VERSION NO: 1
VERSION DATE: 01.10.2024

UNIVERSITI MALAYA

PUSAT PERUBATAN
Medical Centre

RESEARCH PROTOCOL

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3. Research Proposal

TITLE OF RESEARCH PROPOSAL
Feasibility Randomised Controlled Trial of Intensive Music Therapy on Cognitive Function in Subacute Stroke Rehabilitation in Malaysia
KEY WORDS
Music therapy; randomised controlled trial; rehabilitation; stroke; cognition; attention

BACKGROUND/ JUSTIFICATION

Stroke is a leading cause of long-term disability worldwide, often resulting in cognitive impairments, particularly in memory, attention, and executive function, which significantly impact patients' quality of life and daily functioning. Research indicates that music therapy can enhance cognitive recovery during neurorehabilitation by engaging multiple brain networks and promoting neuroplasticity. There is still limited evidence on the specific effects of intensive music therapy during the subacute phase, a critical period for neurorehabilitation. In addition, there is no published report on the efficacy of structured music therapy as part of a cognitive rehabilitation program in Malaysia, despite a concerted move to promote the use of music for therapeutic purposes in this country over the last decade. Music therapy has not been a part of a formal therapeutic modality in most neurorehabilitation program locally, unlike the more established music therapy practice in neighbouring countries such as Singapore. This study proposes to investigate the effects of intensive music therapy on cognitive functions in subacute stroke patients, while also assessing its feasibility within regular rehabilitation program in Malaysian setting. If successful, this approach could support the integration of music therapy into clinical neurorehabilitation settings, promoting its wider use for cognitive recovery post-stroke.

OBJECTIVES/OUTCOMES

Objectives:

1. To assess the feasibility of recruiting, retaining, and ensuring adherence of subacute stroke patients to an intensive music therapy program within a neurorehabilitation setting.
2. To evaluate the practicality of integrating music therapy into existing stroke rehabilitation protocols, including the training requirements for staff, resource availability, and logistical considerations.
3. To gather preliminary data on the impact of intensive music therapy on cognitive function, specifically memory, attention, and executive function, to estimate effect sizes and inform the design of a larger, fully powered randomized controlled trial.

Expected outcomes:

1. The study successfully recruits and retains the target number of subacute stroke patients, with a high adherence rate to the intensive music therapy sessions.
2. The intervention is effectively integrated into the existing stroke rehabilitation program, with staff adequately trained and resources efficiently utilized.
3. Preliminary data show trends of improvement in cognitive functions (e.g., memory, attention, executive function) among patients receiving music therapy

METHODOLOGY

Study design

This study will be a feasibility randomised controlled trial (RCT) in one centre, with two parallel groups: an intervention group receiving intensive music therapy in addition to standard neurorehabilitation, and a control group receiving only standard neurorehabilitation. A certified music therapist will conduct the intervention and a trained assessor will evaluate the outcome. The assessor is blinded to the patients' allocation group and will evaluate the cognitive outcomes at baseline, at two weeks (after 8 sessions) and at 1 month post intervention. All patients who

are admitted to the rehabilitation ward for stroke rehabilitation will be screened and approached. Informed consent will be obtained from eligible patients before randomisation.

To ensure that there are exactly 15 patients in both the control and intervention groups, block randomization will be used using a random number generator. After randomization, the group assignments will be kept in a password-protected file that only the study coordinator can access. The assessor will not have access to this information because the patients will be labelled with anonymous codes that do not reveal whether they are in the control or intervention group. The assessor will only know the code, not the group assignment, ensuring unbiased evaluation.

Intervention group
The music therapy session described follows a structured and engaging approach, aimed at enhancing the patient's cognitive skills during neurorehabilitation. Here's a summary of the session components:

1. Relaxation Phase: The session begins with a five-minute deep breathing exercise to help the participant relax and prepare mentally for the activity.

2. Song Selection: The therapist presents a list of 50 well-known pop songs from the past three decades, available in four languages (Malay, English, Mandarin, and Tamil). The participant chooses a song based on personal preference, promoting cultural relevance and personal connection.

3. Instrument Selection and Familiarization: The therapist offers five percussion instruments (kompang, djembe, tambourine, maracas, shaker) for the participant to explore. The participant selects one instrument to accompany the chosen song.

4. Rhythmic Training: The participant learns to play a rhythmic pattern that complements the song. Once mastered, they sing along with the therapist while playing the rhythm.

