Review Article
A meta-analysis of the effect of music therapy on Alzheimer's disease

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Abstract: Objective: To evaluate the effect of music therapy on Alzheimer's disease (AD) patients and to provide evidence in support of the implementation of music therapy in the management of AD. Methods: We explored works published in the medical literature in English and Chinese from January 2000 to December 2017 on the evaluation of the effect of music therapy on AD after intervention. We searched the relevant databases, including PubMed, Chinese Biomedical Literature, the full-text databases of Chinese periodicals, the Wanfang databases, and other network resources. The literature was screened according to the criteria of inclusion and exclusion. The bias risk assessment tool recommended by the Cochrane work manual and the randomized controlled study model were used (extensions of the CONSORT statement). The quality of each study was used as the reference standard to evaluate the quality of the literature. The intelligence and daily energy ability of the patients with AD were taken as the effective indexes to extract the relevant information that had been included in the literature. Stata 11.0 software was used to collect the data of 15 final studies, and the random effect model was used to combine the effect quantity and the meta-analysis. Results: The 15 studies on the effects of music therapy on Alzheimer's cognitive function show that the data are heterogeneous (I^2=90.3), and combining the effect of the random effect model, SMD=0.139, 95% CL [-0.36, 0.63], P=0.443>0.05, there is no statistical significance. The 6 studies on the effects of music therapy on the activities of daily living (ADL) in AD show the heterogeneity of the data (I^2=92.8). Combining the effect of the random effect model, SMD=-0.03, 95% CL [-0.81, 0.75], P=0.933>0.05, and there was no statistical significance. Conclusion: The effect of music therapy on cognitive function and ADL in patients with AD is not significant. Music therapy for AD patients also needs further research involving a multi-center study, a larger sample size, and various musical models. We also need to explore whether music therapy is suitable for use in Chinese pension institutions, including whether it is convenient and feasible. The low-cost and effective music therapy mode for the prevention of Alzheimer's disease has a profound influence and a great significance.

Keywords: Alzheimer's disease, music therapy, meta-analysis

Introduction

As the Chinese population is ageing rapidly, the prevalence of AD is increasing and multiplying [1]. AD is a progressive neurodegenerative disease with a hidden onset and the clinical manifestations of cognitive impairment [2] (most notably short-term memory loss and functional impairment) are central, and may be accompanied by aphasia, apraxia, agnosia, visual spatial skills impairment, executive dysfunction, personality and behavioral changes, and other mental and behavioral symptoms, a group of diseases that affect an individual's social function and lead to a decline in daily life and the quality of life. The common types of dementia in clinical work are AD, which accounts for about 60% of all dementia types, and there are also vascular, frontotemporal, and mixed dementia. AD has become one of the top four causes of death after cardiovascular and cerebrovascular disease and cancer.

Since the pathogenesis of dementia has not yet been clarified, at present, the treatment of it is still a challenging problem in clinical work, although the drug treatment of dementia is more mature, but is often accompanied by unavoidable side effects and complications, especially atypical antipsychotics, which are used to treat the mental and behavioral symptoms of dementia, and although they are effec-

tive, they are associated with severe adverse cardiovascular and cerebrovascular events and extrapyramidal symptoms [3]. In view of the limitations of drug therapy, more and more studies are beginning to explore the effectiveness of non-pharmacological therapy for AD. As a promising non-pharmacological therapy for dementia, music therapy has become one of the hot research topics of scholars and is becoming more and more popular.

Music therapy is usually carried out by professional music therapists or systematically trained rehabilitation trainers and a caretaker for dementia patients. According to the patient's preferred type of music, a pleasant and warm environment or atmosphere is created through active music therapy that includes singing, dancing, or instrument performance or passive music therapy which involves listening to live or recorded music, so as to realize a personalized goal in the relationship of music therapy. In 2006, the American Music Therapeutics Association (AMTA) defined music therapy (MT) [4] "achieving individualized goals in therapeutic relationships through clinical and evidence-based music interventions". Music is beyond the communication of language and has a magical power that can break the barrier of isolation. Music therapy is not a cure for dementia but it is based on the systematic use of musical instruments to improve communication between music therapists and patients, which may have beneficial effects on one's social, cognitive and psychobehavioral symptoms. It improves the quality of life of dementia patients. The effectiveness of music therapy in the intervention of AD patients was evaluated by MMSE, ADL/QOL and the treatment progress was monitored at the same time, and it was done according to the new data collected in the field of research to guide the next step of practice.

Available evidence suggests that music therapy may be a useful treatment or can effectively manage Alzheimer's symptoms. At the same time, music therapy is a low-cost, safe, effective, and enjoyable non-invasive treatment that can be designed and delivered by professional music therapists and other nursing staff in the home [5]. However, based on the analysis of evidence-based medicine, the current research has not established reliable evidence to prove the practical clinical value of music therapy, which greatly limits the generality of music therapy. The purpose of this paper is to systematically search, screen, and evaluate the literature published in recent years through the methodology of meta-analysis in evidence-based medicine, and to integrate the evidence of music therapy of AD from 2000 to 2017, to provide a reference for dementia prevention and treatment policies with elderly patients.

Data and methods

Search strategy

To search the database of Chinese scientific and technological journals, the Chinese biomedical literature database, the Chinese periodical full-text database, the Wanfang database, PubMed, and other related data of network resources. The retrieval period is from January 2000 to December 2017. The literature retrieval strategy adopts the principle of the combination of subject words and free-text words. The key words are "Alzheimer's disease" and "music therapy". "Alzheimer disease", "Alzheimer", "dementia", "music", "musical", "melody", "singing", "Music therapy", and "Music intervention". The retrieval process is based on *Entries for the Systematic Review and Meta Analysis Priority Report*. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) are divided into four processes: retrieval, initial screening, integration, and synthesis.

