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Searching for Memory Lane: The Extent that Music can Aid in the Treatment of Patients with Alzheimer's Disease

Tristan Latchford
Durham University

ABSTRACT

There are numerous academic articles that draw links between listening to music and retrieved memory functions in patients with Alzheimer's Disease. Whilst many of these studies explain the process of memory recall in patients, they do not address the clinical applications of their findings. The aim of this study is to draw together four separate studies and discuss to what extent their findings suggest music could provide treatment solutions for patients with Alzheimer's Disease. Critically appraising these studies and synthesising them enables us to answer to what extent current studies link memory processes with music, whether those processes are agreed upon between the studies, and how the findings of the studies can be used to improve the clinical environment. The appraisal of these studies shows promising results for music as a therapeutic tool, and for future models of mapping memory processes (e.g. proteinopathy, separate memory encoding spaces, etc.).

1. SEARCHING FOR 'MEMORY LANE'

There are countless studies that discuss the link between music and increased performance in memory function. Although there is much evidence for links between music and working memory, a much smaller body of research exists to explain the links between music and improvements in other forms of memory. In this essay, I will discuss two recent studies that look at music based memory enhancement in patients with Alzheimer's disease, and examine their findings. I will then look at a study discussing the neurophysiology of why long term musical memory is preserved in Alzheimer's disease, and another discussing applying musical therapy to patients with Alzheimer's disease. I will then conclude by discussing the ramifications of these studies, and the clinical applications of their findings.

2. 'MUSIC-BASED MEMORY ENHANCEMENT IN ALZHEIMER'S DISEASE: PROMISE AND LIMITATIONS'

In their study in 2010, Simmons-Stern, Ally, and Budson concluded that patients with Alzheimer's disease (AD) recognised visually presented lyrics better when they were presented in conjunction with music (when being encoded in the brain). Attempting to build off this, as part of their follow up study in 2012 (Simmons-Stern et al., 2012) they hypothesised that musical memory encoding would enhance familiarity and recollection within their test-group.

They first addressed a number of oversights in their previous study, including distortions in their findings due to 'false recognition.' This is a particularly common trait of patients with AD, and thus makes discussing results difficult if there is no measure to counteract this. Citing Schacter (1999), they note that 'Minimization of false recognition and other memory distortions is essential to normal memory function' (Simmons-Stern et al., 2012: 3297). They made it their goal to analyse the rate of false recognition, and hypothesised a lower rate in sung stimuli. Whilst this seems a reasonable assumption at the outset, it quickly becomes problematic as they attempted to minimise this factor so as not to affect the study's overarching results. Perhaps further study could shed closer light on any correlation between false recognition and sung stimuli.

They also used 'Pr,' a measure of discrimination that accounts for false recognition first used by Snodgrass and Corwin (1988). To counteract the fact that this measure was outdated, Simmons-Stern et al. (2012) hypothesised that the conditions of the experiment would mediate the participants' response bias. The extent to which this is true cannot be discerned from their article, as no account was given of what clinical stage of AD each patient suffered from at the time of taking the test. It is highly likely that patients in middle stages of AD would have higher rates of false recognition than those in early stages. Regardless, a more recent alternative to Snodgrass and Corwin's framework could have been provided by Budson et al. (2002).

Twelve participants with clinical diagnosis of AD and seventeen healthy adults participated in the study. The healthy adults were screened for first-degree relatives with AD, and any other physiological or psychiatric illness that would hinder the study. Three participants were excluded as a result of a neuropsychological test battery, and two further were removed because of an experimental error. This leaves a small sample size from which to draw conclusions.

All participants were tested individually in a single session lasting one and a half hours. A key factor that was overlooked here is that patients with AD often experience worsening symptoms with low energy levels (Poehlman and Dvorak, 2000). Patients with AD are thus likely to show worse symptoms of impaired memory function when tired. Differing energy levels in participants is therefore likely to affect the results of the study, especially as it lasts over an hour.

