This Week in The Journal

Encoding of Pitch Trajectories in Mouse Auditory Cortex

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(see pages 4469–4482)

Vocalizations vary not only in their predominant frequency (pitch) and amplitude, but also in how pitch and amplitude change over time. These features contain information about the purpose of the vocalization as well as the species and age of the vocalizer. For example, mouse pups, when isolated from their mother, produce brief ultrasonic vocalizations that elicit retrieval, whereas adult males produce vocalizations that elicit approach by females for mating. Pup and adult calls can be distinguished partly by frequency range, duration, and repetition, but auditory cortical neurons can discriminate pup and adult vocalizations even when the initial frequency and duration are similar. Therefore, Chong et al. hypothesized that the frequency trajectory, that is, how the pitch changes during the call, also helps to distinguish adult and pup vocalizations. To test this hypothesis, they recorded single units in primary and secondary auditory cortex of adult female mice while presenting natural and simulated vocalizations.

The authors reasoned that if a neuron encodes the frequency trajectory of calls, it must be active after the whole trajectory has been presented—that is, after the call ends. Approximately 44% of call-responsive single units in auditory cortex showed spiking after the call ended (Off responses). To test whether pitch changes during the call influenced these responses, the authors created a six-parameter tone model that allowed them to reproduce natural vocalizations, then modulate the frequency, duration, and other attributes of the call. Consistent with their hypothesis, Off responses in single units were much stronger for models simulating natural calls than for narrow-band noise using the same frequencies. Furthermore, when frequency modulation was added to the best pure tone stimulus for a given unit, the Off response of the unit increased.

Further analyses suggested that the amplitude of frequency modulation was greater in pup than in adult calls and that auditory cortical neurons of mice with maternal experience preferred calls with greater frequency modulation than neurons of inexperienced mice.

These results suggest that neurons in primary and secondary auditory cortex of mice are responsive to the frequency trajectory of calls and that maternal experience increases the responsiveness of neurons to pup calls. Future work should determine how responsiveness to frequency trajectory is produced and how it is altered by maternal experience.

Neuronal activity (pERK, blue) and serotonergic innervation (5-HT, magenta) in the telencephalon (outlined by DAPI, yellow) of a juvenile zebrafish exposed to a novel tank. Social isolation during development changes serotonergic signaling and behavior in fish. See Varga et al. for details.

Effects of Isolation on Behavior and 5-HT in Larval Zebrafish

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(see pages 4551–4564)

All of our experiences shape brain circuitry and influence how we react to future events; but experiences that occur early in life, while the brain is still

developing, may have the most profound effects on future behavior. Mild challenges early in life may make one more resilient to stress later in life, whereas severe adversity can increase one's susceptibility to behavioral and psychiatric disorders. Such effects are not restricted to humans or even to mammals: social isolation during development alters later behavior in zebrafish as well.

Young zebrafish larvae [8 d postfertilization (dpf)] prefer light areas over dark areas of a novel tank, but this preference normally reverses with age. Indeed, Varga et al. found that larvae at 14 and 28 dpf preferred the dark half of an unfamiliar tank. If fish were housed in isolation from 14 to 28 dpf, however, they subsequently preferred the light part of the tank and showed fewer-than-normal transitions between light and dark areas. These behavioral changes were accompanied by changes in serotonin (5-HT) levels in the brain. Specifically, whereas serotonin levels decreased when group-reared fish were introduced to the light-dark tank, baseline levels were lower in fish raised in isolation and increased when these fish were placed in the light-dark tank. Isolated fish also showed abnormal behaviors in other tests. For example, whereas the appearance of a moving object increased swimming in socially reared fish, it reduced swimming in isolated fish. Furthermore, whereas socially reared fish preferred to be near another fish in a U-shaped tank, isolated fish preferred to stay away from the other fish. Notably, treating isolated fish with buspirone, which suppresses serotonin release by acting on 5-HT_{1A} autoreceptors, reversed the effects of isolation on behavior in all three tasks.

These results suggest that social isolation of larval zebrafish alters responses to potentially dangerous stimuli by disrupting the development of serotonergic signaling pathways. These effects are reminiscent of the effects of early-life stress in mammals. Therefore, zebrafish might be a useful model for studying how early stress alters neural circuitry to produce abnormal behavioral responses in adults.

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