impairing the ability for patients to form new networks[54]. This damage is linked to alterations such as neuronal network disarrangement and cell death, proposing that synaptic dysfunction may be a key contributor to cognitive decline in AD patients[34]. Music therapy can help improve neuroplasticity by having patients engage in different tasks that enhance their cognitive abilities, thereby amplifying neural network connections and cognition in AD patients. Furthermore, fMRI studies have shown that music therapy leads to improvements in neuronal network connections as well as neuronal efficiency, helping AD patients recover neuroplasticity.

Music therapy effects on neurotransmitters

Neurotransmitters are often imbalanced in AD patients[55], leading to cognitive impairments. Excitatory and inhibitory neurotransmitters such as Glu and GABA play important roles in the regulation of cognition and behavior in the human body[56]. Glu, an excitatory neurotransmitter, is linked closely with learning and memory and it is the metabolic precursor of GABA[56,57] . GABA, an inhibitory neurotransmitter, is associated with memory and mood[58]. Neurotransmitters like dopamine and serotonin also play essential roles in cognitive functions. Dopamine plays an essential role in learning and motor control while serotonin regulates mood and many neuropsychological processes[59]. Music therapy helps to alleviate neurotransmitter imbalance in AD patients, resulting in cognitive and behavioral improvements.

Excitatory and Inhibitory Neurotransmitters

In AD, the balance between excitatory and inhibitory neurotransmitters, crucial for cognitive function, becomes disrupted, leading to cognitive decline[60]. For example, a major hallmark of AD, beta-amyloid plaques (Aβ), interfere with GABA levels and cause cognitive dysfunction in AD patients[61]. Furthermore, studies have shown that Glu levels are also significantly lower in AD patients, affecting dopamine levels in the body as well[62].

Many factors contribute to the progression of AD symptoms, one of which is a reduction in gamma oscillations. A reduction in gamma oscillations is associated with memory dysfunction, one of the more prominent symptoms of AD. GABA, an inhibitory neurotransmitter, is linked closely with memory and mood and plays an important role in regulating gamma oscillations. Studies have found that music therapy influences GABA levels in the brain as well as enhances gamma oscillations in music listeners. Moreover, listening to more somber music is found to increase GABA levels and reduce Glu levels, while listening to more uplifting music can decrease Glu levels and increase GABA levels[4]. In AD patients, significantly lower levels of GABA and Glu are observed, leading to deficiencies in synaptic function and neuronal transmission. These results suggest that music therapy may improve and regulate levels of excitatory and inhibitory neurotransmitters in AD patients, potentially improving synaptic function and cognition.

In a clinical study conducted by Juanjuan Hao et al., Chinese Traditional Five Element Music Therapy was used on rats to test the effects of music on neurotransmitters and behavior. Different types of music were tested on rats to examine changes in GABA and Glu levels. Groups exposed to more powerful and upbeat music demonstrated a more significant increase in motor activity and Glu levels, whereas groups exposed to more depressive music experienced a reduction in motor activity

and an increased GABA levels. These results indicate that different types of music can differentially affect inhibitory and excitatory neurotransmitters. The data from this experiment was calculated to be significant, however, bigger group sizes can be used to further validate the results of the study. In AD patients, neurotransmitters like Glu and GABA are lower than normal, which affects their cognition and behavior. As music can increase the levels of these neurotransmitters, it may be an effective treatment to help improve behavioral symptoms in AD patients[63].

Dopamine and Serotonin

Dopamine and serotonin are crucial neurotransmitters that regulate various bodily functions. In AD patients, levels of these neurotransmitters are significantly reduced compared to healthy individuals, with up to 40% decreases in serotonin and 67% decrease in dopamine levels[64,65]. This reduction adversely affects mood, cognitive functions, and reward pathways. Dopamine (DA) and serotonin (5-HT) have their own monoaminergic systems. Music therapy can affect dopaminergic pathways like nigrostriatal and mesocorticolimbic pathways, which regulate reward systems, emotion, and motor control (See Figure 1). Similarly, music also increases the activity of serotonergic neurons that have the ability to activate sleepiness, appetite, and positive mood as serotonin is released from the raphe nuclei (See Figure 2)[66]. These neurotransmitters are essential for motor control, reward systems, and emotional regulation[59]. In addition, dopamine and serotonin are more concentrated in areas like the caudate-putamen (CPu) and nucleus accumbens (NAcc), regions of the brain that connect to motor control and the reward system[67].

