Targeting Worry to Improve Sleep

NCT03684057

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Procedures:

Individuals will be recruited primarily via online advertising (e.g. Facebook and Google AdWords). Those who learn about the study via social media will be prompted to complete an online screening questionnaire. Those who learn about the study via other means (e.g. flyers, word of mouth) will review the questions from the online screener during the initial screening phone call. After the screening call, eligible participants will be scheduled for their baseline visit at the Brown Mindfulness Center (1 Davol Square, Suite 203). Study staff will send potential participants a copy of the consent form to review prior to the baseline visit. Participants will be asked to complete four study visits in total: three visits will be in-person and one will be completed online.

At the baseline visit, potential participants will be asked to review the consent form, ask any questions they may have about the study and if they decide to participate in the study, they will be asked to sign the consent form. Study participants will be given a copy of the signed consent form for their records.

Randomization Plan: A research team member who is not involved with the study will prepare sealed envelopes with an individual's group assignment using a block randomization scheme designed by an independent statistician. After the consent process and prior to administration of assessments, study participants will be randomized into one of two groups: 1) Group A – the treatment as usual group; 2) Group B - the UA intervention group. The participant will be given a sealed envelope and asked to open it to determine their group assignment.

Based on the participant's group assignment, the research team member will pull up the appropriate survey in Qualtrics and ask the participant to complete the first portion of the baseline assessment. After they have concluded, they will be instructed on how to complete the shape-matching task and then left alone to complete it on the study laptop while the researcher keeps track of the time from outside.

Upon completion of the assessments, the participant will be instructed to download either the Fitbit app (Group A) or Unwinding Anxiety and the Fitbit app (Group B). Please see below for onboarding specific to group assignment.

<u>If the participant is randomized to Group A</u> - They will be given a Fitbit Inspire to track the quality of their sleep and asked to download the Fitbit app to their smartphone. They will be provided with the information necessary to set up their account and instructed how to use the app to track their sleep. Please refer to the included script, *Fitbit Setup Guide* attachment*,* for more details. They will be asked to wear the Fitbit and record what time they went to bed & woke up in a sleep diary (which will be provided) for one week after the baseline visit, one week before the 3rd visit (in-person), and one week before the 4th visit (in-person). The total number of hours slept per night will be collected for the post-baseline period in Qualtrics via a personalized survey link while data will be collected in person for the other two use periods and recorded in Qualtrics. Upon completion of the third assessment, the UA app will be downloaded to his/her smartphone at no cost and with lifetime access. The participant will be instructed to watch the first module of the app and will review its features with the research team member to ensure they do not have any questions (see *UA Setup Guide* attachment for more details).

<u>If the participant is randomized to Group B</u> - They will be given a Fitbit and the process outlined above will be followed. In addition, the UA app will be downloaded to his/her smartphone and the same process will be followed as outlined above.

Both groups are expected to complete the following tasks / assessments at each research visit:

<u>Baseline – In-person</u>

- Group A will complete the first eight items using a personalized survey link (based on participant ID) via Qualtrics

- Group B will complete the first seven items using a personalized survey link via Qualtrics and the seventh, the GAD-7, will be completed as part of the Unwinding Anxiety assessment.

- Both groups will complete the shape matching task on a study laptop.

1. Demographics. This form will be filled out in Qualtrics (age, gender, socioeconomic status, employment, education, race/ethnicity, relationship status) (approximately 3 minutes)

2. Five Facet Mindfulness Questionnaire (FFMQ) non-reactivity scale. The non-reactivity scale is a subscale of the 39-item FFMQ which is a self-report psychological measure of mindfulness skills. This subscale contains 7 items which are presented on a 6-point Likert scale ranging from 1 (almost always) to 6 (almost never). This questionnaire is included in the protocol. (approximately 1 minute)

3. Penn State Worry Questionnaire (PSWQ). The PSWQ is a 16-item self-report measure of worry with items presented on a 5-point Likert scale ranging from 1 (not at all typical of me) to 5 (very typical of me). This questionnaire is included in the protocol. (approximately 3 minutes)

