Music listening in the rehabilitation of post-ischemic stroke cognitive impairment patients: a randomized controlled trial

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Abstract

Background: Recent and past research has tested the efficacy of music listening on mood and post-ischemic stroke cognitive impairment (PSCI) recovery. Among these studies, those that use preferred self-selected music have been more likely to yield better results. One plausible explanation is that a patient's own selected playlist will integrate music that represent one's inner values and beliefs, manifest one's social, cultural, and spiritual nature, and thus activate mental and unconscious processes, which are essential to cognitive functioning.

Methods: 34 patients with PSCI were randomly divided into music (n=18) and control (n=16) groups. Both groups received standard routine care for stroke. Music group patients received self-administered music listening sessions. For three months, they listened to a customized playlist based on the individual's cultural, ethnic, and social background, life experiences, as well as personal taste for music. Control group patients, on the other hand, listened to white noise as placebo. Cognitive function, neurological function, mood, and activities of daily living (ADLs) were assessed using the Montreal Cognitive Assessment (MoCA), Hamilton Rating Scale for Anxiety (HAMA), Hamilton Depression Scale (HAMD), National Institute of Health stroke scale (NIHSS) and Barthel Index (BI). Caregiver strain was also assessed using the Zarit Caregiver Burden Interview (ZBI).

Results: After three months of treatment, MoCA mean scores were significantly higher in the music group compared with the control group ($p<0.05$), particularly in the domains of delayed memory and orientation ($p<0.05$). NHISS, BI, and ZBI mean scores were significantly better in the music group ($p<0.05$ in BI; $p<0.01$ in NHISS and ZBI) than in the control group. As for mood outcomes, HAMA and HAMD mean differences were nonsignificant within groups.

Conclusions: Music listening can promote the recovery of cognitive and neurological functions, enhance ADLs, and reduce caregiver burden.

Keywords: music therapy; ethnomusicology; post-ischemic stroke cognitive impairment; post-ischemic stroke emotional disorder; caregiver burden

Introduction

It is predicted that 71-80.97% of stroke patients will develop cognitive impairment (Jokinen et al., 2015; Qu et al., 2015). Post-stroke cognitive impairment (PSCI) can aggravate the degree of disability, hinder the rehabilitation process, limit the ability of living independently, and reduce the life expectancy of the patient (Mellon et al., 2015; Nys et al., 2006). It can also increase the probability of post-stroke depression and pose significant stress on caregivers (Nys et al., 2006; Rohde et al., 2019). Additionally, PSCI has a high incidence rate and cause great harm–an important complication that is frequently ignored. Fortunately, research has shown that timely intervention of PSCI can effectively promote functional recovery (Nys, Van Zandvoort, De Kort, Van der Worp, et al., 2005; Zinn et al., 2004), particularly if it is done in the first month after onset (Nys, Van Zandvoort, De Kort, Jansen, et al., 2005).

Recent and past research has tested the efficacy of music listening on mood and PSCI recovery, including post-stroke visual neglect, memory, and attention in experimental settings (Chen et al., 2013; Hommel et al., 1990; Särkämö et al., 2008; Tsai et al., 2013). Among these studies, those that use preferred self-selected music have been more likely to yield better results than those using unpleasant non-selected music. One plausible explanation is that a patient's own selected playlist will integrate music that represent one's inner values and beliefs, manifest one's social, cultural, and spiritual nature, and thus activate mental and unconscious processes, which are essential to cognitive functioning. This idea is embedded in the foundation of medical ethnomusicology that music, the human being, and health and healing are interconnected through the physical, psychological, social, emotional, and spiritual domains (Koen, 2018). Based upon this argument, it is reasonable to believe that interventions designed to account for the patient's unique social, cultural, and spiritual background may be more effective.

In this study, a randomized controlled trial was designed to test the effects of adding music listening to a program of routine rehabilitation care for patients with PSCI. In contrast with previous research, the intervention was designed to incorporate not only the patient's favorite music but also how that music fits into that specific person's cultural heritage and life experiences. The experiment was conducted at a hospital in the Southeastern Chinese city of Xiamen. China provides an ideal setting for this study. First, it is a country filled with an abundant number of culturally and linguistically diverse communities. Second, stroke accounts for more deaths than any other disease in China, which makes it a special case among most regions in the world, where most deaths are due to ischemic heart disease (Z. Li et al., 2019).

