Musical Engagement of brain LObes in Alzheimer's Disease patients studY (MELODY)

Informed Consent Form

NCT05309369

December 21, 2021

Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT

TITLE OF RESEARCH: Musical **E**ngagement of brain **LO**bes in Alzheimer's **D**isease patients stud**Y** (**MELODY**)

SUMMARY

You are being asked volunteer for a research study. This research study will be conducted at the Medical University of South Carolina (MUSC) at the Children's Research Institute. Research studies are voluntary and include only people who chose to take part. This consent form will give you information about the study to help you decide whether you want to participate.

The purpose of this research is to learn about how listening to music may produce meaningful improvements in brain function and increase level of arousal (state of being alert, awake, and attentive) in individuals with Alzheimer's Disease (AD). Music is a safe, non-invasive intervention that needs to be studied more to understand its effects on the brain.

If you agree to participate in the study, you will attend 5 visits with the study team over 5 weeks. Your medical history and medication use will be reviewed, and the following will be performed during some, but not all visits: a fall risk questionnaire, a safety evaluation, vital signs (sitting pulse and sitting blood pressure), an auditory (hearing) assessment, questionnaires, and 3 functional magnetic resonance imaging (fMRI) scans. Details on all study procedures are listed in section "B. Procedures" below. Research participation requires that you have a "study partner" who is expected to provide information about the selection of preferred musical tunes that you will listen to and complete questionnaires to describe your memory, thinking, attention, and mood.

There are minimal risks associated with the auditory (hearing) portion of this study, including the risk of falls and auditory (hearing) injury. For the fMRI scans, the most severe risks include anxiety or claustrophobia (fear of closed spaces), as well as the risk of injury if the participant has metal in their body. These and other possible risks to being in this study will be described in detail in this consent form under section "C. Risks and Discomforts" below. There are other medications or treatments available for Alzheimer's disease care, including the possibility to receive treatment by a professional musical therapist.

If you are interested in learning more about this study, please continue to read below. Ask your study doctor or study staff to explain any words or information that you do not clearly understand as you are considering your participation in the study.

A. PURPOSE OF THE RESEARCH

Experts think that listening to music holds significant potential to support and enrich brain health as people age. Music affects different regions of the brain including those involved in hearing/listening, movement, attention, language, emotion, memory, and thinking skills.

Research shows that memories of music last over years and can often remain intact, even in cases of dementia in advanced Alzheimer's disease (AD) when other memories have been forgotten. Older people with AD can often remember music from their youth. Evidence has emerged that listening to music may boost memory in some patients, specifically music that we like and have positive, emotional connection with. People who

support music-based therapies say that the approach can pay off for dementia patients, as well as their caregivers, by improving communication, cooperation, social interaction, and mood.

Even though we have fairly good evidence that music stimulates the brain, we have not yet established that this stimulation will be beneficial. Therefore, the purpose of this study is to test the effect of emotionally impactful music on participants' general well-being, memory, and arousal. The music will be compared to calming nature sounds such as ocean wave sounds.

This consent form describes a research study and your role as a research subject. This document is intended to inform you about the possible risks and benefits of the research study, other options that may be available to you and your rights as a research subject. Please read this consent form carefully and take your time making your decision.

You are being asked to participate in this research study because you have been diagnosed as suffering from AD at the moderate or severe level. The investigator in charge is Jacobo Mintzer, MD. You may contact Dr. Jacobo Mintzer at 843-367-4260.

The study is sponsored by the National Endowment for the Arts and AARP. Portions of Dr. Mintzer's and his research team's salaries will be paid by the grant. The study is being done at one site. Ten people will participate in the study.

B. PROCEDURES

If you choose to take part in this study, you will be asked to sign this consent form before any study related procedures are done. You will then be given a signed and dated copy of the document.

