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Multimodal Neuroimaging of Insomnia During Non-Rapid Eye Movement Sleep (MNI_NREM)

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Daniel Kay

Application Abstract

The impact of insomnia on brain regions/networks during sleep may represent mechanisms through which insomnia contributes to the risk for mood disorders. As a first step toward understanding the risk relationship linking insomnia to mood disorders, this study will utilize functional magnetic resonance imaging (fMRI) with multimodal techniques to investigate alterations in brain regions and networks during wake and NREM sleep in patients with insomnia relative to good sleeper controls. We also intend to investigate the pathophysiology of insomnia across 8 units of analysis by combining these data with Dr. Kay’s larger study, the MNI_RDoC (IRB #16377). The units of analysis under investigation in that study, specifically, are genes, molecules, cells circuits, physiology, behavior, self-report, and paradigms. These data will be essential in developing further hypotheses and designing future studies.

Evaluation of how well the academic objectives of the proposal were met & Description of results

Specific Aim 1: Investigate alterations in brain regions and networks during NREM sleep in patients with insomnia (n = 12) relative to good sleeper controls (n = 12)

The research for specific aim 1 is still ongoing. As this experiment required data collected from 36 participants to obtain 24 individuals needed for the final analysis sample, the timeline was pushed back due to the withdrawal of several participants that met the exclusionary criteria. We have so far collected full data from 19 participants but will need to recruit 5 more individuals which will be collected Winter term 2019. Preliminary analyses indicate that patients with insomnia have alterations in functional connectivity in brain regions involved in conscious awareness, self-referential processes, and mood. These preliminary results were presented by Dr. Kay at the Sleep 2018 annual conference in Baltimore MD as the chair of a symposium on sleep neuroimaging. This aim will serve as the 2nd year project for Dr. Kay’s current graduate student, Jolynn Jones.

Specific Aim 2: Determine how regional differences in sleep intensity relate to mood in patients with insomnia

Similar to Specific Aim 1, the research for this aim is still ongoing as we have collected and analyzed data from current participants. Our question of interest was about whether regional differences in brain activation and functional connectivity during NREM sleep was associated with daytime impairments in domains of positive affect, negative affect, cognition, social processes, and arousal/regulatory systems. We will conduct these analyses in the coming year.

Supplementary Aims: Several undergraduate students have begun to analyze the data from this project to answer their own questions. One student investigated how patients with insomnia perceive their sleep experience compared to actigraphy. Another student investigated how participants change their self-reported sleepiness rating if they perform more poorly on a cognitive task. In addition, multiple students have utilized other available data in the lab to make meaningful contributions.

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Evaluation of the mentoring environment

The purpose of this proposal was to prepare BYU students for graduate work and for careers in other areas related to sleep medicine research. The analytical skills students gain in a mentored research environment have wide application in any number of fields. The access to research techniques in Dr. Kay’s Sleep Research laboratory has given students a competitive advantage in applying for graduate school, medical/dental school, and other employment opportunities. MEG-supported students spent substantial time working on all phases of the project, including the recruitment and screening of participants, assessment of sleep with state-of-the-art methods and techniques (polysomnography and high-density EEG), collection and analysis of neuroimaging data, collection and preparation of DNA samples, and collection, scoring, and interpretation clinical questionnaires and neuropsychological tests. The mentoring environment for this study addressed the principles of mentorship according to ORCA as discussed in the application for this MEG.

Students (lead authors) who participated and academic deliverables they have produced

**Spencer H** and Kay, DB (2018). Sleep onset latency and discrepancy in young adults. Poster presented at the Mary Lou Fulton Conference. This poster received an honorable mention (Figure 1).


Other Students Supported by the MEG (Figure 1):

Scott Crawford
Jessica Nielson
Zoe Knudsen
Sariah Steele
Brad Albrecht
Hillary Jones

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Description of results

Below are the products produced by students since I received the MEG and are direct products of the data collected using the MEG funds. Please be aware that my lab has several other products as described above that did not use MEG money. Those additional products include a published paper on show sleep relates to serotonin functioning in rhesus monkeys, abstracts on how sleep relates to cognition and mood in patients with Parkinson’s disease and an abstract on how exercise impacts sleep quality in women. These products are available upon request.


