

Study Protocol

Title: Effects of Heart Rate Oscillations During Meditation on Plasma Biomarkers of Alzheimer's Disease

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Research Background

Cross-sectional studies suggest that meditation practices are associated with slower brain aging and improvements in early biomarkers of Alzheimer's disease (AD). However, the underlying mechanisms remain unclear. Most research has focused on the mental training aspects of meditation (e.g., paying attention to the present moment) and linked them to health outcomes. By contrast, the physiological changes that occur during meditation (e.g., heart rate oscillations, breathing rate) and their influence on health outcomes have been largely overlooked.

During some meditative practices, breathing slows down, which induces large oscillations in heart rate at the breathing frequency. In our previous HRV-ER trial (NCT03458910), a 4-week daily intervention designed to induce high-amplitude heart rate oscillations via slow-paced breathing significantly reduced plasma amyloid beta (A β)₄₂ and A β ₄₀ levels associated with AD.

Research Objectives

Based on our prior findings, the present study aims to separate out the mental training and physiological aspects of meditation to better understand their differential effects on plasma A β levels. We will examine how two types of meditation practices (with or without slow breathing) affect plasma A β levels compared with a no-intervention control group. We will also assess the effects of these practices on emotional well-being, given that various types of meditation improve well-being.

Healthy adults aged 18-35 who meet all eligibility criteria will be invited to this study. Participants will be asked to engage in one week of daily meditation practice or no-intervention control task at home. They will also be asked to visit the lab twice, once before and once after the intervention, to provide blood samples to assess plasma A β levels and to complete emotion questionnaires and memory tests.

Methods and Design

Lab Visit 1 (around 1.5 hours)

1) Consent

At the beginning of this visit, the researchers will provide detailed information about the study. Participants will then be asked to sign the consent form on DocuSign. When they sign, participants will have the opportunity to download a copy of the signed consent form for their record.

2) Administer questionnaires

Participants will be asked to complete the following questionnaires at the Emotion & Cognition Lab:

- Profile of Mood States (POMS)
- Depression Anxiety Stress Scales – Short Form (DASS-21)
- Five Facet Mindfulness Questionnaire
- Demographic information

3) Blood draw

Phlebotomists will collect blood samples up to 30 mL via venipuncture. Note that blood draw volume for blood donation in the US is 1 pint (~450 mL); thus, 30 mL should be safe for participants. Fasting is not required for the blood draw.

4) Measure resting heart rate

Give the participant devices and explain how to use them. The devices include a laptop with a customized meditation app, USB-module and an ear sensor that clips onto the earlobe and measures heart rate.¹). Using the devices, the participant will be asked to measure their heart rate for 5 min. During the 5-min resting state, they will be asked to sit in a chair with palms up, both feet flat on the floor, back straight, knees 90-degree angle, and closed eyes.

5) Paced breathing

Next, the app will ask participant to do 5 minutes of paced breathing at 15 breaths per minute by following audio cues. The participant will be asked to inhale when the ball ascends and exhale when it descends. This controlled breathing at around a normal breathing pace will allow us to assess baseline individual differences in heart rate spectral frequency with breathing rates controlled.

6) Intervention instructions

The app will randomly assign participant to one of the three conditions (belly-focus concentration meditation, belly-focus concentration meditation with slow breathing, no-intervention control). The experimenter will go over the instructions below and have them try the assigned practice for 20 minutes.

Instructions for the belly-focus meditation:

The app will show, “You will be asked to sit quietly to meditate for 20 minutes while your heart rate is recorded. During this time, you will listen to a guided meditation (pre-recorded by a meditation expert) to help you focus on the sensations around the belly. Please remember that it is normal for the mind to wander. When this happens, gently bring your attention back to your belly.”

Audio guided meditation

At the beginning of the session:

- Welcome, please sit in a comfortable position in a chair or on a cushion with your back and neck upright and yet comfortable and gently close your eyes. If you wear glasses, feel free to take them off.
- Keep your mouth gently closed and focus your entire attention... entire attention on your belly.
- Remain aware, aware of every breath coming in, every breath coming out.
- On the inhale, allow your belly to receive your breath, on the exhale allow the belly to contract
- Notice the sensations around the belly as the breath comes in and out. As your breath flows in, feel it move down into your belly. Please observe how breathing makes your belly move. Whatever sensations arise, keep your attention here, noticing the arising and passing of sensation from moment to moment.
- As you inhale, feel your belly expanding and as you exhale feel your belly contracting. Noticing moment to moment whatever sensations are present here in the belly.
- As you meditate, many thoughts, feelings, images, and memories may come up. Welcome, all that arises. Letting them rise and fall, staying with the sensations of the breath expanding and contracting the belly.

At 5 minutes:

- If you find yourself in conversation with a thought or feeling, simply acknowledge this is happening, meet yourself kindly, and bring attention gently back to the sensations in the belly.