Description of Visit Activities

The following activities will be done at one or more visits over the course of this study:

- *Eligibility Assessment* (Screening Visit): The study doctor will interview you and your study partner to ask questions about your memory, attention, and reasoning. We will review your medical records and your current state of health to see if any medical conditions contribute to your memory problems. Then we will evaluate your memory using a short test for memory, attention, and reasoning.
- *Auditory Assessment (hearing test)* (Screening Visit): An auditory assessment will be performed to determine if your hearing levels fall within normal limits.
- *Demographic Information* (Screening Visit): You will be asked questions about your age, gender, ethnic and racial identity, your level of education, and your current or previous occupation.
- *Review of Medical History* (Screening Visit): You will be asked to sign a Release of Medical Information Form (if you have not already signed one) so we can receive medical records from your private doctors and medical centers you use. We will ask you questions at every visit to check for any changes to your medical condition.
- *Review of Medication* (Screening Visit): Your study doctor and staff will ask about medications you are currently taking at each study visit.
- *Vital Signs* (Screening Visit): Study staff will check your blood pressure, body temperature, and heart

rate.

- *Risk of Falls Test* (Screening Visit): The doctor will measure the time it takes you to stand up from a chair, walk 10 feet and back, then sit back down to assess your risk of falls.
- *Metal Screening Questionnaire* (Screening Visit): You will be asked questions about if you have metal items in your body that may be harmful to the magnetic resonance imaging (MRI) scanner.
- *Selection of Study Music Interview* (Baseline Visit): You and your study partner will be interviewed to establish your three favorite tunes. One of the tunes will be randomly selected to use to test the effects of music on brain function and level of arousal.
- *Randomization* (Baseline Visit): You will be randomized (assigned by chance like flipping a coin) to receive either the selected musical tune at Visit 1 and nature sounds in the form of ocean wave sounds at Visit 2, or nature sounds at Visit 1 and the selected musical tune at Visit 2.
- *Auditory Intervention* (Visit 1 and Visit 2): You will listen to either the selected musical tune or nature sounds using over-ear headphones delivered as 10-minute segments at the top of each hour over the course of 3 hours. If the musical tune is less than 10 minutes, it will be repeated as many times as necessary to complete the 10-minute period. Before the auditory interventions, we will do a volume test to determine the best volume for the intervention.
- *Questionnaires* (Screening, Baseline Visit, Visit 1 and Visit 2): Memory, thinking, and attention assessments will be conducted. You will be asked about where you are, what is the date, you will be asked to remember words, performs simple tasks, and copy a drawing. You will also be asked about your sleep. You and your study partner will be given an open-ended interview to evaluate your health, memory, thinking, functioning and emotional well-being.
- *Adverse Events* (Baseline Visit, Visit 1, Visit 2, and Visit 3): You will be asked about any adverse events (changes in health, any side effects/ reactions to medications, injuries, or illnesses) that you may have experienced since your last visit.
- *Compliance Assessment* (Visit 1, Visit 2, and Visit 3): Study staff will observe and ensure that you wear the headphones continuously for 10 minutes each session that sound is played. If you are unable to complete the first session, you will be given a 30-minute break and try again. If you still cannot complete the session, you will discontinue from the study.
- *Functional magnetic resonance imaging (fMRI)* (Visit 3)**:** An fMRI uses a large magnet and computer equipment to produce electronic pictures of your brain. You will be placed on a narrow bed on your back and slid into a small tunnel approximately 6 feet in length and 25 inches in diameter. You will hear a loud knocking noise as the scanner operates. You will complete 3 10-minute fMRI scans during one visit. While you are in the scanner, you must hold your head as still as possible. The fMRIs will be performed at a separate location (Center for Biomedical Imaging Building)

  Before the scans are performed, a volume test will be done to make sure the volume is not too high or too low. The volume will be established at the beginning by the study staff asking you if you can hear the sound comfortably. The volume will be fixed at this level.

Summary of Visit Activities

The following charts summarize the activities that will occur over the course of this study. Each visit will last approximately 4 hours.

