This Week in The Journal

Getting to Know Npas1-Neurons in the Ventral Pallidum

Gessynger Morais-Silva, Rianne R. Campbell, Hyungwoo Nam, Mahashweta Basu, Marco Pagliusi, et al.

(see pages 405–418)

The neural network that makes up the basal ganglia, a midbrain collection of multiple structures that handle such brain functions as motivation, reward, aversion and directed movement, includes the ventral pallidum (VP). The VP contains a heterogeneous mix of neurons that remain enigmatic in their function and even structure, although similarities between the VP and external globus pallidus (eGP) are guiding current inquiries. Now, Morais-Silva et al. have undertaken a comprehensive approach to better understand one population within the VP—those that express the neuronal Pas 1 (Npas1) protein, a transcriptional repressor that controls neuronal differentiation during development. The study encompassed inquiries into the circuitry of neurons, molecular makeup, and function within the stress response using multiple techniques in mice. Viral tracing revealed that the Npas1 neurons extended from the VP to a dizzying array of ventral brain structures, many within the basal ganglia, including the ventral tegmental area, nucleus accumbens, septum, habenula, thalamus, hypothalamus, and periaqueductal gray, but were notably absent from others, including the eGP, dorsal striatum, amygdala, substantia nigra, and all cortical structures examined, suggesting a role in emotional processing. The authors then assessed the ribosome-associated mRNA in Npas1 neurons relative to all VP neurons and found that protein-binding and chloride channel-related proteins were most differentially regulated. Experiments using chemogenetic technology and behavioral tests revealed an interesting dichotomy between Npas1 neurons expressing hM3Dq versus hM4Di receptors. Using the social defeat stress test and the chronic witness defeat stress test, the data showed that male mice became more susceptible to social stress with activation of the G-coupled hM3Dq receptor, whereas both male and female mice became more resilient to social stress with activation of hM4Di receptors. The data not only further the understanding of the structural and molecular identity of VP Npas1 neurons; they indicate that the neurons bidirectionally modulate responses to social defeat stress.

Conserved Computational Framework in Pavlovian and Instrumental Learning

Neema Moin Afshar, François Cinotti, David Martin, Mehdi Khamassi, Donna J. Calu, et al.

(see pages 458–471)

In the last century, researchers have made great strides in determining the neural underpinnings of reward-based stimulus responses in animals and humans, with important implications for neurobiological disease states such as addiction. One question that remains is whether the reinforcement-learning systems that guide learning about actions and outcomes (e.g., instrumental learning) are the same that guide learning about environmental stimuli and outcomes (e.g., Pavlovian learning). Now, Moin Afshar et al. provide new insights into how these reinforcement-learning computations may be related across associative learning mechanisms. Pavlovian learning was thought to occur in "model-free" learning, in which reward-predictive cues accrue value over time, but recent theoretical work suggested that Pavlovian learning may also be "model-based," in which individuals acquire an internal model of the relationship between actions outcomes. In the current work, the researchers examined individual differences in rats' behaviors during a Pavlovian autoshaping procedure to determine whether they were predominantly exhibiting sign-tracker (ST) behaviors, which approach and interact with a reward-associated cue, or goal-tracker (GT) behaviors, which, when presented with a cue will instead approach the reward-delivery location. Computational work had suggested that ST behavior was more closely associated with model-free learning, whereas GT behaviors may indicate model-based learning. To test this, the researchers assessed ST and GT behaviors in a Pavlovian conditioned approach task, and then used a multistage decision-making task to characterize learning behaviors as model-free or model-based. They found that ST rats were more likely to use model-free learning than model-based learning, as predicted. Importantly, the study suggests that Pavlovian and instrumental learning mechanisms are not unique but may be driven by a conserved neural framework, and that these processes occur in parallel. The findings shed new light on the biobehavioral underpinnings of incentive-based learning, which could aid in better understanding—and perhaps one day correcting—aberrations in this learning in disease states.

This Week in The Journal was written by Stephani Sutherland

https://doi.org/10.1523/JNEUROSCI.twij.43.3.2023