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EFFECTS OF MUSIC THERAPY ON POST-STROKE APHASIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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ABSTRACT

Objective: To evaluate the evidence on the effectiveness of music therapy in post-stroke aphasia, particularly in language communication function and well-being quality of life compared with speech therapy or no therapy. Methods: We performed computerized electronic databases and websites searches in PubMed, Embase, Cochrane Library, Science Direct, PEDro and Google Scholar on 20 July 2022. The eligible studies, data extraction, and evaluation of the methodological quality were independently screened out by two reviewers. Outcomes were analyzed into four sections of language communication function and well-being quality of life. Results were pooled using standard mean difference (SMD) with 95% confidence interval (CI). Results: We identified a total of six eligible studies involving 231 patients. There was significant mean difference in functional communication for post-stroke aphasia by 0.46 (95% CI: 0.06, 0.85; P=0.02), in naming by 0.34 (95% CI: 0.02, 0.65; P=0.04), and in repetition by 0.37 (95% CI: 0.08, 0.67; P = 0.01). But there was no significant difference in comprehension by 0.15 (95% CI: −0.17, 0.47; P = 0.35) and in well-being quality of life for post-stroke aphasia by -0.05 (95% CI: -0.36, 0.25; P = 0.73). Conclusion: This systematic review and meta-analysis shows a significant effect of music therapy on improving functional communication, naming and repetition but did not significantly improve comprehension and well-being quality of life. Future larger sample size is necessary in order to explore and provide definite evidence on the efficacy of music therapy on the recovery of post-stroke aphasia.

KEYWORDS: Post-stroke, Aphasia, Music therapy, Melodic intonation therapy.

INTRODUCTION

Stroke (cerebrovascular accident) is a global disease which is the second leading cause of death and the third leading cause of disability worldwide.[1,2] In general, stroke patients are often suffering from long-term disability where these will affect and influence the activities of daily living (ADL).[3] Moreover, these patients may experience numerous impairments which varies from body motor function defects.[4,5] swallowing capabilities,[6,7] and particularly in speech language communication function disorder which is known as aphasia.[8] Aphasia, described as a total or partial loss of language functions, is a very common disability among the stroke patients population ranges from 21-38% which severely restricts communication and the ability to engage in social interactions.[9-11] This syndrome arises from damage to the language dominant hemisphere generally the left hemisphere in right-handed people.[12] Fluent aphasia, non-fluent aphasia and global aphasia are the most common 3 major forms of aphasia that may result from stroke.[13] The fluent form known as Wernicke's aphasia is characterized by the impairment to grasp and understand the meaning of spoken words, while speech is abnormal. Reading and writing ability are often severely impaired.[14] Next, the non-fluent form known as Broca's aphasia shows favorable understanding in auditory but difficulty in expression. People with Broca's aphasia may be able to read, but not that capable in writing. The global aphasia patients have difficulties with both communication and understanding. They can only produce few recognizable words, able to understand little or no spoken language and neither have to ability to read nor write.

Understanding how people recover from post-stroke aphasia remain one of the biggest enigma in neuroscience. As a result, concerted efforts in recent years have focused on developing novel strategies to enhance post-stroke aphasia recovery. In particular, music therapy was introduced as an intervention for stroke rehabilitation for more than a decade as it is a affordable, non-invasive and convenient treatment method. Music interventions range from the use of rhythmic auditory stimulation (RAS) to aid in the execution of movement and normalization of gait parameters,[15] music improvisations and composition to enhance sense of well-being,[16] to music listening and singing to reduce pain.[17] Music therapy aims to capitalize on this naturally occurring brain plasticity change by enriching the environment of the person with aphasia to promote functional gains.[18,19] Moreover, melodic intonation therapy (MIT) uses the unimpaired singing ability of a person with aphasia to rehabilitate impaired language skills.[20]

Along with an increasing number of studies that have shown that music therapy has promising outcomes in post-stroke aphasia patients,[21,22] meta-analyses exploring the effect of music therapy on post-stroke aphasia patients were still scarce. Therefore, the purpose of our study is to conduct a systematic review and meta-analysis which primarily focuses, analyses and reviews current evidences regarding the effects of music therapy on post-stroke aphasia by examining whether music therapy can improve the of patients with aphasia after stroke, particularly in language communication function and well-being quality of life compared with speech therapy or no therapy.

METHODS

Search Strategy and Selection criteria

This systematic review and meta-analysis is conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA)[23, 24], and was registered with the PROSPERO, the International Prospective Register of Systematic Reviews (ID CRD42021273868).

The following databases were searched on 20 July 2022. Computerized electronic databases and websites searches were performed in PubMed, Embase, Cochrane Library, ScienceDirect, PEDro and Google Scholar to identify relevant studies. The searches were limited to human studies that are written in English and published until present day. The following keywords or terms used in combinations for database searches: “stroke or cerebrovascular accident,” “post-stroke,” “aphasia,” “language disorder,”“music therapy”, “melodic intonation therapy or MIT,” “speech or language therapy.” and We will also contact authors of relevant papers regarding any further published or unpublished works. Additionally in order to identify relevant articles, manual searches of the reference lists of the pertinent articles will also be conducted.

