This Week in The Journal

Sources of Input to Developing Barrel Cortex

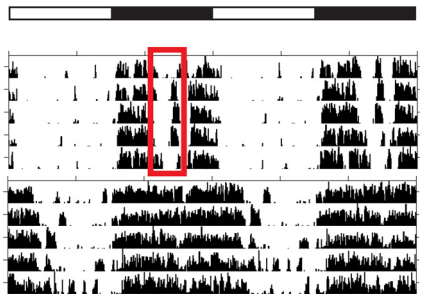
Dinara Akhmetshina, Azat Nasretdinov, Andrei Zakharov, Guzel Valeeva, and Roustem Khazipov

(see pages 9922–9932)

Neuronal activity shapes the development of sensory cortical circuits. Spontaneous activity in retinal cells shapes visual cortical circuits before eye opening, whereas sensory information from whisker movements is thought to shape circuits in the developing somatosensory barrel cortex. Input to barrel cortex can arise from active whisker movements that result in contact with external objects or from passive whisker movements caused by movements of littermates and the mother. To determine the relative importance of these sources of sensory input, Akhmetshina et al. recorded from cortical barrels in unanesthetized rat pups during the first postnatal week.

Active whisker movements produced local field potential oscillations and spike bursts in barrel cortex regardless of whether the whiskers contacted an external object. Activity was nearly twice as great when an object was contacted than when whisker movement was unobstructed, however. Similarly, electrically evoked whisker movements increased activity in barrel cortex, with greater activity produced when an object was contacted. In addition, mechanical deflection of stationary whiskers activated barrel cortex, and this activity was similar in magnitude to activity produced when electrically induced whisker movements resulted in object contact. Likewise, barrel cortex activity was nearly two-fold greater when pups were in contact with littermates than when they were isolated. Finally, cutting the sensory nerve innervating the whisker pad reduced barrel cortex activity to about two-thirds of control level, suggesting that sensory input is not the only driver of activity in this cortical area.

These results indicate that both passive and active whisker movements drive activity in developing barrel cortex. Observation of pups in the home cage revealed that pups' whiskers were in contact with an external object nearly 95% of the time, which together with the electrophysiology results, suggests that barrel cortex is strongly activated while it is developing. The authors note that the analogous period of somatosensory cortex development in humans occurs *in utero*, when fetal movements result in increased contact with the uterine walls. Movements of premature infants may be less likely to result in contact with an external object, which may hinder development of somatosensory circuits. Therefore, ensuring contact with the environment may enhance cortical development in these infants.



Plots of ten individuals' activity level across the light– dark cycle (periods shown in bar at top) reveal that normal mice (top five actograms) take a siesta (marked by red box) in the middle of the dark period, but serotonin-depleted mice (bottom five actograms) do not. See Whitney et al. for details.

Behavioral Effects of Adult Serotonin Depletion

Meredith Sorenson Whitney, Ashley M. Shemery, Alexandra M. Yaw, Lauren J. Donovan, J. David Glass, et al.

(see pages 9828 –9842)

Serotonin regulates many physiological processes and behaviors, including arousal, circadian activity patterns, aggression, locomotion, and respiration. Because serotonin reuptake inhibitors effectively treat depression and anxiety disorders, serotonin is also thought to regulate these affective states. Genetic manipulations that disrupt serotonergic neurotransmission have produced conflicting evidence regarding this hypothesis, however. For example, knocking out tryptophan hydroxylase 2 (Tph2), the rate-limiting enzyme for serotonin synthesis, caused increases, decreases, or no change in depression- and anxiety-like behaviors, depending on the test and/or the laboratory in which tests were performed (Mosienko, et al. 2015 Behav Brain Res 277: 78). Although the reason for these discrepancies is unclear, life-long depletion of serotonin in these animals might lead to compensatory changes that differ depending on rearing conditions and are sensitive to subtle differences in testing procedures.

To avoid this confound, Whitney et al. knocked out *Tph2* selectively in the dorsal and medial raphe nuclei of adult mice. This greatly reduced serotonin levels in the targeted nuclei, forebrain, and suprachiasmatic nucleus, without significantly affecting serotonin levels in the caudal raphe nuclei, which project primarily to the hindbrain. Adult serotonin depletion had no apparent effect on anxiety-like behaviors in the open field, elevated plus maze, or light-dark box tests. Surprisingly, however, serotonin-depleted mice were significantly more active than controls in both the open arena and the home cage. In addition, conditional knockout mice spent less time stationary during the dark (active) period and less time sleeping during the light period than controls. Moreover, the circadian active period began sooner, ended later, and was >2 h longer in serotonin-depleted mice. Finally, serotonin-depleted mice did not take daily siestas, the ~2 h periods of sleep that typically occur during the dark period in wild-type mice.

These results are consistent with previous studies that showed serotonin depletion lengthened the circadian active period and did not alter anxiety-like behaviors. But the hyperactivity and loss of siestas following serotonin depletion are surprising, because previous work has suggested that serotonin promotes arousal and locomotion. Thus, these results add to growing evidence that the raphe nuclei contain functionally diverse classes of serotonergic neurons that may exert opposing effects through activation of distinct receptors (Filip and Bader, 2009 Pharmacol Rep 61:761).

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