The past two decades have seen an increasing awareness of cognitive deficits in multiple sclerosis (MS). Many MS patients have cognitive deficits (Amato, Ponziani, Siracusa, & Sorbi, 2001; Kujala, Portin, & Ruutuainen, 1996; Peyser, Edwards, Poser, & Filskov, 1980; Rao, 1990, 1995). Memory is one of the most prevalent types of cognitive deficit in MS and some memory deficits present in early phases of the disease (Landro, Sletvold, & Celius, 2000). Despite new memory test development (Camp, Thompson, & Langdon, 2001) and several research studies aimed at isolating the memory problems in MS (Deluca, Barbierberger, & Johnson, 1994; Marie & Defer, 2001; Rao, Staubinfaubert, & Leo, 1989), the exact nature of memory deficits in MS remains unclear. More important from a clinical point of view, as Rao has ardently noted for many years (Rao, 1995), is the lack of treatments for memory dysfunction in MS (Bennett, Dittmar, & Raubach, 1991).

Music training and musical accompaniment can also enhance memory for nonmusical material (Ho, Cheung, & Chan, 2003; Jakobson, Cuddy, & Kilgour, 2003; Rainey & Larsen, 2002; Wallace, 1994). Previous evidence has shown music memory provides access to verbal knowledge in patients with memory disorders (Baur et al., 2000; Foster & Valentine, 2001; Haslam & Cook, 2002). Music rehearsal has been shown to be more effective than verbal rehearsal in learning nonmusical materials with learning disabled and developmentally disabled students (Claussen & Thaut, 1997; Gfeller, 1983; Wolfe & Hom, 1993). Structured music listening has been shown to enhance a broad range of cognitive functions in autistic children (Bettison, 1996). Maeller (1996) demonstrated that music can improve memory in MS patients, with a trend toward greater improvement associated with severity of the disease. Thus, there is mounting evidence that music can enhance a variety of cognitive functions in neurologically impaired individuals. But if music can assist learning and memory, what might be the neurophysiologic basis for this effect?

Music and Brain Plasticity

There is a small but growing body of evidence that music modulates brain activity associated with nonmusical functions of the nervous system. We have evidence...
that rhythmic entrainment can be used for sensorimotor rehabilitation: the temporal structure of music can be harnessed to rehabilitate motor function in brain damaged patient populations (Hummelsheim, 1999). Can a similar strategy be used to rehabilitate impaired verbal memory function? If the brain implements verbal learning and memory differently for musical and nonmusical contexts, perhaps impaired nonmusical verbal memory could be ameliorated by unimpaired musical verbal memory. Plasticity in the functional organization of brain networks is important in recovering verbal learning and memory function after, for example, traumatic brain injury (Ricker, Hillary, & DeLuca, 2001). Occipital cortex of congenitally blind individuals plays a prominent role in superior verbal memory performance relative to sighted individuals (Amedi, Raz, Pianka, Malach, & Zohary, 2003). Music can play a role in brain plasticity, through both its pitch characteristics (Shahin, Bosnyak, Trainor, & Roberts, 2003) and temporal structure (Merzenich, Schreiner, Jenkins, & Wang, 1993; Pantev, Wöllbrink, Roberts, Engelien, & Lutkenhoner, 1999).

Present Study

Learning and remembering spoken verbal information is a common and important day-to-day function. Deficits in verbal learning and memory can severely degrade a patient’s quality of life. In this study we investigated whether a musical template for verbal learning improves verbal learning and memory. Given the practical significance of the sequence of verbal information, we specifically investigated whether music would improve learning and memory for ordered word lists in patients with multiple sclerosis. Music is naturally associated with ordered word list recall in the form of lyrics, so perhaps it could selectively enhance ordered word recall even in the absence of rhyme and syntactic and semantic structure.

