Mindfulness-Augmented Cognitive Behavioral Therapy for Insomnia as a Phase 3 Treatment for Non-remittent Insomniacs - An Open-label Pilot Study

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1. Statistical Analysis Plan

Study outcomes were downloaded directly from Qualtrics and all analyses were performed in SPSS 241 version 26 (IBM Corp) with a significance value of .05. We first examined descriptive data for sample 242 characteristics, including sociodemographics, insomnia treatment history, and presenting clinical symptoms. 243 Study hypotheses were tested using a complete case analysis approach, which included all patients enrolled in 244 MBTI. As the study was a single-arm proof-of-concept clinical trial, we conducted paired samples t-tests to test 245 acute pretreatment to posttreatment effects of MBTI on mindfulness, sleep symptoms, depression, and cognitive 246 arousal. To test long-term effects, we conducted paired samples t-tests comparing study outcomes at 247 pretreatment and 6-month follow-up. Paired samples t-test effect sizes are expressed using Cohen's dz; 248 small=.20, medium=.50, large=.80, very large ≥1.00. In addition, we conducted posthoc analyses to further 249 explore our data, which included examining frequency of Rx and OTC sleep aid use at posttreatment and 250 follow-up (note: reducing sleep aid use can be a goal of insomnia therapy, but this was not the case in the 251 present study; rather we observed spontaneous changes in sleep aid use), as well as rates of insomnia remission 252 and major depression among patients with high vs low cognitive arousal at posttreatment and follow-up.

2. Protocol

1. **<u>STUDY AIM, BACKGROUND, AND DESIGN ABSTRACT</u>**
   Millions of people with untreated insomnia suffer from impaired daytime functioning, depression, and poor quality of life. Cognitive-behavioral therapy for insomnia (CBT-I) is a specialist-driven multicomponent treatment that is recommended as a first-line intervention with superior safety and durability relative to pharmacotherapy. Despite the demonstrated success of CBT-I, ~50% of patients do not achieve full remission.

   Our research (NINR R01 and others) suggests that inadequate CBTI response is linked to residual symptoms of cognitive-emotional arousal (i.e., rumination, worry) (Cheng et al., 2020; Kalmbach et al., 2019). Despite its role in insomnia etiology and maintenance, cognitive-emotional arousal is not a primary therapeutic target in standard CBTI, which has minimal effects on these symptoms. The link between residual cognitive-emotional arousal and treatment-resistance emphasizes a critical unmet need to address residual cognitive-emotional arousal symptoms in non-remitters. Though initial remission rates of 50-60% are good, this still leaves millions exposed to the harmful consequences of insomnia such as depression, daytime impairment, and decreased quality of life.

   To address this critical limitation of CBTI, researchers have placed the behavioral sleep strategies of CBTI into a mindfulness intervention framework to create mindfulness-based therapy for insomnia (MBTI). Like CBTI, MBTI substantially reduces insomnia symptoms. Unlike CBTI, MBTI also substantially alleviates cognitive arousal (Ong et al., 2008; Ong et al., 2014). These data suggest that MBTI may be highly effective for treatment-resistant insomnia, which is marked by refractory cognitive arousal.

   In this internally funded pilot study, we propose to test whether MBTI significantly reduces symptoms of insomnia and cognitive arousal in patients with highly treatment-resistant

insomnia. Forty patients who did not remit after at least one round of CBTI will be recruited from an ongoing stepped care trial (IRB # 11586) and will receive telemedicine MBTI in this open-label trial. Specifically, after patients in the stepped care trial do not fully remit after one (digital CBTI) or two (first-line digital CBTI followed by face-to-face in-person CBTI) rounds of treatment, we will invite them to participate in this trial in which all patients would receive telemedicine MBTI. We will assess insomnia, cognitive arousal, and other relevant symptoms before and after the 8 sessions of MBTI and then again 6 months following the end of treatment.

