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Original Article

Music therapy improves cognitive function and behavior in patients with moderate Alzheimer's disease

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Abstract: Alzheimer's disease (AD) is in an increasingly common affliction among the world's aging population, involving a steady decline in mental function and the onset of dementia. Music therapy has been demonstrated to provide health benefits when used as an adjuvant treatment. To determine whether music therapy can improve clinical outcomes of AD, we analyzed its effects on cognitive function and behavior in patients with mild AD in conjunction with conventional drug treatments. Sixty patients with mild AD were selected as the research subjects and randomly divided into an observation group and a control group. Patients in the control group were treated with drug therapy only, while the patients in the observation group were treated with music therapy and drug therapy. Scoring according to the mini-mental state examination (MMSE), the Montreal cognitive assessment (MoCA), and the neuropsychiatric inventory (NPI) was used to assess patients before beginning treatment (t_0), at the end of treatment (t_1), and three months after the completion of treatment (t_2). We found that the MoCA and MMSE scores of patients in both groups improved over the course of treatment, but that patients in the music therapy group demonstrated a greater magnitude of improvement over patients in the control group. This finding suggests that music therapy can improve cognitive function and behavior in patients with AD, helping to delay the progression of the disease and improving prognosis.

Keywords: Music therapy, Alzheimer's disease, cognitive function, dementia, behavior, therapeutic effects observation

Introduction

Alzheimer's disease (AD) is a chronic degenerative disease of the central nervous system, characterized by progressive memory loss, cognitive dysfunction, and a decline in psychological and mental health [1, 2]. The cognitive impairments of AD include memory loss, aphasia, apraxia, agnosia, and executive dysfunction, manifested as significant damage to memory, judgment, abstract thinking ability, and inferential capability, complicated by abnormal behavior and decline in social function [3, 4]. The primary pathological changes associated with AD include diffuse cerebral cortical atrophy, the formation of senile plaques (SP) containing β-amyloid protein (Ap), and the formation of neurofibrillary tangles (NFT) made of hyperphosphorylated tau protein [5]. Recent studies have shown that the soluble β-amyloid protein oligomer deposits in AD patients interfere with brain synapses and synaptic signaling pathways resulting in a decline in brain synaptic density and plasticity [6, 7].

The development of systematic neuropsychological assessment scales has aided in the classification of cognitive dysfunction and helped to establish diagnostic criteria for AD and other neurodegenerative disorders [8, 9]. Subjective cognitive decline (SCD) and mild cognitive impairment (MCI) have both been recognized as pre-clinical AD based on recommendations from the National Institute on Aging and the AD Association. Researchers have recognized that, during the course of disease progression, patients go through an SCD stage before MCI, providing an important strategy for

Table 1. Study participant clinical data

		Observation group (N=30)	Control group (N=30)
Gender (Cases)	Male	10	12
	Female	20	18
Age (years)		70.4±7.5	69.1±7.2
Education period (years)		6.92±2.94	6.99±2.89
Course of disease (years)		4.02±2.91	3.90±2.81
MMSE scores		22.85±1.22	22.92±1.28

Table 2. MMSE, MoCA and NPI scores in music therapy of mild Alzheimer's disease

Score Items		Observation group	Control group	F value	*P* value
MMSE	t_0	22.85±1.22	22.92±1.28	F=51.000	P=0.003
	t_1	23.62±1.55	23.29±1.53		
	t_2	24.15±1.55	23.80±1.53		
MoCA	t_0	12.42±2.18	12.48±2.14	F=47.633	P=0.000
	t_1	13.08±2.19	12.56±2.31		
	t_2	13.39±1.17	12.75±2.32		
NPI	t_0	16.35±1.95	16.29±2.05	F=41.165	P=0.000
	t_1	15.78±1.95	15.98±1.89		
	t_2	15.39±1.98	15.78±1.91		

the selection of cognitive impairment patients for clinical study [10, 11].

