Study Protocol

Title: Heart rate variability biofeedback training and emotion regulation

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Research Objectives

The aim of the study is to examine the effects of two types of heart rate biofeedback training on emotional well-being and brain function. One group will be trained to increase heart rate variability (HRV) while the other group will be trained to decrease heart rate (HR) and HRV. We hypothesize that the increase-HRV group will have better emotional health in post-training compared with pre-training whereas the decrease-HR/HRV group will not show such improvements. Furthermore, we predict that the improvements will be smaller in older adults than in younger adults. In addition, we predict training-related changes in brain function. We hypothesize that the increase-HRV training groups will show a better ability to up- and down-regulate the amygdala during an emotion regulation task. We also predict that the HRV-increase training will lead to greater functional connectivity between the medial prefrontal cortex and the amygdala at rest.

Research Background

Heart rate variability (HRV) is defined as the variation in the time interval between heartbeats. High HRV is associated with a number of positive emotional health outcomes including lower depression and better emotion regulation (Geisler, Vennewald, Kubiak, & Weber, 2010; Patron, Messerotti Benvenuti, Favretto, Gasparotto, & Palomba, 2014). One technique to increase HRV is to manipulate breathing. Slow, paced-breathing (approximately 6 breaths/min) leads to a synchronized oscillation between respiration and heart rhythms and results in increasing heart rate variability via the interaction with the baroreflex system (Lehrer & Gevirtz, 2014). Previous research shows that repeating this technique over several weeks improved emotional health outcomes in non-clinical and clinical populations (Lehrer & Gevirtz, 2014). However, studies typically did not have an active comparison group and so it is not clear what the mechanisms of these changes were.

This technique is feasible for most people and they can learn it during a few training sessions. After the initial training, participants will take the HRV biofeedback device home - the device provides visual and/or auditory cues to the participant to control breathing and heart rhythms.

Previous research suggests that aging has negative effects on the efficacy of HRV biofeedback training (Lehrer et al., 2006). However, little is known about how aging influences the effects of HRV biofeedback training on emotional well-being. In addition, it is not clear from prior research whether the benefits of HRV biofeedback occur due to increased HRV during the sessions or due to strengthened prefrontal control over heart rate. In this study, we examine both of these questions. The results of this study will contribute to our understanding on how aging affects the relationship between HRV change and emotional well-being. In addition, this study allows us to examine the neural mechanisms underlying the HRV-emotion link.

There is a minimal risk in our proposed study. A number of previous research studies used the increase-HRV manipulation on adults, children and patient populations (e.g., people with depression, anxiety, asthma). Our decrease-HR/HRV biofeedback condition is also low risk. Certain types of meditation decrease HR/HRV while having positive emotional outcomes. Furthermore, in order to minimize adverse events in our proposed study, we will use strict inclusion/exclusion criteria for recruitment prescreening. We will exclude individuals at high risk of breathing manipulations, such as people who have history of abnormal cardiac rhythm or stroke. In the beginning of training, we will spend a few hours with each participant to monitor their breathing practice and discuss any mental and physical changes experienced by the participants. In case of any aversive event, we will report it to the IRB and reassess the continuation of study participation.

References

Geisler, F. C. M., Vennewald, N., Kubiak, T., & Weber, H. (2010). The impact of heart rate variability on subjective well-being is mediated by emotion regulation. *Personality and Individual Differences, 49(7),* 723–728. http://doi.org/10.1016/j.paid.2010.06.015

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Methods and Design

Week 1:
After telephone screening, a group of eligible participants in the same condition (HRV-increase or HR/HRV-decrease, up to 6 people) will be invited to visit the lab at the same time. 3-5 researchers will conduct this group session, which will take about 3 hours.

First, the researchers will explain the overview of the study and take any questions and concerns that they may have. This should take about 30 minutes.

Second, participants will individually fill out forms including a consent form, demographic information, and emotion questionnaires (e.g., CESD, STAI, relaxation and fatigue questionnaires). We will record their resting HRV for 5 minutes. These will take about 30 minutes.