Music listening has been proved to activate NAcc regions and increase DA response. Menon and Levitin's analysis of music listening and its connection with the mesolimbic structures reported strong correlations between NAcc response and DA release in association with music[68]. In addition, this is further proven through a study by Moraes et al. 2018, who examined studied the the link between exposure to music and dopamine and serotonin levels in rats. Moraes measured the concentrations of DA, 5-HT, 5-hydroxyindoleacetic acid (5-HIAA), and 3,4-dihydroxyphenylacetic (DOPAC) in the brain of the rats after passive music therapy. The results show that exposure to classical music significantly increased levels of dopamine and serotonin. In the CPu, DA concentrations were elevated by 24.1% while DOPAC/DA ratios, which reflect dopamine turnovers and 5-HIAA/5-HT ratios, which indicate serotonin turnovers, were not greatly influenced. This shows that while DA levels increased, regular DA and 5-HT metabolism remained stable and were not disrupted by the increase of DA levels. In NAcc, the DOPAC/DA ratio was increased by 61.6%, while 5-HIAA/5-HT ratios were unaffected. The increase in DOPAC/DA ratio indicates a more significant breakdown of DA, which could result from enhanced dopaminergic neuron activity and increased production of DA. Meanwhile, 5-HIAA/5-HT ratios were not affected, showing that the changes in DOPAC and DA did not impact dopamine turnover[66]. In summary, music therapy can induce increases in DA and 5-HT levels, which may help raise the levels of DA and 5-HT in AD patients, improving their cognitive function. In the context of AD, music therapy can potentially serve as a therapeutic to improve DA and 5-HT imbalances. Future research can focus on the specific affects of music on AD patients regarding DA and 5-HT levels.

Discussion

This review analyzes how music therapy can impact main symptoms of AD-BPSD, reductions in neuroplasticity, and imbalances in neurotransmitters, highlighting how music therapy has benefitted AD patients in clinical studies and provides evidence for mechanisms underlying how music therapy can alleviate AD symptoms, slow disease progression, and offer potential future treatment for AD patients.

Music therapy has proven effective in alleviating BPSD symptoms in AD patients. When combined with other therapeutic approaches, music therapy helps reduce symptoms like restlessness, irritability, and anxiety by creating a soothing environment through its rhythmic and melodic elements[20]. fMRI studies indicate that passive music listening increases functional connectivity between neuronal networks, thereby enhancing neuroplasticity[53]. However, the underlying biological mechanisms regarding this have still not been discovered, and there is still limited evidence as to whether or not music therapy can serve as a long-term treatment for the enhancement of neuroplasticity. Music is often paired with activities to help generate new neural networks or enhance existing ones for new specific tasks[46]. For example, patients engaging in activities while listening to music can strengthen neural pathways related with these functions. These findings highlight the potential of music therapy to facilitate neural adaptations and improvements, offering promising avenues for future treatment of AD patients. Furthermore, music therapy has been shown to regulate levels of neurotransmitters such as Glu and GABA, which are crucial for cognitive function and behavior in AD patients[61,62] . Music therapy also increases dopamine concentration and serotonin levels, contributing to improved mood and cognition in AD patients[66]. As music is known to elevate important neurotransmitter levels, why this happens can be further investigated. Furthermore, there is still a limited amount of research regarding elevations of neurotransmitters in the context of AD. Using music as a therapeutic provides a non-pharmacological intervention that enhances emotional and behavioral regulation in AD patients.

Although many studies have demonstrated the benefits of

music therapy for AD patients, others did not, suggesting variability in music therapy efficacy. For instance, a study involving 10 patients with dementia engaged in a 10-week singing intervention aimed to analyze the effects of music on cognitive behavior in dementia patients. The findings revealed a decline in cognition, behavior, and psychological issues[69]. Furthermore, another study involving 120 patients with moderate to severe dementia and BPSD were treated with music therapy. The study found no significant improvements of BPSD in the patients, but did show reductions in delusions, anxiety, and disinhibition[70]. The variability in results can be due to limited data and a lack of primary research studying mechanisms of music therapy in improving BPSD or cognitive symptoms. As many existing studies have small sample sizes, there is a need for studies with larger sample sizes to improve on result accuracy and holistic representation of the AD patient population. Moreover, there is a need for a more rigorous and systematic standard for music therapy to ensure accurate study results and optimal patient outcomes[71]. For instance, variations in the type of music used, duration of therapy, and patient characteristics can all influence outcomes and make it challenging to draw accurate conclusions. Researchers are currently developing music therapy toolkits to enhance the quality of music and health research[72] . In the future, more research utilizing neuroimaging techniques such as fMRI should be conducted to better understand the effects of music therapy on different neural pathways. Additionally, further exploration of integrating music therapy with other therapeutics may enhance its effectiveness.

Overall, while music therapy shows promise as a non-pharmacological intervention for improving cognition and behavior in AD patients, additional research is necessary to fully understand its mechanisms and optimize its application. Addressing research gaps, such as long-term outcomes and potential side effects of AD, and gaining a more holistic understanding of how music therapy enhances AD pathology will help establish it as a standard component of AD patient care.

Methods

This review includes meta-analyses and clinical trials taken from PubMed from June, 2024 through August , 2024. Studies published within the last decade were used as evidentiary support, and older studies were used to further validate recent research. Bibliographical references were checked for relevant studies related to the topic. The search strategies used were as follows: “Alzheimer’s Disease”, “music therapy”, “neurotransmitters”, neuroplasticity”, and “BPSD”. Clinical trials and meta-analyses using music therapy interventions on patients or non-patients were selected. Studies involving the use of any type of music therapy on AD patients were included, and studies with statistical evidence were also evaluated. Most studies involve patients over the age of 65 and often reside in a care-home setting for treatments. Other non-pharmological intervention studies like bright-light therapy were excluded from this review. The overall effect of music therapy on rats and non-patients was first evaluated. The results from these preclinical studies were then compared with effects of music therapy on AD patients, drawing conclusive evidence of how music therapy affects AD pathology. Articles were considered if they were published within the last decade and were evaluated based on relevance to the topic.