The inclusion criteria of the study were the studies are randomized controlled trials and/or clinical controlled trials with crossover or parallel group design, more than 5 participants are recruited, the participants are adults (≥18 yrs) who are diagnosed with a post-stroke aphasia and the articles are published in English journals. Exclusion criteria were the studies are not a randomized controlled trial and/or clinical controlled trials with crossover or parallel group design, the participants are healthy, the participants had neurological disorders other than stroke of the cerebral hemisphere, participants with a history of language impairment before the stroke or cerebral hemorrhage of the cerebral hemisphere, information require to perform a meta-analysis (e.g., mean scores, standard deviations) are missing and the articles are not published in English journals.

Procedure

The studies were retrieved according to the search strategy. The search results were merged with the reference management software (EndNote 20) and duplicates were removed. The evaluation of study eligibility according to inclusion and exclusion criteria was performed by two reviewers (TYL and WJL) by screening the titles and abstracts of the studies. After examining the titles and abstracts, potential eligibility studies were further screened by reading through the full text.

The following information was extracted and included in the form of data collection: study details (author), sample characteristics (sample size, mean age, duration of post-stroke), study design, study duration, allocation and blinding process, feasible sources of bias, intervention characteristics (types, frequency, duration), amount of participants assigned to each study group, and number of outcomes in each study group. During the above process, we had contacted with the authors of relevant papers directly when there were missing data. Also, any disagreement between reviewers were resolved by discussion.

The methodological quality of the studies are evaluated by two reviewers using the Physiotherapy Evidence Database (PEDro) scale, where this scale includes a total of 11 categories[25]. The score is either 1 or 0 according to whether each category is fulfilled. The grade of methodological quality was subdivided into: a score of 9–10 was excellent, 6–8 was good, 4–5 was fair, and less than 4 was poor.

Two reviewers assessed the quality and the risk of bias of each study independently based on the following categories in the Cochrane handbook of systematic reviews of interventions: sequence generation, allocation sequence concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential sources of bias.[24] Any dispute or disagreements were resolved by discussion until consensus was achieved.

The language communication function and well-being quality of life were evaluated as outcomes where the language communication function was subdivided into 4 sections which were the functional communication, naming, repetition and comprehension. The functional communication was measured by a formal assessment with validated tools which included the Amsterdam Nijmegen Everyday Language Test (ANELT),[26] Boston Diagnostic Aphasia Examination (BDAE)[27] and the Communicative Activity Log (CAL).[28] The naming was measured by Aachen Aphasia Test (AAT).[29] The repetition was measured by Aachen Aphasia Test (AAT)[29] and MIT repetition task.[20] The comprehension was measured by Boston Diagnostic Aphasia Examination (BDAE),[27] Aachen Aphasia Test (AAT)[29] and nonverbal Semantic Association Task (SAT).[30] The well-being quality of life was measured by Barthel Index (BI),[31] Hamilton Anxiety Rating Scale (HAM-A), Hamilton Depression Rating Scale (HDRS),[32, 33] Stroke and Aphasia Quality of Life Scale (SAQOL)[34] and Modified Reintegration to Normal Living Index (mRNLI).[35]

In brief, the ANELT test measures the level of oral communicative abilities and their changes over time. The BDAE splits into five subtests which consisted of oral expression communication, conversational and expository articulation speech, listening apprehension, reading and writing. Next, the CAL evaluate daily life oral communication with people. The AAT evaluates six subtests which are spontaneous language, token test, naming, repetition, written language and speech comprehension. Furthermore, MIT repetition task consists of repetition of words or sentence based on the intonation of rhythmic melody. The SAT is utilized to evaluate the association capability in visuoperceptual form. Finally the BI, HAS, HDS, SAQOL and mRNLI measures the well-being, performance in activities of daily living and health-related quality of life of the patients.

The Review Manager 5.4 software was utilized for statistical analysis. The data collected for each outcome were mean and standard deviation after the treatment period as well as the number of participants in the experimental and control groups. The data and results were summarized as standardized mean differences (SMD) and 95% confidence intervals (CIs) since the results were continuous data. We performed conversions through calculations as different studies expressed the results in different forms. In order to obtain a more comprehensive analysis of the global effect across studies, the results from tests evaluating the same outcome were pooled in forest plots. Heterogeneity across the studies was evaluated using the chi-square test and I^2 statistic. A fixed effects model was used for meta-analysis if $P>0.1$ and $I^2<50\%$, indicating no heterogeneity among studies. A random effects model was used for meta-analysis if $P\leq0.1$ and/or $I^2\geq50\%$, indicating heterogeneity among studies. Finally, if there were possible sources of heterogeneity, sensitivity analyses will be performed.

RESULTS

Study selection

A total of 227 studies were retrieved in the databases according to the search strategy. After removing duplicates studies, 60 articles remained. After screening the titles and abstracts of the remaining studies, 14 potentially eligible studies were yielded because they meet the inclusion criteria. Then, through reading the full text article, 6 studies involving 231 patients[36–41] were finally included in this meta-analysis. Figure 1 shows the detailed selection of the flow chart.