Aim 1: Determine whether MBTI reduces insomnia symptoms in highly treatment-resistant insomnia. We predict that patients will report a significant decrease in insomnia symptoms from pre-MBTI to post-MBTI.

Aim 2: Determine if MBTI reduces cognitive arousal in highly treatment-resistant insomnia. We predict that patients will report a significant decrease in cognitive arousal symptoms from pre-MBTI to post-MBTI.

These findings would be important as they would support the hypothesis that sleep can be improved in a highly resistant population of insomnia patients and that this improvement may be due to a decrease in cognitive emotional arousal. These findings would also allow clinicians to triage patients into more helpful therapies that better fit their cognitive emotional profiles and improve sleep and emotional well-being more quickly by targeting specific sleep issues.

2. SUBJECT POPULATION AND ELIGIBILITY

Subject Population – Inclusion criteria

- Previous participation in both Phase 1 and/or Phase 2 of the STRIDE (Sleep to Reduce Incident Depression Effectively, IRB 11586) clinical trial will serve as the recruitment entry point for this pilot study. Insomnia patients (DSM-5) will have all received standardized digital CBTI (dCBTI) (Sleepio) (Phase1). Although most insomnia patients respond to dCBTI, only ~50% fully remit. dCBTI non-remitters (ISI >7) and participants who were then re-randomized to standard face-to-face CBTI (Phase 2), but were still non-remittent, will be offered mindfulness-augmented CBTI (MBTI) delivered by nurse via telemedicine real-time video (Phase 3).
- Patients who were non-remittent following face-to-face CBTI with a Behavioral Sleep Clinician are also eligible to participate in the study. These would be identified using chart-review.
- No vulnerable populations will be involved, although participants who are Henry Ford employees will be offered the chance to participate if they meet the study criteria (still non-remittent for insomnia after dCBTI and/or face-to-face CBTI therapy).
- English literacy
- Participants must have access to a device (cell phone, computer, or tablet) with audio and video capability.

Enrollment and/or Screening

- Participants will be identified by:
    - 2-year follow-up questionnaires from STRIDE (Sleep to Prevent Incident Depression Effectively, IRB 11586). Participants must have an ISI (Insomnia

Severity Index) > 7 at the 2-year follow-up to qualify for this pilot study.
    - Chart-review from HFHS Epic records
- Prospective participants will be approached by email and phone (Drake_MBTI-STRIDE_Recruiting Materials). No additional screening other than what has previously been described is necessary.

3. STUDY PROCEDURES

1. Potential participant is identified based on Insomnia Severity Index (ISI) score from STRIDE Timepoint 5 (2-year follow-up questionnaire), referral, or chart-review. ISI score greater than 7.
2. Prospective participant is contacted by email and/or phone and the additional study is described by the RN-Research Coordinator (RC) or Clinical Research Assistant (RA). Interested participants will be emailed the Informed Consent Form (ICF) in the form of a Qualtrics questionnaire. At the end of the Qualtrics questionnaire, the participant is given the option of a) Declining to participate, b) Agreeing to participate, or c) Expressing interest but would like more information. A video visit will be scheduled for the latter two options.
3. During the video visit, the RC or RA will review the ICF with the participant, explaining in detail the components of the study and answering all questions the participant has. If the participant would still like to move forward and participate, a second ICF Qualtrics questionnaire will be emailed with a signature page for the participant to sign and submit. A digital version of the HIPAA consent will also be discussed, and participants will be invited to sign. Participants will be able to have digitally signed copies of both documents for their records.
4. Once consent has been received, a baseline questionnaire (Drake_MBTI-STRIDE_Questionnaires) will be sent by email to the participant through the Qualtrics platform.
5. A tentative schedule for the 8 sessions will be determined and sent to the participant for reference. Schedules are flexible and can be changed by either the participant or the nurse therapist as required.
6. Eight sessions will be completed according to the Session Outlines (Drake_MBTI-STRIDE_Session Guide). Homework, consisting of a meditation log (Drake_MBTI-STRIDE_Participant Handouts) and a sleep diary (Drake_MBTI-STRIDE_MBTI Sleep Diary), are assigned to the participant each week for completion. Immediately prior to each session, a short Qualtrics questionnaire (Drake_MBTI-STRIDE_Treatment survey) will be emailed to the participant to complete; this questionnaire asks the participant questions about sleepiness, mood, and insomnia severity) to allow the clinician an opportunity to monitor the well-being of the participant each week.
7. At the conclusion of the eight sessions an end-of-study questionnaire (Drake_MBTI-STRIDE_Questionnaires) will be sent to the participant to complete.
8. Six months after completion of the treatment sessions, a 6-month follow-up questionnaire (Drake_MBTI-STRIDE_Questionnaires) will be sent to the participant to complete.