We hypothesized that patients receiving the active treatment will have significantly better cognitive outcomes than those receiving conventional treatment only. We also expected an improvement in mood and activities of daily living (ADLs). The goal is to raise evidence for a practical, cost-effective, and non-invasive treatment for PSCI, which is urgently needed to improve the health and wellbeing of stroke survivors, and to reduce the global stroke burden.

Methods

Trial design

A two-arm parallel randomized controlled trial was conducted for three months to measure the effects of music listening on PSCI. Music listening therapy plus standard routine care was compared with standard routine care plus a white noise placebo. At baseline and three months after treatment, cognitive function, mood, neurological function, ADLs, and caregiver burden were evaluated. This study was approved by the ethics committee of the First Affiliated Hospital of Xiamen University and has been registered in the Chinese Clinical Trial Registry (ID: ChiCTR190021484).

Participants

34 patients diagnosed with PSCI were recruited by the Department of Neurology of the First Affiliated Hospital of Xiamen University. All patients enrolled in the study signed an informed consent form. Their families also knew about and were aware of the treatment study. All patients recruited met the following inclusion criteria: (1) cognitive impairment after a first-ever stroke, (2) less than one month after the stroke, (3) ≤75 years old, (4) no neurological or psychiatric comorbidity, (5) no drug or alcohol abuse, (6) no serious audio-visual impairment, (7) no previous formal musical education, (8) able to speak Mandarin and cooperate, (9) have a caregiver and reside in Xiamen.

Intervention

Patients were randomly divided in two groups, the music and control groups. Music group patients received the active treatment, which consisted of listening to music every day for one hour for three months. Control group patients received a placebo treatment, in which they listened to a one-hour playlist of white noise sounds (rain, waves, bird sounds, etc.) every day for three months. Over the course of the experiment, both groups received standard routine care for stroke based on aspirin and atorvastatin.

After agreeing to participate in the study, music group patients went through a music-related interview with a non-licensed therapist—a postgraduate student of Ethnomusicology at Xiamen University. During the interview, the therapist gathered information about each patient's cultural and ethnic background, religious and philosophical beliefs, meaningful past experiences and memories, hobbies and interests, as well as taste for different musical genres and instruments. The therapist would then aggregate this information and design a customized playlist for each patient. The control group patients went through a similar friendly conversation where the therapist simply explained the treatment.

The therapist maintained close communication with patients and/or their caregivers to monitor patients' compliance with the treatment and assess potential adverse effects. Patients were encouraged to listen to music every day for an hour and fill out a listening diary.

Outcomes

Primary outcome:

Cognitive function was measured with the Montreal Cognitive Assessment (MoCA) (Ver. 7.1 Beijing) (Nasreddine et al., 2005) before and after three months of treatment.

Secondary outcomes:

Mood was evaluated using the Hamilton Rating Scale for Anxiety (HAMA) (Hamilton, 1959) and Hamilton depression scale (HAMD-24) (Hamilton, 1960). Neurological function and ADLs were assessed with the National Institute of Health stroke scale (NHISS) (Kwah & Diong, 2014) and Barthel index (BI) (Li et al., 2020) respectively. The Zarit Caregiver Burden Interview (ZBI) (Lu et al., 2009) was additionally used to measure the caregiver burden. All assessments were performed by a neurologist at baseline and after three months of treatment.

Sample size

The initial estimated sample size was 39. It was rounded to 40 to allow for even group sizes. The sample size was calculated considering a 5% alpha, 80% power, a MoCA effect size of 1, and a known standard deviation of 2.5. MoCA standard deviation can range from 1.7 to 2.2 for subjects aged 65-75 (Borland et al., 2017). A standard deviation of 2.5 was chosen to be more conservative[1].

Randomization and allocation concealment

Due to the relatively small sample size, blocked randomization was used to ensure an equal number of subjects in the music and control groups. As the estimated sample size was 40, 20 envelopes labeled "music" and 20 envelopes labeled "control" were grouped in blocks of ten and four. Each block of ten contained five envelopes labeled "music" and five envelopes labeled "control", while each block of four contained two envelopes labeled "music" and two envelopes labeled "control". In total, there were two blocks of ten and five blocks of four. Each block was shuffled thoroughly and placed in separate piles. A coin was flipped to choose the order in which each block was put one on top of the other.

