This Week in The Journal

Cellular/Molecular

Novel Stressor Reverses Effect of Repeated Stress

Jaclyn I. Wamsteeker Cusulin, Laura Senst, G. Campbell Teskey, and Jaideep S. Bains

(see pages 6177–6181)

Parvocellular neuroendocrine cells (PNCs) in the hypothalamic paraventricular nucleus activate stress responses by secreting corticotropin-releasing hormone, leading to glucocorticoid release from the adrenal glands. Glucocorticoid feedback onto PNCs triggers endocannabinoid synthesis in these cells, and the endocannabinoids retrogradely inhibit glutamate release from presynaptic terminals, thus attenuating the stress response. In rats, repetitive stress disrupts this feedback by downregulating endocannabinoid receptors (CB1Rs) on both glutamatergic and GABAergic terminals. Wamsteeker Cusulin et al. now report that presenting a novel stressor after repetitive homotypic stress reverses CB1R downregulation on GABAergic terminals. As shown previously, depolarizing PNCs in hypothalamic slices from unstressed rats caused CB1R-dependent, depolarization-induced suppression of inhibition (DSI), and DSI was reduced in rats exposed to a single stressor for 5 d. If a novel stressor was administered on the fifth day, however, DSI returned to control levels. This recovery was paralleled by increases in the ability of a CB1R agonist to reduce IPSC amplitude, suggesting it was mediated by restoration of CB1Rs.

Development/Plasticity/Repair

TNFα Reduces Surface Levels of AMPA Receptors in Striatum

Gil M. Lewitus, Horia Pribiag, Rachna Duseja, Michel St-Hilaire, and David Stellwagen

(see pages 6146–6155)

Tumor necrosis factor α (TNFα) is released by glia in healthy brains, where it regulates synaptic function. For example, it promotes insertion of AMPA receptors (AMPARs) in hippocampal neurons, and it appears necessary for maintaining optimal levels of AMPARs in these neurons. TNFα also increases in the brain after injury, infection, or onset of neurodegenerative diseases, and in these conditions it can promote apoptosis or survival of different neurons, depending on which receptors and downstream signaling molecules the neurons express. Because TNFα levels increase in the striatum after chronic treatment with antipsychotics and in people with Huntington's and Parkinson's diseases, Lewitus et al. asked how TNFα affects the principal striatal cells, medium spiny neurons. In contrast to its effects in hippocampus, TNFα reduced surface levels of AMPARs—particularly those that are permeable to Ca^{2+}—in mouse striatal slices. Interestingly, knocking out TNFα increased involuntary facial movements induced by chronic haloperidol treatment, suggesting that TNFα normally attenuates the effects of this treatment.

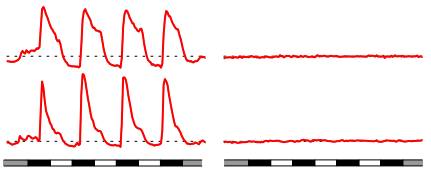
Systems/Circuits

Kainate Receptors Mediate All Cone Bipolar Cell Responses

Bart G. Borghuis, Loren L. Looger, Susumu Tomita, and Jonathan B. Demb

(see pages 6128–6139)

Cone photoreceptors release glutamate on two broad classes of bipolar cells: OFF bipolar cells, which are depolarized by light decrements, and ON bipolar cells, which are depolarized by light increments. OFF bipolar cells are further divided into those with sustained responses and those with transient responses. A widely accepted hypothesis is that transient OFF bipolar cells express AMPA receptors (AMPARs), which quickly recover from desensitization, while sustained OFF bipolar cells express kainate receptors (KARs), which recover more slowly. Surprisingly, however, Borghuis et al. provide strong evidence that all OFF bipolar cells in mouse retina depend on KARs, and not on AMPARs. Light-evoked activation of bipolar cells—detected either with a glutamate biosensor expressed in postsynaptic neurons or via electrophysiological recordings in bipolar cells or postsynaptic ganglion cells—was blocked by KAR antagonists but not by AMPAR antagonists. Furthermore, despite their slow recovery, KARs in OFF bipolar cells were able to encode changes in illumination with temporal frequencies up to 20 Hz.



Neither OFF-sustained (top traces) nor OFF-transient (bottom traces) responses are blocked by AMPAR antagonists (left), but both are blocked by KAR antagonists (right). Light stimulus shown below each set of traces. See the article by Borghuis et al. for details.

Behavioral/Cognitive

Negative Reinforcement Is Subject to Devaluation

Anushka Fernando, Gonzalo Urcelay, Adam Mar, Anthony Dickinson, and Trevor Robbins

(see pages 6286–6293)

Animals can be conditioned to perform a behavior with either positive or negative reinforcement. For example, rats will press a lever more frequently if doing so results in getting food or avoiding a shock. While much is known about how positive reinforcement drives operant behavior, considerably less is known about how negative reinforcement shapes behavior. For example, allowing free access to a food is known to cause devaluation, reducing the animal's motivation to perform the food-reinforced behavior; but devaluation of a negative reinforcer has not been demonstrated until now. To do so, Fernando et al. trained rats to press a lever to avoid shocks, then treated rats with morphine or vehicle while delivering shocks without lever access. When rats were subsequently given lever access without shocks, morphine-treated rats pressed the lever less frequently than controls, indicating that reducing the pain associated with the shock reduced operant responding. When shocks were reintroduced after drug withdrawal, however, operant responding rapidly returned to control levels.