At 8 minutes:

- Whatever sensations arise, just observing. Observe how long the sensation lasts, how it changes with each passing moment. It may become stronger for some time, but sooner or later it passes away. No sensation is eternal, each arising and passing away. It is the same with any sensation, whether it be a tingling, an itching, warmth, coolness, or vibration, heaviness; simply observe whatever sensation is present, noticing how they change moment to moment.

At 12 minutes:

- It's quite normal for the mind to wander, if and when you notice your mind wandering, gently bring your attention back to the sensations of breath in the belly right here and now, what sensations are present?

At 15 minutes:

- Noticing where the mind is now, and gently bringing attention back to the sensations of breath and the belly. Moment to moment what sensations are

present in the belly. Each moment of the inhalation ... exhalation, what sensations are present now?

At the end:

- This is the end of the session. Close your practice by setting an intention to stay connected to your body as you move slowly out of the meditation.

Instructions for the belly-focus meditation with slow breathing:

The app will show, "You will be asked to sit quietly to meditate for 20 minutes while your heart rate is recorded. During this time, you will listen to a guided meditation (pre-recorded by a meditation expert) to help you focus on the sensations around the belly. You will also be asked to breathe slowly during the entire meditation session. Please remember that it is normal for the mind to wander. When this happens, gently bring your attention back to the upper lip area."

Audio guided meditation

At the beginning of the session:

- Welcome, please sit in a comfortable position in a chair or on a cushion with your back and neck upright and yet comfortable and gently close your eyes. If you wear glasses, feel free to take them off.
- Keep your mouth gently closed and focus your entire attention... entire attention on your belly.
- Remain aware, aware of every breath coming in, every breath coming out.
- On the inhale, allow your belly to receive your breath, on the exhale allow the belly to contract.
- Take long slow breaths as I guide you. Inhale for a count to 5 and exhale for a count to 5. Breathe slowly and gently at this pace during the entire meditation exercise. I'll count with you for the first few breaths. Then you can count on your own. Inhale, 2, 3, 4, 5, exhale 2, 3, 4, 5. Inhale, 2, 3, 4, 5, exhale 2, 3, 4, 5. Continue breathing this way on your own.
- Notice sensations around the belly as the air moves in and out. As your breath flows in, feel it move down into your belly. Please observe how breathing makes your belly move. Whatever sensations arise, keep your attention here, noticing the arising and passing of sensation from moment to moment.
- As you inhale, feel your belly expanding and as you exhale feel your belly contracting. Noticing moment to moment whatever sensations are present here in the belly.
- As you meditate, many thoughts, feelings, images, and memories may come up. Welcome, all that arises. Letting them rise and fall, staying with the sensations of the breath expanding and contracting the belly.

At 5 minutes:

- If you find yourself in conversation with a thought or feeling, simply acknowledge this is happening, meet yourself kindly, and bring attention gently back to the sensations in the belly. Remember to breathe slowly and gently for a count of 5 while inhaling and a count of 5 while exhaling.

At 8 minutes:

- Whatever sensations arise, just observing. Observe how long the sensation lasts, how it changes with each passing moment. It may become stronger for some time, but sooner or later it passes away. No sensation is eternal, each arising and passing away. It is the same with any sensation, whether it be a tingling, an itching, warmth, coolness, or vibration, heaviness; simply observe whatever sensation is present, noticing how they change moment to moment. Remember to breathe slowly and gently for a count of 5 for each inhalation and a count of 5 for each exhalation during the remaining session.

At 12 minutes:

- It is normal for the mind to wander, if and when you notice your mind wandering, gently bring your attention back to the sensations in the belly right here and now, what sensations are present? Remember to breathe slowly and gently.

At 15 minutes:

- Noticing where the mind is now, and gently bringing attention back to the sensations of breath and the belly. Moment to moment what sensations are present in the belly. Each moment of the inhalation ... exhalation, what sensations are present now?

At the end:

- This is the end of the session. Close your practice by setting an intention to stay connected to your body as you move slowly out of the meditation.

Instructions for the no-intervention control condition:

The app will show, "You will be asked to sit quietly for 20 minutes while your heart rate is recorded. Please feel free to do whatever you would like to do (e.g., use your phone or computer, read a book, watch TV, listen to music) as long as your activity does not involve head motion."

Before each practice session, participants in all conditions will view 6 images from the Nencki Affective Picture System (NAPS; uploaded on section 21.2) and rate them on a scale of 1-9 (1 = very negative to 9 = very positive, with 5 = neutral). At the post-intervention lab visit (i.e., Lab Visit 2), they will be given memory tests for these images (see below for more details).

One week intervention at home

Participants will be asked to engage in the assigned practice for 40 minutes (20 min x two times) each day for a week.

Lab Visit 2 (around 1 hour)

Participants will be asked to return their devices and complete the assessments listed in Lab Visit 1 Steps 2-5. In addition, participants will complete a free recall test in which they will describe as many images as they can that were viewed right before each meditation practice in the past week. They will also complete a recognition memory test in which they will be given 3 response options for each image; Remember, Know and New (Remember = "I vividly remember," Know = "I have a sense of familiarity with the image, New = the image was not seen before").