All participants were presented with the lyrics to 40 songs, in order to equalise intelligibility. Only a single set of lyrics was studied for each object. The lyrics were presented in a uniform format to all participants. 20 were accompanied by a sung recording and 20 by a spoken recording. Immediately following this, participants answered two questions about the objects. After a short break of 40 minutes, participants were presented with the stimuli and asked to make new decisions on each.

Their results showed that the AD patients had significantly more false alarms than the healthy older adults, and also showed that false alarm rates were lower for the sung condition than the spoken condition. Their results showed that general content information studied in sung lyrics may be remembered better than that studied in spoken lyrics. This was found for both AD and healthy participants. They did also note that memory for specific content information did not benefit from musical encoding.

Whilst the study shows promising results, the small sample size and the variation in participants indicate that it cannot be conclusive. Simmons-Stern et al. (2012) do provide a strong argument as to why music does affect the memorial processes however, proposing that musical encoding of memory creates a robust but non-specific representation in the brain, outside of the medial-temporal lobe. They support this proposal with evidence from Curran and Dien (2003), that familiarity may be derived from a distributed neural network. Their proposal also links to studies of the relationship between music and 'working memory,' a form of short-term memory that has been shown to be enhanced by music (see Burunat, Alluri, Toiviainen, Numminen, & Brattico, 2014). The proposed network suggests that working memory is imprinted in wider neural networks over time via an 'episodic buffer' (Baddeley , 2000). It therefore seems logical that an enhanced working memory would lead to wider neural encoding.

3. 'EVALUATING THE EFFECTS OF SINGING SONGS IN ETHNIC MUSIC THERAPY FOR DEMENTIA PATIENTS WITH A NOVEL NEAR-INFRARED SPECTROSCOPY'

These findings were supported by a study by Tanaka and Nogawa (2013) into the effects of singing songs in ethnic music therapy. The aim of this study was to evaluate the effectiveness of ethnic-oriented music therapy in brain rehabilitation. To discover this, Tanaka and Nogawa performed two separate experiments with two participant groups. They also provide a table outlining their research aims.

The first experiment was questionnaire based. There were 86 participants in the study, including 77 dementia patients. The patients were sorted into categories according to the degree of care that they required in day-to-day life. The participants all required some level of care, with 37 requiring light levels of care, 22 further care, 16 mid-level care, and 2 heavier care. The pieces selected only used two scales (C major and minor), and were performed instrumentally, and then sung. The melodies were played on the piano, and lyrics were provided for the participants.

The questionnaires contained four questions for each piece. Tanaka and Nogawa then attempted to calculate how 'positive' the responses were from the participants. Responses such as 'know', 'like', and 'bright', that are left hemisphere responses were placed over the number of effective respondents and then multiplied by 100 to give a percentage. This form of questionnaire is lacking in effectiveness, as the options possible limit the wide range of responses a participant may give. More effective solutions may have had participants marking on a sliding scale, perhaps linked for clarity to a set of illustrations such as the Wong-Baker pain rating scale (Wong & Baker, 1988). This would enable participants to give more precise responses, and therefore gain a more accurate sense of positive feedback from participants.

In their second experiment, the researchers used a Near-Infrared Spectroscopy (NIRS) device to monitor blood oxygenation in the brain. They chose to focus on the total concentration of Hemoglobin in the brain, as the brain is activated by increased blood volume. They then applied a power-spectrum analysis to this on the assumption that it responds in a similar manner to an Electroencephalography (EEG). There were six participants in the experiment.

The results that they presented for the questionnaire experiment were highly positive. Similarly to Simmons-Stern et al. (2012), their results show that the probability of patients remembering the music of the song is higher than it is for the text. The results of the questionnaire also showed that the preference of music by the dementia patients is not influenced by the words (or language). The results also show that dementia patients were able to successfully differentiate between the mood of major and minor scales, but did not understand the tonality of the Japanese music that they were presented with.
The researchers do not highlight some other interesting results within the study such as the high value (of high and low frequency) that the 'Classical scale' achieved in both Dementia and Border-region participants, compared to the Japanese music, which featured at a lower high frequency value in both of these cases. This is especially interesting in the light of the healthy participants, who showed much higher (high and low frequency value) responses to Japanese music, to the extent that the classical scale is not labelled on their graph.

