Neuropsychol Rev (2009) 19:85–101
DOI 10.1007/s11065-009-9085-2

REVIEW

Memory for Music in Alzheimer's Disease: Unforgettable?

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Received: 16 November 2007 / Accepted: 3 October 2008 / Published online: 13 February 2009

Abstract The notion that memory for music can be preserved in patients with Alzheimer's Disease (AD) has been raised by a number of case studies. In this paper, we review the current research examining musical memory in patients with AD. In keeping with models of memory described in the non-musical domain, we propose that various forms of musical memory exist, and may be differentially impaired in AD, reflecting the pattern of neuropathological changes associated with the condition. Our synthesis of this literature reveals a dissociation between explicit and implicit musical memory functions. Implicit, specifically procedural musical memory, or the ability to play a musical instrument, can be spared in musicians with AD. In contrast, explicit musical memory, or the recognition of familiar or unfamiliar melodies, is typically impaired. Thus, the notion that music is unforgettable in AD is not wholly supported. Rather, it appears that the ability to play a musical instrument may be unforgettable in some musicians with AD.

Keywords Alzheimer's disease · Dementia · Memory · Music

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Introduction

> *Magical music never leaves the memory* (Sir Thomas Beecham 1962).

Over the last few decades there have been several case reports of patients with probable Alzheimer's disease (AD) showing preserved memory for music. Given that the hallmark feature of AD is impaired memory function, these studies have highlighted an intriguing phenomenon. Recent case studies of patients demonstrating new learning and recall of novel music are particularly noteworthy as they suggest relatively spared musical memory against a background of impaired non-musical memory, providing support for the notion of a specialised memory system for music that appears to be distinct from other domains such as verbal and visual memory (Peretz 1996; Peretz and Coltheart 2003).

The goal of this review is to determine if memory for music is spared in AD by carefully examining the literature concerning this topic to date. This issue has both clinical and scientific relevance. Assessment of musical memory function may provide insights into preserved cognitive skills that can be utilised in rehabilitation or therapeutic strategies. The potential sparing of any cognitive function in dementia provides promising prospects for clinical interventions to aid communication and other cognitive functions. Furthermore, if musical memory is found to be intact in AD, it suggests that this material is unique and engages brain regions that are not affected by AD pathology. Therefore, an examination of this literature may provide unique insights into the neural correlates of memory for music.

In accordance with theoretical models of memory proposed by Tulving (1972) and Squire and Zola-Morgan (1988), we propose that different types of musical memory can be distinguished, as described in the non-musical domain, and these may be differentially impaired in AD.

In this review, we will explore the validity of preserved musical memory in AD by relating the current findings to different types of memory systems, and characterising the profile of musical memory disturbance in AD patients. Our focus is on long-term musical memory involving melodies, or sequences of tones with different rhythms, rather than other auditory parameters (i.e. pitch, duration and timbre). Articles examining musical memory in AD were ascertained using the database "PubMed", using the keywords 'dementia', 'music', 'memory' and 'Alzheimer's Disease', and limiting the search to studies published in English. The references of articles obtained from this database were also searched to identify other relevant studies.

Neuropsychology of Musical Memory

Forms of Musical Memory

According to multi-systemic models of memory, several authors have distinguished short and long-term memory (Squire et al. 1993). Although memory for music involves both these forms of memory, we will focus on the different forms of long-term memory throughout this review. Long-term musical memory comprises two different forms, explicit and implicit. Explicit or 'declarative' memory involves 'remembering that', and enables conscious recollection of events and facts. In the non-musical domain, explicit memory has been defined as having two divisions, episodic and semantic memory. Initially, these two systems were distinguished on the basis of the source and type of information to be remembered, namely personally experienced events and general facts (Tulving 1972). Over the subsequent years, Tulving et al. (Tulving 2002; Wheeler et al. 1997) proposed that episodic and semantic memory systems are associated with different kinds of conscious awareness; 'autonoetic' (self remembering) and 'noetic' (knowing) awareness, respectively. Based on these distinctions, episodic musical memory can be defined as the ability to retrieve the spatiotemporal (where and when), personal and emotional contexts of the musical experience (what). In contrast, semantic or conceptual musical memory can be defined as memory for factual musical knowledge or memory for associative or emotional concepts that is not linked to the retrieval of a specific personal experience or autobiographical event. Implicit or 'non declarative' memory involves 'knowing how' and is mediated by non-conscious processes, including priming, procedural memory or motor skill learning, which is critical for playing a musical instrument.

Conceptualisation of Musical Memory in Research to Date

Current neuropsychological research into musical memory has primarily examined explicit musical memory, typically assessing recognition. Evaluation of musical memory has employed different types of musical stimuli comprising unfamiliar or familiar melodies, with or without lyrics, using various paradigms. The type of stimuli used is an important consideration as it has implications for the form of musical memory that is engaged by the task. For example, using music with lyrics (songs) involves language, which could potentially facilitate musical memory, depending on the autonomy or integration of these two cognitive systems, which is an issue of ongoing debate (see Schon et al. 2005). A single presentation of familiar music before a recognition test may be considered a means of assessing not only episodic encoding but also semantic retrieval of musical information. In contrast, a 'familiarity decision-based task' requiring the participant to judge whether the musical excerpt is familiar or not, without previous exposure to the melodies during the experimental session, mainly engages semantic or conceptual musical memory. The presentation of both familiar and unfamiliar melodies enables activation and assessment of the integrity of the musical lexicon (Peretz 1993) or schematic knowledge (Bharucha 1987). Episodic musical memory, in terms of the recall of spatiotemporal and personal contexts of music encoding, has not been investigated to date. Indeed, semantic and episodic memory for musical stimuli are not as well distinguished as in other domains, and the tasks reported in the literature do not easily match these different forms of musical memory. Thus, although it is useful to distinguish different forms of musical memory in order to develop our understanding of this cognitive function, the practical assessment of musical memory does not currently reflect these distinct memory forms.

Neural Correlates of Musical Memory

Our current understanding of the neural substrates of musical memory is based on neuropsychological studies of patients with focal brain lesions, and a few functional neuroimaging studies of healthy individuals. These studies have primarily focused on explicit musical memory and have demonstrated the critical involvement of temporal and frontal lobe regions (e.g. Platel et al. 2003; Samson and Zatorre 1992). In the next sections we will provide a brief summary of the main findings of lesion and neuroimaging research into musical memory.