4. Multidimensional Assessment of Interoceptive Awareness (MAIA). The MAIA is a 32-item self-report questionnaire comprised of 8 subscales including: noticing, not-distracting, not-worrying, attention regulation, emotional awareness, self-regulation, body listening, and trusting. Items are rated on a 6-point Likert scale ranging from 0 (never) to 5 (always). This questionnaire is included in the protocol. (approximately 5 minutes)

5. PROMIS Sleep & Anxiety items. The PROMIS Sleep & Anxiety includes 5 questions taken from the PROMIS v1.0 Sleep Disturbance questionnaire which focus on the interaction between worry and sleep. This questionnaire is included in the protocol. (approximately 1 minute)

6. Worry Interfering with Sleep scale (WIS). The WIS is a single item self-report question that asks individuals to rate what percent of time worry interfered with their ability to get to or stay asleep. This questionnaire is included in the protocol. (approximately 1 minute).

7. Expectancy. These three questions assess treatment usefulness, confidence, and likelihood to recommend on a 9-point Likert scale from 1 (Not at all confident or Not at all useful) to 9 (Very confident or Very useful) and from 0 to 100%. This questionnaire is included in the protocol (approximately 1 minute).

8. Generalized Anxiety Disorder 7-items (GAD-7). The GAD-7 is a 7-item measure of anxiety rated on a 4-point Likert scale ranging from 0 (Not at all sure) to 3 (Nearly every day). This questionnaire is included in the protocol. (approximately 2 minutes)

9. Shape Matching Task. The shape matching task assesses cognitive control, or resistance to distraction. Individuals are presented with probe and target shapes and must decide whether they are the same shape. On some trials a distractor shape will be present, which the individual is instructed to ignore. (approximately 25 minutes)

Module 14 (Group B) or 1 Month (Group A) – Online

- Both groups will receive a personalized survey link via Qualtrics.

1. FFMQ non-reactivity (approximately 1 minute)
2. PSWQ (approximately 3 minutes)
3. MAIA (approximately 5 minutes)
4. PROMIS Sleep & Anxiety (approximately 1 minute)
5. WIS (approximately 1 minute)
6. GAD-7 (approximately 2 minutes)

Module 30 (Group B) or 2 Months (Group A)

- Group A will complete the first five items using a personalized survey link via Qualtrics and the sixth, the GAD-7, will be completed as part of the Unwinding Anxiety assessment.
- Group B will complete the first seven items using a personalized survey link via Qualtrics
- Both groups will complete the shape matching task on a study laptop.

1. FFMQ non-reactivity (approximately 1 minute)
2. PSWQ (approximately 3 minutes)
3. MAIA (approximately 5 minutes)
4. PROMIS Sleep & Anxiety (approximately 1 minute)
5. WIS (approximately 1 minute)
6. GAD-7 (approximately 2 minutes)
7. Net promoter score (approximately 1 minute)
8. Shape matching task (approximately 25 minutes)

2 Months post-intervention (Group B) or 4 Months (Group A)

- Both groups will complete the first six items using a personalized survey link via Qualtrics and the shape matching task will be completed on a study laptop.

1. FFMQ non-reactivity (approximately 1 minute)
2. PSWQ (approximately 3 minutes)
3. MAIA (approximately 5 minutes)
4. PROMIS Sleep & Anxiety (approximately 1 minute)

5. WIS (approximately 1 minute)

6. GAD-7 (approximately 2 minutes)

7. Shape matching task (approximately 25 minutes)

4. **Participant Population.**

Description of participant population:

We will recruit people who experience sleep disturbances related to anxiety in order to address Aims 1 & 2 of this study. We will recruit people who live within a 30-minute drive of Providence, RI because people who live within close proximity to Providence are more likely to return for follow-up visits and complete the study.

