Quantifying the Influence of Yogic Breathwork on Cerebrospinal Fluid Circulation

Unique Protocol Identification Number: STUDY00019281

National Clinical Trial (NCT) Identified Number: NCT03858309

Principal Investigator: Selda Yildiz

Sponsor: Oregon Health & Science University

Grant Title: Quantifying the Influence of Yogic Breathwork on Cerebrospinal Fluid Circulation

Grant Number: K99AT010158

Funded by: NCCIH

November 11 2019

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1) Protocol Title

Quantifying the Influence of Yogic Breathwork on Cerebrospinal Fluid Circulation

2) Objectives

The purpose of this protocol is to determine the influence of an 8-week yogic breathwork intervention on cerebrospinal fluid (CSF) dynamics among healthy subjects using a non-invasive magnetic imaging (MRI) technique. We will examine this aim by studying the changes in each subject's pre- and post-intervention CSF dynamics using the non-invasive RT-PCMRI technique during two MRI scans (one before and one after the 8-week intervention). This aim will test the hypothesis that a regular yogic breathwork practice will enable participants to sustain slow and rhythmical breathing patterns and create larger modulations in their CSF dynamics.

3) Background

Yogic breathwork (YB) is an appealing mind-body therapy for healthcare management purposes because it is a low-risk and low-cost practice that can be easily learned and performed without any additional equipment. It is important to understand the mechanisms for the benefits of YB practices. Based on our preliminary results, we believe that another - less explored- potential mechanism for the positive effects of YB can be its direct influence on cerebrospinal fluid (CSF) circulation, which to date has not yet been quantified due to lack of non-invasive methodology.

CSF circulation. CSF, a clear colorless fluid secreted by the choroid plexuses, moves by bulk flow (*macrocirculation*) around the central nervous system (CNS), and ensures the health of the CNS[6]. Impaired CSF circulation can comprise the normal physiological functions of the CNS, which then may contribute to CNS diseases including neurodegenerative conditions[7]. Furthermore, CSF circulation plays a key role in maintaining glymphatic transportation of CSF (*microcirculation*). Recent research efforts[8,9] have defined a "*glymphatic function*", a brain-wide clearance mechanism facilitates the clearance of solutes and metabolic wastes from the brain interstitium. Sleep and arousal state are critical regulators of glymphatic function, since CSF tracer influx and interstitial solute clearance are increased during both sleep and anesthesia compared to the wakefulness[1], which is associated with slowed amyloid beta clearance and more rapid amyloid plaque deposition[2]. The impairment of glymphatic function underlies the development of CNS diseases in the aging brain remains unknown, so it is critical to better understand the complete mechanisms supporting CSF circulation in the human CNS by i) developing non-invasive approaches to measure CSF circulation, and ii) potentially identifying therapies that can regulate and enhance CSF circulation. For this aim, we recently developed novel non-invasive imaging approaches to quantify CSF dynamics [12] and we aim to study YB as a potential therapy for regulating and enhancing CSF circulation.

4) Study Design

This study is the K99 phase of the NIH-NCCIH K99/R00 study K99AT010158.

Protocol. The study protocol consists of 20 healthy young subjects undergoing an 8-week intervention (10 subjects in arm 1 and 10 subjects in the active control arm 2), and outcome measures within a 2-week period of pre-and post-intervention. We will test the hypothesis that the yogic breathwork practice with sophisticated breathing practices, compared to active control will enable participants to sustain slow and rhythmical breathing patterns and create larger modulations in their CSF dynamics.

Optimization Scans: In order to optimize the study MRI protocol, we will implement optimization scans with healthy volunteers (18-65 y-o) who will only undergo ~1-hour optimization scans including the non-invasive MRI scan (which is to be optimized for the study intervention scans). We have included a separate consent form for the optimization scan volunteers. Optimization scans will be conducted with healthy population (18-65 y-o).