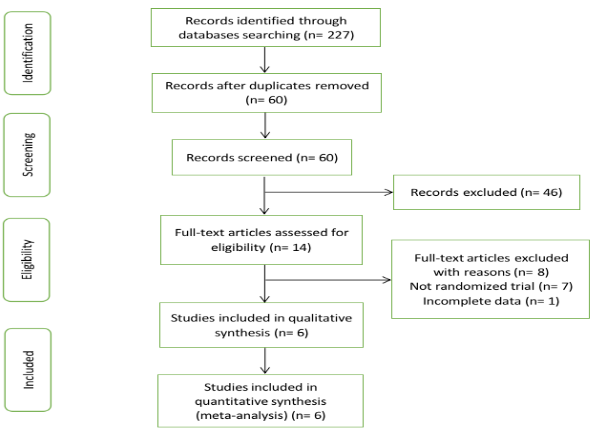

Figure 1: PRISMA flowchart of the selection of eligible studies.

Study characteristics of the included studies

The included studies were published between 2014 and 2021. The sample size ranged from 17 to 79 patients. The mean age ranged from 52 to 69 years. Van der Meulen et al.[36] was a single-blinded waiting list randomized controlled trial with a multicentre design. A total of 27 early subacute stroke survivors with non-fluent aphasia were randomly assigned to the experimental group (MIT) which consisted of 16 patients or the control group consisted of 11 patients which carried out control intervention followed by delayed MIT. Outcome measures were the ANELT,[26] AAT,[29] MIT repetition task,[20] and SAT.[30]

Another study from Van der Meulen et al.[37] also used a multicentre single-blinded waiting list randomized controlled trial design. A total of 17 patients with chronic post-stroke non-fluent aphasia were randomly assigned to the experimental group which consisted of 10 patients receiving 6 weeks of MIT or to the control group which consisted of 7 patients receiving 6 weeks of control treatment intervention followed by 6 weeks of delayed MIT. Assessments were done at baseline (T1), 6 weeks later (T2), and 12 weeks later (T3). The outcome measures were the ANELT,[26] AAT,[29] and MIT repetition task.[20] The MIT repetition task comprised 11 trained and 11 untrained matched sentences.

Haro et al.[38] was a single-blinded randomized, crossover, unicentre pilot trial. Participants were the chronic post-stroke survivors with non-fluent aphasia. 20 patients were included in this study. Due to the inability to attend the intervention based on the assigned dates, 4 of the patients allocated to group 2 crossed over to group 1 to receive the treatment first. Patients randomized to the experimental group 1 received MIT first for the first 3 months followed by a washout period of three months without therapy. Without receiving speech therapy treatment in the first 3 months, patients in control group 2 started active treatment between 3 and 6 months after their inclusion in the study, thus serving as waiting list controls for the first phase and as the active experimental group in the second phase. Main measures were the BDAE[27] and the CAL questionnaire[28] which were assessed at baseline, 6 and 12 weeks.

Aravantinou-Fatorou et al.[39] conducted a double-blinded randomized, unicentre clinical trial. Time since post-stroke of the 79 included participants were not limited and subdivided into the experimental group and the control group. Patients in the music group received daily traditional experimental music listening of 4 training sessions per week (45 min per session) accompanied with standard care for 6 months. For the control group, patients received only standard care. BI[31] and AAT[29] were the main outcome measures in this study.

Another double-blinded randomized, unicentre clinical trial is carried out by Zhang et al.[40] 40 stroke survivors patients ranging from subacute to chronic stage of stroke were included in this study and they are divided equally into half for the intervention melodic intonation therapy (MIT) group and the control speech therapy (ST) group. The intervention group received MIT training for 30 min per session, five sessions a week, for 8 weeks while the control group received ST for 30 min per session, 5 sessions a week, for 8 weeks. BDAE, HAM-A and HDRS were utilized for the measure of the outcomes.[27, 32, 33]

Tarrant et al.[41] was a single-blinded randomized, multicenter pilot trial. There are no restriction for the the time since post-stroke of the 48 included patients and they are divided equally into half for the singing with post-stroke aphasia group (SPA) and the control group. The patients in the SPA group had 10 weekly sessions with each session lasting 90 minutes while the control group patients received only standard care. The main outcome measures of this study are SAQOL[34] and mRNLI.[35]

Based on the outcome measures, 4 studies[36,37,38,40] assessed functional communication, 4 studies[36,37,39,40] assessed naming, 5 studies[36-40] assessed repetition, 4 studies[37-40] assessed comprehension, and 3 studies[39-41] assessed well-being quality of life. Table 1 shows the detailed characteristics of the included studies.

Table 1: Main characteristics of the included studies.

Studies	**Van der Meulen et al.[36] 2014**	**Van der Meulen et al.[37] 2016**	**Haro-Martínez et al.[38] 2019**	**Aravantinou-Fatorou et al.[39] 2021**	**Zhang et al.[40] 2021**	**Tarrant et al.[41] 2021**
Methods	Randomized, waiting list, single-blind, multicenter clinical trial	Randomized, waiting list, single-blind, multicenter clinical trial	Randomized, crossover, single-blind, unicenter, pilot trial.	Randomized, double-blind, unicenter clinical trial	Randomized, double-blind, unicenter clinical trial	Randomized, parallel mixed, single-blind, multicenter, pilot trial.
Inclusion criteria	• Age 18–80 years • Time post-stroke: 2–3 months • Non-fluent aphasia after left hemisphere stroke • Native language Dutch • Premorbid right-handed	• Age 18–80 years • >1-year post stroke • MIT candidate •Native language Dutch • Right-handed before stroke	• Age: no restrictions • > 6 months post-stroke • Non-fluent aphasia due to unilateral stroke in the left hemisphere • The patient had received a standard program of conventional speech therapy after stroke.	• Age 18–75 years • Time post-stroke: no restrictions • Aphasia due to single left hemisphere stroke • Greek-speaking and able to cooperate • Right-handed prior patients for all day to day and not forced	• Age 18–70 years • Time post-stroke: <3 months. • Mild to moderate to severe non-fluent aphasia diagnosed with fMRI or CT imaging, showing left ischemic or hemorrhagic stroke • Participants	• Age 18 years and above • Time post-stroke: no restrictions • Diagnosis of aphasia following a stroke • Conversational English pre-stroke • Willingness to be randomized to either the SPA intervention or