Lesion Studies

Neuropsychological research into musical memory has been conducted in patients with focal lesions due to stroke or neurosurgery for epilepsy. Such neurological conditions offer a unique opportunity to investigate the neural correlates of musical memory. Accumulating evidence from

neuropsychological research in patients with temporal lobe lesions has suggested that bitemporal mechanisms underpin musical memory function. Studies of patients who have undergone unilateral temporal lobe resection for intractable epilepsy (Milner et al. 1965; Samson and Peretz 2005; Samson and Zatorre 1991, 1992; Zatorre 1985) and patients with unilateral hippocampal sclerosis (Samson 1999; Samson and Peretz 2005) have demonstrated that learning and recognition of unfamiliar tunes depends on the integrity of both right and left temporal lobe structures. Delayed recognition of these tunes, however, predominantly involves the right temporal lobe (Samson and Zatorre 1992). A number of cases of music agnosia, or an inability to recognise familiar melodies, have been reported subsequent to bitemporal damage (Peretz 1996; Peretz and Gagnon 1999). These findings suggest the existence of a memory system specialised for music that involves the temporal lobe regions. Furthermore, they provide support for the two-stage model of recognition that distinguishes between perceptual analysis and memory representations. This model predicts that impaired recognition in music agnosia can result from either disrupted perceptual or memory based mechanisms, corresponding with a form of apperceptive or associative agnosia respectively (Peretz 1993). Specifically, impaired recognition of music can result from a perceptual deficit that would prevent formation of, and access to long-term memory representations. Alternatively, it can be due to damage to previously formed long-term memory representations. The observation of dissociated musical perceptual and recognition deficits in two patients with ischaemic brain damage supports this notion (Eustache et al. 1990). The first patient, with a left temporoparietal lesion, demonstrated impaired recognition of familiar melodies, as assessed by naming the title, identifying lyrics or background information of the tune, but he showed intact perceptual discrimination of familiar melodies, as assessed by a task requiring detection of pitch, rhythm or tempo changes in familiar melodies. The reverse pattern was observed in the second patient, who had an infarct of the right lenticular nucleus, external capsule and postero-inferior region of the right frontal cortex. In addition to demonstrating a double dissociation of perceptual and memory components of auditory information, these findings also identified a laterality effect in the mediation of these two components, involving the right and left hemisphere respectively. This laterality effect has been further supported by a group study of the neural correlates of apperceptive and associative music agnosia (Ayotte et al. 2000).

Three neuropsychological studies have examined musical memory in patients with frontal lobe damage. Two case studies have demonstrated intact memory for familiar music in patients with right frontal lobe lesions (Eustache et al. 1990; McChesney-Atkins et al. 2003). These observations suggest that the right frontal lobe region is not crucial for memory of familiar music, but no information regarding recognition of unfamiliar melodies was provided. There has been one previous group study of musical memory function in patients with frontal lobe lesions (Zatorre 1985). This study used an incidental encoding memory task of unfamiliar melodies that had been presented previously in a melodic discrimination task. The results revealed no significant difference in recognition performance between 17 patients who underwent frontal lobectomy (ten right, seven left) and controls. In addition, there was no difference between the patient and control groups on the discrimination task. These findings do not support the contribution of frontal lobe regions in recognition of unfamiliar music.

Neuroimaging Studies

In support of the wealth of findings from brain lesion studies, there is also neuroimaging evidence of temporal lobe involvement in musical memory, although only some studies have observed participation of mesial temporal lobe structures (Plailly et al. 2007; Satoh et al. 2006; Watanabe et al. 2007; Zatorre et al. 1996). Apart from Plailly et al. (2007) and Watanabe et al. (2007) who used functional Magnetic Resonance Imaging (fMRI), these studies are all Positron Emission Tomography (PET) investigations (Halpern and Zatorre 1999; Platel et al. 2003; Satoh et al. 2006; Zatorre et al. 1996). Three studies have used both familiar and unfamiliar music (Plailly et al. 2007; Platel et al. 2003; Satoh et al. 2006), one has used only unfamiliar music (Watanabe et al. 2007) and the remaining two used only familiar music (Halpern and Zatorre 1999; Zatorre et al. 1996). Although there are methodological differences between these studies, the majority have reported activation within the auditory association areas of the superior temporal gyrus, which was bilateral (Satoh et al. 2006; Watanabe et al. 2007; Zatorre et al. 1996) or right lateralised (Halpern and Zatorre 1999), depending on the nature of the tasks and stimuli. In addition, all of these neuroimaging studies found frontal lobe activation.

Zatorre et al. (1996) observed significant activations bilaterally in the inferior frontal poles associated with musical imagery of familiar songs with lyrics, and a subsequent musical imagery study using familiar melodies *without* lyrics demonstrated activation in the right inferior frontal region and middle frontal lobes which was predominately right sided (Halpern and Zatorre 1999). This activation was interpreted as reflecting retrieval of familiar songs from semantic musical memory. An alternative explanation acknowledged by the authors was that the right frontal activation might reflect episodic retrieval of the point at which they were trained to stop imagining the

melody. Two recent neuroimaging studies found predominately left sided activation associated with familiar music, including the left superior and inferior frontal gyri, (Plailly et al. 2007; Platel et al. 2003). This is in keeping with Ayotte et al's (2000) finding of reduced performance on musical memory tasks (the majority involving familiar melodies) in patients with left-sided brain lesions. One study has differentiated episodic and semantic musical memory using both familiar and unfamiliar melodies. Platel et al. (2003) observed frontal lobe activations in both semantic and episodic musical memory tasks. Specifically, comparison of the semantic and control tasks revealed predominately left hemispheric activation, involving the inferior frontal regions and angular gyrus in addition to bilateral medial frontal activation. In contrast, comparison of episodic and control tasks revealed activation of bilateral middle frontal regions and precuneus, which was predominately right-sided. Comparison of the *familiar* episodic and control tasks revealed activation of the right precuneus and frontal gyrus only, while comparison of the *unfamiliar* episodic and control tasks showed activation of the superior and middle frontal gyri and medial frontal cortex bilaterally. Thus, both familiar and unfamiliar melody recognition during the episodic task elicited frontal lobe activation, which was right lateralised and bilateral respectively.

Two other fMRI studies have examined the neural correlates of unfamiliar music recognition. Watanabe et al. (2007) found that successful retrieval of unfamiliar musical phrases (defined as the number of hits minus correct rejections) was associated with significant activations in the left inferior frontal gyrus, and to temporal lobe regions including the right hippocampus. In addition, a negative correlation was observed between the haemodynamic response and the 'corrected recognition rate' (defined as hits minus false alarms) in the left inferior frontal gyrus. This pattern of frontal activation was attributed to retrieval effort. Plailly et al. (2007) found that *unfamiliar* music elicited activation of the right superior frontal gyrus and superior middle gyrus, in addition to the left central and superior precentral sulci and left parietal operculum.

In summary, lesion and neuroimaging research has primarily focused on explicit musical memory and demonstrated the involvement of temporal and frontal lobe regions. Methodological and task differences between the studies make it difficult to generalise the findings in regard to specific structures within these brain regions. Nevertheless, the majority of neuroimaging studies have reported activation within the auditory association areas of the superior temporal gyrus and inferior and middle frontal regions, with the lateralisation of activation patterns dependent on the nature of the task and the form of memory it engages (e.g. semantic or episodic). In regard to the issue at hand, the critical role of the temporal lobes in musical memory and the prediliction of AD pathology to affect this brain region suggests that explicit musical memory would be impaired in this population. Nevertheless, the involvement of frontal brain regions may compensate in some cases, and other forms of musical memory that may not be as dependant on the temporal lobes (e.g. procedural musical memory) could potentially be relatively preserved in AD patients.