Inclusion criteria

(1) The literature about music therapy of AD at home and abroad (clinical study, not basic science or animal experiments), the type of investigation is a randomized controlled study; (2) First-hand research materials, not reviews; (3) The subjects of the study were AD patients; (4) the research design is reasonable and the statistical method is correct; (5) Outcome indicators should include MMSE, ADL/QOL of AD patients.

Exclusion criteria

(1) the type of investigation is a non-randomized controlled study, such as a case control study; (2) repeated reports; (3) unreliable literature.

Evaluation of document quality

The bias risk assessment tool and the quality of random controlled study reports recommended by the working manual of Cochrane collaboration Network (extensions of the CONSORT statement, CONSORT extension) were used to evaluate the literature quality. Bias risk was evaluated in terms of selection, implementation, measurement, follow-up, reporting, and other bias items, and each index was judged to have either a "low bias risk", a "bias risk uncertainty", or a "high bias risk".

Data extraction

The investigator set up a data extraction table to describe the general characteristics of the study period, type and the sample size of the selected literature and to extract the indexes of intelligence, daily life ability, and the life quality effect, and to describe the research results of music therapy on AD respectively.

Statistical analysis

<u>Heterogeneity analysis</u>

The most commonly used heterogeneity test is the Q test, in the case of a small number of combined studies, we usually change $\alpha=0.05$ to $\alpha=0.10$, in order to make up for the low test efficiency of the Q test method, and to eliminate the influence of the number of studies on the statistical test efficiency. Q is usually converted to get an I^2, and $I^2=0\text{-}25\%$ indicates no heterogeneity, 25-50% indicates low heterogeneity, 50-75% indicates moderate heterogeneity, and 75-100% indicates high heterogeneity. Using Stata 11.0 software, if the heterogeneity of each study included is acceptable, that is, the test level $P>0.10$ and $I^2<50\%$, the fixed effect model is selected for the meta-analysis. If there were heterogeneity at $P\leq0.10$ and $I^2\geq50\%$ among the results of the study, the random effect model was used to analyze the heterogeneity source of the meta-analysis. The heterogeneity test was performed by using Q and I^2 statistics, and the combined effect was determined using the Der Simonian and Laird method (the D-L method), verifying that the consolidated statistics are statistically different using the hypothesis test, $P<0.05$, and it shows that the combined statistics are statisti-cally significant, or $P>0.05$, when there was no statistical significance.

According to the manual of the Cochrane system evaluation and the viewpoints of the similar studies the effect of intervention can be divided into three grades according to the value of the effect: SMD<0.2, the effect of intervention is small, 0.2<SMD<0.5, the intervention effect is moderate, and SMD>0.5, the effect of intervention is high.

Forest plots are based on the statistical indicator and the statistical analysis method, a graph drawn from the result of a numerical operation. It is in a plane rectangular coordinate system, centered on a vertical invalid line with a horizontal coordinate scale 1 or 0, and multiple lines parallel to the horizontal axis are used to describe the amount of the effects and the confidence intervals that are included in the study. The effects and confidence intervals of the multiple studies are described by a single prism (or other graph). It describes very simply and intuitively the statistical results of the meta-analysis and it is the most commonly used expression of results in meta-analyses.

Forest graphs of continuous variables: When the measurement data (continuity variable) is used, the weighted mean difference (WMD) or the standardized mean difference (SMD) are used as the combined statistics to calculate the confidence interval of 95%.

When the 95 CI of a certain study contains 0, that is, the 95 CI horizontal line in the forest map intersects with the invalid vertical line (the horizontal coordinate scale is 0), the average value of a certain index in the test group is equal to that of the control group, and the experimental factors do not reach the ideal effect.

When the upper and lower limits of 95 CI in a certain study are greater than 0, that is, in the forest map, the 95 CI horizontal line does not intersect with the invalid vertical line, and the horizontal line falls on the right side of the invalid line, the average value of a certain index in the test group is greater than that in the control group. If the index studied by the researcher is an adverse event, the test factor is a harmful factor (risk factor), and if the event studied by the researcher is a beneficial event, the experimental factor is a beneficial factor.

When the upper and lower limits of 95 CI in a certain study are less than 0, that is, in the forest map, the 95 CI horizontal line does not intersect with the invalid vertical line, and the horizontal line falls on the left side of the invalid line, the average value of a certain index in the test group is smaller than it is in the control group. If the index studied by the researcher is an adverse event, the experimental factor is a beneficial factor (protection factor), and if the event studied by the researcher is a beneficial event, the experimental factor is a harmful factor.

Forest graphs with binary variables: The 95% confidence interval (CI) was calculated using RR or OR as a statistical indicator when the study object was a binary variable (such as occurrence and non-occurrence).

When the 95% CI of a study RR (OR, RD) contains 1, that is, the horizontal line of 95% CI in the forest map intersects with the invalid vertical line, it can be considered that the incidence rate of the test group is equal to that of the control group, and the test factor is not effective.