Third, participants will be asked to complete two computer-based cognitive tasks (i.e., Stroop Task and Paced Auditory Serial Addition Test), while their heart rate, breathing, blood pressure, skin conductance and pupil size are being recorded using the lab biofeedback devices and the eye tracker. In the Stroop task, a color name (blue, green, or red) is presented on a computer monitor in a color that was either congruent or incongruent with the name. The participants' task is to press a key on the keypad corresponding to the color in which the word is presented rather than the color name. In the PASAT, the participant will be presented with single digit numbers and asked to sum the two most recent digits. The two tasks together take about 30 minutes.

Fourth, participants will be asked to complete cognitive and emotion tasks, which together take about 40 min: 1) Flanker Inhibitory Control and Attention Test, 2) List Sorting Working Memory Test, 3) Dimensional Change Card Sort Test, 4) Pattern Comparison Processing Speed Test, 5) Sustained Attention to Response Task (SART) and 6) emotion questions. The first four tests are part of the NIH Toolbox Cognition Battery. See "Watch Demo Video" in the below link for the description of each test:
http://www.healthmeasures.net/explore-measurement-systems/nih-toolbox/intro-to-nih-toolbox/cognition

The fifth test, SART, measures sustained attention. In this task, participants will be asked to respond to target stimuli (e.g., "3") but inhibit responding to non-target stimuli (e.g., "8" or any other digits). https://www.youtube.com/watch?v=gCrB3l_ffpU
The emotion questions are part of the NIH Toolbox Emotion Measures:
http://www.healthmeasures.net/explore-measurement-systems/nih-toolbox/intro-to-nih-toolbox/emotion

Lastly, phlebotomists will will collect blood samples up to 25 mL via venipuncture (http://tendertouchmobilelabs.com). Note that blood draw volume for blood donation in the US is 1 pint (~450 mL). Thus, 25 mL should be safe for our participants.

For the rest of Week 1, participants will be asked to complete short questionnaires daily (e.g., POMS, SAI, Sleep, Stress), which takes about 5-10 minutes. In addition, they will be asked to wear a wristband that monitors their heart rate continuously until the end of the study.

After the Week 1 session, we email participants once asking to provide the details of the medications that they are currently taking (e.g., dosage, uses, ingredients). They will be asked to report any changes in medications on the following lab visits (21.2). During the following lab visits, we will also ask participants safety questions, such as "Did you notice any changes in your health or well-being this past week?" to ensure their safety and well-being throughout the study (21.2). Additionally, we will ask female participants the following questions:
- Did you have a menstrual period since your last visit?
- If so, when was the first day of your period?

Week 2:
In the morning of Week 2 visit, participants will be asked to collect saliva samples at home using provided swabs, which will take a few minutes. Participants will individually visit the lab once, which will take about 3 hours.

First, the participant will be asked to fill out emotion questionnaires (e.g., CESD, STAI), and to provide saliva samples in the lab. The participant will be asked to answer a few questions about an upcoming decision-making task, which will be administered on Week 7 (e.g., If you want to split $10 between you and someone else, how much money do you offer to the other person?). Additionally, we will assess body measures including height, weight, waist and hip circumferences. This part will take about 20 min.

Second, the participant will practice a computer-based emotion regulation task, which they will be asked to do in a fMRI scanner later on. In this emotion regulation task, participants will see a series of pictures (neutral, emotional from IAPS uploaded to 21.2) while they try to increase, decrease or just feel the emotion elicited by the picture. After each picture, they will be asked to rate the strength of the emotion they are currently feeling. The practice session will take about 20 min.

Third, we will walk the participant over to DNI and put them in a scanner. The participant will complete a computer-based emotion regulation task while their heart rate, breathing, blood pressure, skin conductance, CO2 levels and pupil size are being recorded. In addition, the participant will undergo structural and functional scans while they rest. This part of the study will take about an hour and 15 min.

Fourth, we will escort the participant back to the lab. The participant will undergo the first HRV training session, which will take up to an hour. The researchers will give step-by-step training instructions to the participants using Lehrer et al.'s protocol (Lehrer et al., 2013). Please note that we will adapt the text to omit discussion of "your symptoms." For example, we will say "control your heart rate" instead of "control your symptoms." Participants in the increase-HRV group will be asked to breathe at a slow and steady

rate that maximally increases HRV (approximately 6 breaths/min). The decrease-HR/HRV group will undergo a similar procedure except that they will be asked to breathe normally. Then, the researcher will work with the participant to practice the assigned exercise using the home biofeedback devices. The researcher will ensure that these breathing manipulations would not cause any discomfort to the participant. Participants will then be asked to use the home biofeedback devices to record their heart rate variability (HRV) during a 5-minute resting period while the researchers assist them and make sure they understand the instructions.