Musicians Versus Non-Musicians

There is accumulating evidence of structural and functional neuroanatomical differences between musicians and non-musicians (see Munte et al. 2002; Schlaug 2001 for reviews). The first authors to propose such functional differences were Bever and Chiarello (1974) in their seminal study demonstrating cerebral lateralisation differences in musical functions. Subsequent structural neuroimaging studies have demonstrated a range of neuroanatomical differences. For example, increased volume of the cerebellum (Hutchinson et al. 2003) and increased grey matter concentration in the right auditory cortex (Bermudez and Zatorre 2005). Such changes may be instrument specific and dependant on the time of onset of musical training (e.g. Bangert and Schlaug 2006; Elbert et al. 1995). Findings of functional differences include enhanced visuospatial and attentional functioning (e.g. Patston et al. 2007) in musicians compared with non-musicians. Several authors have examined the neural correlates of motor skills in musicians and non-musicians using functional neuroimaging. Pianists have demonstrated activation of specific motor areas, including the primary and pre-motor cortex and supplementary motor area, during the performance of complex finger movement tasks. Some studies have found greater activation in some of these motor regions in non-musicians, and this has been interpreted as reflecting either their increased effort in performing the task (Krings et al. 2000), or less effective motor representations in non-musicians than pianists (Meister et al. 2005). Interestingly, a recent study found increased activity in secondary motor cortices in pianists compared with non-musicians while listening to a piano piece (Baumann et al. 2007).

The findings of brain differences between musicians and non-musicians raise the question of whether these alterations are innate or induced by experience. In support of the latter notion, numerous studies have demonstrated experience dependant modification or plasticity of sensory and motor brain regions elicited by learning or practicing a musical instrument (e.g. Pascual-Leone 2001). These changes occur in sensory and motor brain regions. Overall, the brain regions that show structural or functional neuroanatomical differences between musicians and non-musicians are not

typically affected by AD pathology, at least in the early stages. Thus, while preservation of particular musical abilities and forms of musical memory may be more apparent in patients with AD who have had prior musical experience, non-musician patients may also demonstrate relative preservation of these functions, particularly procedural musical memory. In addition, findings of brain plasticity in response to learning and practising a musical instrument may be particularly relevant in patients with AD who are musicians and continue to play after the onset of their dementia. In these patients, it is possible that playing music may elicit involvement of musical memory substrates in brain regions that are not affected by AD pathology.

In summary, given the structural and functional differences in the brains of musicians compared with non-musicians, it is likely that the nature of musical memory representations and their neural correlates differ between these two groups. Preservation of some forms of musical memory in patients with AD may only be evident in musicians, and is yet to be explored in non-musicians.

Musical Memory in AD

Relationship Between Pathology and Forms of Musical Memory

In the early stages, the neuropathological and atrophic changes associated with AD are relatively focal, predominately affecting the temporal lobes, giving rise to the hallmark feature of impaired episodic and semantic memory function (see Carlesimo and Oscar-Berman 1992 for a review of memory deficits in AD patients). As the disease progresses, these changes become more widespread, resulting in diffuse brain dysfunction (Braak and Braak 1995; Thompson et al. 2007). Given that the pathology of AD initially affects the temporal lobes, we would expect long-term explicit musical memory, both semantic and episodic forms, to be impaired in this population from the early stages. In contrast, the brain regions mediating some forms of implicit musical memory, specifically procedural musical memory, are relatively spared by AD pathology until the very late stages (Carlesimo and Oscar-Berman 1992). Thus, we hypothesise that this form of musical memory may remain relatively preserved, particularly in musicians.

Differences Between Case and Group Studies

The current literature examining musical memory in patients with AD comprises only eight case studies and three group studies. AD was confirmed by autopsy in one patient (Beatty et al. 1997). Table 1 shows a summary of the details of these studies.

There are three important differences between the case and group studies. Firstly, all the case studies demonstrated some form of preserved musical memory. In contrast, the three group studies did not support the observation of spared musical memory, with all showing impaired explicit musical memory (Bartlett et al. 1995; Halpern and O'Connor 2000; Quoniam et al. 2003), and only one demonstrating preserved implicit musical memory (Quoniam et al. 2003). Secondly, all the case studies described patients with moderate to severe AD as determined by mini-mental state examination (MMSE) scores (Perneczky et al. 2006), while the group studies comprised patients with mild to moderate AD (see Table 1). Thirdly, of specific interest is the fact that all eight patients reported in the case studies were musicians or had considerable musical experience prior to the onset of dementia, whereas the group studies involved non-musicians (see Table 1). It is likely that the premorbid musical abilities of the eight patients reported in the case studies were the reason that they came to attention, representing a form of selection bias. In the next sections we will describe how these studies assessed musical memory in terms of the different forms of musical memory described above (see "Forms of Musical Memory").

Explicit Musical Memory

Familiar Music

In seven case studies, explicit musical memory has been examined using *familiar* music, or well known music previously known to the individual (Beatty et al. 1994, 1988; Cowles et al. 2003; Crystal et al. 1989; Cuddy and Duffin 2005; Polk and Kertesz 1993). Only two out of these seven patients (29%) showed preserved memory for familiar melodies (Cuddy and Duffin 2005; Polk and Kertesz 1993). In their case study of an 83 year old female amateur musician 'EN' with severe dementia as determined by her MMSE score (see Table 1), Cuddy and Duffin (2005) used three tasks that included familiar songs and instrumental pieces to explore musical memory function. Two of these tests were familiarity decision-based tasks; the '*familiarity decision test*' from the 1998 version of the Montreal Battery of Evaluation of Amusia (Liegeois-Chauvel et al. 1998), and the '*famous melodies test*' (Steinke et al. 2001), both of which involved identifying which excerpts are familiar, while the latter also required recalling the name of the excerpt. The other task was the '*distorted tunes test*' (Drayna et al. 2001), which involves detecting the melodies that have been altered by a pitch change, and is considered a perceptual task of pitch recognition rather than a memory task per se. EN's performance on these tasks was in keeping with controls.