Tanaka and Nogawa give little explanation as to why these data were overlooked, aside from the fact that dementia patients showed a tendency to confuse the classical scale for different music. Whilst this shows a difficulty with specific recollection, it shows a good level of general recollection such as that described by Simmons-Stern et al. (2012).

The experiment using the NIRS device showed that there was a lower volume of power in the left brain of dementia patients (as would be expected). As a result of the experiment the researchers speculated that dementia patients were unable to control small blood-flow changes in the brain, which would account for the low readings they received from them.

The study did show that Japanese music acted as effective music therapy, and that music therapy was an effective treatment for dementia patients within the clinical care phase. Unfortunately, the NIRS experiment didn't seem relevant to the study overall as it only provided evidence that Japanese music could act as an effective rehabilitation (evidence already provided as part of the questionnaire experiment), and acted as the basis of the researchers' hypothesis that dementia patients have little control over their cerebral blood flow (a useful explanation, but unrelated to the studies aims). Also, with such a limited sample size for the NIRS experiment, it is impossible to draw any large-scale conclusions. Separating the two studies, and providing a larger sample size may have yielded more meaningful results, and perhaps supported the hypothesis more clearly.

4. DISCUSSING THESE STUDIES

Both studies draw interesting results, and function to show part of the relationship between music and memory. Particularly interesting is the revelation that these two studies provide that musical memory links to a more general, familiar memory as opposed to a specific one. These findings by Simmons-Stern et al. (2012) account for patients' responses to the text in the study by Tanaka and Nogowa (2013), as well as working to explain the high results from both Japanese and Classical pieces within their study. The studies also both provide a strong argument for the value of music therapy within the clinical environment, as both studies were clear that music does aid memory in AD patients to some extent. Simmons-Stern et al. (2012) particularly points out the use of music in helping calm AD patients and understand their environment within the facility or ward more quickly. Encoding methods such as this also have other applications, such as teaching dementia patients spatial location by playing different music in different areas of a facility.

There are, however, areas in which the studies contradict one another. One such contradiction is that if the observation of non-specific memory by Simmons-Stern et al. (2012) is accurate, then there should be no difference as a result of text. From Tanaka and Nogowa's results, it seems more likely that music is effective at enhancing memory, and that there is only an incremental further positive effect by picking ethnic music. This would align more comfortably with the research by Simmons-Stern et al. (2012).

The other unfortunate problem with these studies is the lack of a standardised classification of the patients. Simmons-Stern do not classify the AD patients at all, whilst Tanaka and Nogowa classify them according to Japanese clinical guidelines. As a result of this, it becomes impossible to draw comparable conclusions across their studies, as we have no reference point from which to understand the participants.

5. 'WHY MUSICAL MEMORY CAN BE PRESERVED IN ADVANCED ALZHEIMER'S DISEASE'

Recent further research has highlighted the findings of these two studies. A study by Jacobsen et al. (2015) has used more recent imaging techniques to study this further. Using music as a model for understanding complex brain patterns, Jacobsen et al. discuss why musical memory is preserved in advanced AD. The researchers hypothesised that due to a large body of research strongly suggesting that the temporal and frontal lobes are not involved in recalling musical memory, the network encoding musical memory is at least partly independent of other memory systems. Quoting Baird and Samson (2009), they propose that the preserved memory function of patients with AD is due to the intact functioning of brain regions that have been relatively spared. Specifically, they set out to prove that late degenerating brain structures play 'a fundamental role in encoding long-known music' (Jacobsen et al. 2015: 2442) .

