This Week in The Journal

Paraventricular Thalamus Influences Approach and Avoidance

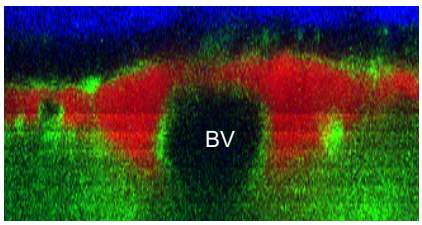
Eun A Choi and Gavan P. McNally

(see pages 3018–3029)

Two opposing motivational forces drive animal behavior: approach and avoidance. These opposing drives are often activated simultaneously in the natural world. For example, a place where an animal's food is abundant often attracts its predators. Numerous studies have investigated the neural circuits involved in approach toward rewards and avoidance of threats, but little is known about how these circuits interact in the presence of conflicting cues. Choi and McNally addressed this question and provide evidence that such interactions take place in the paraventricular thalamus.

When rats were trained to press a lever to obtain food and then underwent fear conditioning in the same arena, they froze less in response to shock-paired cues than rats that had not undergone lever training. Silencing neurons in the paraventricular thalamus further reduced freezing in lever-trained rats, suggesting it added weight to the food-seeking drive. When a separate group of rats was first trained to associate cues with shock in an arena without food available and then underwent a second round of fear conditioning in an arena where they had previously learned to seek food, they exhibited less freezing in the food-associated arena. In these rats, silencing paraventricular thalamus neurons increased freezing during the test phase, apparently reducing the influence of the food-seeking drive. Importantly, silencing neurons had no effect on either lever pressing or freezing behavior in rats that underwent only one type of training.

These results suggest that the paraventricular thalamus contributes to behavioral choices only when conflicting motivations are present. Why silencing this nucleus increased fear responses in one circumstance and reduced such responses in the other is unclear. One possibility is that the effect depended on the rats' most recent experience in the chamber: when the most recent experience included both food and shock, paraventricular thalamus activity increased fear responses, whereas when the most recent experience involved only food, paraventricular thalamus activity reduced fear responses. Future work will be required to more clearly define the role of paraventricular thalamus in shaping behaviors in the presence of conflicting motivational cues.



Dye injected into mouse cortex fills the paraventricular space (red) surrounding a blood vessel (BV), but it does not fill the subarachnoid space (unlabeled area under blue skull). Green labels parenchyma. See Schain et al. for details.

Spreading Depression Impairs Glymphatic Flow

Aaron J. Schain, Agustin Melo, Andrew M. Strassman, and Rami Burstein

(see pages 2904–2915)

Brain cells are bathed in interstitial fluid, which fills spaces between neurons and glia. Cellular waste is dumped into this fluid and diffuses toward blood vessels. Although some secreted molecules are transported into local capillaries and are cleared from the brain via blood, others are thought to be carried longer distances in the fluid-filled channels that run along vessels. These paravascular channels comprise the glymphatic system, and they have been proposed to be a major pathway for removing toxic molecules such as β-amyloid peptides from the brain.

Schain et al. report that glymphatic transport is impaired during cortical spreading depression (CSD), an electrophysiological phenomenon that contributes to neuronal death after ischemia and brain injury and likely underlies the sensory auras that precede migraine headaches in many patients. CSD results from sudden, simultaneous depolarization of all cells in a small cortical area, leading to near complete breakdown of transmembrane ion gradients and thus to neuronal silence lasting >30 s. Because depolarization causes glutamate release, it initiates a wave of depolarization/depression that propagates across gray matter. When the depolarization wave enters a new cortical area, it causes immediate, severe constriction of local arteries, followed by brief arterial dilation, and then a prolonged period of milder arterial constriction lasting >25 min. Schain et al. found that arrival of the CSD wave was quickly followed by nearly complete closure of paravascular spaces surrounding both surface and penetrating arteries and veins. Paravascular spaces remained partially constricted for >30 min. Moreover, the CSD-induced collapse of the paravascular space forced a fluorescent marker into arterial walls and slowed movement of the marker through the brain.

These results indicate that cortical spreading depression causes constriction of the paravascular space and thus impairs glymphatic clearance of solutes. By slowing the removal of inflammatory agents and other toxic molecules, this could exacerbate the damaging effects of CSD after ischemia and might contribute to the development of headache after migraine aura. How CSD waves cause collapse of the paravascular space is unclear, but swelling of astrocytic endfeet that form the wall of the paravascular space is a likely contributor, given that such swelling has been documented in previous studies.

This Week in The Journal was written by Teresa Esch, Ph.D.