Table 1 Summary of studies of musical memory in patients with probable Alzheimer's Disease

Authors (year)	N/sex	Musical Background	AD: diagnostic criteria and 'severity'[a] at time of testing.	Medications (dosage, duration)	Neuroimaging	Main findings in regard to forms of musical memory
Case studies						
Beatty et al. (1988)	1/F	Music teacher	Neuropsych assessment. MMSE declined from 17 to 8/30 over the year of testing ('moderate' to 'severe').	Lorazepam (3 mg/day), Haloperidol (0.5 mg/day), Trazo-done (150 mg/day).	EEG: diffuse slowing, no focal signs. MRI: diffuse cortical atrophy.	Intact procedural memory (piano). Impaired recognition of familiar music.
Beatty et al. (1994)	1/M	Amateur musician	NINCDS-ADRDA criteria MMSE 20/30 'moderate'. AD confirmed at autopsy (Beatty et al. 1997).	None reported.	MRI: Possible lacuna in left globus pallidus and substantial atrophy of cerebellar hemispheres and marked temporo- parietal atrophy.	Intact procedural memory (trombone), mildly impaired recognition of familiar music.
Cowles et al. (2003)	1/M	Amateur musician	MMSE 14/30 'moderate'.	Aricept (10 mg/ day ongoing)	MRI: bilateral atrophy of mesial temporal lobes and prominent sulci, ventricles and cisterns. Small infarcts in L thalamus and L basal ganglia, and punctate infarct in R cerebellar hemisphere.	Relatively intact. Learning and recall of a novel violin piece. Preserved procedural memory (violin and piano), mildly impaired recognition of familiar music.
Crystal et al. (1989)	1/M	Musician and music editor	Neuropsych assessment annually for 7 years. Initial diagnosis of amnestic disorder but changed to AD in Year 7 when intellectual and nominal functioning declined. MMSE not reported.	None reported	CT normal	Impaired recognition of familiar music, intact procedural memory (piano).
Cuddy and Duffin (2005)	1/F	Amateur musician	MMSE 8/30 'severe'	Donezepil (2 yrs), Rivastigmine (2 mths), Galantamine (ongoing). Dosages not reported.	None reported.	Intact recognition of familiar music.
Fornazzari et al. (2006)	1/F	Musician	MMSE 10/30 to 5/30 'severe'.	Donepezil (ongoing) Dosage not reported.	MRI diffuse mild cerebral atrophy and scattered foci of altered signal intensity in deep and peri-ventricular white matter. SPECT: L fronto- temporal and parietal hypoperfusion.	Relatively intact. Learning and recall of a novel piano piece. Preserved procedural memory (piano) (memory for familiar music not formally assessed).

Polk and Kertesz (1993)	2/ M & F	Case 1 & 2: Music teachers	Case 1: MMSE=3, 'severe'. Neurol and neuropsych assessment[b]. Case 2: Neurol and neuropsych assessment[c].	None reported.	Case 1 MRI: enlarged ventricles and diffuse cerebral atrophy, L>R. Case 2 MRI: Prominent parieto-occipital atrophy, R>L. PET scan: hypoperfusion in parieto-occipital region, R>L.	Case 1: Mildly impaired familiar music recognition, intact procedural memory (guitar). Case 2: Intact semantic memory, impaired procedural memory (piano).
Group studies						
Bartlett et al. (1995)	15/ 5F,10M	Some patients had musical training but there were no professional musicians	NINCDS-ADRDA criteria. MMSE 15-25 (Mean 19.9) 'mild' to 'moderate'.	None reported	MRI performed but not reported.	Impaired explicit recognition of unfamiliar and familiar melodies.
Halpern and O'Connor (2000)	15/8F,7M	Nine patients with musical training, i.e. instrumental/ choral.	NINCDS-ADRDA criteria. MMSE 15–25 (mean 22.5) 'mild' to 'moderate'. One patient did the Dementia Rating Scale (128/40) 'mild'.	None reported.	MRI performed but not reported. Noted that patients with ischaemic changes not included.	Impaired explicit recognition and implicit memory in the form of mere exposure effect for unfamiliar melodies.
Quoniam et al. (2003)	10/N/A	Not reported	MMSE[d] 22–25 (mean=23.1) 'mild'.	None reported	None reported	Impaired explicit recognition of unfamiliar melodies. Intact implicit memory in the form of mere exposure effect for unfamiliar melodies.
Effect of music on autobiographical memory						
Foster and Valentine (2001)	29/N/A	Not reported	Diagnosed by psychiatric consultant based on MEAMS performance. 'Mild-moderate' (n=7) or 'moderate' (n=16).	None reported	None reported	Facilitatory effect of music listening.
Irish et al. (2006)	10/4F,6M	Not reported	NINCDS-ADRA criteria MMSE 17–28 'mild' to 'moderate'.	None reported	None reported	As above.
Lord and Garner (1993)	20 14F/ 6M	Not reported	Not reported	None reported	None reported	As above.

AD Alzheimer's Disease, *assess* assessment, *MEAMS* Middlesex Elderly Assessment of Mental State, *Meds* medications, *MMSE* mini-mental state examination, *mths* months, *MRI* magnetic resonance imaging, *NINCDS-ADRA* National Institute of Neurological and Communicative Disorders and Stroke—Alzheimer's Disease and Related Disorders Association, *neurol* neurological, *neuropsych* neuropsychological, *PET* Positron Emission Tomography, *SPECT* single photon emission tomography, *yrs* years, *N/A* not available

[a] According to MMSE score (Perneczky et al. 2006), [b] Diagnosis of primary progressive aphasia or possible AD, [c] Diagnosis of posterior cortical degeneration due to AD or Heidenhain's disease, [d] Personal communication.

Given EN's severe language difficulties and agraphia, the authors utilised qualitative assessment and allowed behavioural responses such as humming and changes in facial expression. While this method of assessment is necessary in patients with severe cognitive impairment, it is difficult to objectively evaluate such responses. The authors also explored EN's ability to generate melodies from spoken lyrics, and found that she could sing 12 familiar tunes, although the lyrics were not always accurate. Unfortunately, no neuroimaging results were reported, but the wealth of behavioural data compensates for this. Given the preservation of her memory for familiar music, we predict that her semantic musical memory may be relatively intact, as in the case described below.

The second patient to show intact memory for familiar music is Case 2 described by Polk and Kertesz (1993). This 53 year old female piano teacher was able to name 15/15 familiar melodies (only one phrase presented) and sing the last note of 5/5 familiar melodies. She could also name 4/4 familiar melodies written in treble clef from examination of the written notation. Unfortunately, the details of the nature of the stimuli were not provided, and there was no control group for comparison. In contrast to her errorless performance on familiar melody recognition tasks, she demonstrated an inability to play the piano, described as 'bimanual instrumental music apraxia'. She reported that she no longer knew where to place her fingers on the keyboard. This could also be conceptualised as impaired implicit, specifically procedural musical memory (see below). Interestingly, this patient showed parieto-occipital abnormalities on neuroimaging investigations (see Table 1). It is likely that her 'music apraxia' (and/or impaired implicit musical memory) is due to her parieto-occipital dysfunction. In contrast, her intact explicit musical memory for familiar music may reflect the relative integrity of her semantic musical memory. It is noteworthy, however, that two alternative diagnoses were proposed for this patient; AD or Heidenhain's disease. In both EN and this patient (Cuddy and Duffin 2005; Polk and Kertesz 1993), the relative preservation of semantic musical memory may be explained by the absence of temporal lobe dysfunction.

