This Week in The Journal

Cellular/Molecular

Diverse Treatments Increase ΔFosB in Striatal Neurons

Mary Kay Lobo, Samir Zaman, Diane M. Damez-Werno, Ja Wook Koo, Rosemary C. Bagot, et al.

(see pages 18381–18395)

Chronic exposure to stress, drugs of abuse, antipsychotics, or natural rewards all increase levels of the transcription factor ΔFosB in the striatum; but as Lobo et al. demonstrate, they affect the two functionally distinct classes of medium spiny neurons (MSNs) differently. Whereas cocaine, ethanol, and cannabinoids induced ΔFosB expression only in MSNs that expressed D1-type dopamine receptors (D1-MSNs), the antipsychotic drug haloperidol increased ΔFosB expression selectively in D2-MSNs. In contrast, natural rewards (sucrose and environmental enrichment), increased ΔFosB levels in both D1-MSNs and D2-MSNs. Interestingly, the effects of stress differed across mice: in mice that were susceptible to the deleterious effects of social defeat stress, such stress induced ΔFosB expression selectively in D2-MSNs; but in resilient mice and those treated with an antidepressant, stress induced ΔFosB expression only in D1-MSNs. The effects of different treatments on D1-MSNs and D2-MSNs stems from their effects on striatal inputs, and optogenetic stimulation of different afferent regions also induced different patterns of ΔFosB expression in MSNs.

Systems/Circuits

Oral PYY Reduces Food Intake without Taste Aversion

Maria D. Hurtado, Valeriy G. Sergeyev, Andres Acosta, Michael Spegele, Michael La Sala, et al.

(see pages 18368–18380)

When food is consumed, intestinal cells secrete peptide YY (PYY) into the blood. Activation of Y2R receptors by PYY produces the feeling of satiation and thus reduces food intake. Exogenous PYY might be useful for weight reduction, except systemic administration causes nausea and taste aversion. Y2Rs are expressed in several brain nuclei, on abdominal sensory nerves, and in the oral mucosa; to determine which of these sites are responsible for satiation and taste aversion in mice, Hurtado et al. compared behavioral responses and neuronal activation patterns induced by PYY delivered by injection and an oral spray. Unlike systemic PYY, oral PYY reduced food intake without inducing taste aversion. Although both oral and systemic PYY increased neuronal activation in hypothalamic nuclei involved in hunger and satiety, only systemic PYY activated a brainstem area that processes visceral satiety information. Furthermore, oral PYY produced less activation than systemic PYY in an area involved in aversive responses. Therefore, oral PYY might help reduce food intake in humans.

Behavioral/Cognitive

Longer Viewing Reduces Saccadic Suppression of Displacement

Eckart Zimmermann, M. Concetta Morrone, and David C. Burr

(see pages 18396–18401)

During saccades, visual motion detection is suppressed to maintain a stable percept as the image of the world rapidly shifts across the retina. We can determine whether objects moved during saccades by comparing the relative position of objects before and after saccades; but studies in which targets were displaced while saccades were in progress have found that people are less sensitive to displacement during saccades than during fixation. Zimmermann et al. note, however, that in these studies, saccades were initiated immediately after targets appeared. Because previous work suggested that spatiotopic representations develop over time, they hypothesized that subjects' ability to detect object displacement during saccades would improve if targets were viewed for longer periods before a saccade. This was in fact the case. As the previewing duration increased (up to 500 ms), the threshold for discriminating target displacement decreased. Importantly, discrimination sensitivity as a function of preview duration was similar for displacement occurring during saccades and masked displacement occurring during fixation.

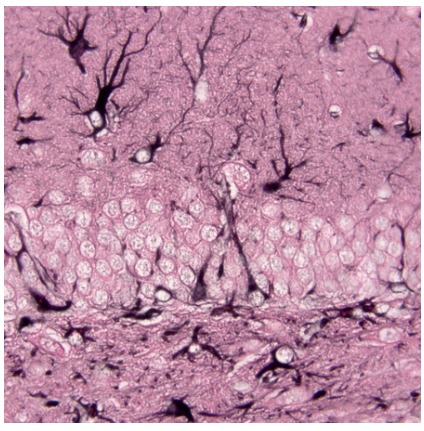
Neurobiology of Disease

Neurogenesis Is Impaired in a Model of Alexander Disease

Tracy L. Hagemann, Richard Paylor, and Albee Messing

(see pages 18698–18706)

In Alexander disease (AxD), gain-of-function mutations in glial fibrillary acidic protein (GFAP) cause aggregation and deposition of this intermediate filament protein and result in developmental delays, motor impairment, and ultimately, death. In the mature CNS, GFAP is expressed predominantly in astrocytes, but it is also expressed in neural progenitors in the dentate gyrus. This, along with the fact that astrocytes can influence adult neurogenesis, prompted Hagemann et al. to investigate neurogenesis in mice expressing an AxD-like mutation in GFAP. The number of proliferating precursors and immature neurons was greatly reduced in the dentate gyrus of 2-month-old mutant mice, indicating that adult neurogenesis was impaired. Mutant mice showed deficits in spatial learning and contextual fear conditioning, but whether this resulted from reduced neurogenesis or other pathological features—such as reactive gliosis, abnormal regulation of synaptic transmission by astrocytes, or stress pathway activation—remains to be determined. Furthermore, whether reduced neurogenesis results from defects in radial glia or mature astrocytes is unknown.



In a mouse expressing an AxD-linked mutation in GFAP (black), radial glia-like cells in the dentate gyrus are greatly hypertrophied. See the article by Hagemann et al. for details.