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Music-based memory enhancement in Alzheimer's Disease: Promise and limitations

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ABSTRACT

In a previous study (Simmons-Stern, Budson & Ally, 2010), we found that patients with Alzheimer's disease (AD) better recognized visually presented lyrics when the lyrics were also sung rather than spoken at encoding. The present study sought to further investigate the effects of music on memory in patients with AD by making the content of the song lyrics relevant for the daily life of an older adult and by examining how musical encoding alters several different aspects of episodic memory. Patients with AD and healthy older adults studied visually presented novel song lyrics related to instrumental activities of daily living (IADL) that were accompanied by either a sung or a spoken recording. Overall, participants performed better on a memory test of general lyric content for lyrics that were studied sung as compared to spoken. However, on a memory test of specific lyric content, participants performed equally well for sung and spoken lyrics. We interpret these results in terms of a dual-process model of recognition memory such that the general content questions represent a familiarity-based representation that is preferentially sensitive to enhancement via music, while the specific content questions represent a recollection-based representation unaided by musical encoding. Additionally, in a test of basic recognition memory for the audio stimuli, patients with AD demonstrated equal discrimination for sung and spoken stimuli. We propose that the perceptual distinctiveness of musical stimuli enhanced metamemorial awareness in AD patients via a non-selective distinctiveness heuristic, thereby reducing false recognition while at the same time reducing true recognition and eliminating the mnemonic benefit of music. These results are discussed in the context of potential music-based memory enhancement interventions for the care of patients with AD.

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1. Introduction

Alzheimer's disease (AD) affects approximately 5.2 million Americans age 65 and older. By 2030, this number is expected to reach 7.7 million (Alzheimer's Association, 2011; Hebert, Scherr, Bienias, Bennett & Evans, 2003). Globally, there may be as many as 80 million people living with AD by 2050 (Alzheimer's Disease International, 2009). Episodic memory and instrumental activities of daily living (IADL; e.g., housework, medication adherence, use of transportation, management of money, etc.) are affected early in the course of AD, and are major contributors to the functional disability associated with the disease (Gaugler,

Yu, Krichbaum & Wyman, 2009; Tomaszewski Farias et al., 2009; McKhann et al., 2011). In order to alleviate the significant detriment to quality of life for the affected patient (Schölzel-Dorenbos, van der Steen, Engels & Olde Rikkert, 2007) and burden of care for his or her caregivers (Razani et al., 2007) there exists a major interest in the development of interventions designed to reduce the impact of memory loss and IADL impairment in AD.

There are numerous studies of potential disease modifying drugs currently underway, many in Phase 3 clinical trials (for reviews see Budson & Kowall, 2011; Budson & Solomon, 2011). With the growing number of individuals with AD and the likelihood of a more slowly progressive disease as a result of the new treatments, there will be a growing need to improve the daily functioning and quality of life of AD patients in the years ahead. Music therapy, of which traditional forms consist of basic active (e.g., instrument playing, singing) or passive (e.g., listening) music engagement, represents a low cost intervention with a wide range

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of benefits. These benefits include improvements on measures of anxiety and depression (Guétin et al., 2009), agitation (see Witzke, Rhone, Backhaus & Shaver, 2008 for review), autobiographical memory recall (Foster & Valentine, 2001; Irish et al., 2006), and a variety of cognitive functions (e.g., Thompson, Moulin, Hayre & Jones, 2005; Janata, 2012). However, to the best of our knowledge no work to date has examined the potential benefit of music-based therapies specifically targeted to enhance new memory formation and improvement in IADL functioning in patients with AD. Furthermore, despite some anecdotal reports of effective use of musical mnemonics in a therapeutic setting, there are no accepted music-based memory enhancement therapies for the care of patients with AD.

In a previous study (Simmons-Stern et al., 2010) we demonstrated that patients with AD remember song lyrics better on a recognition memory test when those song lyrics are accompanied by a sung recording than when they are accompanied by a spoken recording at encoding. However, healthy older adults showed no benefit of musical encoding on subsequent recognition memory. This original experiment provided some of the first empirical evidence that musical mnemonics may serve as an effective therapeutic tool for the care of patients with AD, but was limited by the scope of its design. Because we only tested recognition for the lyrics of studied songs, we were unable to make any claims about the practical benefits of musical mnemonics. We showed that music does enhance basic recognition for a set of lyrics, but did not test content recognition or comprehension, both of which are requisites of an ecologically valid music-based therapy designed to improve memory and IADL functioning in AD patients. For example, recognition memory may be driven differentially by both familiarity and recollection (Eichenbaum, Yonelinas & Ranganath, 2007; Yonelinas, 2002), and it is likely that the latter is particularly important to the functional transferability of musical mnemonics. However, a familiarity enhancement effect may in itself inform less specific but nevertheless highly impactful music-based memory enhancement therapies, as well as provide further support for the benefit of music interventions in general for AD patients.