Additional Information

- Assessments will occur at baseline, at completion of the 8-week intervention, and 6 months following completion of the intervention.
- Data will be collected using questionnaires on the Qualtrics survey platform for the following assessments at Pre-Treatment, Acute Post Treatment and then 6-Month

Follow-up time points

- Insomnia Severity Index (ISI)
- PHQ9
- Five-Facet Mindfulness Questionnaire – a measure of mindfulness insight
- Pre-Sleep Arousal Scale (PSAS) – a measure of nocturnal cognitive arousal
- PSWQ – a measure of cognitive arousal
- RRS Brood – a measure of cognitive arousal
- Perseverative Thinking Questionnaire (PTQ) – a measure of repetitive negative thinking
- Epworth Sleepiness Scale (ESS)
- Daytime Insomnia Symptom Response scale (DISRS)
- COVID-19 Questions

- Data analysis plan:
  - Power Analysis: Although MBTI produces large reductions in insomnia symptoms in prior trials (Cohen's d > .80), patients in this study are treatment resistant. Therefore, we anticipate that MBTI may have a reduced effect on insomnia symptoms. Based on a medium anticipated effect (Cohen's d = .50) for a two-tailed test with alpha = .05, a N = 34 sample size will have a .81 power to detect significant effects using within samples t-tests. To account for potential subject attrition, we thus request to recruit a sample size of 40 participants. Notably, in many of our prior insomnia therapy trials, attrition rates were <5%, therefore we are confident that a N=40 sample size will provide sufficient power to detect symptom changes in our primary and secondary outcomes
  - AIM 1: We will use an intent-to-treat approach using the last observation carried forward, which is a conservative method to address missing data/attritors in clinical trials. We will test changes in insomnia symptoms using paired-samples t-tests from pre to post MBTI. We will use a two-tailed test with significance set at alpha=0.05. Cohen's d will be used to describe effect size.
  - AIM 2: Analyses for Aim 2 will be the same as those for Aim 1, except we will examine changes in cognitive arousal.
  - The team member performing the statistical analysis will be provided with de-identified demographic data and questionnaire answers.
- Therapy Content
  - Session-by-session outlines –Drake_MBTI-STRIDE_Session Guide
  - Participant handouts – Drake_MBTI-STRIDE_Participant Handouts

- Treatment Fidelity:
  - For this project, Dr. Fellman-Couture will be supervised by the PI, Dr. Chris Drake, who is a licensed clinical psychologist with extensive training and clinical practice in CBTI, mindfulness-based interventions, and MBTI. In addition, MBTI sessions will be audio-recorded as permitted by the participant. After study completion, 5% of these sessions will be randomly selected (40*6*.05=10 sessions) and rated for fidelity by Dr. Drake.
- Nurse Therapist: Cynthia Fellman-Couture, RN, PhD, is the therapist delivering the intervention to subjects. In addition to providing Cognitive Behavioral Therapy for Insomnia as the research therapist since February, 2014, she has completed the following training in Mindfulness:

- Mindfulness-Based Stress Reduction (8-week course through the Beaumont Center for Mindfulness)
- Mindfulness-Based Cognitive Therapy (8-week course through Brown University School of Public Health)
- 5-Day MBSR Silent Retreat through the Beaumont Center for Mindfulness
- MBSR Foundations to become a Mindfulness-Based Stress Reduction teacher (8-week masters-level course through Brown University School of Public Health) which prepares individuals to begin teaching workshops in mindfulness-based interventions
- Additional certificate level training includes:
    - MBSR: Mindfulness-Based Stress Reduction (PESI, a 2-day program)
    - Integrating mindfulness-based stress reductions (MBSR) skills in clinical practice: A retreat (PESI)
- She has received direct training in Mindfulness-Based Therapy for Insomnia (MBTI) from Drs. Cheng and Drake.