When the 95% CI upper and lower limits of a certain study RR (OR, RD) are all greater than 1, that is, in the forest map, the 95% CI cross line does not intersect with the invalid vertical line, and the horizontal line falls to the right of the invalid line, so the incidence in the test group is higher than it is in the control group. If the events studied by the researchers were adverse events (such as morbidity, illness, death, etc.), the experimental factors in the trial group would increase the occurrence of the adverse events, and the test factors were harmful (risk factors). If the events studied by researchers are beneficial events, (such as effective, relieving, survival, etc.), the test factors will increase the beneficial events, and the experimental factors are beneficial factors.

When the upper and lower limits of 95% CI in a study are less than 1, that is, in the forest map, the 95% CI horizontal line does not intersect with the invalid vertical line, and the horizontal line falls on the left side of the invalid line, the incidence of the trial group is considered to be less than that of the control group. If the events studied by the researchers were adverse events (such as morbidity, illness, death, etc.), the experimental factors in the trial group would reduce the occurrence of the adverse events; if

the event studied by the researcher is a beneficial event (such as effective, relieving, survival, etc.), the experimental factor will reduce the occurrence of the beneficial event, and the experimental factor will be a harmful factor.

Sensitivity analysis

A sensitivity analysis is based on the characteristics of each study (such as design type, follow-up, etc.) to reconsider the number of studies included in the meta-analysis, and to compare the changes of the results of the two meta analyses before and after the analysis. The aim is to investigate the stability and reliability of the meta-analysis results. If there is no essential change in the results of meta-analysis or the systematic reviews, the sensitivity and reliability of the analysis results are better, if the conclusion is reversed, the conclusion is prudent.

Bias analysis into literature

Funnel plots analysis

The detection of the publication bias is shown by funnel plot. A funnel graph is a visual observation to identify the existence of publication bias. It is recommended by the Cochrane handbook. In this method, the estimated value of the effect quantity of each study is shown on the x axis, the sample size is shown on the y axis to a scatter plot drawn, and a visual observation of whether it is symmetrical or not. A funnel graph is the most commonly used method to identify the existence of publication bias in the study, and the presupposition is that the accuracy of the effect estimator increases with an increase of the sample size. In studies involving small sample sizes, the estimated value of the effect quantity is distributed at the bottom of the graph with a wide range, and the estimation value of the effect quantity of the large sample size is distributed at the top of the graph, and the range is narrower.

The key to seeing whether there is a published bias from the funnel diagram is to see if the tests are funnel-shaped distributions centered on vertical lines. Generally large samples are distributed at the top of the funnel and concentrated near the vertical line. When the sample size is small, the test is evenly scattered in the lower part of the funnel graph. If the included study has no bias or less bias, the figure shows
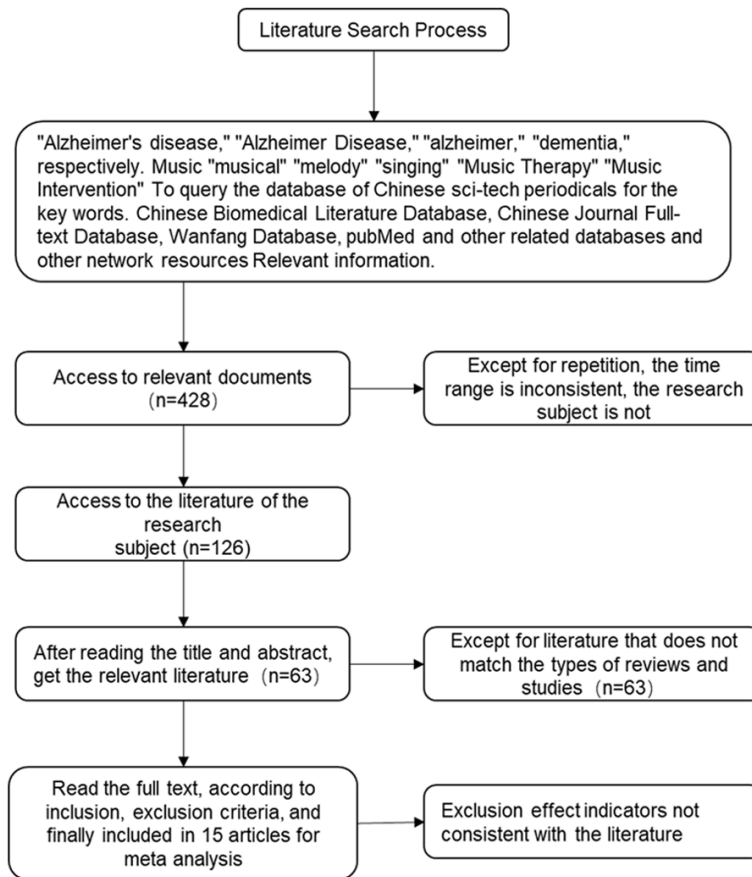
Figure 1. Literature screening flowchart.

a similar inverted funnel with a small top and a large bottom. If there is an asymmetric funnel graph, there may be a greater bias, and the more obvious the asymmetry, the greater the degree of bias, which is mostly caused by publication bias. However, funnel diagrams usually have a lot of subjectivity, and this method is specific, intuitive and simple, but it cannot accurately test the symmetry of the graph. It is better to use an Egger test or a Begg test to get a more objective *p* value, thus avoiding the subjectivity of judging from the funnel diagram alone.