As the global population ages, the incidence of AD also increases annually. In Western countries, the prevalence of AD is about 2% among individuals older than 60 and up to 5% of those older than 85 [12], while in China, the prevalence of AD is only 3-5% among those over 60 [13]. Recent studies have found that AD is closely correlated with hypertension, diabetes, high cholesterol, hyperhomocysteinemia, craniocerebral injury, sleep disorders, high-fat diet, and epilepsy [14]. According to the World Health Organization (WHO), AD underlies 60%-70% of new dementia cases diagnosed each year throughout the world [15]. Since the mechanisms of the pathogenesis and progression of AD are not well understood, studies tend to focus on developing treatments to help alleviate some of the symptoms of AD, but no treatments exist to fully reverse the progression of the disease. Biological treatment options typically involve neurotransmitter substitution therapies, neurotrophic factors, drugs that promote the metabolism of nerve cells, and neuroprotective agents [16, 17]. Stem cell therapy also has made some progress in treating AD by reconstructing cell cycle and function, providing neuroprotection and nutritional support, inhibiting the formation of amyloid protein, and mediating immune function [18, 19]. However, the reliability and safety of these therapies still needs to be assessed.

Music is the common language of all humans, and is understood by people with different levels of education, backgrounds, languages, disease states, mood disorders, and physical limitations. Music therapy is an emerging interdisciplinary subject, known to bring about changes in the physical and psychological states of patients. Music therapy embodies the biopsychosocial medical model and has made great progress in Europe and America since the 1940s, while gaining traction in China [20]. Music therapy provides specific types of music to help patients achieve unified physical and emotional harmony and helps to alleviate the stress response caused by adverse physiological and psychological factors [21]. In recent years, music therapy has successfully helped to alleviate surgery- and trauma-related pain and anxiety [22], chemotherapy-related suffering [23], and fears of dental work [24]. To determine whether music therapy is an effective adjuvant to pharmacological treatment of AD symptoms, here we describe the effects of music therapy on cognitive function and behavior of mild AD patients receiving pharmacological intervention.

Materials and methods

Patients

Sixty mild AD patients treated in the first affiliated hospital, Henan Polytechnic University between January and December 2014 were selected to participate in the study. There were 22 males and 38 females, with a mean age of 69.8±7.9, mean education period of 6.95±3.01 years, mean disease duration of 3.95±2.86 years, and mean mini-mental state exam (MMSE) score of 17.63±3.69. All 60 patients met the AD diagnostic criteria established by the National Institute of Neurological Disorders and Stroke and the Alzheimer's Association and were confirmed by head CT, MRT, and other imaging. The Clinical Dementia Rating (CDR) of the patients fell between 0.5-1.0, and any