5. Progression and Adjustment: If the participant successfully plays the rhythm for over 50% of the song duration, they are invited to choose another song and instrument. If struggling, they are prompted to select another song to prevent frustration. Rest breaks are included, and the therapist adjusts the session based on the participant's endurance.

6. Session Frequency: Each session lasts 45 minutes and is conducted four times a week for two weeks, integrated with the patient's standard neurorehabilitation.

7. Customization: The therapist tailors the sessions according to the patient's preferences, medical condition, and emotional state, with real-time adjustments based on feedback and continuous coordination with the rehabilitation team.

This individualized approach aims to enhance patient engagement and recovery by integrating music, rhythm, and therapeutic interaction into the neurorehabilitation process.

Control group
In the control group, participants will receive the standard neurorehabilitation program prescribed by the rehabilitation team, without the addition of music therapy. This will provide a baseline to compare outcomes with the intervention group and evaluate the feasibility and preliminary effects of the music therapy intervention. The usual cognitive rehabilitation program during the subacute stroke period focuses on restoring cognitive abilities such as attention, memory, executive functions, and communication. The key components typically include:

1. Attention Training: Exercises that improve sustained, selective, and divided attention, crucial for regaining concentration in daily activities.

2. Memory Aids: Tools like mnemonic strategies, repetition tasks, and external memory aids (e.g., calendars, notes) help rebuild short-term and working memory.
3. Executive Function Training: Targeting skills such as problem-solving, planning, and organizing tasks through structured exercises, gradually improving independent thinking.
4. Communication and Language Therapy: Speech-language pathologists work with patients to improve verbal and non-verbal communication, focusing on both comprehension and expression.
5. Problem-Solving Exercises: These help patients break down real-life problems into smaller, manageable steps, encouraging better decision-making skills.

The control group's daily rehabilitation sessions will last for 45 minutes, mirroring the music therapy group's session duration, ensuring a fair comparison of outcomes across both groups. This comparison will help assess the unique contributions of music therapy on cognitive functions like attention, memory, and executive functions in stroke patients.

Inclusion Criteria:
1. Diagnosed with ischemic or haemorrhagic stroke confirmed by CT scan
2. Duration of stroke within the first 3 months
3. Aged 18 - 75 years old
4. Ability to provide informed consent
5. Understands Bahasa Melayu or English with basic communication abilities to follow instructions during therapy sessions
6. Mild to moderate cognitive impairments with MoCA score of 10-25.

Exclusion Criteria:
1. Severe aphasia
2. Significant uncorrected hearing or visual impairments preventing engagement in music therapy.
3. Severe or unstable medical conditions (e.g., uncontrolled hypertension or diabetes).
4. Medications that significantly impair cognition or motor function (e.g., high-dose sedatives).
5. History of neurological diseases other than stroke (eg, Parkinson's disease).

Outcome measures
This will be assessed at baseline, after completion of 8 sessions and also at 1 month after completion. Primary outcome measures are Montreal Cognitive Assessment (MoCA), Trail Making Test (TMT), Digit Span (Forward and Backward) and Clock Drawing Test (CDT). The secondary outcome measure is MBI.

Sample size calculation:

A sample of 30 subacute stroke patients (15 control and 15 intervention) will be recruited from the UMMC rehabilitation ward. This number is chosen based on practical considerations to evaluate feasibility metrics and exploratory analysis as in the objectives. For these purposes, a sample size of 30 is typically adequate to gather enough information about the practical aspects of the trial. This number could also ensure that the feasibility objectives are met even with at least 20% dropouts. The average stroke admission to the rehabilitation ward in UMMC is five patients per week, and the number of potential patients that will be eligible is estimated about 2 per week. This total number of 30 will be sufficient within the study period and the grant duration.

Statistical Analysis:

Descriptive Statistics and Exploratory Inferential Statistics will be used in this study.

The means, standard deviations, and 95% confidence intervals (CIs) for cognitive outcome measures (e.g., memory, attention, executive function scores) at baseline, post-intervention, and

follow-up will be used. This will provide a preliminary understanding of the data distribution and effect sizes.

For the exploratory Inferential Statistics, independent t-test (or Mann-Whitney U Test) will be used to compare the mean changes in cognitive scores between the intervention and control groups. The independent t-test if the data are normally distributed. If not, we will use the Mann-Whitney U test as a non-parametric alternative.

Within each group, we will compare the baseline and post-intervention scores using the paired t-test for normally distributed data or the Wilcoxon signed-rank test for non-parametric data. Cohen's d will be used for independent t-tests (between groups) or r for non-parametric tests.