Memory for familiar music was reportedly impaired relative to the performance of controls in five out of the seven patients (71%) assessed. In three of these patients, recognition performance was considered to be *mildly* impaired (Beatty et al. 1994; Cowles et al. 2003; Polk and Kertesz 1993 Case 1), and in the remaining two patients it was *severely* impaired (Beatty et al. 1988; Crystal et al. 1989). In accordance with neuropsychological research demonstrating the integral role of the temporal lobes in music recognition, four of the five patients with impaired recognition of familiar music showed cerebral atrophy on MRI brain scans, which was noted to be specific to the temporal regions in two patients (Beatty et al. 1994; Cowles et al. 2003). In the remaining patient, only Computed Tomography (CT) brain scan was performed which was reportedly normal (Crystal et al. 1989).

There has been only one group study of explicit recognition of familiar melodies in AD patients to date using intentional encoding (Bartlett et al. 1995). The authors also examined episodic retrieval of familiar (i.e. traditional) and unfamiliar (i.e. novel) tunes previously heard during the experimental session. Bartlett et al. (1995) presented a series of eight familiar melodies including Christmas and children's tunes followed by an old/new recognition test (requiring yes/no response) comprising 16 familiar melodies (eight old and eight new) to a sample of 15 patients with mild to moderate AD and age matched healthy controls. It was noted that a few participants in each group had some musical training but none were professional musicians. A similar test using eight novel compositions was used to test unfamiliar melody recognition. A third familiarity decision-based task comprised all the 16 familiar and 16 unfamiliar melodies played randomly and involved identifying each melody as known before the experimental session (i.e. familiar or unfamiliar), and for familiar tunes recalling the title, lyrics or tune category. AD patients showed impaired recognition performance on both familiar and unfamiliar recognition tasks relative to age matched controls and were slightly impaired on the familiarity decision-based task. The patients also performed more poorly on the title/lyrics recall task, and this score was positively correlated with MMSE score, suggesting a relationship between naming ability and degree of impairment. Interestingly, the patients demonstrated a significantly higher false alarm rate only for the familiar tunes in the recognition task. In other words, they showed a more liberal use of 'old' judgements for recognition test lures that were highly familiar (Bartlett et al. 1995). Even if semantic musical memory is impaired in AD patients as compared to matched controls, AD patients seem to be able to utilise their prior schematic knowledge of the stimuli in that they perceive well known stimuli (familiar tunes) as more globally familiar than unfamiliar stimuli.

Unfamiliar Music

In addition to the study by Bartlett et al. (1995), two other group studies have examined recognition of unfamiliar melodies using incidental encoding in patients with mild to moderate AD (Bartlett et al. 1995; Halpern and O'Connor 2000; Quoniam et al. 2003). The purpose of both studies was to examine implicit memory (see below), thus the tasks were incidental memory tests as the participants were not

informed that they had to memorise the melodies. This is the same method of assessment as the recognition test used by Ayotte et al. (2000). Halpern and O'Connor (2000) used the same unfamiliar stimuli as Bartlett et al. (1995) and found that the 15 patients with mild to moderate AD showed poorer recognition performance than age matched controls, but this difference did not reach significance as both groups scored near chance. Quoniam et al. (2003) used a paradigm inspired by Johnson et al. (1985) to examine recognition of unfamiliar melodies in ten patients with mild AD (MMSE score 22–25, personal communication). In comparison with age matched healthy controls and depressed patients, AD patients showed significantly impaired recognition of unfamiliar melodies.

Explicit Musical Memory Summary

In summary, there have been three methods of assessing explicit memory for *familiar* music in AD patients; (1) familiarity decision-based tasks which involve judging whether the musical excerpt is familiar or not (Cuddy and Duffin 2005), (2) recall of the title/composer (Beatty et al. 1988), or a completion task that requires recall of the last pitch of the musical excerpt by singing (Polk and Kertesz 1993), and (3) presenting a series of melodies followed by a yes/no recognition task (Bartlett et al. 1995). Using these tasks, the current research suggests that explicit recognition of *familiar* melodies, engaging conceptual (or semantic) musical memory, is typically impaired in AD patients relative to healthy controls, as demonstrated by the findings of the majority of published case studies (5/7) (Beatty et al. 1994, 1988; Cowles et al. 2003; Crystal et al. 1989; Cuddy and Duffin 2005; Polk and Kertesz 1993) and in the one group study to date (Bartlett et al. 1995). This is consistent with previous literature that has documented semantic impairments in AD patients (Barbarotto et al. 1998, 2001; Harley and Grant 2004; Whatmough et al. 2003) or difficulties in accessing the semantic representation or a deterioration of the representation itself (Hodges et al. 1992) in non-musical domains. It can also be explained by a failure to retrieve episodic information. Patients with AD appear to use a different criterion of response, being strongly biased by the overall familiarity of the well-known tunes (Bartlett et al. 1995). During recognition tests, they tend to respond yes to *all* familiar melodies, being unable to distinguish familiar melodies heard during the experimental session from the melodies stored in long-term memory (not previously heard during the experimental session). In rare cases, memory for familiar melodies may be relatively preserved, even in severe dementia (Cuddy and Duffin 2005; Polk and Kertesz 1993). This may be most apparent in patients with relative integrity of temporal lobe function (Polk and Kertesz 1993), but this hypothesis requires further investigation.

The three group studies examining explicit memory for *unfamiliar* music in AD patients have used yes/no recognition tests, two of which were incidental encoding tasks. Explicit recognition of *unfamiliar* melodies appears to be consistently impaired relative to healthy controls, even in mild AD (Bartlett et al. 1995; Halpern and O'Connor 2000; Quoniam et al. 2003). These findings are in keeping with the evidence that AD pathology predominately affects the temporal lobes and that this brain region is critical in mediating explicit memory for familiar and unfamiliar music (Peretz 1996).

Assessment of memory using yes/no recognition tests is most comparable with recognition memory tasks used in verbal and visual domains, while a familiarity decision-based task is equivalent to a lexical decision task. Nevertheless, assessment of memory using recognition tests, without further questioning or justification of responses does not allow for a distinction between familiarity and recollection, the two processes that are widely assumed to underlie recognition memory. Specifically, a feeling of 'familiarity' or 'knowing' can be associated with previously studied items, whereas 'recollection' involves actual 'remembering' of the studied items, such as when or where they occurred, reflecting episodic memory function (Aggleton and Brown 2006; Yonelinas 2001). Unfamiliar melody recognition tasks involve recent encoding and learning which can create a feeling of familiarity or knowing. Thus, successful performance on such tasks may be underpinned by familiarity rather than recollection. Therefore, this does not solely reflect intact episodic musical memory function. Interestingly, there has been no study of the explicit learning of unfamiliar melodies with repeated presentations in the AD population to date, but one study has used repeated presentations to explore implicit musical memory (Quoniam et al. 2003, see "Mere Exposure Effect" below). Previous studies using this paradigm in patients who had undergone temporal resections for intractable epilepsy have demonstrated the involvement of both left and right temporal lobes in the learning and recognition of unfamiliar melodies (Samson and Zatorre, 1992). Future research will need to characterise musical learning in the AD population.