The Begg and Egger methods

In fact, this method uses a statistical method to test the funnel graph. The Egger method uses linear regression, while the Begg method uses a linear correlation test. The general formula of the regression equation can be expressed as: OR/SE=a+b*1/SE, that is, the inverse of the standard error of the OR value of

the check variable is an argument, and the OR value is divided by its standard error as the dependent variable. It is actually a test of whether the intercept is zero or not. If the intercept is zero, there is no publication bias. Otherwise, it indicates the existence of publication bias. The Begg method is similar to this, and it is considered that Egger is more sensitive to Begg when the number of studies is less or less biased.

Result

Literature retrieval results and retrieval process

Document retrieval process

This study retrieved 428 relevant articles, including 290 in English and 138 in Chinese. We eliminated duplicate documents, documents outside our time scope, and irrelevant documents using the document management software. We initially selected 126 papers on the contents of the match, and after reading the titles and abstracts, 63 articles were excluded because the literature review and other research types did not match. Further, by reading the full text of the literature screening effect index, 46 articles were excluded because of the difference of the effect index, and the heterogeneity of the research object was larger. We eventually ended up with 16 randomized controlled trials.

Literature screening flow chart (**Figure 1**)

Evaluation of literature quality (offset risk): This meta-analysis did not specifically distinguish between different types of dementia or severity, nor did it compare the validity of various musical patterns between the groups. The intervention of music therapy to AD patients includes music therapists, dementia rehabilitators, nursing staff of old-age institutions and so on, and the place of implementation was not uniform, so there is a certain publication bias.

Table 1. Data on the effects of music therapy on dementia intelligence

First Author & Publication time	Data Source	sample capacity	Intervene personnel	Intervention mode	Intervention time (month)	Conclusion
Liu Jinyu, 2013 [14]	Chinese Journal of Practical Neurodiseases	60	Professional training Dementia rehabilitation trainer	Passive music therapy	1	Music rehabilitation training can improve the cognitive function of AD patients.
Zhong Weia, 2015 [18]	Chinese Medical Journal	57	Music therapists and nurses	Passive music therapy	6	Group music therapy contributes to the recovery of Alzheimer's patients.
Mai Suzhen, 2014 [19]	International Medicine and Health Guidance News	64	Rehabilitation instructor	Passive music therapy	6	Music therapy can improve cognitive function of AD patients.
Chen Lian, 2012 [6]	Sichuan Mental Health	53	Music therapist	Combination of active and passive music therapy	6	Music therapy can improve cognitive function of AD patients.
Gao Zhihong, 2013 [15]	Health Studies	60	Trained doctors and nurses	Passive music therapy	9	Music therapy can improve cognitive function of AD patients.
Lv Jihui, 2014 [7]	Chin J Neurol	93	Music therapist	Active music therapy	6	Music therapy can improve memory function in AD patients.
Liu Gang, 2005 [8]	Acupuncture and Moxibustion	41	doctor	Passive music therapy	4	Music therapy can improve the curative effect of AD patients.
Liu Lichun, 2017 [20]	Chinese Journal of Gerontology	25	Music therapist	Active music therapy	4	Music therapy can improve cognitive function of AD patients.
Yang Yuefeng, 2017 [16]	Modern Diagn Treat	40	Music therapist	Passive music therapy	4	Music therapy can improve the curative effect of AD patients.
Teppo Sarkam, 2013 [9]	The Gerontologist	55	Music therapist	Combination of active and passive music therapy	12	Music activities can improve the cognitive function of patients with mild and moderate AD.
Chien-Hsun Li, 2015 [10]	Neuropsychiatric Disease and Treatment	41	paramedic	Passive music therapy	6	Music therapy has no significant effect on the overall cognition of mild AD patients.
Masayuki Satoh, 2015 [11]	Dement Geriatr Cogn Disord Extra	20	Professional singers and pianists	Combination of active and passive music therapy	6	Music therapy has no significant effect on the overall cognition of mild AD patients.
AnnVande Winckel, 2004 [17]	Clinical Rehabilitation	25	Therapeutist	Active music therapy	3	The effect of music training on cognition of patients with moderate to severe dementia is beneficial.
Hsin Chu, 2013 [12]	Biological Research for Nursing	104	Music therapist	Combination of active and passive music therapy	2	Group music therapy can delay the cognitive function of AD patients.
EvaM.Arroyo-Anll, 2013 [9]	BioMed Research International	27	Music therapist	Passive music therapy	3	Familiarity with music can enhance self-awareness in patients with AD.

Table 2. Data on the effects of music therapy on the daily life ability of dementia patients

First Author & Publication time	Data Source	Sample capacity	Intervene personnel	Intervention mode	Intervention time (month)	Conclusion
Liu Jinyu, 2013 [14]	Chinese Journal of Practical Neurodiseases	60	Professional training Dementia rehabilitation trainer	Passive music therapy	1	Music therapy can effectively improve the ADL ability of AD patients.
Zhong Weia, 2015 [18]	Chinese Medical Journal	57	Music therapists and nurses	Passive music therapy	6	Group music therapy contributes to the recovery of Alzheimer's patients.
Mai Suzhen, 2014 [19]	International Medicine and Health Guidance News	64	Rehabilitation instructor	Passive music therapy	6	Music therapy can effectively improve the ADL ability of AD patients.
Gao Zhihong, 2013 [15]	Health Studies	60	Trained doctors and nurses	Passive music therapy	9	Music therapy can effectively improve the ADL ability of AD patients.
Liu Gang, 2005 [8]	Acupuncture and Moxibustion	41	doctor	Passive music therapy	4	Music therapy can effectively improve the ADL ability of AD patients.
Liang Disai, 2016 [13]	Hebei Journal of Traditional Chinese Medicine	128	Trained doctors and nurses	Passive music therapy	3	Music therapy can effectively improve the ADL ability of AD patients.