Interventions. YB protocol will incorporate a set of yogic breathing practices that will create larger

modulations in CSF dynamics. Active control protocol will include slow breathing. Both 8-week interventions will consist of 60-minute weekly group on-site sessions (1day/week) with a 20-minute daily home sessions (in between on-site sessions; 6 days/week) using home-aid practice materials. We will define a benchmark of at least 8 on-site sessions and 15-min daily[13,14] home practice (4 days/week) in order to see the effects we propose. We will objectively track subjects' respiration using a wearable device, e.g., Spire[15]or Oura ring[16] We plan to buy one of each and pilot each for 2 weeks on several study team members to assess prior to the interventions. In addition, subjects will be instructed to report the frequency and duration of their daily home practice in a logbook provided.
We have tested the Spire[3] health tag and Fitbit tracker, and plan to include in the protocol to objectively determine subjects' home practice. Participants may have one or both of these devices for the study team to track participant's home practice.

Interventionists. The YB and the control intervention will be guided by two separate certified experienced yoga teachers. Prior to being involved in the study and guiding the study interventions, the two interventionists will go through the necessary trainings for human subject research and IRB protocol.

Outcome measures will be i) blood pressure, ii) body mass index (BMI), iii) CSF flow velocities measured with the non-invasive MRI technique during ~1-hour MRI scans, iv) physiological data from wearable devices. We will also review response to self-report questionnaires.

5) Study Population

a) Number of Subjects

We plan to recruit 20 healthy subjects (18-65 years; 10 for each of the two groups) from the Portland community through IRB approved flyers posted around the OHSU campus and the city, and advertised in local media. While we do not expect that any participants will voluntarily drop from the study, unavoidable circumstances may arise and we expect to retain enough participants to collect sufficient data on intervention development, decisions on the appropriateness of our instruments, and burden to participants. In order to assure we have sufficient qualitative and quantitative data for this proposed study and any potential lost-to-follow up, we may recruit 13 people for each arm.

b) Inclusion and Exclusion Criteria

Inclusion criteria: 18-65 years of age, able to provide their consent to be in the study, available and able to participate in study activities, who can lie in supine, able to walk 15 feet, who have no prior/current regular mind-body practice inducing breath awareness or training such as yoga, meditation, Ta-Chi, Qi-Gong; a compatible device for physiological data trackers.

Exclusion criteria: inability to provide informed consent, MRI contraindications, need for muscle relaxants or anti-anxiety drugs in order to tolerate MRI, history of neurological disorders, head trauma with loss of consciousness, craniospinal disorders, spinal injury, sleep disorders, allergic or respiratory disorders, major or uncontrolled psychiatric illness or major depression, lung and heart problems, any condition requiring the use of medication that acts on the brain like stimulants, sedatives current substance abuse issues, pregnancy or nursing.

Optimization Scans:

Inclusion criteria: 18-65 years of age, able to provide their consent to be in the study, available and able to participate in 1-hour MRI scan, who can lie in supine, able to walk 15 feet.

Exclusion criteria: inability to provide informed consent, MRI contraindications, need for muscle relaxants or anti-anxiety drugs in order to tolerate MRI.

c) Vulnerable Populations

This study (K99 or R00 phase) will not include any vulnerable populations. We will not collect any information about subjects' status as prisoners, and will actively exclude pregnant women, children, neonates, and adults lacking capacity to provide informed consent.

d) Setting

OHSU will be the site of operations. The study screening visits will be conducted at OHSU's Hatfield Research Center. The outcome measures will be conducted at the OHSU's Advanced Imaging Research Center (AIRC). The yogic breathwork and active control interventions will take place at the OHSU's March Wellness Center.

e) Recruitment Methods

All recruitment materials will be IRB approved before utilization including those intended for posting to online media. The study will be posted on OHSU's Study Participation Opportunities Website, Oregon Brain Institute email list serve, and Oregon Center for Clinical and Translational Research Institute (OCTRI)'s Research Match for Recruitment. Flyers will be distributed at the OHSU's New Employee Orientation, which occurs bi-monthly, in employee break rooms at both OHSU and the adjacent VA Portland Health Care System Hospital, in student centers, OHSU's March Wellness Center, OHSU affiliated buildings, community centers and libraries in Portland. Recruitment will tap into a research subject Healthy Control Registry that is managed by the OCTRI. We will also consider posting flyers on social media (Facebook recruitment through group pages -TBD). We will consider recruiting any interested individual in the larger Portland, and surrounding communities, but will not be able to supply funds for non-local travel for the purposes of participation.