Visit:	Screening	Baseline	Visit 1	Visit 2	Visit 3
	Day 1	Day 7 +/- 3 days	Day 14 +/- 3 days	Day 21 +/- 3 days	Day 28 +/- 3 days
Activities:					
Informed Consent	X				
Eligibility Assessment	X				
Auditory Assessment	X				
Demographics	X				
Medical History	X				
Vital Signs	X				
Risk of Falls Test	X				
MRI Metal Screening Questionnaire	X				
Selection of study music interview		X			
Randomization		X			
Auditory intervention (music or nature sounds)			X	X	
Questionnaires		X	X	X	
Adverse Events (AEs)		X	X	X	X
Compliance Assessment			X	X	X
Functional magnetic resonance imaging (fMRI)					X

Withdrawal/termination

Your participation in this research study is entirely voluntary. You have the right to refuse to participate and you have the right to change your mind and decide to leave the study at any time in the future without jeopardy to the medical care you receive at this institution.

To withdraw from the study, you must notify the study doctor listed on page one of this consent form in person, by telephone, or in writing.

An investigator may discontinue or withdraw you from the study for the following reasons:

- If you fail to accurately follow the study procedures

- If it would not be in your best interest to continue to participate in the study because of a specific medical condition or situation
- Progression of your disease state that prevents further study participation
- If you meet an exclusion criterion (either newly developed or not previously recognized) that prevents further study participation

If you chose to interrupt your participation in the study or the conditions are not appropriate for you to continue to participate in the study, the last visit you participate in will be considered the final visit of the study.

C. DURATION

Participation in this study will consist of 5 visits lasting approximately 4 hours each over approximately 5 weeks, with each visit scheduled one week apart.

D. RISKS AND DISCOMFORTS

Risks associated with increased activity

While the emotionally impactful musical tune is played, you may experience increased arousal and increased desire to move due to music stimulation, which may result in increased activity, potentially causing injuries or falls.

Risks associated with auditory stimulation

Your auditory system may be harmed if the music intervention or the nature sounds are played at excess volume. The study staff will ensure that the volume level is comfortable.

Risks associated with fMRIs

There have been no ill effects reported from exposure to the magnetism or radio waves used in this test. A known risk is that the magnet could attract certain kinds of metal. Therefore, we will carefully ask you about metal within your body (this includes certain dyes found in tattoos). If there is any question about potentially hazardous metal within your body, you will be excluded from participation in this research study. We will also keep the examining room locked so that no one carrying metal objects can enter while you are in the scanner. Please inform the study staff if you have a history of claustrophobia (extreme anxiety in close spaces). This may also be a contraindication to participation in the study.

Risks associated with assessments and questionnaires

Memory and cognitive testing may cause you to become upset, frustrated, or tired. You have the right to decline to answer any questions and may ask to stop testing at any time for any reason.

Unknown Risks

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks associated with confidentiality

There is a risk of a loss of confidentiality of your personal information as a result of participation in this study.

E. MEDICAL RECORDS

Information about your study participation will not be in your medical record. This means that neither your research participation nor any of your research results will be included in any MUSC medical record.

F. BENEFITS

Being in this study may not benefit you, however, you may find the experience of listening to music and/or nature sounds enjoyable, which could reduce stress or anxiety. If the auditory intervention is effective, your cognitive brain functions may improve, and you may become more alert. This information could be shared with your primary care doctor for your benefit.

If the study proves to be beneficial, it may provide the scientific community with a new treatment tool to be to enhance clinical well-being and alertness in AD patients.

G. COSTS

There will be no cost to you as a result of participation in this study.

H. PAYMENT TO PARTICIPANTS

You or your legally authorized representative will be paid $30 per visit upon completion of each visit.

Payment is intended offset the cost of travel expenses associated with participating in study visits (up to $150 total).

If the study is not completed, you will only receive payment for the study visits completed.

Payment for study visits will be issued in the form of a prepaid debit card called a ClinCard. It works like a bank debit card, and you may use the card to purchase goods or services everywhere Debit MasterCard is accepted. You will be given a ClinCard at the beginning of the study. Each time you complete a study visit, the money will be added to the card and available to you within 24-48 hours. Instructions for using the debit card system are explained on an additional sheet that will be provided to you by the study team.