To ensure an effective allocation concealment, the method of sequentially numbered, opaque, sealed envelopes (SNOSE) was used. Envelopes were numbered before handed and opened in sequence as participants were enrolled in the study. Carbon paper was put inside the envelope along with the allocation paper to ensure the information written on the envelope (date, patient's name and signature) was transferred to the allocation

[1] Sample size was calculated as $\frac{\sigma^2(z_{1-\beta}+z_{1-\alpha})^2}{(\mu_0-\mu_1)^2}$, where $z_{1-\beta}$ corresponds to the z score of a 80% power, where $z_{1-\alpha}$ corresponds to the z value of a 5% significance level, σ^2 corresponds to the known variance, and $\mu_0 - \mu_1$ corresponds to the expected effect size.

paper. Foil paper was put inside the envelope to cover both the carbon paper and the allocation paper and make sure the allocation was not deciphered.

Finally, as participants were enrolled in the trial by the neurologist, the therapist would sequentially select an envelope, write down the patient's information, and then open the envelope. This allocation process was done in the presence of the participant but not the neurologist, preventing selection bias from the recruiter.

Blinding

Blinding of participants: To ensure blinding of participants, white noise listening was assigned as a placebo treatment. In addition, patients were not informed about the hypothesis of the study and which treatment was the active treatment.

Blinding of the outcome assessor: As described in the allocation process, the assessor was not given any information regarding the treatment assignment of each participant. Moreover, participants were advised and reminded by their therapist not to provide any information about their therapy to the assessor.

Blinding of the therapist: Although in this study it was impossible to blind the music therapist, to minimize performance bias, the therapist was given a treatment manual and was taught about the treatment fidelity procedures.

Statistical method

Statistical analysis was performed using R. Mean and 95% confidence interval are shown for outcome scores. Group comparison was done using a two-sample unique variance t-test.

The analysis was intention-to-treat and involved all patients who were randomly assigned, except for those who discontinued the treatment and were unable to follow up.

Results

Participant flow

The trial was run from March 2019 to October 2019. Figure 1 shows the participant flow chart. A total of 172 ischemic stroke patients receiving outpatient rehabilitation therapy were assessed for eligibility. Among those, 109 did not meet the inclusion criteria, and 23 declined to participate. Of the 40 patients enrolled in the study, 20 were assigned to the music group and 20 to the control group. Six patients discontinued treatment (two in the music group and four in the control group).

Figure 1. Study design and participant flow.