Payment for participation.

All enrolled subjects will receive payment in gift cards to offset the time and inconvenience involved in participating in this study.

f) Consent Process

For this study, the study staff will need to receive both identifiers and health information. The study subjects will be screened for preliminary eligibility prior to consent in order to avoid the expense, time, and effort having each potential candidate travel to OHSU. All potential subjects will be asked to sign an OHSU IRB approved informed consent form prior to study participation. At the time of screening, the potential subject will be encouraged to contact study staff with any questions before their consent visit.

During the consent visit, the investigator or designee will explain the research study to the subject and answer any questions that may arise. Extensive discussion of risks and possible benefits of study participation will be provided to all potential subjects. An IRB-approved consent form describing in detail the study procedures and risks will be given to the subject. Project staff will review the informed consent with the potential subject providing ample time for the potential subject to read the consent as needed. The consent process will include a verbal review of the contents of the consent form with particular emphasis on the participation activities, possible risks and benefits, research subject rights, and the voluntary nature of the research. Subjects will be given the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The subject will sign the informed consent document prior to any study-related assessments or procedures. A copy of the signed informed consent document will be given to subjects for their records. Subjects may withdraw consent at any time throughout the course of the study.

To complete the informed consent process at the end of study participation, study staff will inform the subject when his/her participation has come to an end and will document the discussion in the study record.

Non-English Speaking Subjects

This study will not specifically recruit non-English speaking individuals.

Assent of Children and Parent Permission

This study will not include children.

Adults Unable to Consent/Decisionally Impaired
Subjects unable to provide informed consent, decisionally impaired subjects, subjects with cognitive impairment will not be included in the study. Study staff will be instructed to repeat key points, use simple language, and ask targeted questions when seeking informed consent from people. Example questions might be, “Can you tell me in your own words what this study is about?” or “Can you tell me how risks for this study might affect you personally?”

6) Procedures
All procedures involved in this study will be conducted as research rather than standard of care procedures. Study team will monitor the procedures. The study protocol consists of 20 healthy subjects undergoing the 8-week interventions (10 in each of the two groups), and outcome measures within a 2-week period of pre-and post-intervention.

Subjects will have an initial visit of approximately 1-hour for the purposes of informed consent, review of eligibility criteria, and to receive instruction regarding the study visits.

If enrolled, each subject’s first pre-intervention data collection will involve blood pressure, BMI, response to self-report questionnaires, an hour of MRI scan including CSF flow measurements. Subjects additionally will be provided with a wearable device in order to track home practice respiration objectively over the 8-week intervention. Subjects who successfully complete pre-intervention study procedures will go through an 8-week intervention while attending weekly on-site sessions, continuing daily home practice, and using the wearable device for respiration tracking. At the end of the 8-week intervention, we will collect post-intervention outcome measures that will involve the same measures as in pre-intervention visit. Subjects will be instructed to return their wearable device during the post-intervention visit.

Subject participation. It is expected that the K99 study first participant enrollment will begin by October 2019, and that the human subject’s activity, including all interventions and follow-up visits, will be completed approximately by March 2020.

Subjects may be withdrawn from research if they no longer qualify for the study or if anything is discovered that might increase the risks involved for them to complete the study procedures (e.g. high fever on the day of scan, pregnancy, or usage of contraindicated medication, inability to attend intervention sessions, etc.)

If a subject decides to terminate their participation in this research project, any partial data that may have been collected for them may still be analyzed unless they also withdraw their consent for use of their data.

Study Procedure Details.

	Visit 1 Consent	Visit 2 MRI	Visit 3-10 Intervention	Visit 11 MRI
Consent Discussion, Screening, and Study Education	X			
Review of Consent and Screening		X		X
Vitals: Temp, BP, BMI		X		X
MRI		X		X
Physiological measures during MRI		X		X
Questionnaires		X		X
Breathing Practices			X	
Physiological Data Tracking			X	
Total time	1-hour	Up to 3 hours	Up to 24 hours	Up to 3 hours

