Postprint of a Meta-Analysis of the Intervention Effects of Music Therapy on Patients with Alzheimer' s Disease

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Abstract

Abstract

Background: Alzheimer' s disease (AD), as a neurodegenerative disorder, is characterized by high incidence and rapid progression, severely affecting patients' quality of life. In recent years, research on music therapy interventions for AD has gradually increased, but there remains a lack of effective systematic evaluation and analysis.

Objective: To conduct a meta-analysis of the intervention effects of music therapy on cognitive function, emotion, activities of daily living, and sleep disorders in AD patients.

Methods: A computer-based search was conducted for randomized controlled trials on the intervention effects of music therapy in AD patients from CNKI, Wanfang, VIP, Medline, Elsevier ScienceDirect, PubMed, and Embase, with the search period spanning from database inception to February 2023. Review Manager 5.4 software was used for data analysis.

Results: The study included 15 RCT articles, with a total of 1,077 patients. Meta-analysis results showed that the music therapy group had better intervention effects than the control group on cognitive function (MD=4.35, 95%CI=1.64-7.05, Z=3.15, P=0.002), negative emotion (SMD=-0.71, 95%CI=-1.26 to -0.15, Z=2.51, P=0.01), and activities of daily living (SMD=-0.91, 95%CI=-1.55 to -0.27, Z=2.77, P=0.006). There was no statistically significant difference between the two groups in sleep disorder intervention (MD=-1.04, 95%CI=-3.10 to 1.02, Z=0.99, P=0.32). Subgroup analysis revealed that music intervention groups with treatment duration <12 weeks (P=0.01), session length <45 min/time (P=0.02), frequency $ $3 times/week (P<0.001), individual implementation mode (P<0.001), individual+group implementation

mode (P=0.002), and receptive music therapy intervention (P<0.001) had better intervention effects on cognitive function than the control group. Music intervention groups with treatment duration $ $12 weeks (P=0.004), frequency <3 times/week (P=0.01), individual+group implementation mode (P=0.02), receptive music therapy intervention (P=0.002), and active music therapy intervention (P=0.002) had better intervention effects on negative emotion than the control group.

Conclusion: Music therapy can improve cognitive function, emotional state, and activities of daily living in AD patients. However, due to the low quality of the included studies, further verification through additional large-sample, high-quality evidence-based research is still needed.

Full Text

Intervention Effect of Music Therapy on Patients with Alzheimer' s Disease: A Systematic Review and Meta-analysis

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Abstract

Background: Alzheimer' s disease (AD) is a neurodegenerative disease with high incidence and rapid progression that seriously affects patients' quality of life. In recent years, research on music therapy interventions for AD has gradually increased, but effective systematic evaluation and analysis remain lacking.

Objective: To conduct a meta-analysis of the intervention effects of music therapy on cognition, emotion, living ability, and sleep disorders in AD patients.

Methods: Computerized searches were conducted in CNKI, Wanfang, VIP, Medline, Elsevier ScienceDirect, PubMed, and Embase for randomized controlled trials examining the intervention effects of music therapy methods on AD patients. The search period spanned from database inception to February 2023. Data analysis was performed using Review Manager 5.4 software.

Results: Fifteen RCT studies were included, comprising 1,077 patients. Meta-analysis results showed that the music therapy group demonstrated superior intervention effects compared to the control group in cognitive function (MD=4.35, 95%CI=1.64~7.05, Z=3.15, P=0.002), negative emotions (SMD=-0.71, 95%CI=-1.26~-0.15, Z=2.51, P=0.01), and living ability (SMD=-0.91, 95%CI=-1.55~-0.27, Z=2.77, P=0.006). No statistically significant difference was found between the two groups in sleep disorder intervention (MD=-1.04, 95%CI=-3.10~1.02, Z=0.99, P=0.32). Subgroup analysis revealed that music intervention groups with treatment duration <12 weeks (P=0.01), session length <45 min (P=0.02), frequency $ $3 times/week (P<0.001), individual implementation (P<0.001), individual+group implementation (P=0.002), and receptive music therapy (P<0.001) showed better cognitive function intervention effects than the control group. Additionally, music intervention groups with treatment duration $ $12 weeks (P=0.004), frequency <3 times/week (P=0.01), individual+group implementation (P=0.02), receptive music therapy (P=0.002), and active music therapy (P=0.002) demonstrated better negative emotion intervention effects than the control group.

Conclusion: Music therapy can improve cognitive function, mental status, and daily living ability in AD patients. However, due to the low quality of included studies, further verification through more large-sample, high-quality evidence-based research is needed.

Keywords: Alzheimer's disease; music therapy; treatment outcomes; cognition; emotion; quality of life; meta-analysis

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Methods

Literature Search and Selection Computerized searches were conducted in CNKI, Wanfang, VIP, Medline, Elsevier ScienceDirect, PubMed, and Embase for randomized controlled trials on the intervention effects of music therapy methods on AD patients. The search period extended from database inception to February 2023. Two researchers independently screened the literature, extracted data, and cross-checked results. Any disagreements were resolved through discussion with a third researcher. Data were organized using Excel spreadsheets, extracting: (1) basic information (author, publication year, country, sample size, age); and (2) trial information (trial format, implementation method, intervention measures, intervention period, intervention duration, outcome evaluation indicators).