An additional limitation of our original experiment was its inability to assess false alarms or false recognition – the incorrect belief that a novel stimulus has been previously encountered – with respect to presentation condition. Because participants studied the lyric stimuli bimodally at encoding (i.e., the lyrics along with sung or spoken audio) but were then tested unimodally (i.e., the lyrics alone), we were only able to generate an overall rate of false alarms. That is, we were unable to assess false alarm rate as a function of sung or spoken test condition. False recognition and memory distortions are common in patients with AD (Mitchell, Sullivan, Schacter & Budson, 2006; Pierce, Sullivan, Schacter & Budson, 2005). Minimization of false recognition and other memory distortions is essential to normal memory function (Schacter, 1999) and thus if musical mnemonics reduce false memory they may have additional practical value in the life of a patient with AD.

The present study was designed to address three main goals given these results and limitations of our 2010 study. First, we sought to determine whether the benefit of musical mnemonics on basic lyric recognition in patients with AD extends also to content memory. That is, if an AD patient studies musical song lyrics designed specifically to enhance new learning of relevant IADL-related material – what we will call *functional musical mnemonics* – can the content information encompassed by those lyrics be retrieved at a later time? Specifically, we tested both general and specific content memory in order to assess the utility of these functional musical mnemonics. Based on our previous finding and evidence that at least some forms of musical memory may be preferentially spared by the degenerative effects of AD (see Baird & Samson, 2009 for review; Hsieh, Hornberger, Piguet

& Hodges, 2011; Vanstone & Cuddy, 2010), we hypothesized that both general and specific content information would be better remembered for lyrics studied with a sung recording than for lyrics studied with a spoken recording.

Second, we were interested in understanding music-based memory enhancement in the context of the familiarity/recollection dual-process model of recognition memory. As noted, the ability of music to enhance familiarity, recollection, or both will necessarily affect the scope of its therapeutic applications. Although our paradigm of general and specific content questions is novel, it shares characteristics with many dual-process models of recognition memory (see Yonelinas, 2002 for review). In a standard dual-process model, familiarity is often illustrated by the experience of recognizing a person's face as generally familiar, whereas recollection encompasses the ability to remember specific qualitative information such as the name of that person and where he or she was first encountered. Analogously, we sought to isolate familiarity in the present experiment by reducing lyrics to their most general content form (i.e., as the main topic of a lyric, or its "face"). The retrieval of additional information about the context in which that main lyric topic was encountered – the specific content of the musical mnemonic – may involve familiarity as well, but relies predominantly on recollection. By testing general (i.e., familiarity-based) and specific (i.e., recollection-based) content memory separately, we hoped to examine the relative benefit of musical mnemonics across each of these components of recognition memory. Thus, if music affects the familiarity and recollection components of recognition memory independently, we predicted a dissociation of performance on the two content memory tasks.

Furthermore, while healthy older adults exhibit impaired recollection relative to familiarity (Craik & Jennings, 1992; Light, 1991), patients with even mild AD demonstrate nearly complete degradation of recollection (Ally, Gold & Budson, 2009; Ally, McKeever, Waring & Budson, 2009). As a result, we predicted an interaction between the benefit of music and group for recollection-based memory, such that any benefit of music on specific content memory would be more pronounced in healthy older adults than in AD patients. Correspondingly, we predicted that any benefit of music on the familiarity-based general content memory would be of similar magnitudes across subject group.

Our third goal for the present study was to analyze the relative rate of false recognition for sung as compared to spoken stimuli. We tested participants in an audio-based recognition task that included both sung and spoken stimuli, unlike our previous experiment in which the test was independent of condition. We predicted lower rates of false recognition for sung stimuli, and thus expected the benefit – which we assessed using Pr, a measure of discrimination that accounts for false recognition (Snodgrass & Corwin, 1988) – of musical encoding to be more pronounced in the current paradigm for both patients with AD and healthy older adults. Furthermore, we hypothesized that stimulus condition would mediate participants' response bias, or their overall tendency to rate items as studied or unstudied. Participants in tests of recognition memory who respond, "yes, that item was studied," disproportionately are considered to have a liberal response bias, whereas participants who respond, "yes," more infrequently are considered to have a conservative response bias.

2. Methods

2.1. Participants

Twelve patients with a clinical diagnosis of probable AD and 17 healthy older adults participated in this experiment. Patients with probable AD (MMSE: $M=24.67$, $SD=3.45$; MOCA: $M=14.50$, $SD=5.83$) met the criteria outlined by the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's