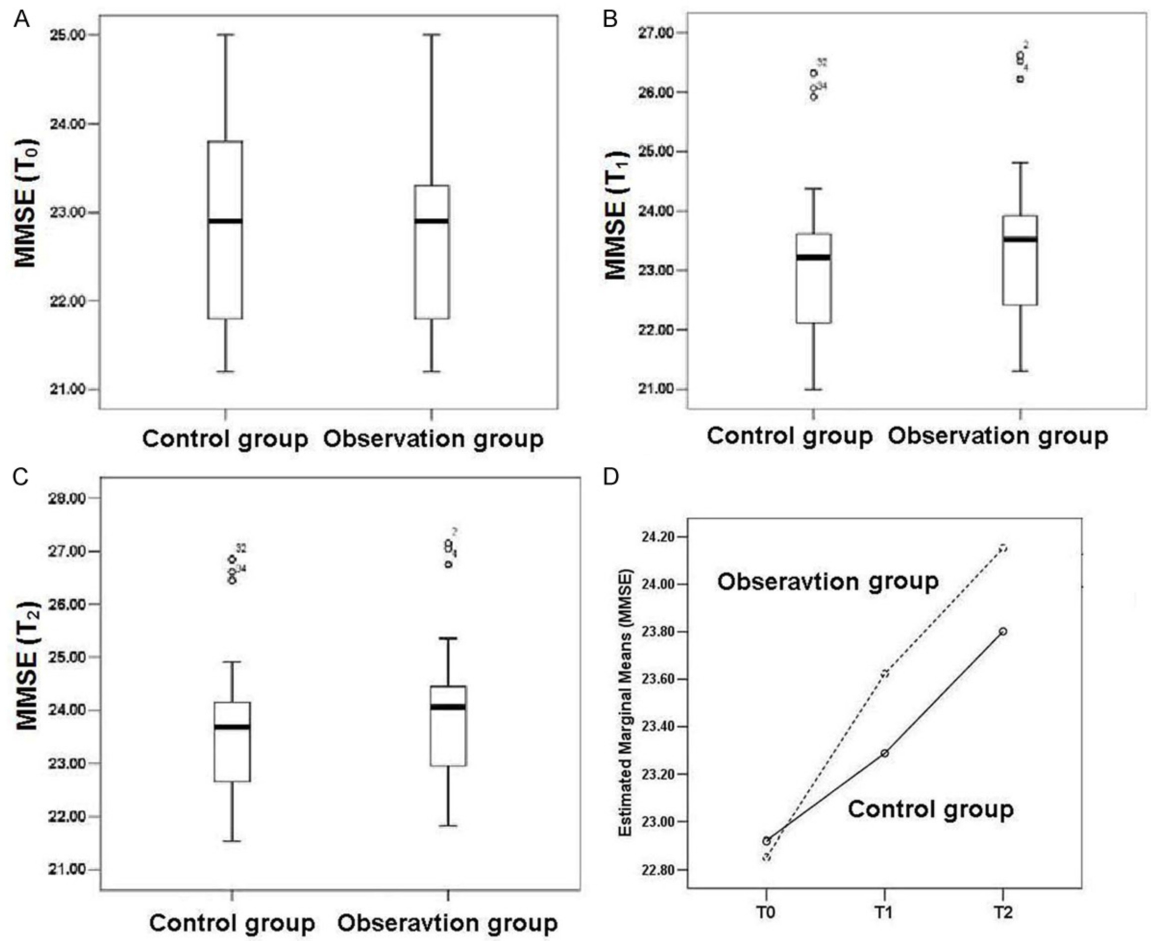

Figure 1. MMSE scores in AD patients who received music therapy (observation group) and those who did not (control group). A. Beginning treatment; B. At the completion of treatment; C. Three months after treatment; D. Estimated marginal means of MMSE scores before (t_0), immediately following (t_1), and three months after treatment (t_2).

patients that exhibited severe hearing loss or severe damage to vital organs and those who could not complete the study were excluded. The 60 patients were divided into two groups of 30, one group for observation and one for control, using a random number table. There were no statistically significant differences in gender, age, education, disease duration, or MMSE score between the two groups (**Table 1**). Patients in both groups maintained their original drug treatment plans. All patients and family members were informed of the study and provided informed consent. The study protocol was approved by the ethics committee of the first affiliated hospital, Henan Polytechnic University.

Music therapy

Patients in the observation group received music therapy in addition to their original drug plans. An indoor treatment site with soft lighting and little noise or interference was chosen, and songs were selected by the first author of this article according to patients' pathogenic condition, education level, and personal preferences. Typically, older songs familiar to the elderly were chosen. The sound volume was controlled at 40 decibels, and the patients sang along with the therapist three times per day for 30-50 min per session. The frequency and duration could be adjusted according to patient's condition. Both groups underwent treatment for three consecutive months and followed up three months after the end of treatment.