				to change hands as a child	did not had professional musical experience	control group and attend the intervention venue
Participants	Total sample: 27 Experimental MIT group: 16 Control group: 11	Total sample: 17 Experimental MIT group: 10 Control group: 7	Total sample: 20 Experimental MIT group: 10 Control group: 10	Total sample: 79 Music group: 34 Control group: 45	Total sample: 40 Intervention MIT group: 20 Control ST group: 20	Total sample: 48 SPA group: 24 Control group: 24
Participant's baseline characteristics	Mean age: • MIT group: 53.1 (SD 12) % Males: 25 • Control group: 52 (SD 6.6) % Males: 63.6 Time from stroke onset, mean (SD), weeks: • MIT group 9.3 (2.0) • Control group 11.9 (5.9)	Mean age: • MIT group: 58.1 (SD 15.2) % Males: 70 • Control group: 63.6 (SD 12.7) % Males: 57.1 Time from stroke onset, mean (SD), months: • MIT group 33.1 (19.4) • Control group 42.6 (23.7)	Mean age: • MIT group: 66.9 (SD 14.7) % Males: 60 • Control group: 61.1 (SD 14.1) % Males: 60 Time from stroke onset, median (months) (IQR): • MIT group: 21.8 (17.5) • Control group: 27.7 (18)	Mean age: • Music group: 69 ± 4 % Males: 16.4 • Control group: 68.1 ± 5 % Males: 27.8 Time from stroke onset, mean (SD), months: Not applicable	Mean age: • Intervention group: 52.90 ± 9.08 % Males: 80 • Control group: 54.05 ± 10.81 % Males: 75 Time from stroke onset, (months):• Intervention group: 2.57 ± 1.74 • Control group: 1.96 ± 1.38	Mean age: • SPA group: 65.2 (12.2) % Males: 60 • Control group: 67.7 (8.3) % Males: 62 Time since stroke, mean (SD), years: • SPA group: 4.6 (3.8) • Control group: 5.6 (6.7)
Intervention group	MIT 5 hours per week for 6 weeks with minimum 3 h per week through face-to-face therapy plus iPod-based homework assignments	MIT 5 hours per week for 6 weeks with minimum 3 h per week through face-to-face therapy plus iPod-based homework assignments	MIT 12 sessions over a 6 weeks period where each session lasted 30 minutes	Daily traditional experiential music listening of 4 training sessions (45 min per session) accompanied with standard care for 6 months	MIT training for 30 min per session, five sessions a week, for 8 weeks	SPA consisted of 10 weekly sessions with each session lasting 90 minutes
Control group	Waiting list (control treatment intervention followed by delayed MIT)	Waiting list (control treatment intervention followed by delayed MIT)	Waiting list (control treatment intervention followed by delayed MIT)	Receiving standard care only	ST for 30 min per session, five sessions a week, for 8 weeks	Receiving standard care only
Outcomes	• ANELT • AAT •MIT repetition task • SAT	• ANELT • AAT • MIT repetition task	• BDAE • CAL	• AAT • BI	• BDAE • HAM-A • HDRS	• SAQOL •mRNLI

Comments	• MIT group: 3 dropouts and 2 loss to follow-up at main outcome visit • Control group: 1 loss to follow-up at main outcome visit	• MIT group: No dropouts or loss to follow-up at main outcome visit • Control group: 1 dropouts and loss to follow-up at main outcome visit	• MIT group: 1 dropouts and 1 loss to follow-up at main outcome visit • Control group: 4 patients allocated to control group crossed over to the MIT group, receiving the treatment first. 1 dropouts and 2 loss to follow-up at main outcome visit	• No dropouts or loss to follow-up at main outcome visit for both music group and control group	• No dropouts or loss to follow-up at main outcome visit for both MIT group and control ST group	• SPA group: 3 dropouts and 3 loss to follow-up at main outcome visit • Control group: 1 dropouts and 3 loss to follow-up at main outcome visit

SD: Standard Deviation; MIT: Melodic Intonation Therapy; ST: Speech therapy; SPA: Singing for People with Aphasia; ANELT: Amsterdam-Nijmegen Everyday Language Test; AAT: Aachen Aphasia Test; SAT: Nonverbal Semantic Association Task; BDAE: Boston Diagnostic Aphasia Examination; CAL: Communicative Activity Log; BI: Barthel Index; HAM-A: Hamilton Anxiety Scale; HDRS: Hamilton Depression Scale; SAQOL: Stroke and Aphasia Quality of Life Scale; mRNLI: Modified Reintegration to Normal Living Index