Fifth, participants will be asked to take an olfactory test where they identify 12 different smells (e.g., orange) by choosing one of the four options (e.g., orange, strawberry, blackberry, pineapple).
http://www.usneurologicals.com/index.php?app=ecom&ns=prodshow&ref=ST_SniffinSticks

For the rest of Week 2, participants will be asked to do the assigned practice (increase-HRV or decrease-HR/HRV described above) for 10-20 min twice a day using the home biofeedback devices and record their HRV data.

Week 3:
The same group of participants formed in Week 1 will visit the lab together, once in the beginning of Week 3. This lab visit will take about 2 hours. First, the researchers will download and check their weekly data to make sure that they have completed the assigned task daily. The researcher will work with participants one-on-one to complete the assigned breathing practice using the home biofeedback devices and give them tips to increase HRV or decrease HR/HRV. For instance, the researcher will ask them to try sometimes doing the session with their eyes closed without attending to the feedback until after the session is over, to see if that works better for them. Each participant will be given a target score for the remaining days of Week 3 and will be asked to complete the assigned practice for 10-20 min twice a day using the home biofeedback devices and record their data.

The participants are allowed to talk to each other, share their experience of home practice and exchange tips. The researchers will also share how all the other participants in the same condition are doing (e.g., we will present a chart showing a completion rate of daily assignment of each participant without their identifiable information, and how many extra practices they attempted within a week), and as detailed in the payment section, give everyone an incentive if everyone has completed the target number of practice sessions - this is to encourage participants to carry out training with other participants in this study. Lastly, participants will be asked to complete some questionnaires (e.g., altruism questions) and cognitive tasks.

Weeks 4-5:
Participants will go through a similar procedure as Week 3 and get tips from the researchers regarding best practices for improving the assigned biofeedback exercise. We will also administer memory tests (see below for description). At home, they will be

asked to do the biofeedback exercises up to 20 min twice a day. Each of the weekly lab visits should last about 2 hours.

Memory tests: Participants will be asked to view a series of pictures (i.e., NAPS or IAPS in 21.2) and rate them. Sometime later, participants will be asked to indicate whether they have seen each picture or not (recognition memory test). They will also be asked to recall pictures (recall memory test). A week later when they return to the lab, participants will be asked to indicate whether they have seen each picture or not by pressing the yes or no keys (recognition memory test). They will also be asked to recall stories that they created in the previous week (recall memory test). During the task, their heart rate, breathing and pupil size may be recorded.

Week 6:
The participants will visit the lab as a group. We will record their resting HRV for 5 min using the home devices and repeat measures from Week 1 (i.e., questionnaires, Stroop, PASAT, cognitive and emotion tasks, blood draw). As a group, the participants and researchers will discuss their experience in this study. The participants will be encouraged to share as much or as little as they would like, and the researchers will take any questions or concerns that they have. This lab visit should last about 3 hours.

For the rest of Week 6, they will be asked to continue the assigned practice for up to 20 min twice a day. Participants will also be asked to continue to fill out questionnaires and wear a wristband every day.

Week 7:
In the morning of Week 7 visit, participants will be asked to collect saliva samples at home using provided swabs, which will take a few minutes. Participants will also be asked to visit the lab individually to complete the same assessments as in Week 2. The entire visit (both the lab and MRI sessions) will take about 3 hours. In the MRI session, there will be additional scans including paced-breathing (e.g., 10 sec/breath), training-mimicking and decision-making scans. The training-mimicking scan is where we ask participants to do the biofeedback exercises that they have been practicing at home. During the decision-making scan, the participant will be asked to decide whether to accept or reject monetary offers from other participants in a decision game. At the end, they will be asked about the tasks they completed and their experiences during this study.

References

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*For more details of the study protocol, see Yoo et al. (2023).

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