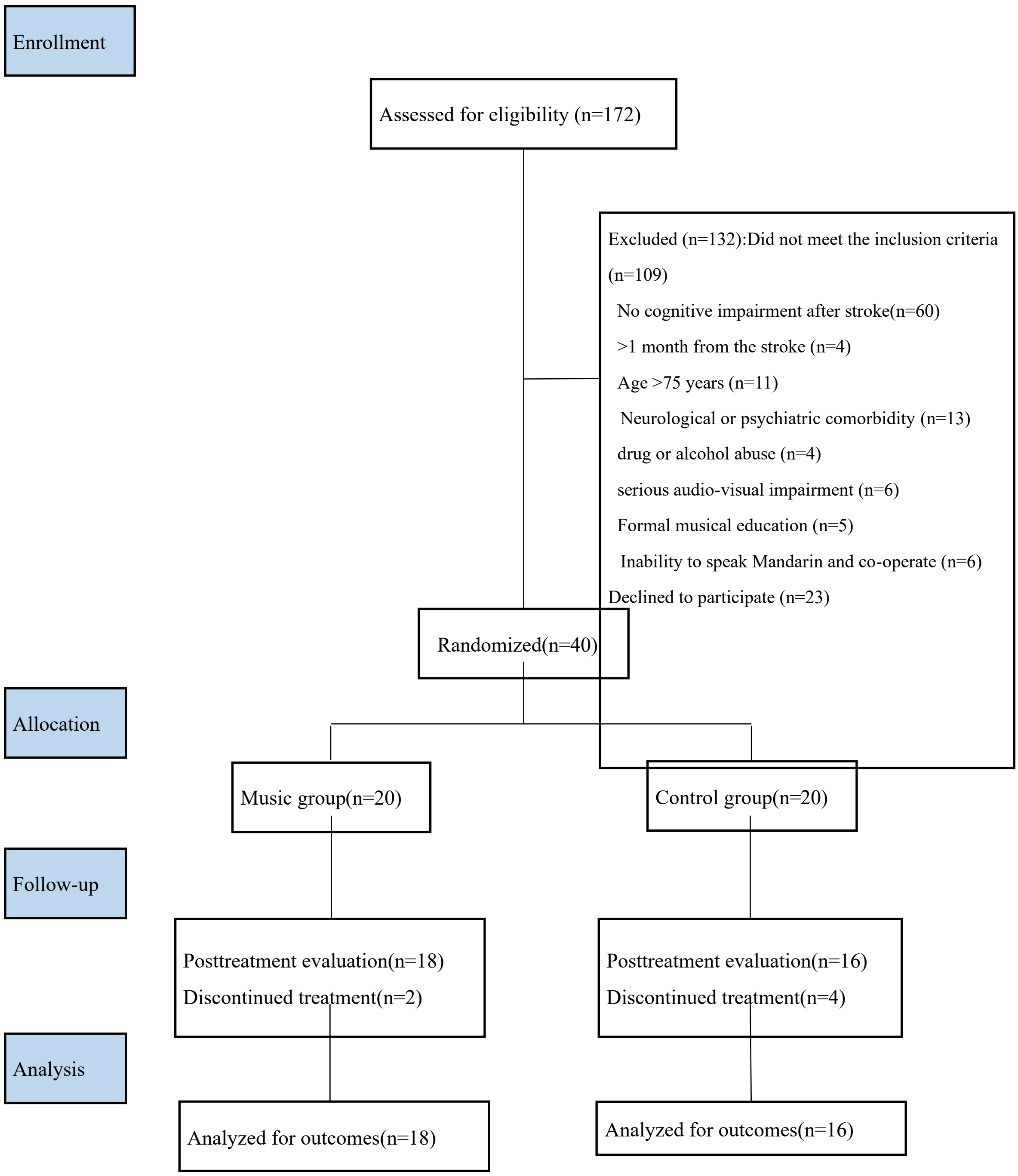

Figure 1. Study design and participant flow. Flow diagram with the phases of the two-arm randomized controlled trial and the number of participants per group in each of the phases.

Baseline analysis

Table 1 reports baseline characteristics for both groups. There were no significant differences in demographic and clinical variables between groups at baseline.

Table 1. Baseline demographic and clinical variables of the music and control groups

	Music group (n=18)	Control group (n=16)	P value
Gender (male) (%)	16 (88.9%)	14 (87.5%)	1.000 ($\chi2$)
Age ($\bar{x}$±t*se)	58.00±5.33	60.88±5.82	0.446 (T)
Smoke (%)	9 (50.0%)	11 (68.8%)	0.447 ($\chi2$)
Hypertension (%)	10 (55.6%)	8 (50.0%)	1.000 ($\chi2$)
Diabetes (%)	8 (44.4%)	6 (37.5%)	0.951 ($\chi2$)
Atrial fibrillation (%)	2 (11.1%)	0 (0.0%)	0.519 ($\chi2$)
Hyperlipidemia (%)	9 (50.0%)	6 (37.5%)	0.699 ($\chi2$)
Lesion laterality (left) (%)	14 (77.8%)	9 (56.3%)	0.331 ($\chi2$)
Lesion number (multiple) (%)	11 (61.1%)	10 (62.5%)	1.000 ($\chi2$)
Lesion location			
Frontal lobe (%)	5 (27.8%)	2 (12.5%)	0.500 ($\chi2$)
Temporal lobe (%)	7 (38.9%)	4 (25.0%)	0.619 ($\chi2$)
Parietal lobe (%)	10 (55.6%)	6 (37.5%)	0.479 ($\chi2$)
Insula (%)	2 (11.1%)	3 (18.8%)	0.887 ($\chi2$)
Other (%)	3 (16.7%)	5 (31.3%)	0.551 ($\chi2$)

Note: Mean and 95% confidence interval are shown for age, and absolute frequencies are shown for the rest of the variables. Group comparison was done using a two-sample unequal variance t-test for continuous data and $\chi2$ test for categorical data.

Primary outcome

Table 2 shows MoCA average scores for music and control groups at baseline and after three months of treatment, as well as score improvement between the two periods. There were no significant group differences on cognitive performance at baseline. After three months of treatment, the music and control group had an average score of 25.33 (±1.28) points and 22.12 (±2.58), respectively. Difference in average score between groups was statistically significant (p=0.027). Moreover, average score improvement was significantly higher in the music group than that of the control group (p=0.003). This further shows that cognitive improvement was considerably greater in the music group.