Participants will meet the following criteria:

Inclusion:

1. 18 years or older
2. PSWQ > 40 based on established cut-off suggesting GAD
3. ≥ 5/10 on Worry Interfering with Sleep scale (WIS)
4. Able to read and speak English, because the Unwinding Anxiety app is available in English only.
5. Owns a smartphone (UA app can only be used on a smartphone)
6. Willingness to wear the Fitbit Inspire tracker

Exclusion:

1. If using psychotropic medication - not on a stable dosage for at least 6 weeks
2. Medical disorder of the severity that would interfere with ability to participate (e.g. cancer, multiple sclerosis, Parkinson's disease, ALS, etc. These disorders impact sleep quality which could confound study outcomes.)
3. As needed (i.e. prn) benzodiazepine or hypnotic sleep aid
4. Known sleep disorder (e.g. obstructive sleep apnea, restless leg syndrome – because these disorders impact sleep quality.)
5. Psychotic disorder (Mindfulness meditation has to be carefully monitored with people experiencing psychosis. We are not able to provide this type of monitoring given budget constraints.)
6. Post-Traumatic Stress Disorder (Mindfulness meditation has to be carefully monitored with people experiencing PTSD. We are not able to provide this type of monitoring given budget constraints.)
7. Severe Depression (PHQ-2 score > 3) (People experiencing severe depression may also experience sleep disorders which could confound study outcomes.)
8. Current shift work employment (People working alternate shifts may have sleep quality problems which could confound study outcomes.)
9. BMI > 30. (People who are obese may have sleep quality problems which could confound study outcomes.)
10. Evening caffeine use (Caffeine use late in the day can impact the quality of a person's sleep, hence the possibility of confounding study outcomes.)
11. Pregnancy (Women in various stages of pregnancy often have sleep quality problems, hence the possibility of confounding study outcomes.)
12. New parents whose child is not sleeping through the night (New parents are often awakened every 3 – 4 hours by a newborn which could confound study outcomes)
13. Lives in same household as someone already enrolled in this study (To prevent study participants from sharing study information with one another.)

Participant enrollment target:

Our goal is to collect 64 complete and usable data sets, so our plan is recruit and enroll 80 participants.

Enrolling 80 participants will be sufficient to cover any participants who don't complete the study and it will allow us to meet our *N* of 64.

Check-ins

The Project Coordinator will check in with participants regarding their experience with the app at 7, 14, and 45 days after they receive access. The purpose of these calls is to encourage engagement with the app in addition to providing a time for the participant to address any questions, comments, likes/dislikes with the Project Coordinator. These will be done via the participants preferred contact method (phone call or text message) and the Project Coordinator will establish preferred times at the baseline assessment. In the event that the Project Coordinator cannot reach the participant, an additional outreach attempt will be made within 24 hours. If this is unsuccessful, no additional contact will be made until the next check-in point. If two consecutive check-ins are missed, an additional email will be sent. Responses may be recorded in Qualtrics and coded solely by participant ID to ensure confidentiality.

5. Recruitment Methods

We will recruit residents who live within a 30-minute drive of Providence, RI primarily using social media advertising (e.g. Facebook, Google AdWords), flyers and info cards, and the Brown Mindfulness Center website.

Social Media

Web page advertisement that briefly describes the study and link to a landing site where potential participants can complete the PSWQ and WIS to determine their eligibility and submit their name, phone number, and email address if interested (see *Landing Page* and *Online Screener* attachments for more details). The contact information will be transferred securely using Stronghold by our Brown-approved consultant, Kevin Danaher (PSA is already in place). Please see *Social Media Ad* attachment for more details.

Flyers

Physical copies of the flyer will be posted on bulletin boards, in waiting rooms, etc. Digital copies will be provided upon request for use on Facebook, websites, and listservs. Please see *Flyer* attachment for more details.

- Brown University campus and surrounding areas
- RISD campus and surrounding areas
- Cafes, grocery stores (e.g. Whole Foods), community boards

Website

Information about the study will be provided on the Brown Mindfulness Center website along with a link to the landing site where potential participants can determine their eligibility. Please see *MC@B Website Ad* attachment for more details.

Brown Mindfulness Center

Information about the study will be on display at the Brown Mindfulness Center. This will be a smaller version of the flyer that is easy for individuals to take with them.

Procedure for all recruitment channels

Both the Project Coordinator and Project Director (both CITI/GCP certified) will be responsible for screening potential participants on the phone. This section is denoted in brackets and underlined and does not refer to one individual specifically.

Potential participants enter the screening pipeline either by reaching out to the Project Coordinator directly or by completing the online initial screening questions.