Trial-to-Trial Inconsistency in Reaction Time on the Psychomotor Vigilance Test Alters Self-Reported Sleepiness Authors: Spencer A. Nielson, Spencer R. Henry, and Daniel B. Kay

Background: Daytime sleepiness is associated with impaired attention processes, including slower and more variable reaction time. Although results are mixed, recent research has started to show the positive association between insomnia severity, greater daytime sleepiness and impaired simple attention processes. In this study, we aimed to determine whether performance on an attention task influences self-reported sleepiness of individuals across the sleep disturbance spectrum.

Methods: Participants (N=50) included individuals across the insomnia spectrum from good sleepers to patients with insomnia disorder. Insomnia severity was assessed using the Insomnia Severity Index. Simple attention was assessed using a computerized Psychomotor Vigilance Test (PC-PVT) administered in the morning. Participants’ rated their sleepiness on a scale from 1 (not sleepy) to 10 (extremely sleepy) before and after they completed the PVT. Spearman’s correlation coefficient was used to assess associations between insomnia severity, sleepiness, and PVT performance. Multiple regression was used
to determine whether mean or trial-to-trial variability in reaction time predicted post-PVT sleepiness, adjusting for pre-PVT sleepiness and Insomnia Severity Index score.

Results: Greater trial-to-trial variability in PVT reaction time predicted greater post-PVT sleepiness after adjusting for pre-PVT sleepiness and insomnia severity, $t=2.9$, $p=0.005$. Insomnia symptom severity was associated with greater sleepiness at pre- and post-PVT, $r(50)=0.41$, $p=0.003$ for both. After adjusting for pre-PVT sleepiness, insomnia severity was not a significant predictor of post-PVT sleepiness. Average PVT reaction time was not associated with sleepiness.

Conclusion: Participants with greater inconsistency in simple attention performance reported greater sleepiness than they had reported 10 minutes previously. Trial-to-trial variability in reaction time performance may have raised participants’ awareness of their sleepiness. Alternatively, participants with inconsistent performance may have altered their self-report to match their performance. Although insomnia symptom severity was associated with sleepiness it did not make participants more prone to biased sleepiness reports based on performance on the PVT.

**Product 2: Poster presented by Spencer Henry at the Mary Lou Fulton Conference in 2018.**

**Sleep Onset Latency and Discrepancy in young adults**

**Background**

- Insomnia is characterized by difficulty initiating or maintaining sleep.
- Participants with insomnia tend to report being more sleep-deprived, although objective measures suggest they are alert.
- This sleep discrepancy (SSD) may occur across and within sleep-disordered populations.
- We hypothesized that sleep discrepancy in simple attentional tasks was associated with sleepiness even when controlling for mean sleep time or rightward-weighting in insomnia patients than post-PVT patients.

**Methods**

**Sample**

- Sleep-disordered, age 18-35
- Insomnia diagnosis with insomnia severity (ISI) > 17
- Good sleepy controls (ISI < 7)

**Measures**

- Insomnia symptomatology using the PVT and the ISI.
- Sleep-onset discrepancy (SSD) = Post-SVT - Pre-SVT
- Mean item score on the ISI
- Sleep discrepancy = subjective sleep latency - observed sleep latency

**Analysis**

- Correlation analyses using Spearman's r
- Multiple linear regression

**Results**

- Greater discrepancy in simple attentional tasks
- Greater variability in sleep efficiency
- Greater discrepancy in subjective sleep latency vs. observed sleep latency
- Greater discrepancy in sleep efficiency vs. ISI

**Discussion**

Sleep discrepancy varies from right to left in chronic insomnia. Variability in rightward-weighting in simple attentional tasks may be related to differences in sleep efficiency and subjective sleep latency. The discrepancy between observed and reported sleep latency is thought to be related to reduced vigilance, increased daytime sleepiness, and reduced performance on attentional tasks.

**Description of how the budget was spent**

To-date we have spent $18,685.41 of the $20,000 on student payment, participant compensation, and MRI scanning. In addition, I have contributed funds to this project that exceeds this amount to allow for the collection of morning MRI scans, structured clinical interviews (SCIDs), pregnancy tests, drug tests, blood draws, DNA samples, and neuropsychological testing, totaling over $3000. We still need to obtain data on 5 more participants and my lab funds will cover those costs. Originally, I had requested $1000 for student travel to the SLEEP conference. However, students in previous years have not required these funds either because they were not able to attend the meeting, or they obtained college/department funds that covered the cost. Our lab has 6 students planning to attend the annual SLEEP meeting in June 2019; 1 student will present preliminary results from this project. I would like to request to use the remaining money ($1314.59) to support student travel to the conference.