4. ANTICIPATED RISKS

Risks include (1) excessive sleepiness and (2) rare mild emotional distress related to participants experiencing potentially distressing thoughts and emotions. Mood and sleepiness are both monitored through weekly questionnaires, the therapy process, and sleep diaries. Additional precautions include bi-weekly consultation with clinical psychologists who are part of the research team and one who is not directly involved in the study (P. Cheng). Participants who show significant psychological distress will be removed from the study and referred to Behavioral Health. Low risk-Medium benefit.

5. ANTICIPATED BENEFITS

Anticipated benefits include a new treatment option for people who have been shown to be resistant to sleep improvement from standard CBTI and an improvement in cognitive-emotional distress that may be contributing to poor sleep. In turn, this may lower the risk of depression and other disorders related to poor sleep.

An additional treatment option would be beneficial in that it offers hope to those who have not had success with other methods.

6. RENUMERATION/COMPENSATION

No monetary compensation will be provided.

7. COSTS

We do not anticipate there being any costs for participation.

8. ALTERNATIVES

Alternatives for taking part in this study include participants talking their doctor, getting treatment in a clinical setting, participating in another research study, or getting no treatment.

9. CONSENT PROCESS AND DOCUMENTATION

a. The consent will be presented in a Qualtrics questionnaire format. At the end of the Qualtrics questionnaire, the participant is given the option of a) Declining to participate, b)

Agreeing to participate, or c) Expressing interest but would like more information. A video visit will be scheduled for the latter two options.

b. During the video visit, the Research Coordinator (RC) or Research Assistant (RA) will review the ICF with the participant, explaining in detail the components of the study, the participant's responsibilities, and answering all questions the participant has. If the participant would still like to move forward and participate, the participant will be invited to sign the Qualtrics questionnaire. A completed ICF will be emailed to the participant for their record.
c. Prospective participants will have all the time they need to answer the questions so long as recruitment is still occurring.
d. A digital copy of the consent will be stored in a password-protected folder on the HFHS shared drive.

10. WITHDRAWAL OF SUBJECTS

- Participants may choose to withdraw from the study at any time.
- The PI may determine that the participant should be terminated from the study if he believes the study is not in the participant's best interest.
- Participants may be asked to meet, virtually or in person, with study staff for safety reasons.
- If a participant withdraws or is terminated from the study, data gathered up until that point may be kept for analysis.

11. PRIVACY AND CONFIDENTIALITY

Research records will not include names, registration numbers, or other information that is likely to allow someone other than the researchers to link the information to the participant. The researchers will label research records with a unique code and keep any master key that links the participant's name and data in a separate location. The researchers will maintain all study records (including any codes) in a locked, secure location. The participant's research information will not be made a part of their regular medical record. All electronic files containing identifiable information will be password protected and only the members of the research staff will have access to the passwords. If researchers share the participant's data with others, the information will be coded as described above to help protect the participant's identity. At the conclusion of this study, the researchers may publish their findings. Information will be presented in summary format and the participant will not be identified in any publications or presentations. The participant's identifiers will be destroyed upon completion of the final report.

The participant's identifiable private information or identifiable biospecimens may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without their additional informed consent.

12. DATA AND SAFETY MONITORING PLAN

TRIAL SAFETY**:** All adverse events that are reported are monitored by the PI and will be determined for seriousness and relatedness to the study procedures. Serious adverse events are immediately reported to the local IRB.