Implicit Musical Memory

In contrast with *explicit* musical memory, *implicit* musical memory functions have received comparatively little research attention, and their neural correlates are relatively unknown. Nevertheless, insights can be gained from previous research using non-musical stimuli. For example,

neuropsychological and neuroimaging studies have implicated cortico-striatal and cortico-cerebellar systems in the learning of new motor skills (Doyon and Benali 2005; Eslinger and Damasio 1986), which may be involved in musical performance. Two forms of implicit musical memory have been assessed in AD patients, (1) the 'mere exposure effect' and (2) procedural musical memory, or musical instrument playing.

Mere Exposure Effect

The 'mere exposure effect', or the preference for previously studied stimuli, has been conceptualised as an implicit memory phenomenon based on perceptual priming (Peretz et al. 1998), although others have argued that it reflects the use of different strategies in task performance (Mandler et al. 1987; Whittlesea and Price 2001) or the possible involvement of emotion (Zajonc 1968).

There have been only four group studies of the mere exposure effect using musical stimuli reported in the neuropsychology literature to date (Samson and Peretz 2005) and two of them have examined in patients with AD, with inconsistent results (Halpern and O'Connor 2000; Quoniam et al. 2003). Using a paradigm inspired by Johnson et al. (1985), Quoniam et al. (2003) presented six different unfamiliar melodies that were played either once, five or ten times (two melodies for each condition) and subsequently tested liking judgements when exposed to the same six melodies mixed with six novel ones. They found that the mere exposure effect was intact in a sample of ten patients with mild AD (MMSE 22–25, personal communication, see Table 1) as compared to normal controls, and the preference increased with the number of presentations. In contrast, Halpern and O'Connor (2000) did not observe the mere exposure effect in 15 patients with mild to moderate AD (MMSE 15–25). In this study, eight unfamiliar melodies were presented twice and liking judgments were obtained when these eight target melodies were represented with eight novel melodies. Methodological differences including the number of presentations of the melodies (twice versus multiple times) and severity of dementia (lower MMSE scores in Halpern and O'Connor's (2000) sample) may explain the inconsistent results of these two studies. The mere exposure effect may only be preserved in the early stage of the disease, when the melodies are repeated multiple times.

Procedural Musical Memory

Six case studies have described preserved ability to play musical instruments in patients with AD, reflecting intact procedural musical memory. According to their MMSE scores (see Table 1), the severity of dementia at the time of testing was moderate in two patients (Beatty et al. 1994; Cowles et al. 2003), and severe in two patients (Fornazzari et al. 2006; Polk and Kertesz 1993). One patient declined from moderate to severe dementia over the year that testing occurred (Beatty et al. 1988), and in one patient MMSE score was not reported (Crystal et al. 1989). All these cases will be discussed below.

Crystal et al. (1989) described a musicologist and amateur pianist with probable AD who could continue playing familiar piano pieces when the examiner played the first few bars, although he was unable to recall or recognise the composers, and could not identify the title if given the name of composer. He also learnt a new skill of mirror writing after the onset of his dementia. Of note, his CT brain scan was normal. The authors attributed the preserved piano playing ability to intact procedural musical memory (Crystal et al. 1989). The notion of intact procedural memory underpinning instrumental playing has been further addressed by Beatty et al. (1994). They described an amateur trombonist who continued playing after the onset of his AD that was later confirmed by autopsy (Beatty et al. 1997). There was no significant difference in observer ratings of recorded performances made by the patient before and after the onset of dementia. The authors noted that this patient had difficulty putting on jackets and tying neckties which they defined as 'dressing apraxia'. They argued that this suggests that his 'perceptual motor skills' are not intact, and therefore cannot be solely responsible for his preserved ability to play the trombone. Interestingly, this patient showed marked cerebellar atrophy on MRI (see Table 1). As described above, this region is typically enlarged in musicians. Despite this, his instrumental playing was not affected, suggesting that other brain regions involved in procedural musical memory may have played a more active role.

In a detailed case study of an 81 year old pianist with probable AD, Beatty et al. (1988) asked three independent raters to compare the patient's recorded performance of six songs with that of four neurologically intact pianist controls. The patients' proficiency was rated as being between a 'rusty' amateur and an elderly, previously accomplished pianist with arthritis. Unfortunately, there was no recording of her playing ability prior to the onset of her dementia for comparison. She could play scales to command and recognised scales when played by others, and was able to perform four Christmas songs that she did not recognise. Of note, she was able to sight read and play a few measures of a novel piece that was published after the onset of her dementia. Furthermore, she could play a simple song (Twinkle Twinkle Little Star) on her first attempt on the xylophone, an instrument that she had not seen or played for over a decade. The authors argued that her ability to sight read a novel piece and play the xylophone suggested that her piano playing ability was more than an

automatic motor response or 'over learned' motor ability. In addition, in contrast with her intact musical instrument praxis, she showed impaired ideomotor apraxia and was unable to perform simple movements such as waving goodbye to command, although this improved with imitation. Receptive aphasia may have contributed to her poor performance to command. Her MRI brain scan showed diffuse cerebral atrophy (see Table 1). Finally, Patient 1 described by Polk and Kertesz (1993) showed intact ability to play the guitar, and his improvised music performances were rated as 'musically competent'. It was noted, however, that his improvisations consisted of many over learned note sequences that resulted in an "impulsive and disconnected production". Furthermore, consistent with the observations of Beatty et al. (1994, 1988), they highlighted the dissociation between musical instrument and limb apraxia. In keeping with the patient described by Beatty et al. (1988), his MRI brain scan showed diffuse cortical atrophy (see Table 1). The two remaining patients with intact procedural musical memory also demonstrated new learning and recall of novel musical pieces and will be described in detail in "New Learning and Recall" below.

Implicit Musical Memory Summary

In summary, there have been two methods of assessing *implicit* musical memory functions in AD patients to date, (1) the mere exposure effect, and (2) playing of a musical instrument in musicians, or procedural musical memory. Findings from two group studies examining the mere exposure effect are inconsistent. This may reflect methodological differences between the studies including the severity of dementia and number of repetitions of the melodic stimuli. Six case studies have shown that the ability to play a musical instrument or procedural musical memory can be retained even in musicians with severe AD. Interestingly, with the exception of one patient in whom familiar melody recognition was not formally assessed (Fornazzari et al. 2006), all the patients who showed intact procedural musical memory had impaired memory for familiar music (see "Familiar Music"). In addition, the opposite pattern was observed in one patient with intact memory for familiar melodies who showed impaired procedural musical memory, as evidenced by her inability to play the piano (Polk and Kertesz 1993). Thus, a dissociation between explicit (semantic) and implicit (procedural) musical memory forms is apparent, supporting our proposal of these distinct types of musical memory. Further group studies are required to clarify the nature and neural correlates of implicit musical memory in AD, and to explore other forms of implicit musical memory such as conceptual priming, learning of new semantic skills or musical structure (Bigand et al. 2003; Regnault et al. 2001; Tillmann et al. 2003) or statistical learning, equivalent to learning of artificial grammar (Tillmann and McAdams 2004) using musical stimuli.

