This Week in The Journal

Role for Calcium as Granule Cells Enter Olfactory Bulb

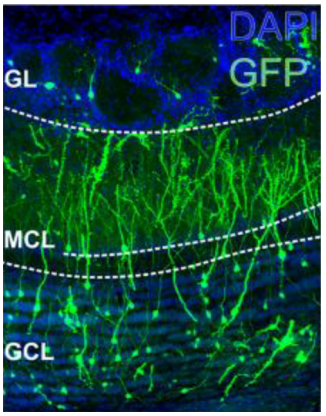
Stéphane Bugeon, Clara Haubold, Alexandre Ryzynski, Harold Cremer, and Jean-Claude Platel

(see pages 2630–2644)

Neural progenitors are generated in the rodent subventricular zone (SVZ) throughout adulthood. These progenitors travel tangentially through the rostral migratory stream until they reach the olfactory bulb, where they switch to radial migration to enter the bulb. The progenitors differentiate into two types of GABAergic interneurons, which settle in different layers: progenitors generated in the lateral wall of the ventricle usually become granule cells, which populate the deepest layer of the bulb, whereas progenitors generated in the medial wall usually become periglomerular neurons, which migrate through the granule cell layer and overlying mitral cell layer to populate the glomerular layer, the most superficial layer of the olfactory bulb.

Although studies have identified many molecular and cellular mechanisms that contribute to migration of SVZ-derived progenitors, whether granule cell and periglomerular neuron precursors depend on the same mechanisms has been unclear. To address this, Bugeon et al. targeted different regions of the SVZ to selectively label each type of progenitor and track its migration. They found little difference between granule cell and periglomerular neuron progenitors as they migrated tangentially in the rostral migratory stream. Both populations alternated between stationary phases and fast nuclear translocation, and the duration of these phases and the overall rate of movement were comparable in the two populations. In addition, calcium transients, mediated by influx through L-type voltage-sensitive channels, occurred at similar frequencies and amplitudes in the two populations. When cells began their radial migration into the olfactory bulb, however, calcium-transient frequency and amplitude increased selectively in granule cells. Inhibiting these transients did not affect tangential migration of either precursor type, but it significantly reduced the entry of granule cell precursors into the olfactory bulb and reduced granule cell survival.

These results suggest that granule cell and periglomerular neuron progenitors rely on similar mechanisms for tangential migration, but rely on distinct mechanisms during radial migration. Future work should determine what causes the selective increase in calcium transients in granule cells; the authors ruled out roles for glutamate, GABA, and glycine receptors, but previous work suggests serotonin or P2Y1 purinergic receptors may be responsible. Whether calcium transients increase in periglomerular neurons as they reach their final destination should also be investigated.



Although some neural progenitors generated in the lateral wall of the ventricle (green) ultimately settle in the glomerular layer (GL) or mitral cell layer (MCL) of the olfactory bulb, the vast majority populate the granule cell layer (GCL). See Bugeon et al. for details.

Response Properties of Dorsal Raphe Dopamine Neurons

Jounhong Ryan Cho, Xinhong Chen, Anat Kahan, J. Elliott Robinson, Daniel A. Wagenaar, et al.

(see pages 2645–2655)

Midbrain dopamine neurons are key drivers of reinforcement learning and goal-directed behavior. Abundant evidence has shown that the firing rate of dopamine neurons in the ventral tegmental area increases when an unexpected reward is received and decreases when an expected reward is absent. These neurons also respond to neutral cues that predict upcoming reward or aversive experiences. Other midbrain dopamine neurons show a different response pattern: their firing rate increases in response to both positive and negative stimuli. Accumulating evidence, including work by Cho et al., suggests that dopamine neurons in the dorsal raphe nucleus (DRN) exhibit this property.

Cho et al. expressed a fluorescent calcium indicator in DRN dopamine neurons and used fiber photometry to measure population-wide increases in calcium as freely moving mice learned to associate sounds with sucrose reward or footshock punishment. Consistent with previous work, population activity increased in response to sucrose or a sucrose-predicting cue, but not a neutral cue. Subsequent fear conditioning with the previously unpaired cue caused DRN dopamine neurons to respond to that cue, but not to the cue that formerly predicted sucrose. Notably, responses to sucrose or shock delivery were greater when the predictive cue was omitted and thus the stimulus was unexpected. Furthermore, responses to sucrose-paired cues were diminished when mice were sated.

The authors next asked whether population responses stemmed from separate sets of neurons that encoded different cues or from a single set of neurons that responded to multiple cues. To answer this, they imaged single neurons in head-fixed mice. As predicted from population recordings, many neurons developed responses to the reward-paired cue. Most of these neurons also responded to reward delivery. Surprisingly, however, no individual neurons responded to the shock-paired cue. Importantly, responses to aversive cues were also absent in population recordings from head-fixed mice, suggesting that this experimental setup eliminated such responses.

These results suggest that DRN dopamine neurons signal salient events, whether aversive or appetitive, but these responses are modulated by internal and external conditions. Why neurons became unresponsive to aversive cues in head-fixed mice is unclear, but one possibility is that mounting a defensive behavioral response is unnecessary or impossible in this condition. Future work should test this hypothesis.

This Week in The Journal was written by Teresa Esch, Ph.D.
https://doi.org/10.1523/JNEUROSCI.twij.41.12.2021