Table 1: Onsite Visit Activities

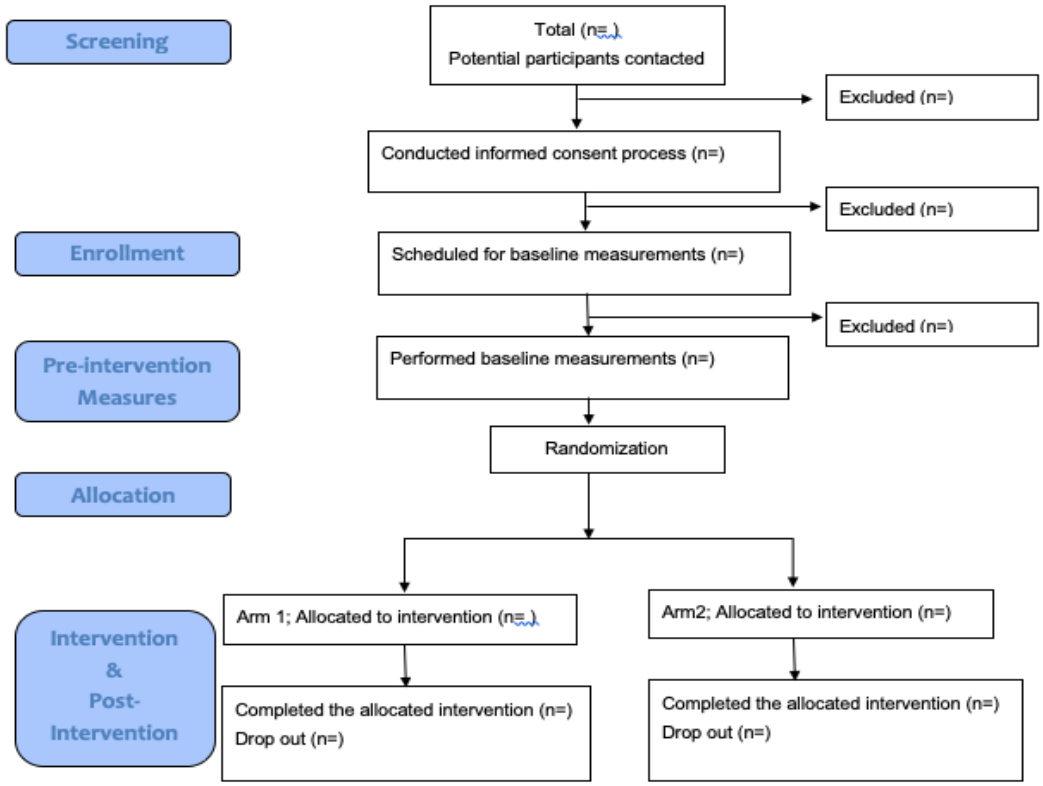

Figure 1: Flow diagram

Phone screening. Potential subjects will be contacted by the study coordinator via telephone to prescreen.

Consent visit. The study coordinator will discuss the informed consent with the subjects as described earlier in this protocol. Subjects who agree to sign the informed consent will be asked to:

- review their inclusion/exclusion criteria including relevant medical history.
- review their current medications for inclusion/exclusion criteria.
- complete an MRI Safety Questionnaire.
- complete an emergency contacts form and an ethnicity questionnaire.
- schedule or verify a tentative date for scheduling their imaging visit.
- receive instructions on how to use the wearable device.

Enrollment and Scheduling. Subjects who are eligible for the study will be enrolled in the study, and will be scheduled for their first imaging visit. Those determined ineligible will be let known why they are not eligible for the study participation.

First imaging visit. Members of the study team will be present for the duration of the data acquisition at OHSU's AIRC.

Ongoing Consent and Safety Screening:

- The study coordinator will review the informed consent and documents collected during the first visit to make sure nothing has changed regarding the subject's eligibility.

Brief Baseline Physical: The trained study member will obtain participants' vital measurements. Subjects within the acceptable vital measurements will receive instructions for the yogic breathing techniques to be performed in the MRI instrument.

MRI Scan:

- After performing the instructed breathing practices, subjects will be instructed to remove all metal on themselves, and will be transferred to the 3T MR instrument.