Evaluation of methodological quality band risk of bias across studies

The results of methodological quality evaluation ranged from 4 to 9 according to the Pedro scale where points are only awarded when a criterion is clearly satisfied. Two studies[37,40] exhibited excellent quality, three studies[36,38,39] exhibited good quality, and one study[41] exhibited fair quality. The results of methodological quality evaluation can be seen in Table 2. The risk of random sequence generation (selection bias) was low in all the six studies[36-41] as all studies used a computer-generated allocation sequence, randomization table or coin-tossing method. Next, three studies[36,37,41] have low risk while the other three studies[38-40] have unclear risk in the allocation concealment (selection bias) where the authors did not mentioned that their studies were concealed. Out of the three low risk studies, two studies[36,37] used consecutively numbered sealed opaque envelopes and in the another one study,[41] minimization algorithm method was used to allocated the participants in order to retained a stochastic element to promote allocation concealment. Allocation was simple but without mentioning concealment in one of the studies,[38] with a 1:1 ratio where the patients who were included in the trial were consecutively allocated to the next available number on the randomization list.

Next, blinding of the participants and the personnel (performance bias) was low in two studies[39,40] which utilized double-blinded method and unclear in four studies[36-38, 41] which utilized single-blinded method. Furthermore, blinding of outcome assessment (detection bias) was considered low in five studies[37-41] and was unclear in one studies[36] that the authors acknowledged that blinding could not be maintained because the patients spontaneously informed the researcher about their therapy allocation. Incomplete outcome data (attrition bias) was low in five studies[36-40] and high in one study,[41] given that some participants had withdrew from trial post-randomization and prior to the randomization due to ill health which caused incomplete or missing data. Moreover, selective reporting (reporting bias) was low in all of the six studies.[36-41] Finally, the other bias was low in four studies[37-40] high in one study[41] and unclear in the another study,[36] given that not all of the pre-specified outcomes were reported. The assessment of the results of risk of bias are shown in Supplementary Figure 1A, 1B.

Table 2: Quality assesment using PEDro scale.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total (0-10)	Study Quality
Van der Meulen et al. [36] 2014	Yes	Yes	Yes	No	No	No	Yes	No	No	Yes	Yes	6	Good
Van der Meulen et al. [37] 2016	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	9	Excellent
Haro-Martínez et al. [38] 2019	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8	Good
Aravantinou-Fatorou et al. [39] 2021	Yes	Yes	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	8	Good
Zhang et al. [40] 2021	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	9	Excellent
Tarrant et al. [41] 2021	Yes	Yes	Yes	No	No	No	No	No	Yes	No	No	4	Fair

Integration of results

Functional communication

Four studies were included in the functional communication of the patients[36-38,40] The included assessment scales were ANELT,[26] BDAE,[27] and CAL.[28] A total of 104 post-stroke aphasia patients were included where there were 56 patients in the experimental group and 48 patients in the control group. Based on the heterogeneity test result, no significant heterogeneity was seen among these studies (P >0.1 and I^2= 0%), thus the fixed-effects model was used. The results of meta-analysis showed that compared with the control group, music therapy can significantly improve functional communication of post-stroke aphasia patients (SMD= 0.46, 95% CI: 0.06, 0.85; P= 0.02) (Fig. 2).

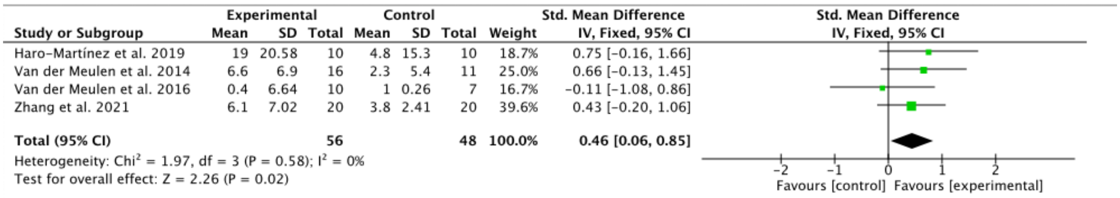

Fig. 2: Forest plot for functional communication.

Naming

Regarding to the naming of the patients, four studies were involved[36, 37, 39, 40]. The assessment scale which was utilized was AAT.[29] A total of 163 post-stroke aphasia patients were included, where there were 80 in the experimental group and 83 in the control group. The heterogeneity test results had shown that there was low or no significant heterogeneity among these studies (P >0.1 and I^2= 0%), therefore the fixed-effects model was used. Based on the results of meta-analysis, music therapy can significantly improve comprehension of post-stroke aphasia patients in compared with the control group (SMD= 0.34, 95% CI: 0.02, 0.65; P= 0.04) (Fig. 3).

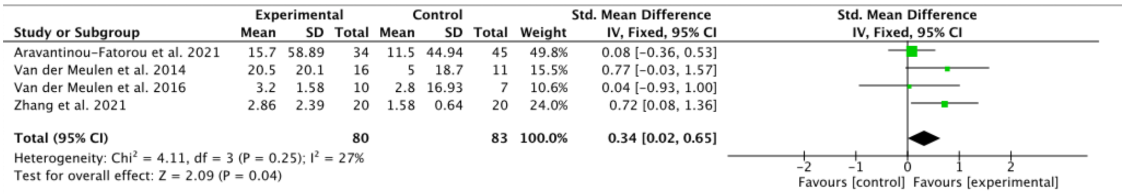

Fig. 3: Forest plot for naming.