Method

Participants

Participants were 20 right-handed volunteers with relapsing-remitting MS, with normal hearing and no history of other neurological or psychiatric conditions. All participants volunteered and provided written, informed consent approved by the institutional review board. Participants were randomly assigned to one of two conditions: with and without a musical template providing temporal structure, hereafter referred to as the “structured” and “unstructured” conditions. Respectively, the groups’ ages were $M = 51.7$ ($SD = 9.3$) and $M = 53.8$ ($SD = 11.2$), years of music training were $M = 5.4$ ($SD = 6.3$) and $M = 10.2$ ($SD = 16.5$), years of education were $M = 15.3$ ($SD = 2.0$) and $M = 16.4$ ($SD = 3.5$), and Expanded Disability Status Scale (EDSS) ratings were $M = 4.6$ ($SD = 1.2$) and $M = 4.3$ ($SD = 1.1$). The two groups did not significantly differ in terms of age, education, music training, or EDSS rating. The two groups performed similarly on the Selective Reminding Test and Logical Memory I subtest. Each group included 9 females and 1 male.

Task and Stimuli

Unlike the more typical in person administration of the Auditory Verbal Learning Test (AVLT, Lezak, 1995), we used prerecorded sound files and remotely recorded voice responses with the participants isolated in a soundproofed booth. This served to maximize consistency of the test procedures. A single standard list of 15 words was repeated in ten trials, and the participant was asked to free recall as many words as possible after each list presentation (see Figure 1). The 15 words in the list were semantically unrelated. The words were presented at a rate of approximately one per second and the presentation order was the same on every trial. On each trial, participants were instructed to listen carefully as they would subsequently be asked to recall as many words as possible. Recall of the list was tested without further presentation of the original list after participants heard and free recalled a distractor list, and again after a 20-minute nonverbal distractor task. Participants were not given feedback on any trials.

Participants were randomly assigned to either a sung or spoken presentation of the AVLT. In the music condition participants were asked to sing back as many words as they recalled. This ensured modality congruence.
between the learning stimulus and recall. In both conditions they were additionally instructed to recall items in the order they were presented on the word list.

The sung and spoken conditions used identical word lists of equal overall duration presented free field at 80 dB SPL. The sound files were recorded using the same female vocalist for both conditions. In the structured condition the word list was presented as lyrics for an originally composed song. One-syllable words were assigned one quarter note of 1 s duration, while two-syllable words were assigned one eighth note of 0.5 sec (500ms) per syllable to generate a melodic-rhythmic phrasing structure and to keep the sung condition at 15 s durations (with one second rest at the end), equal to the spoken condition. We used an originally composed melody that was not familiar but was simple and repetitive in structure (AABA form). We measured the size of word chunks recalled in proper sequence, assessing chunk lengths of 2, 3, 4, 5, 6, and 7 words.

**Results**

In the analysis of pairwise word order learning, a consistent trend emerged for better recall in music than spoken learning, reaching statistical significance at the end of the learning and memory task, when comparing the mean of the last learning trials (T6-10) and the two subsequent memory trials, \( F(1,18) = 4.51, p = .038 \) (see Figure 2). Musical verbal learning induced greater increases in word order recall in early and late phases of learning, whereas spoken verbal learning induced the greatest increases in word order recall during the middle phase of learning. The spoken verbal learners’ performance actually decreased slightly in the last two learning trials, and remained relatively lower than the musical verbal learners’ performance in the later recall trials.

Two-tailed \( t \)-tests for differences in change of learning performance between verbal and musical condition (T6-10 vs. M1) for the higher word order sequences (3-7 words) were all highly significant, 3: \( t(18) = 4.32, p = .0004 \); 4: \( t(18) = 4.27, p = .0004 \); 5: \( t(18) = 4.08, p = .0007 \); 6: \( t(18) = 3.89, p = .001 \); 7: \( t(18) = 2.40, p = .027 \).

**Discussion**

Participants in the music condition showed significantly better word order memory than participants in the spoken condition. The finding that music can improve order memory is significant given the increasingly recognized cognitive deficits in multiple sclerosis (Amato et al., 2001; Peyser et al., 1980; Rao, 1990). Approximately 50% of MS patients suffer cognitive impairment (Rao, Leo, Bernardin, & Unverzagt, 1991), and this commonly manifests in verbal memory impairment (Sweet, Rao, Primeau, Mayer, & Cohen, 2004). This is the first known study to extend earlier work on memory for temporal order in MS (Beatty & Monson, 1991) using an ecologically salient paradigm like the AVLT.

