

This Week in The Journal

● Cellular/Molecular

Nasal Mucus Alters Odor Perception

Ayumi Nagashima and Kazushige Touhara

(see pages 16391–16398)

Individual olfactory sensory neurons (OSNs) typically express one of several hundred odorant receptor molecules, and OSNs expressing the same receptor converge on the same glomeruli in the olfactory bulb. Therefore, the activity pattern produced in the bulb by a particular odorant can usually be predicted by determining what OSNs the odorant activates. Occasionally, however, odorants that activate particular OSNs *in vitro* do not activate the expected glomeruli *in vivo*. Nagashima and Touhara hypothesized that such odorants are altered in the nasal mucosa before activating odorant receptors. They found that odorants containing an aldehyde or acetate group were quickly converted to alcohols and/or acids in the nasal cavity, and this conversion could be blocked by a carboxylesterase inhibitor. The inhibitor also altered the pattern of glomeruli activated by odorants, and mice trained to discriminate odors of this type did not do so after inhibitor treatment, suggesting that odorant metabolites contribute to odor perception *in vivo*.

▲ Development/Plasticity/Repair

Visual SRPs and LTP Are Mutually Occluding

Sam F. Cooke and Mark F. Bear

(see pages 16304–16313)

Visual stimuli evoke local field potentials in layer IV of visual cortex, and if the same stimulus is presented repeatedly over several days, the amplitude of the visually evoked potential (VEP) increases. Such potentiation could enhance visual perception. It is highly specific to the presented stimulus, however: presenting stripes of a given width and orientation does not potentiate responses to stripes of other widths or orientations. Such stimulus-specific response potentiation (SRP) resembles electrically in-

duced long-term potentiation (LTP) in that it requires NMDA receptor activation and insertion of AMPA receptors. Cooke and Bear show that SRP also resembles LTP in that its maintenance requires a constitutively active form of protein kinase C. Furthermore, SRP and LTP of thalamocortical inputs to visual cortex occluded each other, suggesting they involve overlapping molecular mechanisms. In contrast to SRP, however, LTP simultaneously enhanced VEPs for a range of stimuli, suggesting it is less specific.

■ Behavioral/Systems/Cognitive

Optogenetic Activation of Prefrontal Cortex Reverses Depression

Herbert E. Covington III, Mary Kay Lobo, Ian Maze, Vincent Vialou, James M. Hyman, et al.

(see pages 16082–16090)

Recent evidence suggests that decreased activity in medial prefrontal cortex (mPFC) contributes to depression in humans, and electrical stimulation of the anterior cingulate region of mPFC can relieve depression resistant to other treatments. Covington et al. found that immediate early genes up-regulated during neuronal activity were expressed at lower levels postmortem in the medial anterior cingulate cortex of clinically depressed people compared with controls. The same genes were downregulated in ventral mPFC of mice that exhibited depression-like behaviors (i.e., social avoidance and reduced sucrose preference) after chronic social defeat stress, but not in mPFC of mice that were resilient to such stress. Remarkably, laser stimulation of excitatory and inhibitory mPFC neurons expressing the light-sensitive cation channel channelrhodopsin increased social interaction and sucrose preference in mice affected by social defeat stress. Expression of channelrhodopsin under the control of neuron-specific promoters should allow researchers to determine whether specific neuronal types are preferentially involved in depression-related behaviors.

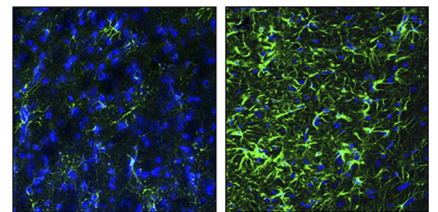
◆ Neurobiology of Disease

Inflammation Increases Nigral Neurons' Susceptibility to Toxins

Michela Deleidi, Penelope J. Hallett, James B. Koprach, Chee-Yeun Chung, and Ole Isacson

(see pages 16091–16101)

Much evidence suggests that Parkinson's disease (PD) can be triggered by exposure to environmental toxins, particularly pesticides, in genetically susceptible people. Viral infections that produce chronic inflammation might also increase susceptibility to future insults. PD-associated loss of nigrostriatal dopaminergic neurons is accompanied by inflammatory processes such as glial activation and cytokine release, but whether this inflammation results from or precipitates neuronal damage is unknown. The latter hypothesis is supported by results from Deleidi et al., who mimicked the effects of viral infection in rats by injecting a synthetic double-stranded RNA (dsRNA) into the substantia nigra, thus activating glia and increasing levels of the neurotoxic inflammatory cytokine interleukin-1 α . The dsRNA did not kill neurons, but it altered neuronal expression of several transport motors and synaptic proteins. Moreover, dsRNA increased the number of neurons killed by subsequent neurotoxin exposure. Degeneration was decreased by infusion of interleukin-1 receptor antagonist, suggesting that this antagonist may slow degeneration in PD.



Injection of dsRNA activated astrocytes in rat substantia nigra, as indicated by greater staining with glial fibrillary acidic protein (green) in injected (right) versus control (left) brain. Blue, Hoechst dye. See the article by Deleidi et al. for details.