New Learning and Recall

There have been only two case studies of patients with AD who have demonstrated new learning and recall in the form of playing novel musical pieces (Cowles et al. 2003; Fornazzari et al. 2006). Severity of dementia according to MMSE scores at the time of testing was moderate in one patient (Cowles et al. 2003) and severe in the other (Fornazzari et al. 2006). An 80-year-old male violinist learnt to play a novel piece without lyrics that was published after the onset of his dementia. He was able to play the piece without sheet music by the third training session and retained it for 10 min within this session. He correctly cued his teacher a further 10 min later, suggesting that he retained the music for a total of 20 min. Three days later he was unable to recall playing the violin and attempts to cue his performance of the piece were unsuccessful, suggesting that learning of this new material was not consolidated after 20 min. However, he was able to perform well-known pieces on the piano to command without music. His MRI brain scan revealed marked bitemporal atrophy, which makes the observations of relative intact new learning even more remarkable. As described above, his recognition of familiar music assessed by asking for the titles of Christmas songs was mildly impaired (Cowles et al. 2003). A 63 year old female pianist learnt a new composition also without lyrics that was presented in aural and written form every day for a week, and played it well on the seventh day of learning, although she transposed it to another key (Fornazzari et al. 2006). Neuroimaging revealed diffuse atrophy on MRI but more focal left sided changes on SPECT (see Table 1). She showed decreased depression and agitation during the study period, as measured by scores on the Geriatric Depression Scale and Neuropsychiatric Inventory respectively. This highlights an important role for music in improving emotional wellbeing in patients with dementia. Although memory for familiar music was not formally assessed, the authors noted that at follow-up a year later, she continued to play familiar music despite further cognitive deterioration as evidenced by a decline in her MMSE score to 5.

Given that both of these patients were unable to learn new verbal or visual material, these observations suggest that music is a unique stimulus. Learning and recall of music by playing may recruit distinct neural correlates that remain functional even in moderate stages of AD. Nevertheless, the lack of control data for instrumental playing in elderly patients makes it difficult to ascertain whether these two cases do actually show special abilities. Without control data we cannot

determine if the limited retention time (20 min) is remarkable, except that in this patient it seemed to be outstanding in comparison to his absence of retention of other material (verbal and visual). A similar profile of selective sparing of new learning and retention of novel songs has also been reported in three amnesic patients by singing with lyrics instead of playing novel musical pieces (Baur et al. 2000; Haslam and Cook 2002). These case studies suggest that information presented in the context of song is encoded and stored in a specialised manner, forming representations that are distinct from those of other domains. These representations may be selectively preserved and accessed in amnesia, providing further evidence of the unique nature of musical stimuli. The observations of Haslam and Cook (2002) are particularly noteworthy given that both amnesic patients were non-musicians. Learning and retention of novel songs (with lyrics) has not yet been explored in AD patients, but these findings suggest that it may be a novel method of aiding verbal memory.

The Effect of Music on Memory Functioning in AD

It has been proposed that musical experience may 'protect' against the development of dementia (Grant and Brody 2004). In their preliminary exploration of this hypothesis, Grant and Brody (2004) surveyed 23 older musicians with an average age of 76.9 years, who were former members of the same orchestra. They found that no participant was aware of any living current or former orchestral member with dementia. Based on population prevalence statistics and the clinical demographics of the 84 older living current and former orchestral members, eight or nine individuals would be expected to have AD. While the hypothesis that dementia may be less common among musicians is intriguing, the evidence remains weak given the rather small number of concerned people in this study. Since all the reported cases of musical memory in AD patients have been musicians, it appears to be a contradiction that musicians are less likely to develop dementia. Nevertheless, a large prospective study showed that participation in 'cognitive' leisure activities including playing a musical instrument was associated with a reduced risk of dementia (Verghese et al. 2003). Further large-scaled research is required to investigate the protective effects of music.

In keeping with the notion that music may protect or facilitate memory, three studies have investigated the effect of music listening on memory functioning, specifically autobiographical recall, in patients with AD (Foster and Valentine 2001; Irish et al. 2006; Lord and Garner 1993). Unfortunately, these studies did not report the musical background of the participants. Lord and Garner (1993) randomly assigned 60 patients with AD (diagnostic criteria and severity were not reported) to one of three activity groups, (1) a music group that involved listening to 1920's and 30's Big band music, (2) a group that completed puzzle exercises, or (3) a recreational group that participated in drawing or watching television. All group participants underwent an evaluation during the initial and final sessions of the 6 month study period using a questionnaire that contained two parts. The first part was given orally to each participant and comprised autobiographical recall questions. Only two examples of these questions were provided, namely 'where were you born?' and 'what was your mother's name?' It is noteworthy that both of these questions assess semantic memory. The second part of the questionnaire involved three 30 s behavioural observations during which the mood and social interaction of each participant was rated by one of the authors on a four point scale from poor to excellent. Patients who participated in the music group performed better on the recall questions and had higher ratings on the mood and social interaction scales compared with patients who participated in the puzzle or recreational groups. Nevertheless, the lack of objectivity of the observer of mood and social behaviour is problematic. Therefore, this study does not provide convincing evidence of the beneficial effect of music on memory functioning.

Memory for personal events has been more specifically examined in the following studies. In a sample of 23 patients with mild to moderate AD (see Table 1), Foster and Valentine (2001) assessed recall of personal facts over three life periods (remote, medium-remote and recent) during exposure to four different auditory conditions; quiet, cafeteria noise, familiar (first movement of Vivaldi's Four Seasons) or novel music. All participants performed once in each auditory condition, presented in a randomised order 1 week apart. This is problematic as practice effects may have influenced performance. Differences when noted were only apparent for recall of memories from medium-remote and remote but not recent life periods. For instance, mean recall performance was significantly better when the mean of all sound conditions (67%, for cafeteria noise, familiar and novel music altogether) was compared with the quiet (61%) condition. However, music elicited only slightly better recall than cafeteria noise (68% and 66% mean recall respectively) and there was no difference between familiar and novel music conditions. The authors proposed that enhanced arousal or attentional processes were responsible for the beneficial effect (Foster and Valentine 2001; Larkin 2001). The lack of significant difference between cafeteria noise and music does not support the notion that music is a 'special' form of auditory stimuli. Rather, it suggests that auditory stimulation (whether music or not) can enhance autobiographical memory.

Only one study to date has explored potential mechanisms underlying the facilitatory effects of music on autobiographical memory in patients with AD. Irish et al.

(2006) found that listening to background music (Vivaldi's Four Seasons, Spring movement) improved performance on the Autobiographical Memory Interview (AMI) in ten patients with mild to moderate AD compared with a silence condition. Conversely, a control group of healthy elderly matched individuals showed no significant difference in AMI performance between silence and music conditions. Arousal was measured with galvanic skin response, attention with the Sustained Attention to Response Task (SART), and anxiety with the State Trait Anxiety Inventory. The order of music and silence conditions was counterbalanced, and participants were seen on two occasions (silence and music) at the same time of day 1 week apart. No differences in galvanic skin responses were found between the music and silence conditions in AD patients or controls. There were no group differences in errors across conditions on the SART, but AD patients showed faster reaction times compared with controls in the music first condition, whereas reaction times for controls were quicker in the silence first condition. Reduced state anxiety was reported during the music compared with the silence condition for both AD patients and controls, but this reduction was only significant in AD patients. Thus, the authors concluded that reduced anxiety in AD patients mediated enhanced autobiographical memory recall in the music condition (Irish et al. 2006). It is noteworthy, however, that his study did not include an 'auditory stimulation' condition (e.g. noise) and therefore does not provide any insight into whether the enhancing effect is due to auditory stimulation (whether musical or not).