Cognitive and behavioral measures

Cognitive function was evaluated and compared between the two groups at three time points: before treatment (t_0), at the end of treat-

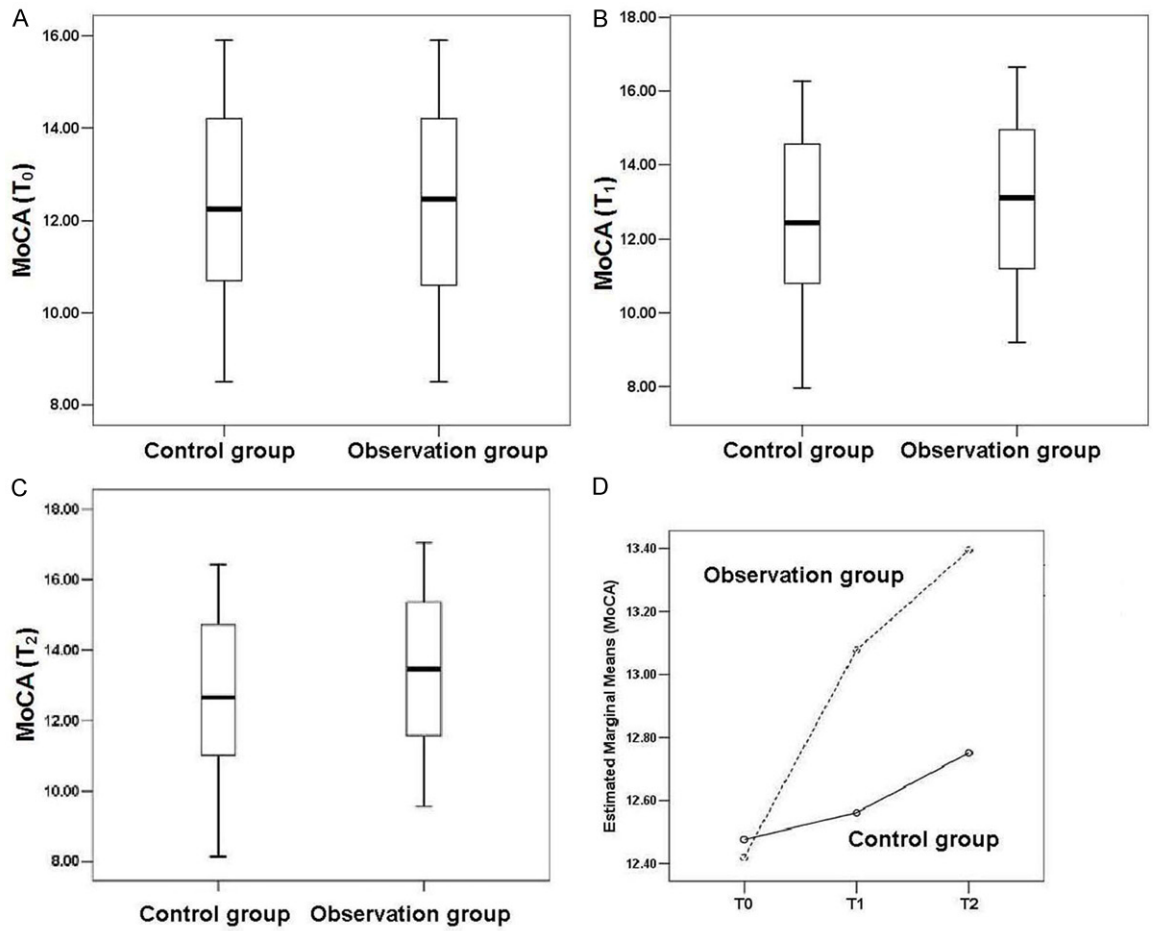

Figure 2. MoCA scores in AD patients who received music therapy (observation group) and those who did not (control). A. Beginning treatment; B. At the completion of treatment; C. Three months after treatment; D. Estimated marginal means of MMSE scores before (t_0), immediately following (t_1), and three months after treatment (t_2).

ment (t_1), and three months after treatment (t_2) using the mini-mental state examination (MMSE) [25] and Montreal Cognitive Assessment (MoCA) scoring [26]. Lower scores on the MMSE and MoCA indicated more severe cognitive impairment. The neuropsychiatric behaviors of patients in the two groups were evaluated using the Neuropsychiatric Inventory (NPI), with higher scores indicating more serious damage to mental behaviors [27].

