This Week in The Journal

Intrinsic Oscillators in the Accessory Olfactory Bulb

Monika Gorin, Chryssanthi Tsitoura, Anat Kahan, Katja Watznauer, Daniela R. Drose, et al.

(see pages 3127–3144)

Rodents rely on the accessory olfactory system to identify potential mates, competitors, and their own offspring. Sensory neurons in the vomeronasal organ detect pheromones released in urine and pass this information to mitral cells in the accessory olfactory bulb. Mitral cells integrate information from multiple vomeronasal glomeruli and send projections to the amygdala and hypothalamus, which drive appropriate responses to other animals based on the pheromones detected.

To investigate how the accessory olfactory system processes chemosensory information, Gorin, Tsitoura, et al. recorded from mitral cells in the accessory olfactory bulb of mice. They discovered that a subpopulation of these cells exhibits rhythmic bursting activity. Blocking fast GABAergic and glutamatergic synaptic transmission disrupted oscillations in some of these cells, suggesting oscillations in this population depended on circuit interactions. But surprisingly, oscillations in other cells persisted after synaptic transmission was blocked, suggesting this population had intrinsic pacemaker-like properties.

Intrinsic oscillatory activity occurs when neurons express appropriate sets of voltage-sensitive conductances. Inward conductances that activate at relatively hyperpolarized membrane potentials depolarize neurons to an "up state" in which neurons fire; activation of outward conductances at relatively depolarized potentials eventually causes a return to the "down state." In mitral cells, Gorin, Tsitoura, et al. found that transitions to the up state were driven primarily by the persistent sodium current (I_{NaP}). In contrast, transitions to the down state depended on calcium influx through R-type Ca^{2+} channels and subsequent activation of big-conductance Ca^{2+}-activated potassium (BK) channels. Blocking I_{NaP} eliminated subthreshold membrane voltage oscillations and spiking, whereas blocking BK channels eliminated oscillations without preventing spiking, so cells spiked tonically and with variable interspike intervals. Finally, blocking R-type channels prolonged burst duration, broadened spikes, and decreased spike amplitude.

Intrinsically oscillating mitral cells were similar to nonoscillating cells in morphology and many physiological properties. Moreover, I_{NaP}, I_R, and I_{BK} were present in both populations. Given these similarities, why does only one population oscillate? Do different populations oscillate under different conditions? Future work should determine whether oscillatory activity varies over time, whether oscillations in some mitral cells drives oscillations in others, and ultimately, how oscillations affect transmission of chemosensory information to the hypothalamus and amygdala and thus influence animals' responses to pheromones.

Intrinsic oscillations in a mitral cell in mouse accessory olfactory bulb (top) are converted to tonic spiking when BK channels are blocked (bottom). See Gorin, Tsitoura, et al. for details.

Role for Subiculum–Accumbens Projection in Relapse

Nathan J. Marchant, Erin J. Campbell, Leslie R. Whitaker, Brandon K. Harvey, Konstantin Kaganovsky, et al.

(see pages 3281–3294)

Alcoholism is a chronic illness, and for those who stop drinking, returning to an environment that previously involved alcohol consumption often triggers relapse. Understanding the neural pathways underlying such relapse may lead to more effective treatments for alcoholism.

Previous studies have suggested that the nucleus accumbens shell is important for context-induced relapse. To determine which inputs to the shell are required, Marchant et al. first trained rats to seek alcohol in one context (A), then extinguished alcohol seeking in a second context (B) by pairing alcohol delivery with a negative consequence, namely, a foot shock. They then measured unreinforced lever pressing when rats were returned to context A or B. Notably, this protocol differs from those typically used to investigate context-induced relapse in that rats voluntarily abstained from alcohol because of its negative consequences—like humans often do—rather than abstaining involuntarily because alcohol was unavailable.

Although neurons in several brain areas were activated when rats were returned to context A, only those activated in the ventral subiculum projected to the accumbens shell. Inhibiting these neurons with DREADDs technology or by injecting GABA receptor agonists into the ventral subiculum decreased context-induced alcohol seeking when rats were returned to context A after abstaining in context B. Neither treatment altered the latency to begin lever pressing, however. Unexpectedly, blocking subiculum–accumbens projections had no effect on a second bout of context-induced relapse after alcohol seeking was re-established in context A and re-extinguished in context B.

These results indicate that projections from ventral subiculum to nucleus accumbens shell promote alcohol consumption in particular environments after a period of abstinence prompted by negative consequences. The lack of effect on latency in these experiments suggests that the projection may support the drive to continue seeking alcohol in the absence of reward, rather than the initial urge to seek alcohol in a previously rewarding environment. Importantly, the retraining results suggest that neural pathways involved in initial and later episodes of relapse may differ. If so, different treatment strategies may be required to prevent relapse to alcohol use depending on an individual's history.

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