Diurnal rhythms across the human dorsal and ventral striatum

Wei Zong, Kyle D. Ketchesin, Mariah Hildebrand, Kelly Cahill, Madeline R. Scott, Vaishnavi G. Shankar, Jill Glausier, David A. Lewis, George Tseng, and Colleen A. McClung

#WZ and #KDK Contributed equally to this work

Background: During the daytime, many neurons are active to facilitate learning, alertness, movement, feeding, and other activities. At night, other neuronal processes take over to promote sleep, consolidate memories, and provide restorative actions. These rhythms in cellular function are primarily governed by a core molecular transcriptional/translational feedback loop which consists of many coordinated circadian genes such as CLOCK, NPAS2 and BMAL1. We previously identified diurnal rhythms in transcripts in human cortical regions that are impacted in aging and schizophrenia. Here, we investigated diurnal rhythms in transcript expression across the human dorsal and ventral striatum in subjects without psychiatric or neurological disorders. The human striatum can be subdivided into the caudate, putamen, and nucleus accumbens (NAc). Each of these structures have some overlapping and some distinct functions related to motor control, cognitive processing, motivation, and reward. This study, together with previous studies, establish a temporal map of rhythms across the human striatum and help in understanding the normal function of rhythms in these regions and how disruption could lead to pathology.

Method: Each gene was fitted with a sinusoidal curve at a fixed 24 hours period to detect circadian patterns of gene expression based on individual time-of-death (TOD). Then the goodness-of-fit coefficient R2 was calculated with corresponding p-values derived from permutation indicating its rhythmicity strength.

Conclusion: Core circadian clock genes are rhythmic across all three regions and show strong phase concordance. However, the NAc and caudate, and caudate and putamen, have several clusters of other discordant rhythmic transcripts, suggesting a temporal wave of specific cellular processes across the striatum. In addition, the top rhythmic transcripts in NAc (but not the other regions) are predominantly small nucleolar RNAs and long noncoding RNAs, which may suggest a completely different mechanism for the regulation of diurnal rhythms in translation and/or RNA processing in the NAc versus the other regions.