A repeated measures ANOVA (if the data is normally distributed) or a mixed-effects model will be used to explore changes over time (baseline, post-intervention, and follow-up). Given the small sample size, these analyses will likely be underpowered but can provide estimates of variability and preliminary trends.

RESEARCH DATA

Where will the data be kept?
The demographic data of the patients, especially the control group will be kept in the EMR as the usual practise, since they receive neurorehabilitation therapy as a standard care. The additional baseline data for the study, data on cognitive performance and other relevant data will be kept in a separate research file. The files are in the laptop will be secured with password and the notes will be kept in a locker in the Department of Rehabilitation Medicine, Faculty of Medicine with one of the co-researchers.

Anonymity of data
All patients will be identified with a code number and not real names in the research files. The data entry into the excel sheet and into the research thumb drive will follow the similar process.

Who will have access to the research data?
All the co-researchers & research assistant

How long will the data be kept?
7 years

BUDGET / FINANCIAL SUPPORT (IF APPLICABLE):

Grant: Yayasan Penyelidikan Otak, Minda Dan Neurosains Malaysia of RM6,000

GANTT CHART

	Dec – Feb 2024/25	March – June 2025	July – Aug 2025	Sept – Feb 2025/26	March –June 2026	July – Oct 2026
1. Development of the project and trial registry						

2. Recruitment and randomisation phase						
3. Data entry & analysis						
4. Manuscript writing						
5. Submission for publication						
6. Promote research outcomes						

REFERENCES (up to 10 references)

1. Thaut, M. H., Gardiner, J. C., Holmberg, D., Horwitz, J., Kent, L., Andrews, G., Donelan, B., & McIntosh, G. R. (2009). Neurologic Music Therapy improves executive function and emotional adjustment in traumatic brain injury rehabilitation. Annals of New York Academy Sciences, 1169, 406-416.
2. Thaut, M. H. (2010). Neurologic Music Therapy in cognitive rehabilitation. Music Perception, 27(4), 281-285.
3. Yoo, G. E., & Kim, S. J. (2016). Rhythmic auditory cueing in motor rehabilitation for stroke patients: Systematic review and meta-analysis. Journal of Music Therapy, 53(2), 149-177
4. Alluri, V., Toiviainen, P., Jääskeläinen, I. P., Glerean, E., Sams, M., & Brattico, E. (2012). Large-scale brain networks emerge from dynamic processing of musical timbre, key and rhythm. *NeuroImage, 59*(4), 3677-3689.
5. Antić, S., Morović, S., Kes, V. B., Zavoreo, I., Jurašić, M. J., & Demarin, V. (2012). Enhancement of stroke recovery by music. *Periodicum Biologorum, 114*(3), 397-401.
6. Cha, Y., Kim, Y., & Chung, Y. (2014). Immediate effects of rhythmic auditory stimulation with tempo changes on gait in stroke patients. *Journal of Physical Therapy Science, 26*(4), 479-482.
7. Fang, R., Ye, S., Huangfu, J., & Calimag, D. P. (2017). Music therapy is a potential intervention for cognition of Alzheimer's Disease: A mini-review. *Translational Neurodegeneration, 6*(2), 1-8.
8. Jeong, E. (2013). Psychometric validation of a music-based attention assessment: Revised for patients with traumatic brain injury. *Journal of Music Therapy, 50*(2), 66-92.
9. Magee, W. L., Clark, I. N., Tamplin, J., & Bradt, J. (2017). Music interventions for acquired brain injury: Reviews. Cochrane Database of Systematic Reviews, 2017(1), 1-130, doi: 10.1002/14651858.CD006787.pub3.
10. Stegemöller, E. L. (2014). Exploring a neuroplasticity model of music therapy. Journal of Music Therapy, 51(3), 211-227.

POTENTIAL IMPACT

This study could provide evidence supporting the integration of music therapy into neurorehabilitation programs for cognitive recovery post-stroke. If proven feasible and effective, it may set a precedent for similar programs globally, contributing to the development of more comprehensive, multidisciplinary rehabilitation approaches. As a feasibility RCT, this study would lay the groundwork for larger, fully powered trials. It can provide essential data on recruitment, retention, adherence, and preliminary effect sizes, informing the design of larger studies that could further validate the effectiveness of music therapy. This study could lead to the development of a structured music therapy programs in Malaysia's public and private healthcare sectors, offering a novel, culturally engaging, and accessible form of rehabilitation to enhance cognitive recovery for stroke patients locally.

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