To do this, the researchers developed two experiments, contrasting one with a similar study of patients with AD (La Joie et al., 2012). The first experiment selected 32 participants with unimpaired hearing and normal or corrected vision between 24 to 32 years old, of which 16 were male and 16 female. Whilst none of the participants were professional musicians, 17 had studied a musical instrument at some time during their life. The researchers then devised a second experiment to source musical extracts that formed three types of stimulus; 'long-known,' 'recently known' (played to participants one hour before the scanning took place), and 'unknown.' These stimuli were selected using different methods. The first stimulus of 'long-known' songs were selected from the German 'media control charts list' of top 10 songs from 1977-2007, and contained a variety of music including nursery rhymes and other related songs. These were then pitched against the statistical listening habits provided by several websites, including www.last.fm, www.amazon.com, and www.pandora.com, as well as being matched by musical experts. The numbers of songs were then reduced by a second behavioural evaluation experiment.

This experiment involved 100 subjects, and asked them to rate their recognition of the piece on a three-point scale, and how much they liked the piece on a five-point scale. The time until recognition of each song was also monitored. The best twenty 'triplets of songs' were then selected for the trial. Using short scales such as these reduced the accuracy of this experiment, and it may have been better to use sliding scales, in order to create a distribution curve of all the songs, and then pick only those values that showed the songs were 'well-known' and 'definitely unknown.' The exact experimental paradigm is outlined by the diagram in their article.

Once they had obtained these triplets, the 32 participants were each presented five experimental runs that each consisted of 12 trials, which in turn consisted of a 20-second stimulus presentation and an 8-second rating. Each run lasted around 5.6 minutes, meaning that the total time the participants were in the scanner was approximately 28 minutes. A ultra-high resolution MRI scanner was used with an isotropic resolution of 1.9 mm. 58 slices of the brain were taken in real time every 2000 ms. The 3D images were acquired after the fact by placing the data into an MP2RAGE sequencer. In order to reduce the noise experienced by the participants, compatible MRI in-ear headphones were used, and in-ear shielding was provided in the form of custom silicone earmuffs to each participant to improve the listening environment. The images were also filtered for head-motion correction.

The results of the experiment were divided into two halves. The first half addressed reporting the findings of their fMRI study. To do this, they tested two classes against each other, and contrasted the data between the two. They state that the group decoding-accuracy maps showed very stable results with a high accuracy (where accuracy was greater than 0.7, and chance level was 0.5). They then took these comparisons, which created hotspots within their maps of the brain, and put them through the MP2RAGE scans. They found that the significant areas of the brain were the caudal anterior cingluate gyrus, and the ventral pre-supplementary motor area (pre-SMA). The comparison between long-known music versus music that was unknown flagged significantly more sections of the brain than when the long-known music was compared against the recently known music. The accuracy for these masks was 0.58, with a *p*-value of 0.0084, both sufficiently low for statistical significance.

The comparison was based on a parcellation using voxel-based morphometry. Scans of the brain were compared to see if the participants in their study used the same sections of the brain during the tasks as those that undergo atrophy in patients with AD. The study found that the mean grey matter loss W-score was lower in the region they had identified than in 98% of all the parcels of the brain. The score of the region of interest for atrophy was 0.012, whereas the mean score for the brain in question was 0.508. This suggests strongly that in AD, the area (parcel) of the brain relevant to music recollection remains mostly undamaged during the progression of this disease.

The research also led to a question over the function of the temporal lobes in long-term musical memory; these are hypothesised as necessary to encode new musical memory, but once these memories are encoded, are not useful for recollection. This explains why patients presenting with heavy atrophy of or lesions on the frontal lobes are still often able to recall music, despite sometimes extensive damage. Jacobsen et al. (2015) also explain that their study is the first using objective data to determine music memory encoding, and suggest that these methods be used to further test patients that suffer from AD, although they do acknowledge that this may prove more complex in practice.

Whilst their research and data shows a high level of rigour, it has a relatively limited sample size (32 participants), of which a disproportionate number had at some point studied a musical instrument in relation to the general public. For example, in the United States, only 27.98 million people played a musical instrument in the last 12 months in a population of 318,388,699 in spring 2014 (census data from U.S. Department of Commerce) - only 8.7% of the general population. Whilst this does not mitigate the studies results, it is possible that there has already been a developmental impact on the brain from that training, which may not be present in the general populace, biasing the results to a greater response rate. A study that looks more closely at the specific formation of musical long-term memory could not be found by the author at the time of writing, but future research of this kind may prove useful to give weight to the argument by Jacobsen et al. (2015).