Inclusion and Exclusion Criteria Studies were excluded if they: (1) included patients with neurological diseases other than AD; (2) were duplicate publications or had poor methodological quality; (3) had unclear trial results or data description that prevented statistical inclusion; (4) were conference papers; or (5) had unobtainable full text.

Quality Assessment and Risk of Bias Two researchers independently assessed the quality of included studies using the Cochrane Handbook for Systematic Reviews of Interventions, which evaluates seven important sources of bias: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, completeness of outcome data, selective reporting, and other bias sources. Results were expressed as "low risk," "high risk," or "unclear risk." Disagreements were resolved through discussion with a third author.

Statistical Analysis Statistical analysis was performed using RevMan 5.3 software. As the selected studies involved continuous variables, either mean difference (MD) or standardized mean difference (SMD) with 95% confidence intervals (95%CI) were used as effect size indicators. Heterogeneity was assessed using P values and I^2 statistics. A random-effects model was adopted when significant heterogeneity was present (I^2>50%, P<0.1); otherwise, a fixed-effects model was used.

Results

Literature Search Results The initial search yielded 1,044 articles: PubMed (n=346), Elsevier ScienceDirect (n=257), Medline (n=162), Embase (n=144), VIP (n=28), Wanfang (n=34), and CNKI (n=73). After removing duplicates (n=238), 806 articles remained for title and abstract screening. Following full-text review of 224 articles, 209 were excluded for various reasons: intervention measures not meeting criteria (n=79), patient population not meeting criteria (n=32), outcome measures not meeting criteria (n=63), insufficient data (n=23), and non-RCT design (n=12). Ultimately, 15 studies [9-23] were included in the meta-analysis [Figure 1: see original paper].

Basic Characteristics of Included Studies The 15 included RCT studies [9-23] comprised 1,077 patients. The basic characteristics of the included studies are presented in .

Risk of Bias Assessment Publication bias was assessed for the 15 included studies [9-23]. Eleven studies mentioned "randomization" [11-18,20,22-23], with seven [11,13-16,22-23] specifying random number tables, computer-generated randomization, or simple randomization. Four studies [8-11] described the randomization method in detail, while four [12,17-18,20] only mentioned "random" without sufficient detail. Two studies [11,14-16] described the blinding process in detail, with two [11,14] implementing blinding for participants, treatment administrators, and statisticians. Three studies [14-16] implemented blinding for outcome assessment or data, while the remaining 12 [9-10,12,17-23] did not mention blinding. One study [11] reported incomplete data as it represented preliminary results, while the other 14 [9-10,12-23] showed no selective reporting

or incomplete data. None of the 15 studies [9-23] had other sources of bias. The risk of bias assessment results are shown in [Figure 2: see original paper] and [Figure 3: see original paper].

Meta-Analysis Results Cognitive Function Intervention: Eight studies [11,15,17-22] reported the intervention effects of music therapy on cognitive function in AD patients, involving 440 patients. All eight studies used the Mini-Mental State Examination (MMSE) for cognitive assessment. Heterogeneity testing revealed I^2=94%, P<0.0001, indicating substantial heterogeneity; therefore, a random-effects model was used. Meta-analysis results showed that the music therapy group had significantly better intervention effects than the control group (MD=4.35, 95%CI=1.64~7.05, Z=3.15, P=0.002) [Figure 4: see original paper].

Negative Emotion Intervention: Eleven studies [9-10,12-15,18-22] reported the intervention effects of music therapy on negative emotions in AD patients, involving 705 patients. Heterogeneity testing revealed I^2=91%, P<0.00001, indicating substantial heterogeneity; therefore, a random-effects model was used. Meta-analysis results showed that the music therapy group had significantly better intervention effects than the control group (SMD=-0.71, 95%CI=-1.26~-0.15, Z=2.51, P=0.01) [Figure 5: see original paper].

Living Ability Intervention: Six studies [10,14-15,18-19,21] reported the intervention effects of music therapy on daily living ability in AD patients, involving 508 patients. Heterogeneity testing revealed I^2=91%, P<0.0001, indicating substantial heterogeneity; therefore, a random-effects model was used. Meta-analysis results showed that the music therapy group had significantly better intervention effects than the control group (SMD=-0.91, 95%CI=-1.55~-0.27, Z=2.77, P=0.006) [Figure 6: see original paper].

Sleep Disorder Intervention: Four studies [14,20,22-23] reported the intervention effects of music therapy on sleep status in AD patients, involving 192 patients. Heterogeneity testing revealed I^2=97%, P<0.00001, indicating substantial heterogeneity; therefore, a random-effects model was used. Meta-analysis results showed no statistically significant difference between the music therapy group and the control group (MD=-1.04, 95%CI=-3.10~1.02, Z=0.99, P=0.32) [Figure 7: see original paper].

