Music therapy as an alternative for Alzheimer's disease patient care

Author: Vishesh Kathuria

Abstract

Alzheimer's disease is the most common form of dementia accounting for 60-80% of dementia cases. Clinical features include progressive memory decline, visual and spatial disorientation, alteration in personality, agitation, irritability, aggression and anxiety caused by the formation of amyloid β plaques and tau neurofibrillary tangles. Despite the high occurrence, we still don't have a reliable treatment for the disease. However, recently music therapy has become a novel way to improve some of the clinical symptoms of the disease. Music Therapy is an established health treatment in which music is used within a therapeutic relationship to address physical, emotional, cognitive, and social needs of individuals. It is a non-pharmacological method, which has proven to be beneficial with dementia patients. Multiple studies indicate that music therapy has the ability to reduce cognitive decline especially in autobiographical and episodic memories, psychomotor speed, executive function domains and global cognition. The aim of this paper is to review the literature on music therapy and after doing so, we concluded that music therapy had positive effects on various skills like spatial temporal reasoning. Parasympathetic nerve activity became dominant. Affective disturbance, anxieties and phobias, paranoid and delusional ideation, and the global rating (which indicates caregiver burden) were reduced. Lastly, the music memory was positively affected.

Introduction

Alzheimer's disease is the most common cause of dementia in the globe. In 2016 in the USA, an individual developed Alzheimer's disease every 66 seconds, which is projected to change to 33 seconds in 2050[1]. Currently, 47 million people live with dementia globally, and it is estimated to increase more than threefold (~131 million) by 2050[2].It is caused by β-amyloid plaque deposition and neurofibrillary tangles of hyperphosphorylated tau[3] which are considered to be the 'hallmarks' of Alzheimer's Disease pathology. This increased production of β-amyloid 42 by β secrete and γ secretase is caused by the mutations in the genes for amyloid precursor protein (APP) and presenilins (PS1,PS2) which are integral membrane proteins .The

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[1] "2016 Alzheimer's Disease Facts and Figures." 2016. *Alzheimer's & Dementia* 12 (4): 459–509. https://doi.org/10.1016/j.jalz.2016.03.001.

[2] Tiwari, Sneham, Venkata Atluri, Ajeet Kaushik, Adriana Yndart, and Madhavan Nair. 2019. "<p>Alzheimer's Disease: Pathogenesis, Diagnostics, and Therapeutics</P>." *International Journal of Nanomedicine* Volume 14 (July): 5541–54. https://doi.org/10.2147/ijn.s200490.

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microtubule which is associated to tau tangles is a phosphoprotein consisting of 80 serine and 5 tyrosine phosphorylation sites. Normal tau count in the brain is 2-3 moles of phosphate per mole of the brain. However, tau is abnormally hyperphosphorylated to a stoichiometry of at least three-fold greater than normal tau, and in this altered state it is aggregated into paired helical filaments forming neurofibrillary tangles[4].The pathology of these molecules is very complex as they consist of many chemical constituents like residue of pathogenic gene mutation, which might result from cellular degeneration, or reflect the acquisition of new proteins by diffusion and molecular binding[5].

A major cause of Alzheimer's is aging. Early onset Alzheimer's disease (EOAD) is characterised for individuals diagnosed with Alzheimer's disease a t age lesser than 65, whereas late onset Alzheimer's disease is diagnosed in individuals with age greater than the age of 65. Indeed, Alzheimer's Disease prevalence increases significantly with age, and AD incidence increases from 2.8 per 1000 person years for people between 65 and 69 years to 56.1 per 1000 person years for people who are older than 90 years[6]. Nearly 60% of Early onset alzheimer's disease have had cases of Alzheimer's disease in their families, and of these cases 13% are inherited in an autosomal dominant manner with at least previous 3 generations affected.

Early signs of Alzheimer's disease include memory loss that disrupts daily life, challenged in planning or solving problems, difficult in completing familiar tasks, confusion with time or place, and problems with words in speaking or writing[7]. In addition to this, symptoms of Alzheimer's disease include loss of memory and procedural memory, disrupted orientation to time and place, language impairment, and behavioral and psychiatric symptoms like depression are very common too.[8]

Despite the high prevalence and mortality rates of Alzheimer's disease, there are only 5 approved medical treatments for it. These treatments don't act to alter the course but just to control the symptoms of the disease[9]. Current treatments include cholinesterase inhibitors for patients with any stage of Alzheimer's disease and memantine for people with moderate- to-severe Alzheimer's disease. In an Alzheimer's disease patients' brain the level of Acetylcholine is lower than the normal range which is responsible for sending messages between certain nerves (parasympathetic nervous system, the part of the autonomic nervous system). Due to the lack of Acetylcholine, the neurons which use this neurotransmitter die which makes the symptoms worse. Donepezil, rivastigmine and galantamine all prevent an enzyme called acetylcholinesterase from breaking down acetylcholine. This means there is a higher concentration of acetylcholine in the brain, which leads to better communication between nerve cells. This may ease some symptoms of Alzheimer's disease for a

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[4] Wang, Jian-Zhi, et al. "Abnormal Hyperphosphorylation of Tau: Sites, Regulation, and Molecular Mechanism of Neurofibrillary Degeneration." *Journal of Alzheimer's Disease*, edited by George Perry et al., vol. 33, no. s1, Dec. 2012, pp. S123–39, doi:10.3233/jad-2012-129031.