Online screening questions –

Contact information (name, email, and phone number) will only be collected from participants who are deemed eligible by the online screener using survey logic (e.g. PSWQ > 40 and ≥ 5/10 on WIS). This will be collected and retained in Qualtrics and only accessed by the Project Coordinator. If an individual is eligible, their contact information will be entered into the key code stored in Stronghold and the study record in Qualtrics will be deleted upon the participant agreeing to participate in the study. If the individual is not eligible after the phone screen, their information will be deleted immediately.

Participants who completed the online screening questions –

[Individuals will be screened for eligibility over the phone. The research team member will first describe the study and ask if the individual is interested in moving forward with the screening process. Upon determination of eligibility based on the inclusion/exclusion criteria, the person will be asked again if they wish to participate (see *Phone Screening – Online Screener* attachment for more details). If they are interested in moving forward with the study, the baseline assessment will be scheduled and a copy of the main consent form and directions to the Mindfulness Center at Brown University will be emailed to them (see *MC@B Directions* and *Baseline Scheduling Confirmation Email* attachments).] The online screener should take no more than 5 minutes and the screening call should take no more than 10 minutes.

Participants who did not complete the online screening questions –

[Individuals will be screened for eligibility over the phone. The research team member will first describe the study and if the individual is interested in moving forward with the screening process, verbal consent will be obtained using the bulleted consent form (covered in detail in Part V). Upon determination of eligibility based on the inclusion/exclusion criteria, the person will be asked again if they wish to participate (see *Phone Screening – No Online Screener* attachment for more details). If they are interested in moving forward with the study the same process will be followed as detailed with the group above. In total this process should take approximately 15 minutes.

Screening forms will be kept for eligible participants who will be assigned a participant ID number. This will allow for their medication information to be entered into Qualtrics without identifiers.

Unwinding Anxiety v. Standard of Care Treatment

Unwinding Anxiety is an app-based treatment modality and therefore is unlikely to be identified as regular treatment. However, language has been added to the consent form stating that standard therapy for anxiety symptoms includes medication (such as selective serotonin reuptake inhibitors) and behavioral treatments (such as cognitive behavioral therapy).

While the Principal Investigator (PI) is a clinical psychiatrist, he will not be providing treatment or clinical care, except in the event of an emergency where he is the designed study clinician. In order to diminish any potential of undue influence, the PI will not be in direct contact with the participants on a day-to-day basis.

6. **Compensation / Reimbursement**

Participants will receive a total of $100 in Amazon gift cards, if they are eligible for and attend all four assessment visits. They will be given a $25 Amazon gift card after each assessment (delivered either in-person or electronically depending on assessment type) visit to compensate them for the time involved with each visit. Participants will not be reimbursed for travel. Participants will also have lifetime access to the Unwinding Anxiety app and will be allowed to keep the Fitbit they were given at the baseline visit.

7. **Analysis**

Participant data will be stored in its deidentified form (coded by unique participant ID). All analyses will be conducted on deidentified data upon completion of data collection. Quantitative data will be analyzed in R, Matlab, and SPSS.

8. **Description of the informed consent process:**

Phone Screen Informed Consent Process

During the screening phone call, the Project Coordinator will provide a basic overview of the study to confirm that the individual is interested and then will review the screening consent document with them. Upon assurance that the individual understands the screening process based on the consent document, they will obtain verbal consent (see *Screening Consent* attachment for more details) and the individual will be offered a copy of the verbal consent document for their records. The participant will be consented for the main study in person by either the Project Coordinator or Project Director and a copy of the main consent document (see *Main Consent* attachment for more details) will be sent to the participant in advance of this meeting. The informed consent process will occur in a private assessment room at the Brown Mindfulness Center and will be conducted by either the Project Coordinator or Project Director. This will begin with an overview of the study followed by a review of the consent document page-by-page. Key areas such as the study procedures, the ability to withdraw consent at any point, their rights as a study participant, and potential risks will be highlighted. In addition, the Project Coordinator will ask questions to be certain that the person has sufficient understanding of study procedures, including required time commitment, and procedures related to using the UA app and Fitbit. The individual will then be asked if they have any questions and if they do not, they will sign and date the consent form. The Project Coordinator will also sign and date the consent form and a copy will be provided to the participant for their records. In order to ensure that participation is obtained voluntarily, study staff will follow Brown University's Human Research Protection Program Policy and Procedure Manual's process for obtaining consent from research participants (HRPP-5). All efforts will be taken to minimize the possibility of coercion or influence including: 1) discussing the study during the telephone screen and sending the consent form ahead of time; 2) giving the potential participant the opportunity to review the consent form prior to the baseline visit.