**Table 3.** A total of 15 studies were included in the meta analysis

First Author & Publication time	experimental group			control group			Weight (%)	SMD (95% CI)
	n1	Mean1	Sd1	n2	Mean2	Sd2		
Liu Jinyu, 2013 [14]	30	21.13	3.09	30	16.57	3.08	6.82	1.48 (0.91, 2.05)
Zhong Weia, 2015 [18]	28	22.51	7	29	31.54	13.45	6.89	-0.84 (-1.38, -0.30)
Mai Suzhen, 2014 [19]	32	9.87	2.61	32	16.05	2.45	6.65	-2.44 (-3.09, -1.79)
Chen Lian, 2012 [6]	25	16.1	2.47	28	15.44	2.33	6.89	0.28 (-0.27, 0.82)
Gao Zhihong, 2013 [15]	30	21.63	2.62	30	19.82	3.15	6.94	0.62 (0.11, 1.14)
Lv Jihui, 2014 [7]	32	17.64	5.3	30	17.91	3.1	6.98	-0.06 (-0.56, 0.44)
Liu Gang, 2005 [8]	20	20.08	6.39	21	18.56	8.41	6.73	0.20 (-0.41, 0.82)
Liu Lichun, 2017 [20]	12	8.24	5.09	13	13.92	5.81	6.18	-1.04 (-1.88, -0.20)
Yang Yuefeng, 2017 [16]	20	26.3	3.5	20	19.2	2.6	6.26	2.30 (1.50, 3.11)
Teppo Sarkam, 2013 [9]	27	19	5.7	28	20.3	5.1	6.91	-0.24 (-0.77, 0.29)
Chien-Hsun Li, 2015 [10]	20	16.7	5.55	21	14.1	3.71	6.71	0.55 (-0.77, 2.05)
Masayuki Satoh, 2015 [11]	10	19.1	3.9	10	20.9	3.5	6.04	-0.49 (-1.38, 0.40)
AnnVande Winckel, 2004 [17]	15	15.53	4.44	10	11	4.3	6.14	1.03 (0.18, 1.89)
Hsin Chu, 2013 [12]	52	14.24	6.39	52	13.5	4.6	7.18	0.13 (-0.25, 0.52)
EvaM.Arroyo-AnlI, 2013 [9]	20	19.5	3.28	20	17.35	3.57	6.68	0.63 (-0.01, 1.26)
Total (95% CI) 0.14 (-.36, 0.63)								

Heterogeneity chi-squared =145.02, (d.f.=14) P=0.000; I^2=90.3% Test of overall effect: z=0.55 (P=0.584).
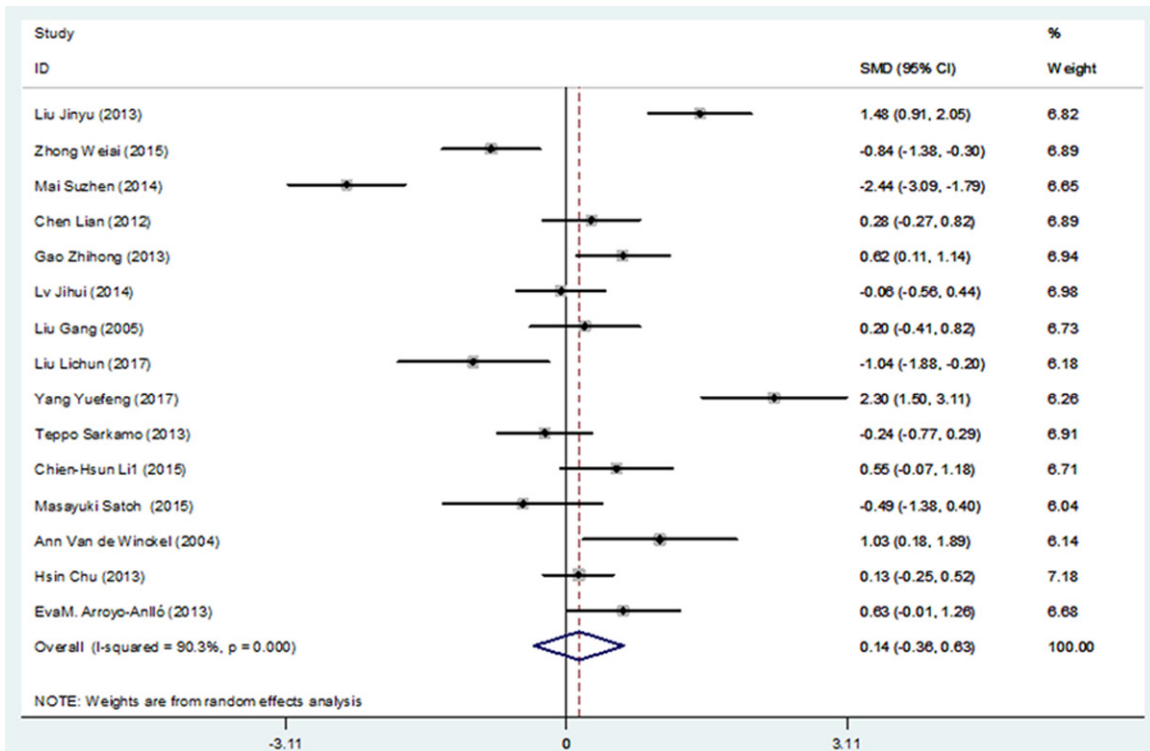
Figure 2. The effect of music therapy on MMSE intervention in AD patients. AD, Alzheimer's disease; MMSE, Mini-mental State Examination.
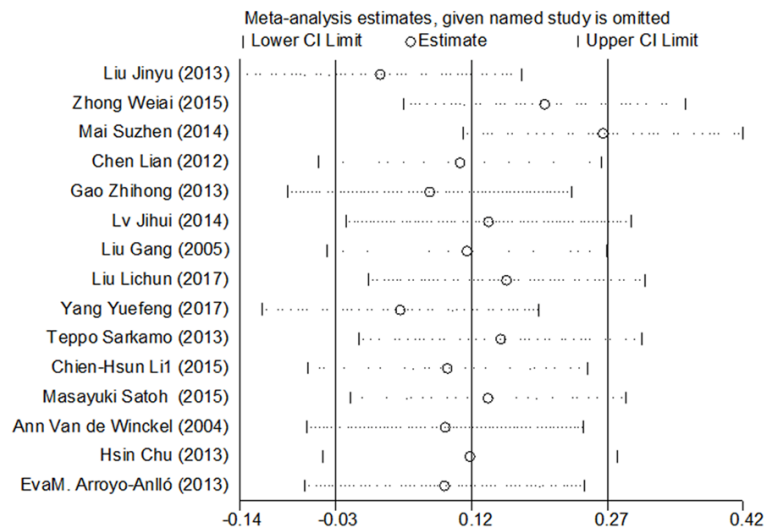
Figure 3. The sensitivity of music therapy to MMSE intervention in AD patients. AD, Alzheimer's disease; MMSE, Mini-mental State Examination.