Subgroup Analyses Cognitive Function: Subgroup analysis was conducted based on intervention characteristics that might cause heterogeneity: treatment duration, session length, frequency, implementation method, and intervention measures . Due to limited literature and some missing data, only partial outcome indicators were analyzed. Results showed that music intervention groups with treatment duration <12 weeks (P=0.01), session length <45 min (P=0.02), frequency $ $3 times/week (P<0.001), individual implementation (P<0.001), individual+group implementation (P=0.002), and

receptive music therapy (P<0.001) had significantly better cognitive function intervention effects than the control group.

Negative Emotions: Subgroup analysis based on the same intervention characteristics showed that music intervention groups with treatment duration $ $12 weeks (P=0.004), frequency <3 times/week (P=0.01), individual+group implementation (P=0.02), receptive music therapy (P=0.002), and active music therapy (P=0.002) had significantly better negative emotion intervention effects than the control group .

Discussion

This systematic review synthesized 15 RCT studies evaluating music therapy effects on cognitive function, negative emotions, living ability, and sleep status in AD patients. Neuroimaging studies demonstrate that music stimulation activates bilateral auditory cortices, left frontal lobe, and cerebellar regions, forming a core component of the brain's ventral attention network that responds to novel or unexpected stimuli [24-25]. This activation helps AD patients relearn or enhance recall of past experiential details, thereby improving cognitive function [26]. Our findings align with EZEGBE et al. [27], confirming that music therapy promotes cognitive function in AD patients.

AD often causes mood disturbances, agitation, anxiety, and tension. Music therapy' s primary advantage lies in transforming music' s physical properties into emotional functions for interpersonal communication, thereby enhancing emotional management capacity in AD patients [28]. Our study demonstrated that music therapy significantly improved negative emotions (SMD=-0.71, 95%CI=-1.26~-0.15), alleviating psychological burden for patients and caregivers [29]. The optimal intervention for cognitive improvement involved treatment duration <12 weeks with frequency >3 times/week, possibly because music-related pleasure is driven by successful prediction (or non-prediction) of musical events and their intrinsic value [30].

Regarding implementation methods, receptive music therapy showed superior effects compared to other approaches, likely related to characteristics of the elderly population. Research indicates that receptive music therapy, which emphasizes listening, is more readily accepted by older adults than active music therapy, and its implementation costs and difficulty are relatively lower.

In terms of daily living ability, our results showed that music therapy significantly improved self-care capacity (SMD=-0.91, 95%CI=-1.55~-0.27). Among four relevant studies, HU Yueqing et al. [22] found that AD patients preferred combined individual and group approaches. Individual music therapy facilitates memory recall and gradual cognitive recovery, while group music therapy leverages social interaction among AD patients to enhance cognitive function [31]. Music therapy stimulates connections between the amygdala (AMYG)

and pregenual anterior cingulate cortex (ACC), AMYG and subgenual ACC, and fusiform gyrus (FFG) and AMYG, improving emotional perception and processing [32]. Long-term music therapy correlates positively with neural plasticity.

Regarding sleep disorders, our meta-analysis found no significant effect (MD=-1.04, 95%CI=-3.10~1.02, P=0.32), contradicting XIAO Jieping et al.' s [22] conclusion that music therapy significantly improves sleep quality. In-depth analysis revealed that differences in intervention duration, session length, and frequency between studies may account for these divergent conclusions, warranting further investigation.

Limitations and Recommendations This study has several limitations: (1) Despite comprehensive search strategies, unpublished studies or relevant literature may have been missed. (2) Some included studies lacked blinding and allocation concealment, and some may have had non-random designs. (3) Comparison methods in retrieved literature may not perfectly match our intended analysis, and some studies had processed sample data. (4) The limited number of included studies and insufficient direct comparison RCTs between experimental and control groups may have introduced heterogeneity.

Future research should: (1) Cite more high-quality journal articles and strengthen meta-analyses of personalized music therapy interventions for AD [33] to provide scientific theoretical foundations. (2) Implement adequate blinding and allocation concealment to minimize bias. (3) Employ more unstructured forms of music therapy to accommodate individual AD patient needs and enhance intervention effects. (4) Emphasize diverse intervention methods, large samples, and long-term randomized controlled trials in clinical practice.

In conclusion, integrating music therapy into AD rehabilitation can improve cognitive function, emotional management, daily living ability, and sleep quality. However, further in-depth exploration is needed regarding disease severity grading, therapeutic mechanisms, intervention formats, duration, frequency, and outcome assessment to provide more scientific and standardized music therapy applications for AD patients.

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Author Contributions: Yong Zhang and Senli Wang were responsible for conceptualization, meta-analysis interpretation, and manuscript writing. Senli Wang and Ronghua Huang developed the search strategy, conducted literature screening, and performed risk of bias assessment. Dan Liu was responsible for quality control and manuscript review. Fengping Xu and Yong Zhang revised the manuscript. Yong Zhang and Dan Liu provided overall supervision.

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Note: Figure translations are in progress. See original paper for figures.