Chronic Sleep Deprivation Induces Brain Inflammation via CCR2-mediated Peripheral Monocyte Infiltration

Wang, Jason (School: Germantown Academy)

Chronic sleep deprivation (CSD), a result of consistent sleep loss, is a global concern in more than half of adults worldwide. Research has shown that people with CSD are more susceptible to developing neurological disorders such as Alzheimer's disease in later life. However, the underlying mechanisms responsible for this link remain to be elucidated. The present study is aimed at uncovering the underlying mechanisms and identifying a potential therapeutic target to ameliorate the effects of CSD. Since inflammatory responses within the brain have been shown to be associated with neurological disorders, I examined whether CSD can induce peripheral monocyte infiltration into the brain of mice and contribute to brain inflammation. By utilizing transgenic mice expressing red fluorescent protein (RFP) under monocyte specific promoter CCR2, this study demonstrated CSD-induced peripheral monocyte infiltration by fluorescent visualization of RFP+ cells in the brain. In addition, I found that peripheral monocyte infiltration led to brain inflammation by fluorescently labeling CD68, a microglia activation marker. Further, by comparing the brains of sleep deprived CCR2 heterozygous mice (CCR2+/RFP) to CCR2 knockout mice (CCR2RFP/RFP), I revealed that depleting the CCR2 receptor reduced peripheral monocyte infiltration and microglia activation in the brain, thus also reducing brain inflammation. Together, the results indicate that CSD-induced peripheral monocyte infiltration leads to brain inflammation, suggesting that maintaining sleep hygiene and improving sleep quality may be critical for preventing neurological disorders in later life. In addition, I identify the CCR2 receptor as a potential therapeutic target to reduce the effects of CSD-mediating neurological consequences.

Awards Won:
Second Award of $2,000