This Week in The Journal

More Neuronal Variability, Slower Learning in Adolescents

Melissa L. Caras and Dan H. Sanes

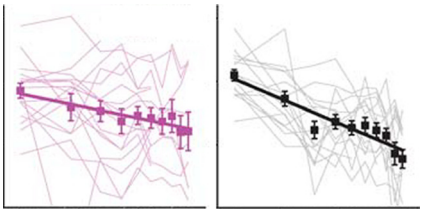
(see pages 2889–2902)

During adolescence, animals become less dependent on parents and begin to seek new social relationships and experiences. The brain undergoes many changes during this period, including changes in reward circuitry and strengthening of executive control by prefrontal cortex. In addition, sex hormones influence circuit plasticity at this time. The combined influence of these numerous changes make adolescence a unique developmental stage, rather than part of a steady progression from childhood to maturity. In fact, in some ways children are more like adults than adolescents are. For example, when undergoing perceptual training—in which individuals learn to distinguish similar sensory stimuli—children and adults improve at similar rates, whereas adolescents improve more slowly.

Caras and Sanes demonstrated this effect in gerbils trained to detect amplitude modulation of broadband noise. Several modulation depths were tested on each day, with depths decreasing as perception improved. Consistent with previous studies of perceptual learning, the detection threshold (that is, the smallest magnitude of modulation perceived) declined at similar rates in young and adult gerbils, whereas adolescents improved at approximately half that rate.

To understand the neural basis of this reduced learning rate, the authors monitored changes in the sensitivity of auditory cortical neurons to noise amplitude modulation across training days. On the first day of training, neuronal sensitivity was similar in adolescents and adults. At the population level, neuronal sensitivity increased with training in both age groups, but like for behavior, the average rate of change in adolescents was approximately half that in adults. This was attributable to greater response variability in adolescents: whereas the sensitivity of most units in adults improved each day, many units in adolescents showed no change or even decreased sensitivity from one day to the next. Furthermore, responses to modulated and unmodulated noise were more variable in adolescents, resulting in a smaller overall signal-to-noise ratio.

These results suggest that slowed perceptual learning in adolescents stems from greater variability in cortical encoding of stimuli. The reasons for this increased variability are unclear, but they may stem from greater variability in internal states such as motivation or attention. Whether similar factors account for the decrease in performance between young and adolescent animals remains to be determined.



Perceptual threshold (*y*-axis) decreases more slowly across training days (*x*-axis) in adolescent gerbils (left) than in adults (right), likely because of greater day-to-day variability in adolescents. Thin lines show trajectories in individual animals, thick lines represent linear regressions. See Caras and Sanes for details.

Increased Influence of M2 on Striatum in OCD Model

Victoria L. Corbit, Elizabeth E. Manning, Aryn H. Gittis, and Susanne E. Ahmari

(see pages 2965–2975)

The striatum is essential for learning complex motor behaviors and for engaging these behaviors either habitually or to obtain specific goals. Striatal selection of specific behaviors is regulated by inputs from frontal cortical areas, including the orbitofrontal cortex (OFC). Altered activity in these corticostriatal circuits is thought to underlie compulsive disorders, in which people feel irresistible urges to perform specific ritualistic behaviors. Evidence for this hypothesis comes from functional imaging studies, which have shown that activity in OFC and striatum are abnormally elevated in people with obsessive compulsive disorder (OCD).

To identify possible neural underpinnings of corticostriatal hyperactivity in compulsive disorders, Corbit et al. used mice lacking the postsynaptic scaffolding protein Sapap3. These mice engage in repetitive grooming behaviors that are suppressed by drugs used to treat OCD. Furthermore, striatal spiny projection neurons (SPNs) in these animals spike at higher rates than those in wild-type. To determine the cause of this elevated spiking, Corbit et al. first examined the intrinsic excitability of SPNs and the fast-spiking interneurons (FSIs) that inhibit them. No effect of Sapap3 knock-out was found. The authors then asked whether activation of FSIs was reduced. It was not; in fact, excitatory drive to FSIs was higher in Sapap3-null mice than in controls. Finally, the authors asked whether cortical inputs to the striatum were altered.

As expected, retrograde labeling revealed that many inputs to the striatum came from the OFC, particularly its lateral region. Surprisingly, however, the greatest number of inputs came from the secondary motor area, M2, in both Sapap3 knock-out and wild-type mice. Moreover, whereas stimulation of lateral OFC axons evoked smaller EPSCs in Sapap3-lacking SPNs than in controls, stimulation of M2 axons evoked sixfold larger EPSCs in Sapap3-lacking SPNs than in controls. These enlarged EPSCs were attributable to increases in currents mediated by AMPA and NMDA receptors.

These results indicate that increased sensitivity of striatal SPNs to inputs from M2 might contribute to excessive grooming in Sapap3 mice. Similarly augmented sensitivity might contribute to compulsive behaviors in humans. Future work should determine whether increased sensitivity occurs predominantly in direct- or indirect-pathway SPNs, which are thought to facilitate or suppress desired or competing behaviors, respectively.

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