daily life abilities, but only 10 demonstrated the effect of music therapy on AD or cognitive function, 1 demonstrated the effect of music therapy on the daily life ability of AD. A total of 914 patients were included. The maximum sample size was 128 cases and the minimum was 20 cases.

Statistical analysis results

We observed that studies [6-13] found music therapy had no significant effect on the cognitive function and activity of daily living of AD, studies [14-17] found it has a remarkable effect, studies [18-20] found it has no effect.

*General information included in the literature (**Tables 1** and **2**)*

In the 16 included randomized controlled studies, there are 5 demonstrating the effect of music therapy on AD of cognitive function and

Evaluation of MMSE intervention effect of music therapy in AD patients

A total of 15 studies were included in the meta-analysis (**Table 3**), MMSE indicators were used to analyze the effect of intervention.
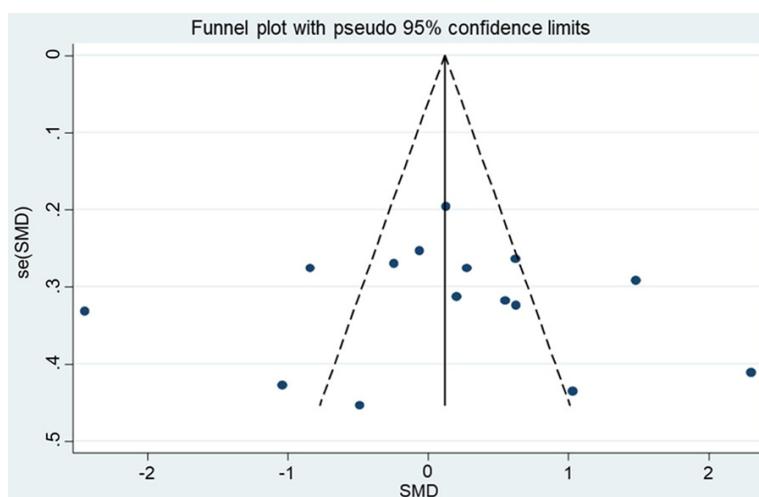
Figure 4. A Funnel diagram was used to evaluate publication bias for the 15 studies. SMD, standardized mean difference.

*Heterogeneity analysis (**Figure 2**):* (1) Results of heterogeneity test: I^2=90.3%, P=0.000; (2) Combined effect quantity of standardized mean difference: SMD=0.139; (3) Combined effect of standardized mean difference 95% CI (-0.36, 0.63); (4) Test after combining statistics Z=0.55, P=0.584.

According to the analysis above, 15 items of RCT into the meta-analysis are heterogeneous, based on the Cochrane evaluation manual suggested that random effect model should be used. The results show the test after combining the statistics Z=0.55, P=0.584, P>0.05, and there was no statistical significance, so it shows that the effect of music therapy on Alzheimer's MMSE is not significant.

*Sensibility analysis (**Figure 3**):* The sensitivity analysis shows that the data is more robust, and without any one of the values, the amount of consolidation effect does not change much. It shows that music therapy has no significant effect on the mentality of Alzheimer's disease.

Publication bias test: A funnel map is drawn for the 15 studies included, as shown in **Figure 4**. Begg's Test: z=0.30, Pr > |z|=0.767 (continuity corrected), P>0.05, and there was no statistical significance, and there was no publication bias.

Evaluation of ADL intervention effect of music therapy in AD patients

A total of 6 studies were included in the meta-analysis (**Table 4**), ADL indicators were used to analyze the effect of intervention.

*Heterogeneity analysis (**Figure 5**):* (1) Results of heterogeneity test: I^2=92.8%, P=0.000; (2) Combined effect quantity of standardized mean difference: SMD=(-0.033); (3) Combined effect of standardized mean difference 95% CI (-0.81, 0.75); (4) Test after combining statistics Z=0.08, P=0.933.