Figure 2 illustrates recovery for both groups in the seven cognitive domains of the MoCA. Table 3 shows average scores and group comparison are shown for these seven domains. At the end of the trial, delayed memory recovery was significantly better in the music group than in the control group (p=0.019). Orientation recovery was also significantly better in the music group than in the control group (p=0.023).

Table 2. Comparison of MoCA scores between two groups at baseline and 3-month treatment.

	Music group	Control group	T	P value
BL	19.61±1.73	19.38±2.66	0.158	0.876
3m	25.33±1.28	22.12±2.58	2.371	0.027*
Improv	5.72±1.30	2.75±1.46	3.226	0.003**

Note: BL=baseline, 3m=after 3 months of treatment, Improv=Difference between BL and 3m. Mean and 95% confidence interval are shown for MoCA. Group comparison was done using a two-sample unequal variance t-test. MoCA scores range from zero to 30, with a score of 26 or higher regarded as normal. *P < 0.05, **P < 0.01, ***P < 0.001.

Figure 2. Group scores for the seven domains of the MoCA at baseline and after three months of treatment.

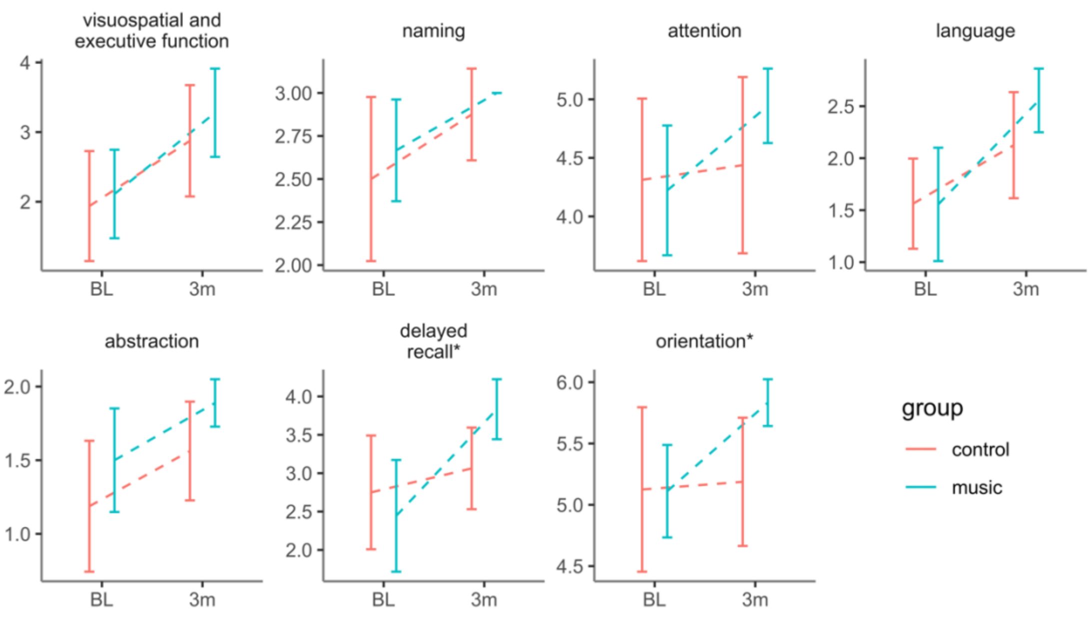

Fig. 2 BL=baseline, 3m=after 3 months of treatment. Mean and 95% confidence interval are shown for MoCA scores. Group comparison was done using a two-sample unequal variance t-test. Score range for the seven cognitive domains assessed are as follows: visuospatial and executive (0 to 5), naming (0 to 3), attention (0 to 6), language (0 to 3), abstraction (0 to 2), delayed recall (0 to 5), and orientation (0 to 6). *P < 0.05, **P < 0.01, ***P < 0.001.

Table 3. The 7 domains scores of MoCA between two groups at baseline and 3 months treatment.