Statistical analysis

The SPSS 17.0 statistical package (IBM, Armonk, NY) was used to establish a database and perform statistical analysis. Measurement data was expressed as mean ± standard deviation. The repeated measurement data at multiple time points were processed by analysis of variance of repeated measurement data. Mauchly's Test of sphericity was used to assess the correlation of the repeated measurement data. The least significant difference (LSD) was used for pairwise comparison and corrected for multiple comparisons with the Bonferroni correction. A $P<0.05$ was considered to be statistically significant.

Results

MMSE scores remained unchanged regardless of therapy

MMSE was used to determine the severity of memory impairment and/or AD progression. At baseline, there were significant differences in MMSE scores between the treatment groups. No significant differences were detected between groups at the first time points (before treatment). In both groups, the scores improved

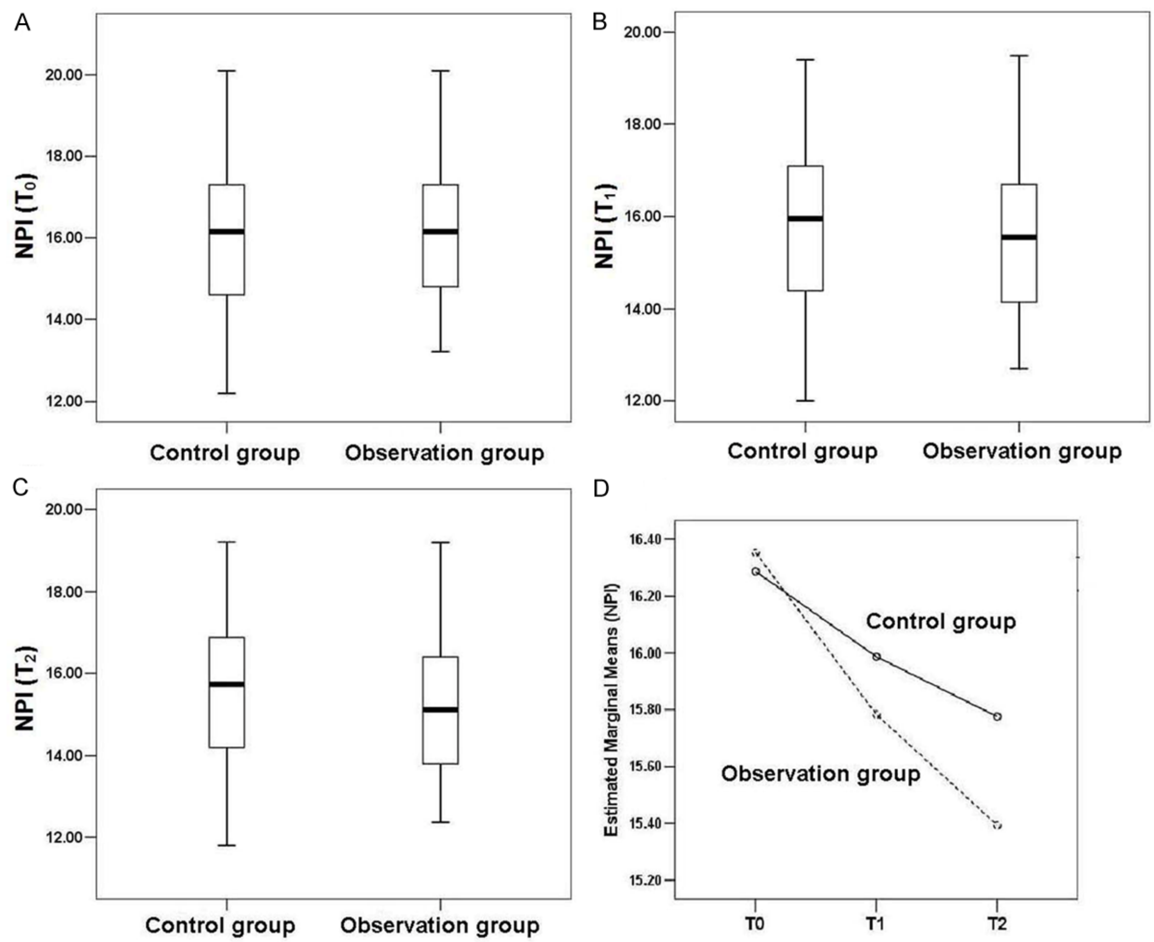

Figure 3. NPI scores in AD patients who received music therapy (observation group) and those who did not (control). A. Beginning treatment; B. At the completion of treatment; C. Three months after treatment; D. Estimated marginal means of MMSE scores before (t_0), immediately following (t_1), and three months after treatment (t_2).

(increased) over the study duration, with tests administered at the conclusion (t_1) and three months after treatment (t_2) (**Table 2**). However, the improvement in MMSE was significantly better in the group receiving music therapy in addition to pharmacological intervention (P=0.003). **Figure 1** depicts the distribution and estimated marginal means of MMSE scores at the 3 time points.

MoCA scores improve with music therapy

The MoCA is a test for the rapid assessment of mild cognitive dysfunction. At t_0, there were no significant differences in MoCA scores between the two groups. As found with the MMSE, scores in both groups improved (increased) over the course of the study. However, at t_1 and t_2, MoCA scores in the observation group were significantly higher compared to those of the control group (P<0.01). Within the observation group, MoCA scores at t_1 and t_2 were both significantly increased compared to pre-treatment values (P<0.01), as shown in **Table 2**. **Figure 2** depicts the distribution and estimated marginal means of MoCA scores at the three time points.

NPI scores improve with music therapy