(1) Potential Risks and Benefits for Participants

Potential Risks: In a recent review of behavioral treatment of insomnia: "Psychological and Behavioral Interventions for Managing Insomnia Disorder: An Evidence Report for a Clinical Practice Guideline by the American College of Physicians," psychological and behavioral interventions we considered low harm. However, rare and mild side effects of sleepiness, irritability, and headache may be reported. Thus, in order to ensure patient safety throughout the present treatment protocol, the following adverse event plan has been put in place to address side effects.

Potential Benefits: The potential benefits to study participants include that participants may experience an improvement in their sleep and/or mood. However, participation may not bring any direct participant benefit, but the medical knowledge regarding treatment of the sleep symptoms associated with insomnia will be advanced.

(2) Adverse Event, Serious Adverse Event, and Unanticipated Problem Collection and Reporting

Definitions

The definitions of events that will be used in this Program Project Include:

Adverse Event (AE):

Any untoward or unfavorable medical occurrence in a human study participant, including any abnormal sign (e.g. abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the participants' involvement in the research, whether or not considered related to participation in the research.

Serious Adverse Event (SAE):

Any adverse event that:

- Results in death
- Is life threatening, or places the participant at immediate risk of death from the event as it occurred
- Requires or prolongs hospitalization
- Causes persistent or significant disability or incapacity
- Results in congenital anomalies or birth defects
- Is another condition which investigators judge to represent significant hazards

Unanticipated Problem (UP):

Defined by DHHS 45 CFR part 46 as any incident, experience, or outcome that meets all of the following criteria:

- unexpected, in terms of nature, severity, or frequency, given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the study population

- related or possibly related to participation in the research (in this guidance document, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research)
- suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Classifying Events

All events occurring in this Program Project will be rated as follows:

Severity

Classifications will include the following:

- ***Mild:*** Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
- ***Moderate:*** Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning
- ***Severe:*** Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating

Severity is not synonymous with seriousness. A ***severe*** rash is not likely to be an ***SAE.*** Likewise, a ***severe*** headache is not necessarily an ***SAE.*** However, ***mild*** chest pain may result in a day's hospitalization and thus is an ***SAE.***

Expectedness

AEs will be assessed as to whether they were expected to occur or unexpected, meaning not anticipated based on current knowledge found in the protocol or scientific literature.

Categories are:

- ***Unexpected -*** nature or severity of the event is not consistent with information about the condition under study or intervention in the protocol, consent form, product brochure, or investigator brochure.
- ***Expected -*** event is known to be associated with the intervention or condition under study.

Relatedness

The potential event relationship to the study intervention and/or participation will be assessed by the site investigator. The comprehensive scale to categorize an event will be:

- *Definitely Related*: The adverse event is clearly related to the investigational agent/procedure – i.e. an event that follows a reasonable temporal sequence from administration of the study

intervention, follows a known or expected response pattern to the suspected intervention, that is confirmed by improvement on stopping and reappearance of the event on repeated exposure and that could not be reasonably explained by the known characteristics of the subject's clinical state.

- *Possibly Related:* An adverse event that follows a reasonable temporal sequence from administration of the study intervention, follows a known or expected response pattern to the suspected intervention, but that could readily have been produced by a number of other factors.

- *Not Related:* The adverse event is clearly not related to the investigational agent/procedure, i.e. another cause of the event is most plausible; and/or a clinically plausible temporal sequence is inconsistent with the onset of the event and the study intervention and/or a causal relationship is considered biologically implausible.

Reporting Responsibilities and Processes

The PI, therapists, and study coordinator will be responsible for all event reporting for the project. They will report events to the Principal Investigator who will report events as outlined to an independent Data and Safety Monitoring Board. The standard definitions of AEs, SAEs, and UPs, as outlined above, will be used and all events will be reported to the appropriate local IRB and the Data Safety Monitoring Committee Chair.