According to the analysis above, 6 items of RCT into the Meta-analysis are heterogeneous, based on the Cochrane evaluation manual's suggestion that the random effects model should be used. The results show the test after combining the statistics Z=0.08, P=0.933, P>0.05, and there was no statistical signifcance, showing that the effect of music therapy on Alzheimer's ADL is not significant.

*Sensibility analysis (**Figure 6**):* The sensitivity analysis shows that the data is more robust, and without any one of the values, the amount of consolidation effect does not change much. There was no statistical significance, and there was no publication bias.

Publication bias test: Because of the small number of studies involved, it is of little significance to draw funnel maps. Begg's Test: z=0.00, Pr > |z|=1.00 (continuity corrected), P>0.05. There was no statistical significance, and there was no publication bias.

Discussion

According to the relevant epidemiological data, in 2006, there were about 26 million AD patients in the world. By 2050, it is estimated that one in every 85 people in the world will suffer from AD [21]. There were 3.68 million AD patients in China in 1990 and 9.19 million in 2010 [22]. AD places a huge economic burden on society as a result of its progressive cognitive decline, resulting in complex treatment and care problems [23], and it has become a worldwide public health problem. How to effectively treat the disease has become a common concern throughout the world. With the increasing

Table 4. A total of 6 studies were included in the meta analysis

First Author & Publication time	experimental group			control group			Weight (%)	SMD (95% CI)
	n1	Mean1	Sd1	n2	Mean2	Sd2		
Liu Jinyu, 2013 [14]	30	48	8.57	30	34	8.65	16.39	1.63 (1.04, 2.21)
Zhong Weia, 2015 [18]	28	31.54	13.45	29	38.65	15.69	16.69	-0.49 (-1.01, 0.04)
Mai Suzhen, 2014 [19]	32	37.87	3.61	32	48.05	8.45	16.52	-1.57 (-2.13, -1.00)
Gao Zhihong, 2013 [15]	30	42.03	6.38	30	38.29	5.36	16.73	0.63 (0.12, 1.15)
Liu Gang, 2005 [8]	20	17.31	7.57	21	20.83	10.22	16.22	-0.39 (-1.01, 0.23)
Liang Disai, 2016 [13]	66	30.02	4.37	62	30.09	4.14	17.45	-0.02 (-0.36, 0.33)
Total (95% CI) -0.03 (-0.81, 0.75)								

Heterogeneity chi-squared =69.83, (d.f.=5) P=0.000; I^2=92.8% Test of overall effect: z=0.08 (P=0.933).
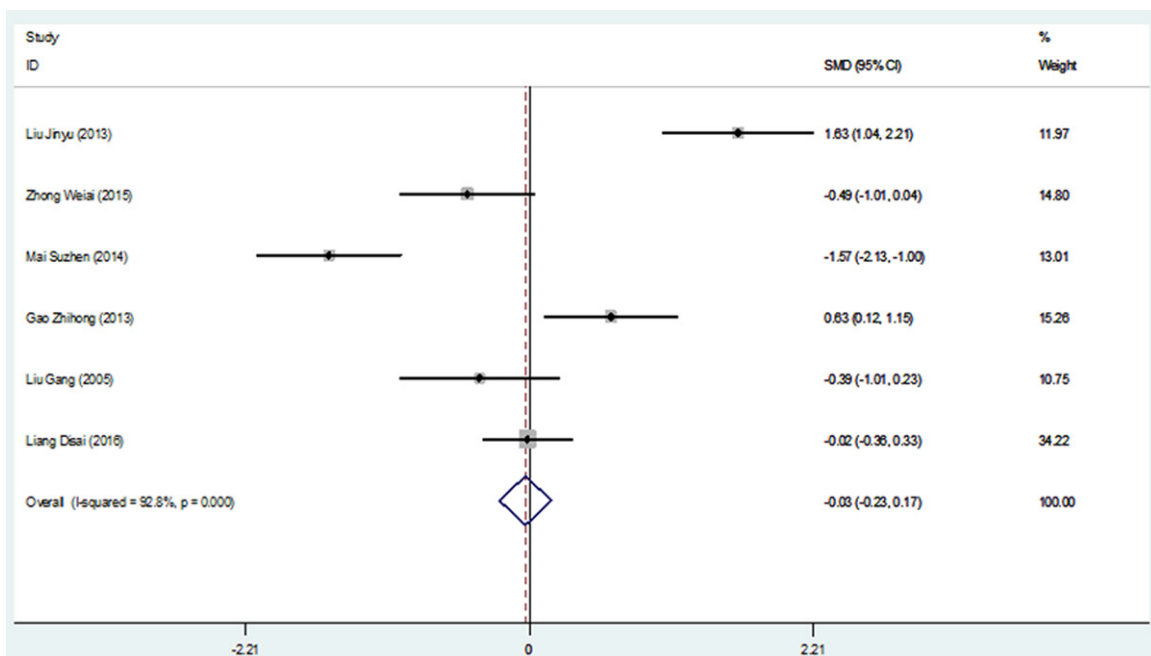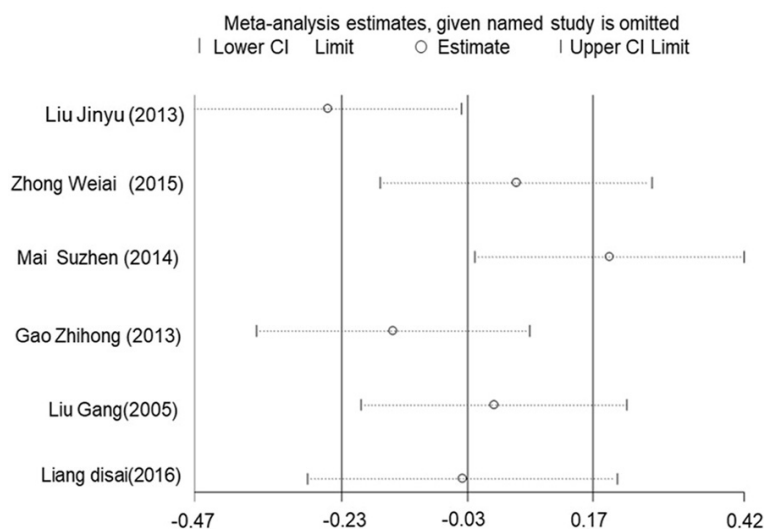