Payments that you receive from MUSC for participating in a research study are considered taxable income per IRS regulations. Payment types may include, but are not limited to: checks, cash, gift certificates/cards, personal property, and other items of value. If the total amount of payment you receive from MUSC reaches or exceeds $600.00 in a calendar year, you will be issued a Form 1099.

I. ALTERNATIVES

You do not have to take part in this study. The US Food and Drug Administration (FDA) recently granted accelerated approval of a new medication, called aducanumab (ADUHELM™), for the treatment of Alzheimer's disease. Accelerated approval requires an additional clinical trial to verify the drug's clinical benefit. FDA's approval was based on studies of individuals with mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's disease dementia and who had evidence of brain amyloid plaque. Brain amyloid plaque is a build-up of abnormal protein in the brain of people with AD. This build up may lead to impairment in memory or thinking.

There are other medications available for treating symptoms of Alzheimer's disease, but these are approved

only for patients who have been diagnosed with AD dementia. Please ask your study doctor if you would like additional details on these alternatives.

J. DATA SHARING

Information about you (including your identifiable private information) will have all of your identifiers removed and used for future research studies or distributed to other researchers for future research without additional informed consent from you or your legally authorized representative.

K. DISCLOSURE OF RESULTS

We may learn things about you from the study activities which could be important to your health or to your standard of care. If this happens, the information will be provided to you, but you will not otherwise receive your study results.

Changes in your cognitive testing scores that warrant further evaluation will be discussed with you.

L. SIGNIFICANT NEW FINDINGS

Any new information about the study that may change your willingness to participate will be given you.

M. CLINICAL TRIALS.GOV

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

N. SPONSOR COMITMENT

The National Endowment for the Arts (NEA) and AARP do not provide compensation for research-related injury.

O. FUTURE CONTACT

Would you like to be contacted regarding future research opportunities as they become available?

I would be willing to be contacted in the future should other studies become available.

☐ Yes ☐No _____ Subject Initials or Legal Representative's Initials

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteer's Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Dr. Jacobo Mintzer at 843-367-4260. I may contact the Medical University of SC Patient and Family Care Liaison (843) 792-5555 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name (print)	_____ Participant's Signature	_____ Date
_____ Name of person obtaining consent (print)	_____ Signature of person obtaining consent	_____ Date

☐ Check here if LAR not applicable

The participant is unable to give informed consent. I, as the legally authorized representative of the participant, give consent for their participation in this study.		
_____ Name of Legally Authorized Representative	_____ Signature of Legally Authorized Representative	_____ Date
_____ Name of person obtaining consent	_____ Signature of person obtaining consent	_____ Date

Indicate below your authority to act as the participant's legally authorized representative:

☐ Spouse

☐ Parent

☐ Adult Child (18 years of age or over) for his or her parent

☐ Adult Sibling (18 years of age or over)

☐ Grandparent

☐ Adult Grandchild

☐ Guardian appointed to make medical decisions for individuals who are incapacitated

☐ Other per local or state law. Specify: _____

STUDY PARTNER INFORMATION & CONSENT

As the participant's study partner, you have important tasks that need to be carried out in order for the study to be conducted in the safest and best manner possible. These responsibilities include:

1) You must have regular contact with the participant (an average of 10 hours per week or more).

1) You must be able to accompany the participant to most study visits.

2) You are an important source of information about the participant. You must agree to be asked questions about your relationship with to participant, as well as their health, memory, thinking, functioning and emotional well-being in order to find out whether there are any changes in the participant.

If for some reason you become unable to carry out your responsibilities, please tell the study team immediately. You may be asked, if possible, to select a substitute who can take over your duties.

You have read all the preceding information which describes both the participant's participation in the study and your involvement as the participant's study partner. The study has been explained to you in detail. All your questions have been answered to your satisfaction.

You voluntarily agree to participate as a Study Partner.

You voluntarily agree to participate as a Study Partner.		
_____ Study Partner's Name (print)	_____ Study Partner's Signature	_____ Date
_____ Name of person obtaining consent (print)	_____ Signature of person obtaining consent	_____ Date