Molecular Resilience to Acute Sleep Deprivation in Female Mice

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Gabriella De La Cruz, Jack Seely, Natalie A. Storch, Lisa C. Lyons
Department of Biological Science, Program in Neuroscience, Florida State University, Tallahassee, FL

Introduction

- According to the CDC, approximately 1 in 3 Americans are sleep deprived. Considered to be public health epidemic, sleep deprivation leads to a myriad of health detriments, including car crash fatalities, weight gain, increased disposition to obesity, diabetes, depression, dementia, anxiety, hypertension, and more. Increased use of smartphones and electronic devices is worsening the epidemic (Chattu, et. al). In the hippocampus (area of the midbrain primarily responsible for learning and memory) sleep deprivation has been shown to impair cAMP and mTOR signaling. This pathway is responsible for initiating neuron growth/consolidation (Havekes, Abel).
- This study seeks to further understand these molecular pathways and how they are effected by sleep deprivation. Observing the effects of introducing different cell signaling hormones and antagonists such as Estradiol and GPER has illuminated the processeses underpinning sleep deprivation resiliency.

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Methods

- C56BL/6 Mice were housed in groups of four and then split into individual cages, where they underwent five hours of acute sleep deprivation. Wellness checks occurred before the experiment in order to ensure that the mice remained healthy and did not exhibit barbering behavior (i.e. abnormal grooming). The mice were maintained under standard conditions approved by the National Institute of Health guidelines and regulated by the Animal Care and Use Committee of Florida State University.
- To measure these fluctuations, two samples (n=6) of mice were acutely sleep deprived (SD) and non sleep deprived (NSD). Sleep deprivation takes place from ZT0 until ZT5 (Zeitgeber time) with dissections proceeding immediately following sleep deprivation. Hippocampal RNA was extracted and ran through qPCR to analyze changes in gene expression.
- Pending the results of the qPCR, a molecular basis for resiliency to acute SD can be established, allowing potential pharmaceuticals to be developed to take advantage of these molecular resiliency mechanisms.

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- Sleep deprivation was performed starting at the beginning of the light cycle and gentle handling through tapping and gentle shaking on their cages was done if necessary to ensure the mice did not fall asleep or undergo periods of micro-sleeping.
- Following the sleep deprivation, mice were euthanized by cervical dislocation, and hippocampal and cortical tissues were collected, flash frozen on dry ice, and processed for RNA extraction and cleanup. Quantitative PCR (qPCR) was used to assess changes in gene expression between hippocampal and cortical samples following sleep deprivation.
- The RNA in these regions demonstrated the changes in gene expression, and it was measured in order to analyze if there were any differing changes in the gene expression of the hippocampus compared to the cortex, and what these changes entailed regarding brain functioning after sleep deprivation.

Results

- Preliminary observations indicate decreased BDNF expression in the hippocampus after sleep deprivation. Ongoing qPCR analysis of cortical tissue will determine whether gene expression changes differ across brain regions, including whether cortical responses oppose or parallel hippocampal changes.
- The results of the qPCR will determine whether there are distinct changes in gene expression between hippocampal tissue and cortical tissue caused by sleep deprivation.
  - For example, decreases in BDNF (Brain-Derived Neurotrophic Factor) in the hippocampus after sleep deprivation were observed, but the changes in the cortex have yet to be determined.
    - These findings will help clarify how acute sleep loss differentially impacts molecular signaling in distinct brain regions.
- The strengths of this experiment include the focus on how the two brain regions are compared through a variety of processes that ensure the RNA has been properly cleaned and prepared for analysis.

Conclusions/limitations

References

Acknowledgements