NPI was used to evaluate neuropsychiatric symptoms. At t_0, there were no significant differences in NPI scores between the two groups. In both groups, the NPI scores improved over the course of the study. Further, at t_1 and t_2, NPI scores in the observation group were significantly lower compared to the control group (P<0.01). In the observation group, NPI scores at t_1 and t_2 were both significantly decreased compared to pre-treatment values (P<0.01), as shown in **Table 2**. **Figure 3** depict the distribution and estimated marginal means of NPI scores at the three time points.

Discussion

AD patients for whom no specific drug therapy can be applied may still benefit from intensified behavioral therapy, environmental changes, functional training, and rehabilitation therapy. Music therapy has become an increasingly popular supportive treatment due to its economical efficiency and simplicity of use, along with its success in delaying disease progression, reducing anxiety, supporting immunity, and improving comfort and quality of life in elderly patients with chronic diseases. Music and language appear to share common neural pathways, and thus music therapy may play an important role in the rehabilitation of language and cognitive function [28, 29]. It has achieved promising results in the treatment and cognitive function rehabilitation of AD [29, 30]. Dassa and Amir revealed that songs from the AD patients' past elicited memories, especially songs related to their social and national identity, and that the participants expressed positive feelings, a sense of accomplishment and belonging [30]. Fukui et al. reported that the secretion of 17 b-estradiol and testosterone, hormones that are supposed to have preventive effects on Alzheimer's disease, is significantly increased by music therapy [31].

MMSE, MoCA and NPI were used to evaluate mild cognitive impairment. Our study showed that music therapy could improve the MMSE, MoCA and NPI scores of AD patients undergoing conventional treatments. Both MMSE and MoCA scores were significantly higher but NPI scores were significantly lower at the end of the treatment and three months after the treatment ended for patients undergoing concurrent music and conventional drug therapy compared to patients who only underwent conventional drug therapies. The higher MMSE and MoCA scores indicate better cognitive function, while the lower NPE score indicates improved neurobehavior. These results suggest that music therapy can be an effective adjuvant to support pharmacological intervention in AD. Music therapy, when combined with pharmacological treatment, led to greater improvements in the cognitive function and mental behavior of AD patients over pharmacological intervention alone. Thus, music therapy may relieve some of the progressive cognitive dysfunction and mental impairment caused by AD, and should be further explored for its potential to delay disease progression while improving prognosis.

Disclosure of conflict of interest

None.

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