AEs, SAEs, and UPs will be collected on the enclosed forms and reported on events occurring from the time of consent to the time of exit interview debriefing for a given participant. Reports will be conveyed by fax to the parties outlined above. All AEs will be rated as to severity, expectedness, and relatedness, as defined above. AEs will be reported within a week of the event being reported to the investigator, and SAEs reported within 24 hrs. The initial SAE report will be followed up with a more detailed report indicating relevant additional information and event resolution when available. UPs which are not SAEs will be reported within 48 hrs. of the event coming to the attention of the investigator and will be forwarded to OHRP within two weeks. UP reports will include a corrective action plan and measures to prevent recurrence.

(3) Protection against Study Risks

Although the occurrence of any adverse events during MBTI is rare, participants will be asked to record any adverse events and will be given the phone number of the PI and study coordinator to report any significant concerns. In addition, at each visit all subjects will be questioned regarding any adverse events that have occurred since the previous contact, including sleepiness. Consenting procedures will also include a thorough review of the risks of performance impairment when sleepy. Per standard clinical and research procedures, all study participants will be advised not to drive or operate machinery if feeling sleepy. Participants reporting any adverse event will be followed by regular contact until resolution.

All recruitment materials and the initial contact script will be submitted and approved by the appropriate IRB. The recruitment materials and initial contact are recognized as the first step in the consent process and these materials will clearly indicate that it is a research study for which participants are being recruited and contacted regarding study participation. No likelihood of direct participant benefit will be offered in recruitment and contact materials, and the potential of risks

will be indicated in the contacts. The participant will be given an opportunity to read the consent and then ask questions by phone or virtual visit about any study aspects they do not understand, at which point the investigator or designee will reiterate the study details and answer questions.

Depression/suicidality: If a participant acknowledges suicidal ideation during their initial screening visit (i.e., via the PHQ-9), then a dedicated Henry Ford Health System process will be initiated to manage suicidal ideation. This protocol includes immediate assessment by an integrated behavioral health provider who determines the appropriate care pathway. Participants who endorse risk of suicide during the online study assessments will be contacted and provided an appropriate mental health referral and/or suicide hotline access by a Senior Staff member who is a licensed clinical psychologist. Thus, any high-risk participants will be provided the 24/7 crisis management hotline (1-800-422-1183). Participants may also be referred directly to the emergency room for immediate admission and treatment. Additionally, we will notify the participant's health provider (preferably behavioral health provider if he/she is receiving care in Behavioral Health Services). If we are unable to reach the participant within 24 hours of the initial phone call, we will dispatch security or law enforcement for a wellness check at the address provided by the participant. This protocol will be made clear to participants during the informed consent, which will also include the Henry Ford Health System's 24/7 crisis number.

In cases where there are clinically significant depressive symptoms present at any assessment participants will be contacted by sleep center clinical staff within 7 days and be directly referred to behavioral health services to receive care or referred to a prior mental health provider with an established relationship with the participant.

Protecting the Confidentiality of Participant Data: The consent process will inform a volunteer about the study, indicate that their participation is voluntary and that he/she has the right to stop at any time. Risks will be enumerated in the informed consent document. The informed consent document will be approved by the appropriate local IRB and will include all the appropriate elements listed in the HFHS informed consent checklist.

Participants will be informed about all study specifics, including full confidentiality of all information, the security of information collected throughout the protocol, and compensation. Specifically, all HIPAA guidelines will be followed, including full data encryption. Data will be analyzed and reported in aggregate. Individual-level data will not be reported. Only the PI and Research Coordinator will have access to these data. All PHI data will be kept in a HIPAA compliant secure password protected database on a secure HFHS computer. All contacts with participants will be conducted in a professional manner and will not impose undue pressure of any kind. All identifying information will be handled with the highest degree of discretion and confidentiality.

External: An assessment of external factors or relevant information (i.e., developments in the literature, results of related studies) that may have an impact on the safety of participants or on the ethics for the research study will be reviewed by study personnel at quarterly meetings as described above. Participants will be informed in a timely manner if new information becomes available that

may be relevant to the subject's willingness to continue participation in the study. The communication of this information will be documented.