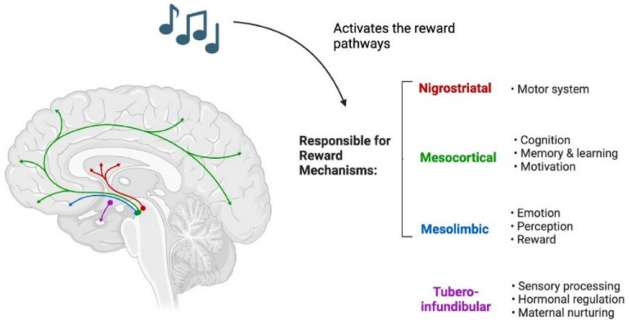

Fig. 1 Music effects on dopaminergic pathways. The dopaminergic system comprises the nigrostriatal, mesocortical, mesolimbic, and tuberoinfundibular pathways[73]. Of the four, the nigrostriatal, mesocortical, and mesolimbic pathways are responsible for the brain’s reward systems, cognition, memory, and motivation- all of which are generally affected in AD patients[66]. fMRI studies have shown that brain regions involving the mesocortical and mesolimbic pathways are highly activated during music listening[66], which in turn regulates impaired cognitive functions like memory, emotion and perception in AD patients[74].

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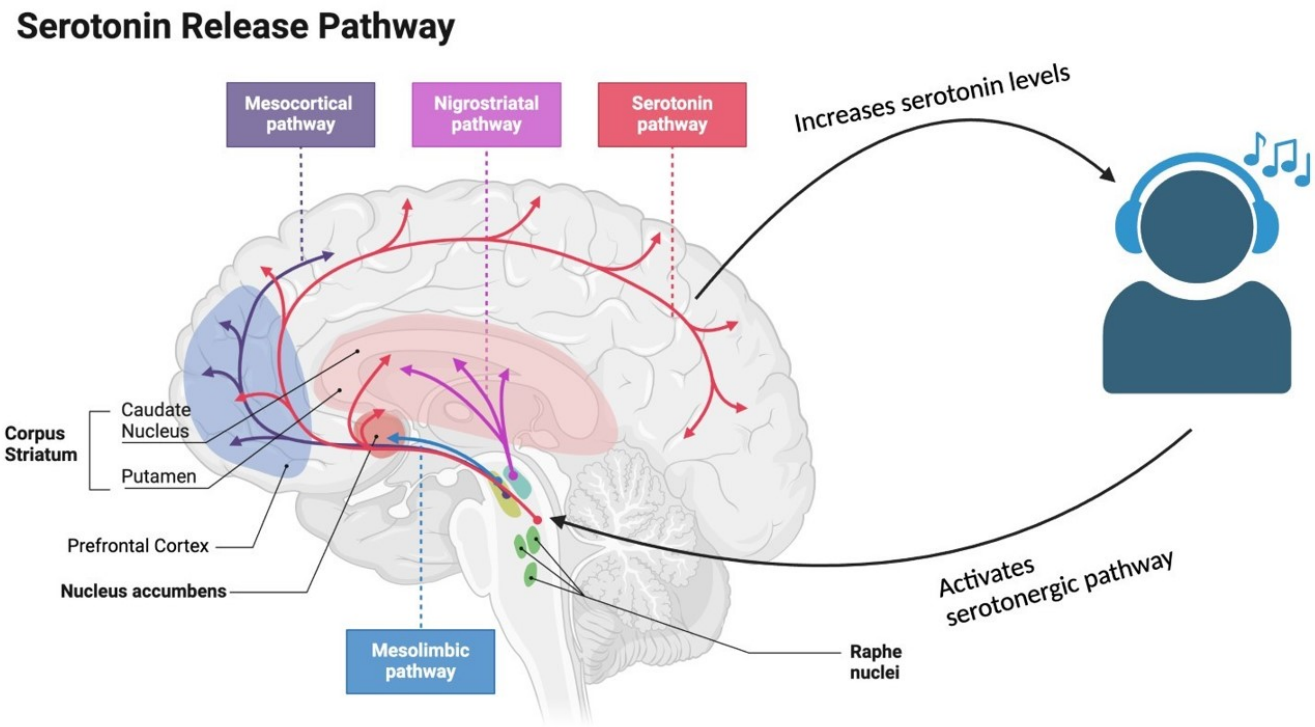

Fig. 2 Music effects on the serotonergic pathway. Serotonin neurons originate from the raphe nuclei and can signal/project to numerous other structures of the brain[75], and the release of these neurons are accompanied by its effects of sleepiness, appetite, and positive mood. Music listening activates the serotonergic pathway and increases serotonin levels in return. The serotonergic pathway also works closely with the mesocortical and nigrostriatal pathways (dopaminergic pathways). As serotonin increases, it also increases DA levels by decreasing the release of GABA[66].

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