Repetition

With regard to the repetition of the patients, five studies were included.[36-40] The included assessment scales were the AAT[29] and the MIT repetition task.[20] A total of 183 post-stroke aphasia patients were included where 90 patients were in the experimental group and 93 patients in the control group. Based on the heterogeneity test result, no significant heterogeneity was seen among these studies (P >0.1 and I^2= 0%), thus the fixed-effects model was used. According on the results of meta-analysis, music therapy can significantly improve repetition of post-stroke aphasia patients in compared with the control group (SMD= 0.37, 95% CI: 0.08, 0.67; P= 0.01) (Fig. 4).

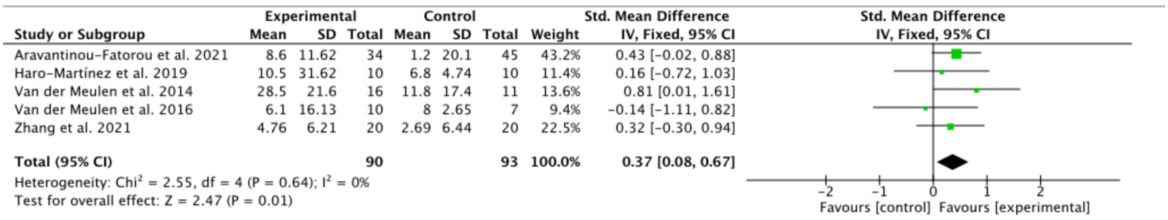

Fig. 4: Forest plot for repetition.

Comprehension

In the comprehension of the patients, four studies were involved.[37-40] BDAE,[27] AAT,[29] and SAT[30] are the assessment scales which were included. A total of 156 post-stroke aphasia patients were included, where there were 74 in the experimental group and 82 in the control group. The heterogeneity test results had shown that there was no significant heterogeneity among these studies (P >0.1 and I^2= 0%), therefore the fixed-effects model was used. The results of meta-analysis showed that compared with the control group, music therapy cannot significantly improve comprehension of post-stroke aphasia patients (SMD= 0.15, 95% CI: −0.17, 0.47; P= 0.35) (Fig. 5).

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Aravantinou-Fatorou et al. 2021	8.5	2.3	34	8	3.4	45	50.6%	0.17 [-0.28, 0.61]
Haro-Martínez et al. 2019	1.8	10.12	10	0	7.9	10	13.0%	0.19 [-0.69, 1.07]
Van der Meulen et al. 2016	-2.2	12.33	10	1.6	4.76	7	10.6%	-0.36 [-1.34, 0.62]
Zhang et al. 2021	6.48	13.15	20	3.39	4.02	20	25.8%	0.31 [-0.31, 0.94]
Total (95% CI)			**74**			**82**	**100.0%**	**0.15 [-0.17, 0.47]**

Heterogeneity: $Chi^2 = 1.32, df = 3 (P = 0.72); I^2 = 0\%$
Test for overall effect: Z = 0.93 (P = 0.35)

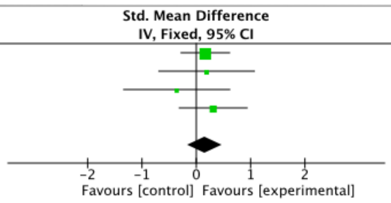

Fig. 5: Forest plot for comprehension.

Well-being quality of life

Three studies were included in the well-being quality of life of the patients.[39-41] The included assessment scales were the BI,[31] HAM-A, HDRS,[32,33] SAQOL[34] and mRNLI.[35] A total of 167 post-stroke aphasia patients were included where there were 78 patients in the experimental group and 89 patients in the control group. Based on the heterogeneity test result, no significant heterogeneity was seen among these studies (P >0.1 and I^2= 0%), thus the fixed-effects model was used. The results of meta-analysis showed that music therapy cannot significantly improve well-being quality of life of post-stroke aphasia patients compared with the control group (SMD = -0.05, 95% CI: -0.36, 0.25; P= 0.73) (Fig. 6).

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Aravantinou-Fatorou et al. 2021	80.3	85.5	34	76.9	81.8	45	47.1%	0.04 [-0.41, 0.49]
Tarrant et al. 2021	2.7	8.81	24	2.1	6.85	24	29.1%	0.07 [-0.49, 0.64]
Zhang et al. 2021	-10.75	4.6	20	-8.65	5.72	20	23.8%	-0.40 [-1.02, 0.23]
Total (95% CI)			**78**			**89**	**100.0%**	**-0.05 [-0.36, 0.25]**

Heterogeneity: $Chi^2 = 1.52, df = 2 (P = 0.47); I^2 = 0\%$
Test for overall effect: Z = 0.34 (P = 0.73)

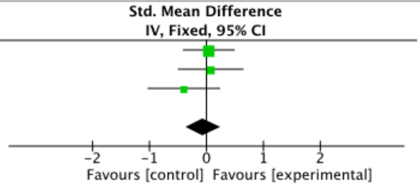

Fig. 6: Forest plot for well-being quality of life.

