MUSE Device to Improve Sleep Quality in Midlife Women

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IRB Minimal Risk Protocol Template

General Study Information

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Study Title: MUSE Device to Improve Sleep Quality in Midlife Women

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Research Question and Aims

Hypothesis:
We hypothesize that the daily use of the Muse-S headband system will be an effective strategy for improving the sleep quality in peri- and postmenopausal women. We anticipate that the women who utilize the Muse-S headband will have improvements in time to sleep onset and sleep maintenance. We also anticipate a positive correlation between duration and frequency of use of the device and the improvement in sleep quality.

Aims, purpose, or objectives:

1. To obtain preliminary evidence regarding the feasibility of using the Muse-S headband system for management of sleep disturbances in peri- and postmenopausal women.
2. To obtain preliminary data on the effectiveness of the Muse-S headband system for management of sleep disturbances in peri- and postmenopausal women and to ascertain whether duration of treatment impacts efficacy.
3. To obtain preliminary data on the effectiveness of the Muse-S headband system in improving secondary outcomes of sleep quality including stress levels, mood and sexual function.

The overarching purpose of this study is to obtain preliminary evidence regarding the efficacy of the Muse-S headband system for management of sleep disturbances (insomnia and sleep disruption) in midlife women. This goal will be achieved with the following specific aims:

Objectives: The overarching goal of this project is to test the feasibility and efficacy of the Muse-S™ Headband, an electroencephalographic device, in management of sleep disturbances in midlife women.

Background:
Sleep problems (insomnia and sleep disruption) affect nearly half the women during the menopause transition and the postmenopausal years. The etiology of sleep disturbances in peri- and postmenopausal women is

multifactorial, resulting from a combination of the direct effect of decline in estrogen level, vasomotor symptoms, mood changes, and chronic pain, among others. It is estimated that there will be 90 million postmenopausal women in the US by the year 2060. Therefore, untreated menopause-related symptoms, including sleep disturbances, have the potential to be a significant public health problem. Unlike several other symptoms of menopause, sleep disturbances often do not improve as the women get farther into menopause. Chronic sleep disturbances have multiple adverse health consequences including negative impact on mood, cognition, work performance, sexual function, and the overall quality of life. There is fairly strong evidence linking chronic sleep disturbance with weight gain and obesity in midlife women. Finally, sleep disturbances are also associated with increased risk for cardiovascular disease (CVD), including greater odds of hypertension, coronary artery disease, and stroke. Given that CVD is the number one killer of postmenopausal women, the importance of managing CVD risk factors cannot be overemphasized in this patient population.

Although prescription therapies such as menopausal hormone therapy, antidepressants, and hypnotics are effective in treating menopause-related sleep disruption and chronic insomnia, many patients avoid their use due to concerns regarding adverse effects, contraindications, or personal preference. The potential for increased breast cancer risk with extended hormone therapy use has caused a dramatic decline in the rates of hormone therapy use. As such, menopausal hormone therapy is not indicated for management of isolated sleep disruption (in the absence of significant vasomotor symptoms) in midlife women. There are concerns regarding side-effects and long-term toxicity even with the non-hormone prescription medications, particularly with chronic use, which is often needed in this condition. Not surprisingly, women frequently have reservations about using medications to manage sleep on a long-term basis. Therefore, investigating non-prescription therapies for management of this common condition in midlife women is of utmost importance.

Behavioral interventions, specifically cognitive behavioral therapy, exercise, and mindfulness/relaxation have been shown to be safe and reasonably effective for management of insomnia and sleep disruption in midlife women. These are typically the first line interventions for management of sleep problems in midlife women. However, the evidence supporting the use of these interventions in midlife women is somewhat weak with a need for further research identified by the experts. Moreover, some of these interventions can be difficult to access, limiting their use. Women can also find it hard to engage in meditation. There is a need to study novel behavioral interventions for management of sleep disruption in midlife women that overcome some of the barriers with the existing treatment modalities. The Muse-S™ headband offers an opportunity to fill this gap by giving patients real time biofeedback with electroencephalogram (EEG) technology to guide them and build confidence in their abilities to incorporate meditation in their daily habits. Once calibrated to an individual, the Muse-S headband distinguishes between active and calm brain states to provide real time performance feedback. This is achieved by converting EEG signals, measured over the frontal and temporal cerebral cortices, into measures of the state of the brain (active versus calm). This biofeedback allows for real time reinforcement of successful meditation. Additionally, the device is portable and easily accessible to the public making it a viable behavioral therapy intervention for patients. The Muse-S headband is being used in studies in the division of General Internal Medicine on patients after breast cancer surgery, those with pain-related to fibromyalgia, and in healthcare providers who are experiencing stress.

The proposed study will assess the impact of the Muse-S headband on the sleep quality in peri-and postmenopausal women experiencing subjective sleep disturbances. The study will also evaluate the impact of the Muse-S headband on the secondary outcomes of mood,quality of life, stress, and sexual function. These

parameters are often negatively affected by poor sleep, and therefore improvement in sleep quality is likely to impact mood, anxiety, quality of life, stress and sexual function favorably.