- Subjects will be instructed to lie still in the supine position during the entire data acquisition.
- Sufficient padding will be provided to minimize head motion artifacts and prevent discomfort.
- Subjects will be provided blankets for warmth.
- MR acquisitions will include anatomical measures and non-invasive CSF flow measures.
- At the end of the MRI scan, a visit questionnaire will be administered to provide the subject with an opportunity to let the study team know how the MRI scan experience was and if there were any problems that need to be addressed.

  Self-report questionnaires:
  - We will assess each subject's response to the following self-report questionnaires during their imaging visits: quality of life (Short-Form Health Survey; SF-36[17]), sleep quality (Pittsburgh Sleep Quality Index; PSQI[18]), perceived stress (Perceived Stress Scale; PSS[19]), Positive Affect Negative Affect Scale - Expanded (PANAS-X)[20], The Patient-Reported Outcomes Measurement Information System (PROMIS)[21], and Cognitive and Affective Mindfulness Scale-Revised (CAMS-R)[22]. Additionally, we will assess subject's attitudes, expectancy and blinding towards the study.

  Physiological Data Tracking:
- *Respiration:* Each subject will be provided with a wearable device in order for the study team to objectively track subject respiration, thus home practice, throughout the intervention. For this purpose, we will use a commercial off the shelf monitor (Spire[3]) . Study staff will assure that these devices remain free of potential identifiers. We will create a respiration tracker account for each user. Subjects will receive instructions on how to utilize the wearable device during the first imaging session.

  Sleep: A sleep tracking methodology may be implemented within the study to investigate the effects of the intervention on long-term sleep patterns – using a Fitbit tracker. Study staff will assure that these devices remain free of potential identifiers, and will create a sleep tracking account for each subject. Subjects will receive instructions on how to utilize the wearable device during the first imaging session.

Randomization. Subjects will be told they will be enrolled in one of the 8-week intervention groups for a set of breathing practices. Group allocation will be performed through a sex and age-based randomization by a study team member who will inform the subjects with which group they will be enrolled in. Neither the subject nor the investigator can choose which group the subject will be in. Subjects will be instructed and reminded not to reveal what group they are in during the study assessment visits. They will be instructed to ask the investigator if they have any questions about this kind of study.

i. 8-week *interventions*.

Breathing practices:
- The yogic breathwork protocol will incorporate breathing practices that will create slow deep rhythmical and large CSF flow patterns. Active control protocol will include slow breathing practices.

Interventions:
- Both 8-week interventions will consist of 60-minute weekly group on-site sessions (1day/week) with 20-minute daily home sessions (in between on-site sessions; 6days/week) using home-aid practice materials.
- We will define a benchmark of at least 8 on-site sessions and 15-min daily[13,14] home practice (4 days/week) in order to see the effects we propose.
- We will objectively track subjects' respiration using the wearable device that were given to subjects during the first imaging visit.
- In addition, subjects will be instructed to report the frequency and duration of their daily home practice in a logbook provided.

ii. *Second imaging visit.* The procedures will be as described in "first imaging visit". Subjects will return their wearable device during this visit.

iii. *Study Follow up:* We may ask study subjects to follow their health and breathwork practice

after the intervention, if any, through the use of phone calls or emails three times for up to 6 months. Follow up questionnaire is uploaded.

iv. ***End of study participation.*** After completion of the second MRI visit, subjects will be asked to complete a set of final questionnaires to let the study team know how their study experiences were and if there were any problems that need to be addressed. These final questionnaires will include a set of post-intervention questions about instructor credibility, breathwork practice feedback, qualitative end point. Documents are uploaded.

v. ***Future research studies:*** Subjects will be asked for participation in future research studies.

7) Data and Specimens

a) Handling of Data and Specimens

The data collected for this study will include health information in the form of current medications, personal and family medical history, and current medical and mental health status to facilitate study screening and define subject variation. Contact information will be gathered to allow scheduling, and follow up. Subjects' blood pressure, body mass index, response to self-report questionnaires, MRI data, ECG and respiration data will be compiled within the study records.

If we find out that our data needs to be saved for future research and/or sharing to other projects, we will revise the protocol to include the necessary repository elements. In that case, we may also use subjects' correlation of data with future studies through a repository.