Facilitate Understanding

In order to ensure that a participant understands all aspects of their involvement in the research, they will be encouraged to ask questions and the Project Coordinator will regularly check-in with them to see if they have any questions. During the screening and consent process, the Project Coordinator will probe, where appropriate, to ensure that the participant understands the study and procedures involved.

Special Provisions for Comprehension

Special provisions should not be necessary but if it appears that an individual is struggling with comprehension of the consent information, the Project Coordinator will take additional time to review the documentation with them and will make accommodations as necessary (e.g. reading it aloud while the individual reviews the

document, asking additional questions, etc). If the Project Coordinator is not sure that the individual fully understands the consent information, the informed consent procedure will be stopped. The individual will be informed that they are not eligible, thanked profusely for their time, and provided with the $25 Amazon gift card.

Ongoing Consent

Study participants are informed during the phone screen consent process and during the main consent process at baseline, that they are free to stop their participation in the study at any time for any reason. During reminder calls and study visits, research staff will check in with study participants and ask how they are doing with the study.

Documentation

Informed consent will be tracked in Qualtrics using the participant ID, date consent was obtained, name of the individual obtaining consent, and whether consent was ever revoked. This will be reviewed quarterly by the Project Director.

Consent forms will be stored in a locked filing cabinet in Brown Mindfulness Center, which is keycode access only. The only individuals with access will be the Project Coordinator and the Principal Investigator.

Statistical Analysis Plan

Analyses will be conducted in R using an intent-to-treat approach (ITT). Fischer's exact tests for categorical and Kruskal Wallis tests for continuous variables will be used to determine any between-group differences in baseline demographics. To examine between-group differences in behavioral outcome measures at the primary endpoint (2 months), Welch's t-tests will be used along with Mann Whitney U tests for data that violates the assumption of normality. A series of Generalized Estimating Equations (GEE) will be used to estimate the adjusted intervention effect by regressing change in outcomes at each follow-up on time, group, time*group and confounders identified a priori (using correlation analysis. GEE's are used for longitudinal data in order to account for within-subject covariance over time. False Discovery Rate will be used to correct for multiple comparisons.

Sleep period time (SPT) will be calculated from the paper sleep diaries (PSDs) by subtracting self-reported bedtime from wake time. Fitbit recorded bedtime, wake time, number of sleep minutes, and number of awake minutes will used to calculate estimated TST and sleep efficiency (SE). To improve reliability, average estimated TST will only be calculated for participants with ≥ 3 days recorded during each wear period. Analysis will utilize the same approach as described for the behavioral measures with the addition of a complete case (CC) approach; participants who did not complete the baseline wear period will be excluded from analysis. For the ITT analysis, we will compare the robustness of our findings using two statistical approaches for handling missing data. First, we will use inverse probability weighting with propensity scores. This is a two-step method: 1) using logistic regression, the probability of missingness is modeled as a function of baseline covariates and baseline values of the outcome and 2) the inverse of the propensity scores (predicted probabilities of dropout from the first step) serve as weights in our regression model of the outcomes. Provided the data is missing at random (MAR) or that the probability of missingness can be fully explained by observable data, this approach produces asymptotically unbiased estimates. To allow for the possibility that the MAR assumption may not hold, we will also use a second approach, pattern mixture models, in which the distribution of the outcome is assumed to follow a mixture of two distributions: one for those who complete follow up and another for those who do not. We will subsequently examine effects under a per-protocol analysis.

Mediation analyses will be conducted using both the Baron and Kenny four-step approach in addition to causal mediation models. In the causal mediation analysis, we will focus on the natural direct and indirect effects and use the bootstrap method with 1,000 bootstrapped resamples to compute the standard errors and 95% confidence interval.