Study Design and Methods

Methods:

All study participants will receive a new Muse-S headband system at study entry and will be asked to utilize it daily for a minimum of 10 minutes day for a period of 6 months (24 weeks). Three of the seven sessions per week will specifically be asked to be mind meditation.

The participants will be provided instructions on setting up the device and connecting it to their smart device. They will also receive general education on the different features of the Muse-S Headband. They will have access to specific education on meditation. They will also have access to sleep tools on their app.

The participants will complete the ASCQ-Me Sleep Impact-Short Form, Epworth Sleepiness Scale and Sleep Quality Assessment PSQI for evaluation of their sleep. In addition they will also completed the the Patient Health Questionnaire (PHQ-9), Generalized Anxiety Disorder Scale (GAD-7), Female Sexual Function Index (FSFI) and Female Sexual Distress Scale (FSDS-R), Quality of Life- (LASA), Perceived Stress Scale (PSS) and Resilience- (CD-RS10). Quality of Life, mood, anxiety, stress and sexual function are often negatively impacted by poor sleep.

The weight, body mass index and blood pressure will be obtained from the MWSHC, Community Internal Medicine, Executive Health, or Family Medicine visit data at 0 and 6 months.
The data will be recorded in REDCap at baseline, 3 months, and 6 months.

All study participants will have access to The Muse-S™ Headband system's customer service team based in Toronto, Canada, by telephone and email for assistance should they experience technical problems with the device.

Server Data: As the subject completes any Muse-SÔ sessions, the information from these sessions will be uploaded to the Muse-SÔ ICloud servers hosted by Google. Each subject will be able to see their own data at the end of each session, and data from the previous session stored in the "me" tab in the app. Subject to the study organizers ensuring that the subjects have signed the appropriate consents, study organizers will have access to each subject's data to monitor compliance, performance and outcomes, but will not get access to Journal entry information (if subject chooses to write a Journal entry). These data that the study organizers will have access to may include the study-specific identification number, gender, and age of the subject, the session type, the time and duration of each session, EEG data, heart rate (PPG) data, and the performance per session. Interaxon's privacy policy, which can be found at

[redacted] will apply to Interaxon's use of the subjects' data. To maximize protection of the individual's privacy, the study organizers will ensure that the subjects are assigned anonymized email address and names for use in the Muse -SÔ application and when contacting the Muse-SÔ customer support. To ensure that no health data is shared with Interaxon, the study organizers have agreed to ensure that no health data will be shared with Interaxon. At the end of the study, the data collected in Google ICloud Server associated with study email addresses will be deleted.

Subject Retention

Participants will not be remunerated for participating in this study, but they will be allowed to keep the Muse-S headbands.

Study Design

We will use standardized procedures to ensure uniform instructions and support for all subjects for the recruitment, screening, and study entry.

Recruitment:

Women that come to the Menopause and Women's Sexual Health Clinic (MWSHC), Community Internal Medicine, Executive Health or Family Medicine at Mayo Clinic Rochester, who are identified as having significant sleep disturbance based on a standard questionnaire used for assessment of sleep quality and duration- the Pittsburgh Sleep Quality Index (PSQI) score >5 are recruited to the study based on the inclusion/exclusion criteria. If the participant is interested in the study the clinician will notify the study coordinator of participants eligibility, study coordinator at that time will set up a designated time to sign consent and get the participant enrolled in the study.

Participants will not be reimbursed for their time spent in the study, but all participants will be given the option of keeping the Muse-S™ Headband system for continued use post study participation.

Consent and Screening:

Study coordinator will meet with the potential participant who has expressed an interest in participating in the study. They will begin by introducing the study details, and after determining that the subject has continued interest in study participation, will move on to the study consent. If the subject chooses to consent, they will screen the participant for study entry inclusion/exclusion criteria. If the study entry criteria are met, the subject will begin their study participation. They will be asked to complete the study questionnaires.

Please note: Participants must have access to an iOS or Android capable device to take part in this study in order to interact with the Muse-S™ Headband system.

Treatment phase:

During the first three months of study, participants will be asked to complete the intervention portion of the study using the Muse-S™ headband. If the MUSE device is not being used at least 3x a week for 10 minutes a day, the participant may get a reminder email or a phone call to remind them to use the Muse-S™ headband

system. Participants will receive an email link at 90 days from REDCap to complete their questionnaires for the study.If not completed in a timely manner there will be reminders by email and/or phone to complete.

Study Follow-Up Visit:
The study will consist of follow up at 3 month and 6 months.