OHSU will be the site of operations for this project. Study pre- and post-intervention outcome measures will be performed within the OHSU's Advanced Imaging Research Center (AIRC). Physical data will be stored within the AIRC's key card secured facilities within a locked cabinet when not in use. Electronic data will be stored on restricted drives on the OHSU network, within encrypted computers, and in a web-accessible REDCap database hosted on an OHSU server. AIRC has a plan for routine back-ups of all data, including encryption and physical security addressed.

Upon enrollment, subjects will be assigned a code that will be used instead of their name or other personally identifying information. Electronic files for data analysis will contain only the subject code. Codes will not contain any part of the 18 HIPAA identifiers (initials, birthdate). The key associating the codes and the subjects personally identifying information will be restricted to the PI and study staff, who must have OHSU IRB approval and therefore the OHSU required training in HIPAA compliance, in the basics of conducting research at OHSU, and in federal, state, and university requirements for conducting human subjects research.

The key will be kept secure on a restricted OHSU network drive in a limited access folder. Encrypted data transmission will be used to share data with the study team. IRB approved study staff will be responsible for gathering study data, for coordinating its analysis, and for its archiving within the data repository in the case our study needs a repository. Data then will be shared to the repository or other investigators by transfer within the secure OHSU network drives. If identifiable data is to be transported in any other way, it will be done by hand or by secure courier with signature confirmation of receipt. All data will be kept for a minimum of three years after the study has ended and stored in a secure OHSU electronic database that has fully patched operating systems and applications including current antivirus software with current virus definitions.

b) Sharing of Results with Subjects

- Subjects will be told in advance of participation that the research data gathered for this study is not intended for diagnoses. Results from this study are experimental in nature and will not be provided to subjects. However, if we discover information that is important for subject health care and/or if there are any significant baseline health risk factors for the subjects, this information will be conveyed to the subjects.

- Subjects will be asked if they want to know the results. Subjects may need to have additional testing in a non-research laboratory. For non-emergency issues, subjects will be referred to their primary care provider. If they have no primary care provider, reference to three providers will be given. They would be responsible for all costs associated with any follow-up testing and medical care.

- The MRI scan is being done to answer research questions, not to examine to subject's brain for medical reasons. The research MRI scan may not show problems that may be picked up by a clinical MRI scan. Any incidental findings during the MRI procedure will be communicated to the subjects. If we find an abnormality that requires urgent follow-up, we will contact subjects to help answer questions and get the right follow-up care for them. Subjects may learn information about their health that is upsetting or impacting their life in other ways.

- To minimize risks related with privacy and confidentiality, all study staff will be trained with regard to the aforementioned strict procedures and policies.

c) Data and Specimen Banking

All study data and identifiers will be banked in a repository and may be used for future research.

Access to the code list will be restricted to the repository PI and study staff. These repository personnel will have full access to the banked identifiers and coded data. Access to coded data, without any PHI, may be provided to outside investigators. IRB approval is required for release of identifiable data from this repository to outside investigators.

8) Data Analysis

Data Analysis Plan

All data recordings and analyses will be performed at OHSU. The PI will be the primary monitor working alongside the other members of the research team. MRI data quality will be assured by the MRI technologist acquiring the study. The study team will record technical notes if quality issues are present that might affect data analysis outcomes.

Post-acquisition, each data set will be examined for quality and completeness by the trained study team.

CSF flow:

- CSF flow data analysis will be performed using a semiautomated pulsatility-based segmentation procedure. The velocity waveform will be averaged over the highly correlated ROI pixels. The maximum and minimum peak values of the averaged CSF flow velocities will then be used for analysis (see details below *Statistical Analysis*).
- The respiration frequency band and the cardiac frequency band will be defined based on the two main distinct peak amplitudes of the frequency spectrum of the averaged CSF velocity waveforms measured with RT-PCMRI.
- The relative contribution of the respiration versus cardiac component of the CSF velocity waveforms will then quantified by defining a power ratio between respiratory component and the cardiac component.

Respiration and ECG data:

- The pulse ox and respiration data collected during the RT-PCMRI acquisitions will be filtered using a 4th order Butterworth to extract only the respiration and only cardiac component.

