This Week in The Journal

Infralimbic–Accumbens Projection Suppresses Taste Aversion

Seth W. Hurley and Regina M. Carelli

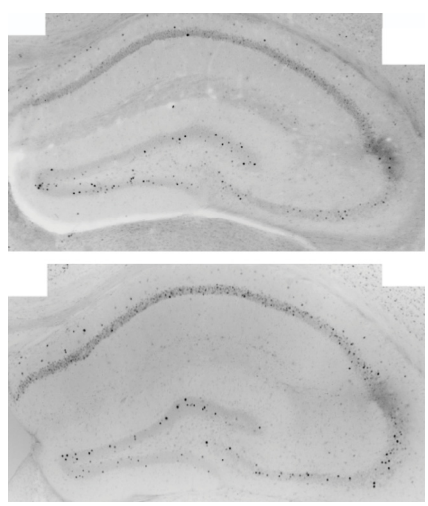
(see pages 6888–6895)

The human ventromedial prefrontal cortex, and the homologous infralimbic cortex (IL) in rodents, regulates responses to appetitive and aversive stimuli. In particular, IL suppresses learned responses to stimuli when conditions change. For example, activation of IL inhibits conditioned freezing in response to a stimulus that previously predicted electrical shock, thus promoting fear extinction. Similarly, the activation of IL inhibits conditioned taste aversion.

Whereas IL likely inhibits conditioned freezing responses via projections to the amygdala, Hurley and Carelli hypothesized that IL inhibits taste aversion via projections to the nucleus accumbens shell (NAcSh), which has previously been implicated in learned taste aversion. To test their hypothesis, they induced aversive responses to sucrose by infusing sucrose solution into rats' mouths, then injecting LiCl to produce malaise. The next day, they examined how photostimulation of IL axons in NAcSh affected facial responses to infused sucrose solution, counting tongue protrusions and lip licks (appetitive responses), as well as gapes and mouth wipes (aversive responses).

As expected, rats primarily showed appetitive responses to sucrose on the first day. After LiCl pairing, however, control rats showed mainly aversive responses. Activation of IL inputs to NAcSh reduced aversive responses in male rats, but surprisingly not in females. Nonetheless, when rats of either sex were given a choice between plain and sucrose-flavored water the next day, those that had experienced IL–NAcSh pathway activation consumed more sucrose than control rats that had undergone aversion conditioning without subsequent stimulation. Furthermore, when given the opportunity to self-stimulate the IL–NAcSh pathway, both male and female rats did so, indicating activation of this pathway was reinforcing. Notably, IL–NAcSh pathway stimulation did not diminish aversive responses to intraoral infusion of the innately aversive tastant quinine.

These results suggest that projections from the IL to the NAcSh acutely inhibit learned taste aversion in male, but not in female rats. The pathway appears to facilitate extinction of learned taste aversion in both sexes, however, leading to increased sucrose consumption the next day. Activation of this pathway is reinforcing in itself, yet insufficient to suppress responses to innately aversive tastes. Future work should determine which NAcSh neurons are targeted by IL projections and further investigate the sex-dependent effects.



Stimulation of the cerebellar simplex lobule (top) or vermis (bottom) produces distinct patterns of c-Fos expression in the hippocampus. See Zeidler et al. for details.

Cerebellar Activation Modulates Hippocampal Function

Zachary Zeidler, Katerina Hoffmann, and Esther Krook-Magnuson

(see pages 6910–6926)

The cerebellum contributes to many functions beyond motor learning and coordination, including working memory, social interactions, and spatial navigation. The role of the cerebellum in spatial navigation has been proposed to involve the use of self-motion information to construct spatial maps represented by the firing of hippocampal place cells. Indeed, place cell firing properties are altered in mice in which cerebellar plasticity is impaired (Rochefort et al., 2013, Front Neural Circuits 7:35). The cerebellum does not project directly to the hippocampus, however, so how it influences hippocampal function is poorly understood.

To address this question, Zeidler et al. photostimulated two regions of cerebellar cortex—the vermis and the simplex lobule—in mice that expressed channelrhodopsin in Purkinje cells. Stimulation of either cerebellar region increased local field potential power at the stimulus frequency in the hippocampus. The rate of calcium transients measured with a fluorescent calcium indicator decreased in the hippocampus during cerebellar stimulation, but after stimulation offset, the amplitude of events increased, suggesting rebound bursting occurred. c-Fos labeling indicated that vermis stimulation increased activation of neurons in the alveus/stratum oriens and pyramidal cell layers of CA1, whereas simplex stimulation increased activation of interneurons in the molecular layer of the dentate gyrus and reduced activation in CA3.

Both simplex and vermis stimulation impaired animals' performance on a hippocampus-dependent object location memory task. But performance on a hippocampus-independent object recognition task that requires similar motor function was unaffected. Effects on object location memory may have stemmed from reduced encoding of object location when Purkinje cells were activated. Object locations were encoded by more place cells in control animals than in stimulated animals; and after an object was moved, the moved object was represented by more place cells than the unmoved object in control animals, whereas both locations were encoded by similar numbers of place cells in stimulated animals.

These results demonstrate that Purkinje cells in different regions of cerebellum modulate activity in different areas of the hippocampal formation and thus influence the encoding of object location by hippocampal place cells. Future work should identify the intermediate targets that mediate this effect and how these pathways function under physiological conditions.

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

https://doi.org/10.1523/JNEUROSCI.twij.40.36.2020