Regulation of Perineuronal Net and Somatostatin Neuron Composition Over the Circadian Rhythm

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In my research I am attempting to determine whether Perineuronal Nets (PNNs) and Somatostatin neurons (SST-IR) vary over the circadian rhythm in mouse brains. All organisms undergo a circadian rhythm and this rhythm helps the organism carry out biological functions at the right time. PNNs are part of the extracellular matrix and surround neurons in mature brains. As a brain matures, unwanted connections are weeded out and important connections are strengthened. One of the last steps that occur when a brain matures is PNNs form around neurons and strengthen these important connections. SST-IR is a neuropeptide that is expressed by some inhibitory interneurons. SST-IR expression is involved in decreasing anxiety levels. Previous work showed that SST expression in the amygdala varies across the circadian rhythm, and is associated with variations in sensitivity to anxiety at different circadian time points. PNNs are involved in strengthening memories and memory strengthening occurs overnight. Until recently, scientists were not sure of why we sleep and how memories are strengthened overnight. PNNs were also not well understood until recently, and it was previously thought that they remained stable after they formed when the brain matured. By studying how PNNs and SST-IR neurons vary over the circadian rhythm, we can work to better understand how memory is strengthened overnight. Previous work in this lab demonstrated that PNN numbers vary across the circadian rhythm. Furthermore, a previous study in mice reported rhythmic changes in expression of the somatostatin gene in the mouse amygdala. However, these studies were conducted in mice that were housed in a 12:12 light-dark cycle. In order to understand if these rhythms are due to internal molecular clocks or if they are instead responses to light-dark conditions, we are replicating these studies in animals that were kept in constant darkness for two 24-hour cycles. Our data support the hypothesis that PNNs are modified across the circadian cycle, potentially allowing for reorganization of synapses through memory consolidation during sleep. In the future we plan to repeat this study in a larger group of mice, and examine more markers for PNN composition and degradation that may be involved in modifying PNNs across the circadian rhythm.

3. Pantazopoulos, Harry, et al. "Decreased numbers of somatostatin-expressing neurons in the amygdala of subjects with bipolar disorder or schizophrenia: Relationship to circadian rhythms." *Biological psychiatry* 81.6 (2017): 536-547.