Wearable device:

- Respiration data from wearable device collected during the 8-week intervention will be analyzed for the respiration rate and peak-to-peak respiration intervals. If collected, sleep data measured with wearable device will be analyzed to measure the influence of intervention on participants' long-term

sleep patterns objectively.

Self-report questionnaires:

- Response to self-report questionnaires will be analyzed for the statistical analysis to compare the changes in subject's quality of life, sleep, and existing stress levels.

Statistical Analysis

- The major dependent variables will be i) CSF flow metrics maximum and minimum (values of average CSF velocities; relative ratio of respiration vs. cardiac component of the CSF velocity; ratio of the maximum CSF velocity during breathing practices to the average of peak CSF velocities at baseline during natural breathing, ii) respiration rate and peak-to-peak respiration intervals and iii) self-reported questionnaire results. The effects of the interventions on these variables will be tested in a multivariate analysis of variance with repeated measures to compared pre- and post-intervention. An alpha value of 0.05 will be used for statistical significance.

9) Privacy, Confidentiality and Data Security

Prior to working within this study, all study members must have OHSU IRB approval and therefore the OHSU required training in HIPAA compliance, in the basics of conducting research at OHSU, and in federal, state, and university requirements for conducting human subjects research. Each member of the study team who will interact with participants, collect qualitative and quantitative instruments will be trained on addressing any participant questions.

Physical data will be stored within the AIRC's key card secured facilities within a locked cabinet when not in use. Electronic data will be stored on restricted drives on the OHSU network, within encrypted computers, and in a web-accessible REDCap database hosted on an OHSU server. AIRC has a plan for routine back-ups of all data, including encryption and physical security addressed.

Any email containing private information, referrals for recruitment for instance, will be encrypted.

At screening, participants will be assigned a unique subject identification number. Wherever possible, documents and data used in the study will be identified only by use of the participants' unique identification code. A master key list containing the subject's names and other identifiers alongside their study identification numbers will be password protected so that only the study team will have access. Any study materials with the subjects' names or other identifiers on them (informed consent forms, recruitment response slips, emergency contacts) will be stored away from the coded subject files in a locked file cabinet.

During this study interventions, subjects will be videotaped / photographed for research/educational purposes, such as for supervision of interventions by the study team, and/or marketing purposes.

- The 60-minute on-site sessions will be videotaped by a study team member for study team's educational / research purposes.
- If subjects do not want their photographs be used for any purposes such as research/marketing publications, they will be instructed to inform the study team.
- If the study team uses a subject's photographs/recordings for research publications or marketing purposes, a black bar may be placed over subject's eyes and/or subject's voice may be disguised at their request/permission.
- If the study team uses a subject's photographs/recordings for a research publication or marketing purposes, the study team may or may not be able to inspect the photographs/recordings before they are released.

10) Risks and Benefits

a) Risks to Subjects

The potential risks to subjects in the proposed research are minimal. They include the following:

- Self-reported questionnaires can cause mild anxiety.
- Interventions can cause mild anxiety or discomfort. Caution will be taken by the interventionists (who are experienced certified yoga teachers) during the classes. Participants will be monitored

at frequent intervals during the study and will be followed for a sufficient period of time after the procedure to ensure stabilization of any distress/strain associated with the intervention, and for any expected and unexpected adverse events related to intervention.

- Participants may experience physical or psychological discomfort while lying supine in the MRI instrument during the MRI experiments. The non-invasive nature and the lack of ionizing radiation make the risks associated with MRI small. FDA guidelines regarding MRI usage will be strictly followed. The MRI procedure will be explained to the subjects while standard safety procedures to remove metal from the patient and screen them for MR unsafe devices will be done. Voice contact with patients will be maintained throughout the scan. The MRI makes loud beeping or thumping noises so all subjects will be offered protective earplugs to wear during scanning. To ensure subject comfort, subjects will be provided with extra paddings around head, bolsters under knees and elbows, and blankets for warmth.
- Confidentiality: Although we have made efforts to protect subject identity, there is a small risk of loss of confidentiality.

Pregnant women and children are excluded in this study.

b) Potential Benefits to Subjects

Subjects will not directly benefit from taking part in this research other than potential benefits of participating in an 8-week intervention, which may enhance quality of life, quality of sleep, and reduce existing stress.

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