		Music group	Control group	T	P value
Visuospatial and executive function	BL	2.11±0.64	1.94±0.79	0.364	0.719
	3m	3.28±0.63	2.88±0.80	0.838	0.409

Naming	BL	2.67±0.30	2.50±0.48	0.632	0.533
	3m	3.00±0.00	2.88±0.27	1.000	0.333
Attention	BL	4.22±0.55	4.31±0.69	-0.216	0.831
	3m	4.94±0.32	4.44±0.75	1.320	0.201
Language	BL	1.56±0.55	1.56±0.43	-0.021	0.983
	3m	2.56±0.31	2.12±0.51	1.538	0.137
Abstraction	BL	1.50±0.35	1.19±0.44	1.171	0.251
	3m	1.89±0.16	1.56±0.34	1.867	0.075
Delayed recall	BL	2.44±0.73	2.75±0.74	-0.624	0.537
	3m	3.83±0.39	3.06±0.53	2.481	0.019*
Orientation	BL	5.11±0.38	5.12±0.67	-0.038	0.970
	3m	5.83±0.19	5.19±0.52	2.471	0.023*

Note: BL=baseline, 3m=after 3 months of treatment. Mean and 95% confidence interval are shown for the 7 domains of MoCA. Group comparison was done using a two-sample unequal variance t-test. *P < 0.05, **P < 0.01, ***P < 0.001.

Secondary outcomes

Figure 3 illustrates score improvement for music and control groups for HAMA, HAMD, NHISS, BI, and ZBI at baseline and after three months of treatment. Average scores and group comparison are shown in Table 4.

Regarding mood, within-group analyses revealed that both groups improved in both HAMA and HAMD mood tests at the end of the study. However, there were not significant group differences in anxiety and depression improvement (p=0.164 in HAMA, and p=0.499 in HAMD).

There were significant differences between groups in neurological function and ADLs after three months of treatment. NHISS scores improved more in the music group than in the control group (p=0.008). Moreover, BI scores showed that patients in the music group had a larger improvement in ADLs compared with the control group (p=0.019). Finally, there were also significant differences between groups in caregiver burden after three months of treatment. Compared with the control group, ZBI indicated that caregiver burden was significantly lower in the music group (p=0.008).

Figure 3. Results for the secondary outcomes.

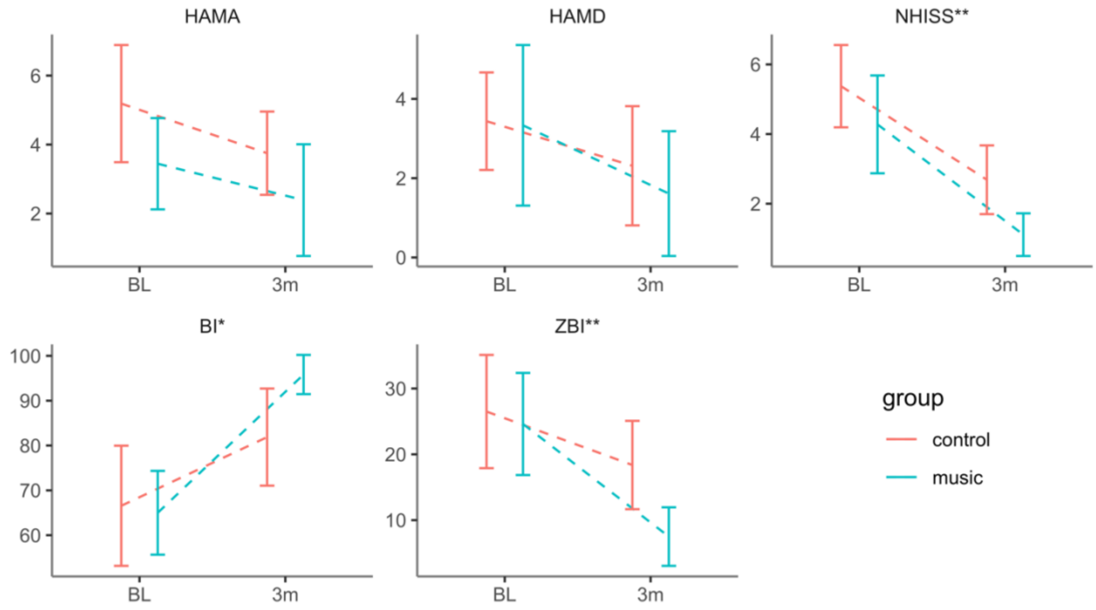

Fig. 3 BL=baseline, 3m=after 3 months of treatment. Mean and 95% confidence interval are shown for scores. Group comparison was done using a two-sample unequal variance t-test. *p< 0.05, **p < 0.01, ***p < 0.001.

