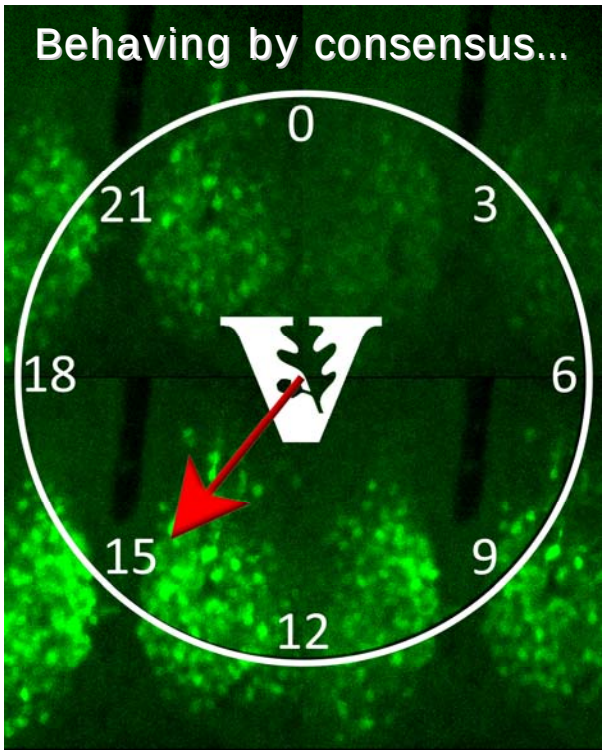

Circadian rhythms are a nearly ubiquitous feature of life on earth, and are controlled in mammals by the suprachiasmatic nuclei of the hypothalamus (SCN). Since its identification as the primary clock more than 30 years ago, how neurons within the SCN control circadian physiology and behavior has been a mystery. In a study recently published in the *Journal of Neuroscience*, Ciarleglio and colleagues demonstrated how neurons within the SCN worked together as a population to control circadian behavioral rhythms.

Circadian rhythms are controlled in mammalian tissues by a set of clock genes that include some that are expressed robustly during the daytime (e.g. *Period1*). Neurons within the SCN are thought to be synchronized by vasoactive intestinal polypeptide (VIP). In this study, the authors used a dual-transgenic reporter mouse with a short half-life *Period1* promoter-driven green fluorescent protein (*Per1*::GFP) and a knockout for *VIP* to study the relationship between neuronal rhythm synchrony *ex vivo* and robust behavioral rhythmicity *in vivo*. *Per1*::GFP mice wildtype, heterozygous or knockout for *VIP* were behaviorally characterized in a light-dark cycle or in constant darkness, then their brains were extracted and their SCN imaged using time-lapse confocal fluorescent microscopy to observe the expression of GFP *ex vivo*.

Behaviorally, $VIP^{-/-}$ *Per1*::GFP mice were arrhythmic, and more phase advanced than $VIP^{+/-}$ and $VIP^{+/+}$ mice, which were found to exhibit strongly rhythmic behavior with normal behavior onsets in LD and in DD. These results support previous reports that $VIP^{-/-}$ mice had disrupted behavioral rhythms. *Ex vivo* (how the authors refer to acute *in vitro* culture) rhythms were also disrupted in $VIP^{-/-}$ mice, such that they expressed much less neuronal synchrony in the phase of *Per1*::GFP expression than $VIP^{+/-}$ and $VIP^{+/+}$ mice. The authors statistically correlated the degree of neuronal synchrony within an SCN to the power of the same animal's behavioral rhythm, and demonstrated a significant relationship between the two measurements. They found that as the amount of neuronal phase variance increased *ex vivo*, the power of the behavioral circadian rhythm decreased, suggesting that the population of neurons as a whole controlled behavioral output.

The authors also reported two other novel findings. First, the proportion of rhythmic neurons in $VIP^{-/-}$ mice was not statistically different from $VIP^{+/-}$ and $VIP^{+/+}$ mice. This is significant because previous studies had suggested that a lack of VIP led to an overall lack of circadian rhythmicity. Instead, the results of this study suggest that it is neuronal asynchrony that results in behavioral arrhythmicity. Second, an advance in *Per1*::GFP expression correlated to the advance of behavioral onset seen in $VIP^{-/-}$ mice, accounting for this strange phenomenon.

This study is significant in that it demonstrated that neurons within the SCN encode behavior as a population, not unlike the population coding seen in the voluntary motor system where the direction of limb movement is controlled by an average population vector in the motor cortex.

Original Research Article:
CM Ciarleglio, KL Gamble, JC Axley, BR Strauss, **JY Cohen**, CS Colwell and DG McMahon (2008). Population Encoding by Circadian Clock Neurons Organizes Circadian Behavior. *Journal of Neuroscience*. **29** (6): 1670-6.

IN THE NEWS...

Vanderbilt University neuroscience researchers received publicity last year for cutting-edge publications.

Zald *et al*. (2008) was covered internationally for the suggestion that a decrease in D_2-like receptors in the human midbrain were responsible for risk-taking and novelty-seeking behaviors (BBC News; ABC News; ScienceNews.org; see "Getting the Dopamine Rush" on the next page).

Mazei-Robison et al. was also covered extensively for characterizing a mutation in the human dopamine transporter that may lead to attention deficit hyperactivity disorder and that responds to amphetamine in an unusual way (Science Magazine; NPR News; Vanderbilt Reporter; see "DAT Leak: A link to ADHD" on the next page).