DISCUSSION

Six studies[36-41] involving 231 patients were included in this meta-analysis. The results indicated that music therapy may have a beneficial effect on functional communication, naming and repetition in patients with aphasia after stroke, but may have no obvious effect on comprehension and well-being quality of life. Zhang et al.[40] has shown that music interventions may be beneficial to communication, naming, comprehension and repetition but no obvious beneficial effect on well-being quality of life in patients with aphasia after stroke. However, only limited sample were included in this study where two participants dropped out of the study, which may have caused the variance in group allocation. Besides, participants with three different types of non-fluent aphasia were included into the trial which can cause an unclear effect comparison. Aravantinou-Fatorou et al.[39] has shown that exercise rehabilitation program accompanied by an enriched sound environment can improve naming, repetition, and comprehension of patients with aphasia after stroke, but has no significant effect on well-being quality of life. This study only carried out in one small center study which is not a multicenter trial where the positive effect of experiential music on recovery from post-stroke aphasia was unable to be generalized. Therefore, our study is needed to more comprehensively explore the effect of music therapy on language function of patients with aphasia after stroke.
However, the internal validity of this study is limited due to the two main challenges in the research on post-stroke aphasia which are the scantiness of published studies that are able to achieve the high standards of well-designed clinical trials, leading to a limited number of included studies for the present meta-analysis as well as the presence of heterogeneity in the outcome measurements. Out of the six randomized clinical trials which were included in this meta-analysis, only two of the randomized clinical trials were carried out by the same research group using the same procedures and endpoints. Thus, the most suitable test for each of the outcomes considered in this review was selected due to the heterogeneity in the outcome measurements of the included studies. Functional communication represents the capability to communicate successfully with others in the daily interactions. The ANELT test was selected over the Sabadel in both of the Van der Meulen et al.[36,37] studies for the functional communication outcome as less statistical dispersion was seen in the ANELT test. Repetition represents the action to repeat something that has already been said or written. Regarding the repetition outcome, the AAT was chosen over the MIT repetition task which compromised of trained items and untrained item tests in both of the Van der Meulen et al.[36,37] studies, as the MIT repetition task are not well-validated tools.

According to sensitivity analyses, the results of functional communication remained the same after removing any of the studies. For naming, the results changed from 27% to 0% when the study by Aravantinou-Fatorou et al. published in 2021[39] was removed, the results changed from 27% to 28% when the study by Van der Meulen et al. published in 2014[36] was removed and the results changed from 27% to 46% when the study by Van der Meulen et al. published in 2016[37] was removed. Moreover, the results also changed from 27% to 14% when we removed the study by Zhang et al., published in 2021.[40] The reasons for the heterogeneity may be as follows: First, the studies did not mention the procedures and methods of random and concealment of allocation. Second, the baseline levels regarding the most important prognostic indicators between the two groups were not equal. Third, the studies did not state and clarify in detail whether there was blinding of all assessors who measured at least one key outcome. For repetition, the results remained the same after removing any of the studies. Same goes to the comprehension, where the results remained the same after removing any of the studies. For well-being quality of life, the results changed from 0% to 16% and from 0% to 19% after respectively removing Aravantinou-Fatorou et al.'s study, published in 2021[39] and Tarrant et al.'s study published in 2021.[41] These findings indicate that the music therapy can improve naming and well-being quality of life in post-stroke aphasia patients are not robust. The detailed results of sensitivity analyses are shown in Supplementary Table 1. Due to the included studies were fewer than 10, therefore we did not carry out funnel plot publication bias analysis.

Limitations

Although this meta-analysis suggests that music therapy has promising effect on functional communication, naming and repetition in patients with aphasia after stroke, however there are still some limitations. First, the some of included studies had a small sample size which were fewer than 30 patients and were only published in English, therefore the results may be biased. Second, the baseline characteristics of patients, the types and procedures of music therapy, and the outcome measurement scales of each study was different, which may cause variations and differences in results. Finally, this study only explored the effects of music therapy on language function and well-being quality of life of post-stroke aphasia patients which did not involve some other outcome indicators such as neuroimaging studies and neuropsychological tests. Many researchers highlight that music therapy can enhance psychological and psychosocial outcomes in post-stroke aphasia patients. Therefore, the diversified effects of music therapy on post-stroke aphasia patients should be emphasized on the future meta-analysis.

CONCLUSION

In conclusion, this systematic review and meta-analysis provides some certain extent of clinical significance and evidence on the efficacy of music therapy in improving functional communication, naming and repetition in post-stroke aphasia patients. These clinical significance and evidence may be further applicable to the treatment of post-stroke aphasia in future rehabilitation practice. Nevertheless, due to the limited sample size of studies included in this meta- analysis, it is necessary to incorporate more studies with larger sample size to further investigate the efficacy of music therapy for post-stroke aphasia patients.

Conflict of interest

The authors declare that there is no conflict of interest.

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Authors contribution

All authors contributed equally to the concept, methodology, data collection, data analysis, composing, revising the article, and giving final approval of the version to be published.

Data availability

Data supporting this study are included in the article.