Table 4. Results for the secondary outcomes between two groups at baseline and 3 months treatment.

		Music group	Control group	T	P value
HAMA	BL	3.44±1.32	5.19±1.70	-1.719	0.096
	3m	2.39±1.62	3.75±1.21	-1.427	0.164
HAMD	BL	3.33±2.03	3.44±1.23	-0.093	0.927
	3m	1.61±1.57	2.31±1.50	-0.683	0.499
NHISS	BL	4.28±1.40	5.38±1.18	-1.267	0.215
	3m	1.11±0.61	2.69±0.99	-2.885	0.008**
BI	BL	65.00±9.34	66.56±13.40	-0.203	0.840
	3m	95.83±4.37	81.88±10.83	2.544	0.019*
ZBI	BL	24.61±7.76	26.50±8.60	-0.346	0.732
	3m	7.50±4.45	18.38±6.71	-2.870	0.008**

Note: BL=baseline, 3m=after 3 months treatment. Mean and 95% confidence interval are shown for HAMA, HAMD, NHISS, BI, ZBI scores. Measurement data use a two-sample unequal variance t-test. *p< 0.05, **p < 0.01, ***p < 0.001.

Harms

Neither the patients in the music group nor those in the control group reported discomfort of adverse effects from the intervention.

Discussion

This study showed the potential benefits of culture-based music listening therapy on cognitive recovery in PSCI patients. Within-group analyses showed that at the end of the trial improvement in cognition, neurological function, ADLs, and caregiver burden was larger in the music group than in the control group.

Three months after treatment, overall cognitive improvement measured from MoCA was significantly larger in the music group than in the control group. Regarding domain-specific scores, delayed memory and orientation recovery were also significantly larger in the music group than in the control group. These findings are consistent with previous research exploring the connections between music and cognition. It has been found that music listening can stimulate neural activity well beyond the auditory cortex to the bilateral networks of the frontal, parietal, temporal, and subcortical areas (Bhattacharya et al., 2001), which are closely related to attention and memory. In addition, music can enhance brain plasticity after stroke by promoting nerve growth in the hippocampal region (Suzuki et al., 2004). Neuroimaging has shown that music can stimulate the activity of these brain structures, enhance attention and memory after stroke, and further improve cognitive function (Alluri et al., 2012; Janata et al., 2002).

As reported from MoCA scores, after treatment nine out of 18 (50.0%) patients still had cognitive impairment in the music group compared with 13 out of 16 (81.25%) in the control group. These results indicate that PSCI can be gradually improved but a complete recovery is not guaranteed. Research shows that PSCI recovery usually occurs between the first three to 12 months after stroke. However, prevalence of mostly minor cognitive impairment can remain high 12 months after stroke (Morsund et al., 2019). Thus, timely intervention is key to improve as much as possible the cognitive functioning, and with that, the ability of stroke survivors to perform independently.

As for secondary outcomes, improvement in anxiety and depression were found to nonsignificant within groups. About 30%-50% of stroke patients will develop an emotional disorder after stroke, particularly anxiety and depression (Hellmann-Regen et al., 2013; Thayabaranathan et al., 2018), which may reduce the effect of treatment, delay the rehabilitation process and increase the risk of death (Knapp et al., 2020). Non significance of mood outcomes in this trial may be due to the small sample size and a true small effect size. Nevertheless, evidence suggests that music listening may still have potential for alleviating post-stroke emotional disorders (Forsblom et al., 2009; Särkämö et al., 2008). One mechanism may be that it regulates the cardiovascular reflexes, and also excite or inhibit the endocrine system through the cardiovascular regulatory center in the ventrolateral medulla, which is connected to the auditory thalamus and amygdala (Koelsch, 2011). Another possible mechanism is that music can directly act on the emotional center of the brain such as the hypothalamus and limbic system, promote dopamine release, and regulate emotional responses (Ashby et al., 1999; Siedliecki & Good, 2006).