6. CLINICAL AND THERAPUTIC APPLICATIONS OF THESE FINDINGS

Whilst it has been demonstrated that music has a close link with ‘working memory’ function, and a separate network for long term memory encoding, it has not yet been discussed how this can be put into therapeutic practice in a clinical environment. In a 2014 study, Dassa and Amir took a small sample set of six participants to explore the role of singing familiar songs in encouraging conversation among people with middle to late stage AD. They begin by explaining that the conversation of patients with AD has a high proportion of words and utterances that convey little or no information. These progressive language failures can lead people with AD to isolation.

The researchers suggested that intervention by reminiscence therapy, communication training for caregivers, and increased social interaction of patients can all improve both the quality of life and the communication in patients with AD. They hypothesised that music could act in a similar way to Fels and Astell’s (2011) findings, that suggested engaging people with dementia in conversation where they are prompted to recall and recount personal stories with the aid of prompts. The act of singing the music was also hypothesised to contain informational recall, such as melody or lyrics, as well as memory recall, quoting Sacks’s (2008) observations that define music as a memory aid that gives patients access to memories, thoughts, and moods.

The six participants of the study all suffered mid- to late-stage AD (judged according to MMSE scores; Folstein, Folstein, & McHugh, 1985). Two participants in the study were male and four were female. The group was randomly selected from a larger study that explored the role of familiar songs in encouraging conversation among people with mid- to late-stage AD. The songs were selected using a systematic process by taking 24 songs popular in Israel (the location of the study) between 1930-1950 (years specifically chosen as participants

would have been adolescents or in their early twenties at that time). These songs were chosen from various books relating to the history of popular songs in Israel. The songs were sung by 12 randomly selected participants that then were divided into two groups of 6 participants. Two sessions were conducted for each group, and the degree of familiarity was rated. The 16 highest scoring songs were then utilised in the research.

Participants in the study were each given a handout that detailed the lyrics for each song that was sung; each song was repeated twice during the study. The format of the sessions remained unchanged so as to retain continuity: the therapist sang and invited the group members to sing, and after the song facilitated a conversation using open ended questions related to the song's lyrics, with the specific aim of eliciting memories. These sessions were documented by video, and subjected to a content analysis in order that the investigators could examine the song's role in the conversation that followed it. This analysis was affected by transcribing all verbal remarks, participants' singing style and verbal content that occurred during the sessions. The data was then condensed into categories based on valid inference and interpretation. A song analysis was also conducted for use in the discussion regarding the link between musical features and conversation topics that followed. This was conducted in line with previous studies and analyses of Israeli folk songs. The researchers' trustworthiness was also measured by keeping a log to examine all therapeutic intervention, and by peer review by a social worker and an occupational therapist that worked with the participants of the study.

The results were split into two categories according to research question. The researchers found that conversation topics discussed by the group during music therapy sessions split into two subcategories: conversation related to the songs and conversation related to the activity of group singing. The researchers found that the core of the 'conversation related to the songs' category was a discussion of memories that were evoked by the songs, which the researchers noted fit into four further subcategories: memories relating to patriotic events, memories relating to social gatherings, memories relating to family and participants' homes, and memories that related to musical experiences. Some of the memories that are discussed by the researchers are quite complex recalled information, but are in line with Sacks's assertion that music acts as a memory aid for mood and thought (Sacks, 2008).

The second category ('conversation related to the activity of group singing') divided into three further subcategories: singing promoting wellbeing, singing promoting self-esteem, and singing together reinforcing a sense of belonging. The researchers also found that the content of the songs did, to some extent, influence the conversations that followed. The pieces were divided into four categories, and the 'lullaby' category did not evoke any memories; the conversation of the group following these songs solely addressed the song's lyrics. These findings are mostly unsurprising, considering the findings of Simmons-Stern et al. (2010) discussed earlier, that showed that musical encoding did not help textual recall. Discussing the lyrics (as in the case of the lullaby category), is therefore not in line with the findings of Simmons-Stern et al.