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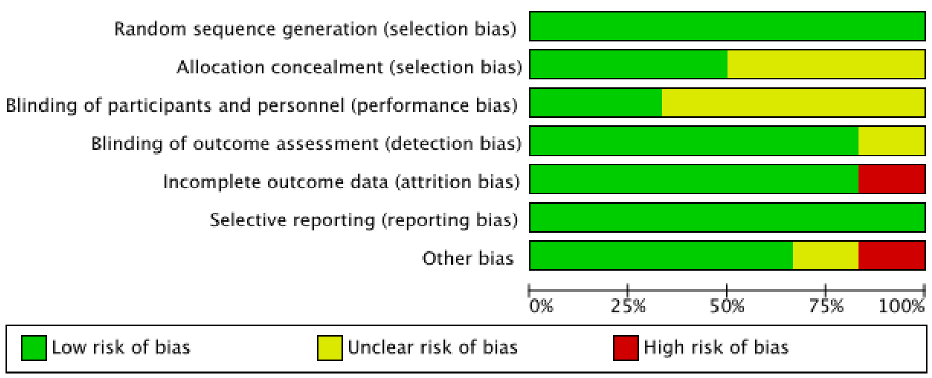
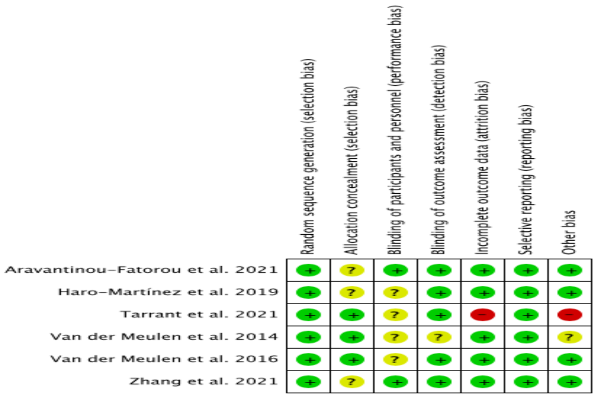
Supplemental



A) Authors' judgement of risk of bias items, Presented as percentages across all included studies.



B) Authors' judgement of each risk of bias item for each included study.

Figure 1: Risk of bias summary.

Supplemental

Table 1: Results of sensitivity analyses.

Outcome indicators	**Study of removal**	**MD（95% CI）**	**Heterogeneity test results (P value and I^2 value)**	**Overall effect (Z value and P value)**
Functional communication	After removing Haro-Martínez, 2019	0.39 (-0.05, 0.83)	P=0.48 I^2=0%	Z=1.74 P=0.08
	After removing Van der Meulen, 2014	0.39 (-0.07, 0.85)	P=0.44 I^2=0%	Z=1.67 P=0.09
	After removing Van Der Meulen, 2016	0.57 (0.14, 1.00)	P=0.82 I^2=0%	Z=2.58 P=0.010
	After removing Zhang, 2021	0.47 (-0.04, 0.98)	P=0.37 I^2=0%	Z=1.82 P=0.07
Naming	After removing Aravantinou-Fatorou, 2021	0.59 (0.14, 1.03)	P=0.45 I^2=0%	Z=2.60 P=0.009
	After removing Van der Meulen, 2014	0.26 (-0.09, 0.60)	P=0.25 I^2=28%	Z=1.47 P=0.14
	After removing Van Der Meulen, 2016	0.37 (0.04, 0.70)	P=0.16 I^2=46%	Z=2.19 P=0.03
	After removing Zhang, 2021	0.21 (-0.15, 0.58)	P=0.31 I^2=14%	Z=1.17 P=0.24
Repetition	After removing Aravantinou-Fatorou, 2021	0.33 (-0.06, 0.72)	P=0.49 I^2=0%	Z=1.64 P=0.10
	After removing Haro-Martínez, 2019	0.40 (0.09, 0.71)	P=0.51 I^2=0%	Z=2.50 P=0.01
	After removing Van der Meulen, 2014	0.30 (-0.01, 0.62)	P=0.74 I^2=0%	Z=1.87 P=0.06
	After removing Van Der Meulen, 2016	0.43 (0.12, 0.74)	P=0.72 I^2=0%	Z=2.69 P=0.007
	After removing Zhang, 2021	0.39 (0.05, 0.72)	P=0.47 I^2=0%	Z=2.26 P=0.02
Comprehension	After removing Aravantinou-Fatorou, 2021	0.14 (-0.32, 0.59)	P=0.52 I^2=0%	Z=0.59 P=0.56
	After removing Haro-Martínez, 2019	0.15(-0.19, 0.49)	P=0.52 I^2=0%	Z=0.84 P=0.40
	After removing Van Der Meulen, 2016	0.21 (-0.12, 0.55)	P=0.93 I^2=0%	Z=1.24 P=0.22
	After removing Zhang, 2021	0.10 (-0.27, 0.46)	P=0.61 I^2=0%	Z=0.51 P=0.61

Well-being Quality of Life	After removing Aravantinou-Fatorou, 2021	-0.14 (-0.56, 0.28)	P=0.27 I^2=16%	Z=0.64 P=0.52
	After removing Tarrant, 2021	-0.11 (-0.47, 0.26)	P=0.27 I^2=19%	Z=0.57 P=0.57
	After removing Zhang, 2021	0.05 (-0.30, 0.40)	P=0.93 I^2=0%	Z=0.30 P=0.76

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