3 month (questionnaire only visit): questionnaires will be sent via email **NOTE:** once questionnaires are complete the study coordinator will check the PHQ 9 score the same day the participant completes the questionnaire via the electronic link. The coordinator will immediately notify the investigators if the score is severe or subject indicates suicidal ideation. The investigators will contact the patient immediately (same day) and if there is concern for active suicidal thoughts, they will recommend the patient pursue emergency evaluation (such as local ED or 988 suicide prevention hotline) or contact local authorities for a welfare check if the patient declines. If severely depressed but no active thoughts of self-harm/plan, we will recommend an appointment with their PCP, EAP (if Mayo Employee) and offer the resource Psychology Today to help find a mental health provider.

6-month (on-site visit /phone visit): Consists of a study coordinator visit at Menopause and Women's Sexual Health Center for a final weight, body mass index, blood pressure check and questionnaires for local participants. Participants that are not local or cannot make an on-site visit, questionnaires will be sent by email to be completed and a phone visit will be scheduled with study coordinator. **NOTE:** The PHQ 9 questionnaire will be reviewed at the time of the visit. If the score is severe (20-27) or the subject indicates suicidal ideation the investigators (Taryn and Amber) will be notified and will discuss with the patient. If concern for active suicidal thoughts, the investigator will initiate immediate emergency evaluation. If severely depressed but no active thoughts of self-harm/plan, we will recommend an appointment with their PCP, EAP (if Mayo Employee) and offer the resource Psychology Today to help find a mental health provider.

Subject Information

Target accrual: 50 women

Subject population (adults):
This will be an open label single-arm clinical trial that will recruit **50 peri- and postmenopausal women** from the Menopause and Women's Sexual Health Clinic (MWSHC), Community Internal Medicine, Executive Health, or Family Medicine at Mayo Clinic, Rochester, who are identified as having significant sleep disturbance based on a standard questionnaire used for assessment of sleep quality and duration- the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a 19-item questionnaire making up 7 clinically derived component scores. Each of the 7 clinically derived components is given a score from 0-3 to obtain a total score ranging from 0-21. Higher scores indicate worse sleep quality, with a **PSQI score >5 indicating poor sleep quality**.

Inclusion Criteria:

- Women between the ages of **45-65 years** (women in the menopause transition or in menopause, based on clinical assessment)
- **PSQI score >5,** with overall sleep quality rating of "fairly bad" or "very bad".

- Motivation VAS score equal to or greater than 5 with overall motivation rating of on a scale of 0-10 with 0 being not motivated at all and 10 being extremely motivated
- Access to an iPad, iPhone, or android device
- Have ability to provide informed consent

Exclusion Criteria:

- Suspected oruntreated obstructive sleep apnea
- Moderate to severe vasomotor symptoms warranting prescription medication use. The FDA categories for hot flash severity are classified as mild (sensation of heat without sweating), moderate (sensation of heat with sweating, able to continue activity), or severe (sensation of heat with sweating cause cessation of activity).
- Use of hormone therapy or hypnotic agents
- Use of supplements known to affect sleep
- A known, active, untreated clinically significant psychiatric condition
- Use of an investigational drug within 30 days of study enrollment or presence of a known history of any condition or factor judged by the investigator to preclude participation in the study or which might hinder adherence.
- Currently (within the past 3 weeks) been practicing mindfulness training on a weekly/regular basis

Potentially eligible participants will be identified from the MWSHC, Community Internal Medicine, Executive Health, or Family Medicine, where midlife women are evaluated for menopause and sexual health-related concerns. All the women seen in these areas willcomplete multiple questionnaires as part of their clinical evaluation, including the PSQI. They also complete questionnaires assessing mood (Patient Health Questionnaire 9, PHQ-9), anxiety (Generalized Anxiety Disorder 7, GAD-7), and sexual function (Female Sexual Function Index, FSFI and the Female Sexual Distress Score-Revised, FSDS-R), Quality of Life- (LASA), Perceived Stress Scale (PSS) and Resilience- (CD-RS10).

Review of medical records, images, specimens

☒ The study involves data that exist at the time of IRB submission and data that will be generated after IRB submission. Include this activity in the Methods section.

Data Analysis

Data Analysis Plan:

Demographic characteristics are described using mean and standard deviations or frequencies and percentages based on the type of variable. For the primary aims being the feasibility and efficacy of the MUSE device, descriptive statistics and graphical displays will be presented for data obtained on frequency and duration of use over the treatment time of six months. A linear mixed model with repeated measures for each time point that

stress and sleep were taken. That information will be utilized to estimate the association between the average of time spent using the Muse-S with the stress and sleep level outcome. As secondary aim, the results of questionnaires for stress levels, mood and sexual function will be analyzed using the same linear mixed model with questionnaires being done at different intervals of the study to determine changes over time. Given the number of outcomes assessed, all analyses will be considered exploratory.

Endpoints:

Primary Hypothesis:

- The regular use of the Muse headband will increase quality and quantity of sleep.

Secondary Hypothesis:

- The regular use of the Muse headband will decrease perceived stress levels, decrease anxiety, and improve sexual health.