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while[10]. These medications have been shown to enhance the quality of life for both patient and caregiver when prescribed at the appropriate time during the course of illness; however, they do not change the course of illness or the rate of decline. So it can be clearly seen that there are no current methods which could "cure" the disease and prevent neurodegeneration but rather help with some of the symptoms of the disease[11].

A novel method to treat the given symptoms is music therapy. Neurologic music therapy is a new scope of music therapy. Its techniques deal with dysfunctions resulting from diseases of the human nervous system. Music can be used as an alternative modality to access functions unavailable through non-musical stimulus. Processes in the brain activated by the influence of music can be generalized and transferred to non-musical functions. Processes in the brain activated by the influence of music can be generalized and transferred to non-musical functions, so in clinical practice, the translation of non-musical therapeutic exercises into analogous, isomorphic musical exercises is performed[12].Various studies and clinical trials have concluded that music therapy does help in improving cognitive, psychological, and behavioral symptoms like memory, orientation, depression and anxiety in Alzheimer patients[13] proving its effectiveness . However, further evidence and analysis is still required to understand the mechanisms and efficacy of this therapy for AD.

Alzheimer's disease and music therapy

In recent years, the use of music therapy has grown in popularity as a method of non-pharmacological and a non-invasive technique for treatment for Alzheimer's patients.

Various studies have shown that music therapy can affect Alzheimer's patients in a positive way. A case study by Johnson and colleagues, in which the subjects were 74 year old monozygotic twins with no family history of dementia in which one twin had Alzheimer's disease and the other didn't have Alzheimer's disease, both having 14 years of education. The mini mental state exam score of the AD twin was 23 (mild dementia) and the score of the NC (for anonymity) twin was 27. To analyse the data the PF&C (Paper fold and cutting task) scores were analysed before and after 3 sessions of listening to a piece by Mozart. For the AD twin when the pre and post test scores of the sessions were analysed there was a remarkable improvement seen in the scores of an average 3.67/8 points showing improvement in spatial temporal reasoning. On the second day of testing, the post-test score again improved. Thus, this improvement was observed across all Mozart listening testing sessions and with two PF&C sets. No improvements, however, were observed in the post-test scores obtained by the AD twin following all of the control conditions. Therefore, this study acts as supporting evidence towards the efficacy of music therapy[14]. However, it needs to be considered that even

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[10] "How Do Drugs for Alzheimer's Disease Work?" 2011. Alzheimer's Society. 2011. https://www.alzheimers.org.uk/about-dementia/treatments/drugs/how-do-drugs-alzheimers-disease-work#:~:text=Cholinesterase%20inhibitors%20(donepezil%2C%20rivastigmine%20and,messages%20between%20certain%20nerve%20cells.

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[14] Julene Johnson, Carl Cotman, Cora Tasaki & Gordon Shaw
(1998) Enhancement of spatial-temporal reasoning after a Mozart listening condition in Alzheimer's disease: A case study, Neurological Research, 20:8, 666-672, DOI:

though the research showed strong correlation the sample size is extremely small which limits the statistical power of the results. Therefore, even though the study does support the efficacy of music therapy, it is not credible enough to provide a conclusion whether music therapy is effective as an alternative for Alzheimer's disease patient care.

A clinical trial conducted by Sakamoto and colleagues recruited 127 dementia patients from which 39 met the eligibility criteria. In the study, 3 groups (Non-intervention Control, Passive music intervention and Interactive music intervention) were compared in which each intervention was performed for 30 minutes once a week for ten weeks. In the Control group, a caregiver and music provider observed participants from a distance without directly interacting with them and any music intervention. The Passive group participants passively listened to the selected music via a CD player, which means there wasn't any interaction like singing along, or dancing. In the Interactive music intervention, the session was conducted individually by a music facilitator who directly interacted with each participant like singing along, dancing, and clapping. The music facilitators watched the participants before intervention and determined each participant's level of cognitive function and Behavioral and Psychological Symptoms of Dementia (BPSD) characteristics. In the Passive group, the comparison of the autonomic nervous system indices. The autonomic nervous system is a control system that acts largely unconsciously and regulates bodily functions, such as the heart rate, digestion, respiratory rate, pupillary response, urination, and sexual arousal.Before and after music intervention the parasympathetic nerve activity (The parasympathetic nervous system is one of three divisions of the autonomic nervous system) became dominant. This was also seen in the interactive group but there wasn't a significant increase in the parasympathetic nerve activity. For long term, which is after 10 intervention sessions for the Passive groups, the phobias of the patients were reduced. In the Interactive group, affective disturbance, anxieties and phobias, paranoid and delusional ideation, and the global rating (which indicates caregiver burden) were reduced. In the control group, activity disturbance and affectivity disturbance were increased. In contrast, three weeks after music intervention BPSD had significantly increased in both the Passive and Interactive groups after the sessions had ceased. The Control group exhibited no changes in BPSD at three weeks after the intervention[15]. This study had a relatively larger sample size of 39 patients compared to the previous study however this still isn't large enough and does not consider different ethnicities and genetic backgrounds. On the other hand, the study displayed particular attention to the control variables, like using the same room for the music sessions everyday and using the same musical facilitators which shows that they paid really close attention to other factors of the study minimising sources of error. Unlike to the previous case study analysed, this clinical trial does provide strong evidence that music therapy can have a positive impact on alzheimer's patients as the BPSD did significantly increase in the passive and interactive groups.