Considering that the demyelination process of the disease will affect and interrupt network dynamics of neuronal cell assemblies required for learning, the results provide evidence that melodic-rhythmic templates, as commonly inherent in the structure of music as a temporal and nonverbal sensory language, may support verbal learning and memory, in spite of an underlying disease process that affects the neurobiological processes of learning. From such circumstantial evidence one may propose that music perception does affect neurobiological processes of learning in some compensatory way, however, with physiological mechanisms to be determined. The differential effect of music may occur during encoding rather than retrieval, because encoding is a phase of memory processing associated with deficits in MS (Marie & Defer, 2001).

While the exact nature of the neurophysiologic mechanisms underlying the differential learning we measured remains elusive, a few theories may be put forth. Musical verbal learning may access compensatory
pathways for memory functions during compromised prefrontal cortical functions associated with learning and recall. Musical learning may also confer a neurophysiological advantage through the stronger synchronization of the same neuronal cell assemblies underlying conventional verbal learning and memory. In both cases, the temporal structure implicit in musical stimuli may sharpen the timing of neural dynamics in brain networks degraded by demyelination in MS. Several researchers (Deutsch, 1982; Janata, Tillmann, & Bharucha, 2002; Wallace, 1994) have—based on Gestalt perception and learning principles—proposed that music provides a highly effective mnemonic for learning by incorporating a temporal structure and redundancy that chunks information into more manageable units (Deutsch, 1999; Gfeller, 1983). "Chunking" is a helpful mechanism not only in declarative learning and recall, but also in motor learning (Verwey, 2001). Indeed chunking is probably an innate feature across a broad phylogenetic range of nervous systems (Matzel, Held, & Miller, 1988). The intrinsic structure of sound patterns in music is a highly effective mechanism to facilitate perceptual grouping and chunking. The present study supports the notion that “musical chunking” can be exploited to rehabilitate verbal learning and memory. It extends recent research in our center regarding the beneficial effect of musical template learning on verbal learning in healthy adult participants (Peterson & Thaut, 2003), as well as pilot research suggesting that music induced enhancements were significantly correlated with increases in severity of disease (Maeller, 1996).

There is a growing body of knowledge about the neurobiological correlates of verbal memory, music, chunking, and plasticity. Lesion (Halpern, 2001; Peretz, 2002), functional imaging (Parsons, Hodges, & Fox, 1998; Platel et al., 1997; Smith, Jonides, Marshuetz, & Koepppe, 1998; Zatorre, Halpern, Perry, Meyer, & Evans, 1996), EEG (Peterson & Thaut, 2002; Ruchkin, Berndt, Johnson, Ritter, Grafman, & Canoune, 1997) and MEG (Maess, Koelsch, Gunter, & Friederici, 2001; Makeig & Jung, 1996; Tecchio, Salustri, Thaut, Pasqualetti, & Rossini, 2000) studies have illustrated that both music and verbal memory recruit widespread networks encompassing many brain regions. Theoretical work is beginning to link the behavioral level phenomenon of chunking to the dynamics of cell assemblies in cortex (Wickelgren, 1999). System-level research into brain plasticity has highlighted the importance of temporal structure in stimuli (Merzenich et al., 1993; Pantev et al., 1999) and associated cortical plasticity with verbal learning (Tallal, 2000). Collectively, the research suggests that physiological measures of brain network dynamics (Fuster, 1997; Garrett, Peterson, Anderson, & Thaut, 2003), such as spectral analysis of the scalp EEG (Basar, Basar-Eroglu, Karakas, & Schurmann, 1999; Lopes da Silva, 1999), can provide a window into how musical chunking may enhance verbal memory. Thus, simultaneous EEG would be a helpful adjunct to the methods used in the present study by providing a measure of how music modulates brain dynamics associated with the learning process. In conclusion, we evaluated a specific strategy for enhancing verbal memory in MS patients. The results are suggestive of the therapeutic potential of musical mnemonics in verbal learning and memory, an area of dysfunction in MS that is definitely underserved in basic research and therapeutic intervention.

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