Figure 5. Effect of music therapy on ADL intervention in AD patients. AD, Alzheimer's disease; ADL, Activities of Daily Living.

attention to AD, the patients' cognitive function and the improvement of the quality of life are also of great concern [24]. Music therapy is a new interdisciplinary subject which integrates music medicine pedagogy and psychology and has made great progress in the field of clinical application in recent years, and it is also widely used in patients with AD. A large number of studies shows that [25] listening to music activates multiple areas of the brain involved in cognitive, sensorimotor, and emotional processing. For example, music involves sensory processes, attention processes, memory-related processes, perceptual and motor regulation ("mirror neuron systems"), and multi-sensory integration. Emotion deals with changes in

activity in the core areas, music syntactic and semantic processes, and social cognition. Music therapy, because of its ability to adjust the mood of Alzheimer's patients, improves their emotions. Maintaining its physical and mental balance and its active rehabilitation role has been accepted by society and medical circles. Music therapy can delay the deterioration of the physical and mental functions of AD patients, so as to play a therapeutic role [26].

This system is based on the evaluation of 15 randomized controlled trials that met the inclusion criteria of the literature, and through the analysis of SMD=0.139, 95% CL [-0.36, 0.63], P=0.584>0.05, they have no statistical signifi-

Figure 6. Sensitivity of music therapy to ADL intervention in AD patients. AD, Alzheimer's disease; ADL, Activities of Daily Living.

cance, suggesting that music therapy has no positive effect on the cognitive function of AD. Analyzing the forest map 2, it shows that studies [14-17] had remarkable effects, and its long-term mechanism may be associated with increased cerebral blood flow in the frontal and temporal lobes, the activation of the cerebral cortical circuit, and a variety of neurotransmitters such as dopamine, neuropeptides (endorphins and naphthenes). And other biochemical media, such as nitric oxide, play a role in the perception and emotional processing of music. A study of Tian Hailin [27] et al. showed that cognitive training on the given music therapy can improve the overall level of each factor and cognition in patients with Alzheimer's, because: (1) by adjusting the patient's mood, it affects cognition, finally obtaining better results in cognitive improvement; (2) music has a kind of stimulation effect on the reticular formation of the brain stem, and it is responsible for promoting the cognitive function of cortical arousal, but the specific mechanism is not clear. Many studies abroad show that [28] MT can improve cognitive function, especially autobiographical memory and plot memory, mental movement speed, executive functional domain and overall cognition, which is consistent with the results of the meta-analysis in this paper. The studies [18-20] shows it's invalid, the studies [6-12, 17] showed that music therapy had no significant effect on the cognitive function of AD, possibly due to the limitation and limitation of MMSE, in

a relatively short period of time after dementia onset, and it is difficult to detect cognitive changes in individuals, that is, MMSE is not sensitive to the evaluation of cognitive function in patients with mild AD. In addition, because the sample size of most studies is too small, the limitation of the methods and the short-term therapeutic effect (less than 4 months of intervention time is more common than Chien-Hsun Li [10] et al., showed that MT had no significant effect on the overall cognitive and daily functions of mild dementia patients, but confirmed their ability to handle temporal and spatial reasoning, language content, and fluency, attention and variant neuropsychological tests of autobiographical memory under the auxiliary cognitive role. So, in future research or clinical work, after a longer period of time or strict music therapy intervention, there is a prospect of significant improvement in the cognitive field.

In this paper, six randomized controlled studies conforming to the inclusion criteria were systematically evaluated, SMD=(-0.033), 95% CL [-0.81, 0.75], P=0.933>0.05. There was no significant difference, and the results showed that the influence of music therapy on the daily life of AD was not significantly affected. The results are in agreement with the results of Chien-Hsun Li [10]. Forest chart 5: show the studies [14, 15] Music therapy had a positive effect on the ADL of AD, while the studies [8, 13, 18, 19] showed it had no significant effect.

In this paper, a meta-analysis was used to analyze the data. Although the sample size was not large enough, the samples were all from randomized controlled studies. Cases included in the literature were screened to make the results reliable; In addition, due to objective reasons we could not collect some of the unpublished articles or data, so there is inevitable publication bias, and this meta-analysis does not specifically distinguish the various types of dementia or severity. There was no comparison of the effectiveness of various

musical patterns between groups, so music therapy for Alzheimer's patients requires further research on multicenter, large sample sizes and multiple musical models. It is of great significance to explore a musical treatment model suitable for Chinese old-age care institutions, which is convenient, feasible, low cost and effective at preventing Alzheimer's disease.

Acknowledgements

Disclosure of conflict of interest

None.

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