(4) INTERIM ANALYSIS

Interim analyses of the proposed project are not planned. The interventions used in this study are not investigational and present low risk to the study participants. The behavioral treatments are treatments previously investigated with no AEs or SAEs reported in those studies or they are treatments with low risks used in clinical sleep centers throughout the US.

13. QUALIFICATIONS OF THE INVESTIGATOR(S)

a) Christopher Drake, PhD, (Principal Investigator) is a Clinical Psychologist at the Thomas Roth Sleep Disorders & Research Center and Associate Professor of Psychiatry and Behavioral Neuroscience, School of Medicine, Wayne State University in Detroit. Dr. Drake completed a two-year fellowship at the National Institute of Mental Health, Clinical Psychobiology Branch in 1994 and is board-certified in Sleep Medicine and Behavioral Sleep Medicine. He is the Associate Editor for the journal SLEEP and serves on the editorial board for the journals Behavioral Sleep Medicine, World Journal of Neurology, and The Open Sleep Journal. Dr. Drake has served as a member of the Board of Directors for the National Sleep Foundation. As well as serving on other national committees, Dr. Drake served as Section Head of Sleep Disorders Research for the Sleep Research Society from 2005 to 2006 and has been an advisor to the World Health Organization on sleep. He has authored numerous publications in the field of sleep medicine and serves as a reviewer for 18 scientific journals. Dr. Drake recently completed a study funded by the National Institute of Health to study the efficacy of Cognitive Behavioral Therapy for Insomnia as a treatment for insomnia concurrent with menopause. He has also recently completed a federally-funded study on predisposition to chronic insomnia. Currently, Dr. Drake is funded by the National Institute of Mental Health to investigate the efficacy of Cognitive Behavioral Therapy for Insomnia in preventing the development of depression. In addition to his federal funding, Dr. Drake has received numerous pharmaceutical grants from companies such as Pfizer, Cephalon Inc., Takeda Pharmaceuticals, and Sanofi-Synthelabo to conduct Phase 2, 3, and 4 clinical trials. His areas of expertise include insomnia, excessive sleepiness, and sleep deprivation.

b) Philip Cheng, PhD, (Co-Investigator) is a well-published clinical psychologist who has maintained an active and federally funded research program in sleep and circadian rhythms. He took a leadership in the design, implementation, data collections, data anylisis, and publication of the previous trial that this research proposal is built on. He has published numerous first author papers from the prior study, with additional manuscripts in preparation.

14. REFERENCES

- Cheng, P., Kalmbach, D. A., Castelan, A. C., Murugan, N., & Drake, C. L. (2020). Depression prevention in digital cognitive behavioral therapy for insomnia: Is rumination a mediator? Journal of Affective Disorders, 273, 434-441.
- Kalmbach, D. A., Cheng, P., Arnedt, J. T., Anderson, J. R., Roth, T., Fellman-Couture, C., ... & Drake, C. L. (2019). Treating insomnia improves depression, maladaptive thinking, and hyperarousal in postmenopausal women: comparing cognitive-behavioral therapy for

insomnia (CBTI), sleep restriction therapy, and sleep hygiene education. Sleep medicine, 55, 124-134

- Ong JC, Manber R, Segal Z, Xia Y, Shapiro S, Wyatt JK. A randomized controlled trial of mindfulness meditation for chronic insomnia. Sleep. 2014;37(9):1553-1563.
- Ong JC, Shapiro SL, Manber R. Combining mindfulness meditation with cognitive-behavior therapy for insomnia: a treatment-development study. Behavior therapy. 2008;39(2):171-182.
- Zoccola, P. M., Dickerson, S. S., & Lam, S. (2009). Rumination predicts longer sleep onset latency after an acute psychosocial stressor. Psychosomatic Medicine, 71, 771–775. doi:10.1097/PSY.0b013e3181ae58e8