From this, Dassa and Amir conclude that songs elicit conversation primarily about past experiences, with the songs eliciting the richest memories being ones that relate to social and national identity. The other noted conclusion was that singing as a group formed the dominant topic, and subsequently encouraged spontaneous conversation between group members. The group members expressed positive feelings and a sense of accomplishment on completing the activity, emphasising the importance of the community feeling that the activity facilitates, actively fighting the isolation brought by lack of communication due to dementia. Group members encouraged each other to sing and emphasised a desire to sing more.

7. FURTHER POSSIBLE CLINICAL APPLICATIONS

Whilst providing interesting results, the scope of Dassa and Amir's (2014) study is not wide enough to draw large conclusions about the effects of music therapy on patients with AD. They do admit to the issue of generalisations; however, with further studies of the same nature, it is likely we can marshal evidence in support of their findings. Indeed, all four studies help explain part of the relationship between music and memory, and in the case of the fourth study, music and association regardless of memory function.

The recall of music being based on a separate encoding system to the recall of words from Simmons-Stern et al. (2010) links with the study by Jacobsen et al. (2015), in that Jacobsen's findings to some extent explain those by Simmons-Stern et al. Establishing that the temporal lobes may have a non-essential role in long-term musical memory processing aligns with the idea presented by Simmons-Stern et al. that the two systems of memory encoding were separate from one another. This also aligns to some extent with the findings of Tanaka and Nogowa (2013), whose ethnic music-based therapy research suggests that patients remember their own culture's music better than that of other cultures, a point echoed in the study by Dassa and Amir (2014), who noted that patriotic music, as a strong part of patients' cultural and social identity, elicited the most memory recall.

Another observation as part of Dassa and Amir's (2014) study was that patients related the music to their families and their homes, and also to social gatherings. The former could be particularly useful if applied in a clinical setting to act as memory cues for patients to remember family members, remember to take medicines, and aid their orientation within the clinical environment. Orientation in particular can be complex in the clinical environment, where there are long, winding corridors, and it is easy to become disorientated. It may be possible to remind patients of their whereabouts by placing different music in different rooms to form associations

between the music and the environment - something not yet discussed in academic study.

Other critical clinical uses relate to combating the isolation that patients with AD experience as a result of loss of communication. As shown by Dassa and Amir's (2014) study, music therapy can be used to actively combat these isolation tendencies, by providing a community environment in which patients can discuss their memories of certain events. Unanimous feedback given by the participants in the study was that they felt a sense of achievement, community, and a boost in self-esteem. These are all important combative factors to mental health decline that may result from isolation felt by the patients. Another factor linked to this is that the music provided a topic of conversation upon which they could fall back.

Finally, a feature of particular interest is the separate memory encoding systems suggested by Jacobsen et al. (2015). Due to the preservation of grey matter that they observe in the sectors of the brain associated with encoding musical memory, it seems likely that further clinical applications can be devised to take advantage of this fact. Whether other thought-processes can follow the same neural pathways is the subject of ongoing study, but there is a possibility that memories could be created by stimulating the music encoding section of the brain. If this is the case, it may be possible to effectively treat the memory loss to some extent, with increased exposure to the correct forms of music (which would have to be determined through future study). This level of neural understanding is still some distance away, but any further information about the functions of brain mechanisms is still useful when applied to the treatment of degenerative brain diseases such as AD.

Further studies such as Warren et al. (2013) also draw links between the brain mechanisms that support musical information and the way that they may explain specific neural architecture and proteinopathies. Whilst there is still not enough evidence to explain the extent to which music has a value in memory encoding in patients with AD, it is clear from these studies that it does have a high inherent value and clinical application. It remains very possible that within the complex sound structure of music lies the key to unlocking memory pathways in patients with AD.

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