Compared with the control group, the neurological function and ADLs in the music group recovered more significantly. Research shows that music can cause changes in the brain's structural gray matter and induce brain remodeling (Särkämö et al., 2008), adaptability, and plasticity (Wan & Schlaug, 2010). When patients in the music group listened to music with which they were familiar and felt socially, culturally, and spiritually connected, the central nervous network should have activated widely, increasing blood flow in the stimulated areas and promoting the connection and remodeling of the neural network. Similarly, music could influence the areas of multisensory and motor integration by stimulating the production and release of neuropeptides and biochemical mediators (such as endorphins and nitric oxide), integrating different senses (auditory, visual, and somatosensory systems), and forming different music experiences (Boso et al., 2006).

Findings from this study also suggest that music listening can significantly reduce caregiver burden. Stroke survivors can become a major burden to family caregivers (Persson et al., 2015), who may as well develop emotional disorders like depression due to restriction of interpersonal communication and subsequent decline in quality of life (Caro et al., 2017; Em et al., 2017; Rohde et al., 2019). Previous research has found that engaging stroke patients in music-based therapy has the potential to produce gains in the general life situation of caregivers (Bunketorp-Käll et al., 2018). We believe that music listening may indirectly reduce stress perceived by caregivers by promoting patients' quick recovery. However, there are relatively few studies that have tested the effects of music-based therapy on caregivers. With caregivers playing an essential role in promoting quicker rehabilitation of stroke patients (Ostwald et al., 2009), more research is needed to assess the efficacy of music-based interventions on caregiver burden.

As the trial was conducted for both sexes, covered a wide age range, and included both left and right-side ischemic stroke, results could be considered fairly generalizable. It would, nevertheless, be important to test this intervention in a larger, more diverse sample that could include more female subjects and people of non-Asian ethnic and linguistic backgrounds.

The music intervention design in this study was based upon the foundation of medical ethnomusicology. As opposed to simply assigning the patient's favorite music as treatment, this study regarded music as an element integral to the person's social, cultural, emotional, and spiritual character and experiences. Taking these findings into account, more research should be encouraged to test culture-based music interventions in clinical studies. We recommend that future research in music interventions apply ethnomusicological principles, consider sociocultural variables, and pay attention to the importance of culture in music and how music fits into the person's ethnic background.

Overall, music listening shows promise in alleviating cognitive impairment, neurological function, ADLs, and reducing caregiver burden, but available data are not yet sufficient to change guidelines or policy. Studies with larger samples and better methodological quality are needed to understand the effects of music listening, how it can be best delivered, and who can benefit from it. Should music listening continue to show positive results in improving stroke recovery, it could be used to seize time spent at the stroke ward or at home while enhancing the cognitive recovery and psychological wellbeing of stroke survivors. One further advantage of this type of treatment is that it does not require a certified music therapist, making it less costly and convenient. It could be delivered by non-specialists, family members, or even the patients themselves to choose the music according to the specific needs of the patients.

Limitations

Findings from this study may be limited by the small sample size. Larger sample size in future studies should provide more accurate and cleared information regarding outcome effects. Another limitation of this study is the lack of imaging data and in-depth exploration of the specific mechanisms for which music therapy promotes PSCI recovery, which should be performed in future analyses.

Conclusions

In conclusion, music listening could be administered effectively for patients with PSCI to promote the recovery of cognitive and neurological functions, improve their emotional state, ADLs, and reduce caregiver burden. Music listening as therapy has the advantage of being inexpensive, simple to execute and supervise, and non-invasive. We suggest that more research should be done to corroborate the results of this study on larger, more diverse samples.

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Conflict of interest

The authors declare that they have no competing interests.

Availability of data and material

The dataset generated and analyzed during the present study is available at https://zenodo.org/record/7294007#.Y2Xv8OyZM-Q.

Ethics approval

This study was approved by the Regional Ethics Committee and the Institutional Review Board of the

First Affiliated Hospital of Xiamen University.

Consent to participate

All patients provided written informed consent.

Consent for publication

All data published here are under the consent for publication.

Authors' contributions

Yi-hong Zhan, Li-ping Fan and Alonso Quijano-Ruiz designed the study; Yi-hong Zhan and Dan-ni Wang recruited the patients; Li-ping Fan and Chen Wang collected clinical data and evaluated the scales; Xian-bao Zhou, Alonso Quijano-Ruiz and Hong-wei Zhao contributed to the music treatment; Alonso Quijano-Ruiz performed the data analysis; Li-ping Fan and Alonso Quijano-Ruiz co-wrote the manuscript. All of the authors have read and approved the manuscript.

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