A case report by Cuddy *et al.,* in which music memory was tested in one subject 'EN' (For anonymity). From the time of diagnosis, the mini mental status examination (MMSE) which is a widely used test of cognitive function among the elderly and includes tests of orientation, attention, memory, language, score had declined

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10.1080/01616412.1998.11740582

[15] Sakamoto, Mayumi, Hiroshi Ando, and Akimitsu Tsutou. 2013. "Comparing the Effects of Different Individualized Music Interventions for Elderly Individuals with Severe Dementia." *International Psychogeriatrics* 25 (5): 775–84. https://doi.org/10.1017/s1041610212002256.

slowly over the two years from 23 to 18. EN was given several tests of music perception and memory and these sessions were conducted in a quiet room for 10-20 minutes. There were 3 tests conducted: Familiarity decision test, Distorted tunes test, and Famous melodies test. In the Familiarity decision test 10 familiar excerpts from vocal (eg happy birthday) and instrumental (eg Blue Danube) pieces mixed with 10 unfamiliar which were the reverse in pitch and time of the familiar excerpts. The task is to determine which excerpts are familiar. The controls found this test to be very easy. EN responded to the familiar tunes by singing along with words and continued with melodies after the song stopped. The subject never responded to the unfamiliar songs and had a perfect score. The Distorted tunes test included 26 popular melodies such as "silent night" from which 17 were distorted by a change of pitch, where the task was to determine which tune had been distorted. Majority of the controls scored 25 or 26. EN responded to the familiarity of the melodies with apparent enjoyment and again hummed or sang along with the tunes long after the test music had stopped. However, she responded to distorted melodies with facial expressions surprise, laughter, or a frown or exclamation "Oh, dear!" Allowing these responses as indicators of detection, the result for EN was a score of 25/26. The last test was the Famous melodies test in which participants are asked to indicate the familiarity of, and to give the name of, a series of melodies. There are also eight novel melodies in the series, for a total of 115 melodies. Song and instrumental melodies were intended to be highly familiar for a Canadian sample of normal controls. There are also eight novel melodies in the series, for a total of 115 melodies. Song and instrumental melodies were intended to be highly familiar for a Canadian sample of normal controls. Given the results for the first two tests, the researchers were concerned whether all the melodies of the Famous melodies test would have been familiar to EN before the onset of Alzheimer's disease. So, they obtained from a family member a selection of 11 test melodies that EN was not likely to have ever encountered. These 11 melodies were presented but not included in the final score (EN did not recognize them). With behavioral observation as the recognition measure, EN's score for song melody recognition was 86% correct and for instrumental melody recognition was 64% correct. These results provide encouraging support that music therapy can have a positive effect on music memory in AD patients[16]. However, the tests which are used are very subjective, for instance in the Familiarity decision test it was assumed that excerpts like happy birthday and Blue Danube would be familiar to EN which might not be the case. Moreover it would have been better if the brain activity was measured using electrodes, as relying on facial expressions isn't very reliable. The unreliability of these tests makes this study not a very credible one, to prove music therapy is a reliable alternative for Alzheimer's disease patient care.

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[16] Cuddy, Lola L., and Jacalyn Duffin. 2005. "Music, Memory, and Alzheimer's Disease: Is Music Recognition Spared in Dementia, and How Can It Be Assessed?" *Medical Hypotheses* 64 (2): 229–35. https://doi.org/10.1016/j.mehy.2004.09.005.

Concluding Remarks

From the literature analysed it can be concluded that music therapy does help to slow down the progression of Alzheimer's disease and also relieve some of its symptoms. However, due to the unreliability of the research, more research is still required to prove whether music therapy is a reliable alternative for Alzheimer's disease patient care.The first study which was analysed showed promising results but the small sample size, reduced its credibility to a large extent. The second study showed positive results which can be relied upon due to the great detail the researchers went in and also because it had a relatively larger sample size of 39 people. The third study cannot be used as evidence to support music therapy, as the methods it used were not credible to rely up. It needs to be considered that there isn't any Uniformity of clinical trials as different trials have completely different areas of research under music therapy which makes it very difficult to compare and analyse them. If more research was to be conducted and had more uniformity it would become easier to compare them and reach a conclusion. Moreover, Research has shown that the auditory cortex is not affected in Alzheimer's disease unlike the visual cortex which makes music therapy a reliable treatment as we will be able to use an unaffected part of the brain to alter the affected parts. Therefore, researching music therapy can provide us with promising results, but as of now we cannot reach any conclusion.

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