The notion that the facilitatory effect of music is due to emotional factors is in keeping with the observation of Sacks (2006) who commented that AD patients can respond emotionally to the 'evocative power of music' and can 'regain their cognitive focus' when exposed to music, particularly familiar music, which may evoke early memories. Previous studies have reported a positive effect of music and/or music therapy on emotional and behavioural functioning in patients with AD (Brotons and Marti 2003). However, a recent review argued that this hypothesis has not been validated to date, given the lack of methodological rigour in many studies that have examined this issue (Vink et al. 2004). The finding that the emotional effect of music underpins its facilitation of memory is in accordance with research demonstrating that changes in the listener's arousal or mood are responsible for the 'Mozart effect', or the observation of improved performance on spatial reasoning tasks when listening to music composed by Mozart or any other classical composers, particularly if the contrast condition is silence (Chabris 1999; Thompson et al. 2001). This effect has typically been reported in healthy individuals, and has only been described in one patient with mild AD (Johnson et al. 1998). Two studies have demonstrated a positive relationship between emotion and memory for music in healthy individuals (Eschrich et al. 2005; Schulkind et al. 1999). Interestingly, this was most apparent in older adults. It was proposed that this may reflect a more pronounced effect of emotion on memory as retention interval increases, given that the older adults retrieved information over a longer retention interval than younger adults. Alternatively, older adults emotional ratings may have reflected their ability to recall the musical information. Thus, it is unclear whether the emotion elicited the memory or vice versa (Schulkind et al. 1999). Further research is needed to investigate the complex relationship between emotion and music both in the healthy and AD population.

Overall, the current data are inadequate to draw firm conclusions of the effect of music listening on memory function in AD patients. Nevertheless, the results are promising and it appears that enhanced autobiographical recall associated with music listening may be due to the emotional and/or arousal effects of the music. Future research could explore the effect of music listening or active participation on other forms of memory (verbal or visual). Some studies have demonstrated improved recall of verbal information when sung rather than spoken in both healthy controls (Wallace 1994) and patients with amnesia (Haslam and Cook 2002), as described above, although other studies in healthy controls have not observed this effect (Peterson and Thaut 2007; Racette and Peretz 2007). Interestingly, a recent study has documented the facilitatory effect of song in learning a language demonstrating the conjoint effect of both attentional (arousal) and segmentation components (Schon et al. 2007). Given the potential benefits to patients with AD and other neurological conditions, further research into the relationship between music and memory and underlying mechanisms such as arousal, attention and mood is clearly warranted. Rehabilitation of memory disorders using music is a promising prospect. Future investigations will need to consider the musical background of participants to explore whether there is a differential effect between musicians and non-musicians.

Conclusions

Methodological Limitations

There are several methodological biases and differences that exist in the studies that have examined musical memory in AD to date. These include small sample sizes, differences in the criteria used to define probable AD, disease severity of the patients, and tasks and stimuli used to assess musical memory function. Few studies have controlled the level of familiarity of musical stimuli used in their assessment of familiar melody recognition, and the

issue of cultural relevance of the musical stimuli is an important consideration in the interpretation of the results. Some tasks have relied on naming responses, which may be affected by anomia, a common symptom of AD. Use of behavioural responses is an option in severely cognitively impaired patients, but this may limit the objective rigour of the results. Many studies lack control data, and this is a particular issue for the cases of preserved instrumental playing. Differences between the group and case studies in terms of the severity of dementia and musical experience of participants are problematic. The preservation of various forms of musical memory has only been observed in case studies of musicians with AD. These observations are difficult to relate to the patient population in general given the evidence of structural and functional neuroanatomical differences between musicians and non-musicians. Thus, although each study makes a valuable contribution to our knowledge, these methodological differences limit the conclusions that can be made from the current research.

Synopsis and Future Directions

Is music unforgettable in AD? Based on the current literature there is not strong evidence for this notion. By reviewing the findings of the eight case studies and three group studies that have been published to date we have characterised the pattern of musical memory function in AD patients. In regard to the different forms of long-term musical memory that we have proposed, it appears that explicit musical memory is typically impaired. Specifically, memory for familiar music, engaging semantic and/or episodic musical memory, is impaired in the majority of reported cases. These observations support the notion that the brain regions affected by early AD pathology, in particular the temporal lobes, mediate explicit musical memory. Episodic musical memory, in terms of recall of spatiotemporal and personal contexts, has not been investigated to date, but we predict that this form of musical memory would also be impaired in this patient population. In contrast with explicit musical memory, implicit (i.e. procedural musical memory, or the ability to play a musical instrument) can be preserved in musicians, suggesting that the pathology of AD does not typically affect brain regions involved in implicit musical memory functions. Interestingly, in synthesising the findings of these studies, a dissociation between explicit (semantic) and implicit (procedural) musical memory functions appears to emerge, supporting our distinction between these two forms of musical memory and their neural correlates.

Future research will need to address the methodological weaknesses that exist in the current literature. Large scales studies that consider the musical background of participants are required. New and innovative paradigms will need to be developed to assess different forms of musical memory and to allow cross modal comparison of memory abilities. Control data is needed, particularly for procedural musical memory tasks. Future large scaled studies should also consider gender differences in musical memory functions, handedness and the overall neuropsychological profiles and the relationship between musical memory functions and other cognitive domains. Characterisation and comparison of musical memory functions in different types of dementia will provide a better understanding of changes that are specific to AD. There are currently only four published studies of patients with non-Alzheimer's dementias (frontotemporal, semantic, and 'mesolimbic') showing preserved or enhanced musical abilities, or a change in musical tastes (Boeve and Geda 2000; Geroldi et al. 2000; Miller et al. 2000; Torack and Morris 1986). Unfortunately, musical memory was not formally assessed in any of these patients, and these studies suffer from similar methodological problems as the AD literature. Finally, future research investigating the neural correlates of musical memory will need to differentiate the various forms of musical memory and delineate specific structures within the temporal and frontal lobes that mediate these.

The research to date has demonstrated the exciting potential for music to be used in neuropsychological assessment and rehabilitation in patients with AD and other neurological conditions. We hope that this review has highlighted the need for further more rigorous research into this issue, which may encourage the future development of assessment tools and cognitive and behavioural interventions using musical stimuli.

Acknowledgements This review was supported by a grant from "Agence Nationale pour la Recherche" of the French Ministry of Research (project n° NT05-3_45987) to Séverine Samson, and a post doctoral fellowship from the same grant to Amee Baird.

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