This Week in The Journal

● Cellular/Molecular

Chloride Concentration Affects GABAergic IPSC Duration

Catriona M. Houston, Damian P. Bright, Lucia G. Sivilotti, Marco Beato, and Trevor G. Smart

(see pages 10416–10423)

Intracellular chloride concentrations are determined in part by chloride transporters, whose expression changes during development and in pathological conditions such as epilepsy. Large shifts in chloride concentration change the effects of GABA from inhibitory to excitatory. Houston et al. now report that smaller changes in chloride concentration also affect GABA-mediated signaling in rat Purkinje cells: increased concentrations prolonged the decay phase of evoked, spontaneous, and miniature IPSCs, thus increasing the duration of inhibition. This effect appeared to result from direct effects of chloride on the GABA receptor. Because the time course of IPSCs influences the integration of excitatory and inhibitory inputs, these results indicate that changes in intracellular chloride concentration might alter network dynamics. Furthermore, because most patch-clamp studies of synaptic inhibition use high internal chloride concentrations, the results suggest that the time course of GABAergic IPSCs *in vivo* might be much faster than previously reported.

▲ Development/Plasticity/Repair

Axonal Translation of Odorant Receptor mRNA Increases During Growth

Caroline Dubacq, Sophie Jamet, and Alain Trembleau

(see pages 10184–10190)

Each olfactory sensory neuron expresses a single odorant receptor gene and projects to a single glomerulus in the olfactory bulb. Odorant receptor mRNA and protein are present in axons of sensory neurons, as well as in the olfactory epithelium, and the proteins are thought to participate in establishing proper connections. Until now, it was unclear whether odorant receptor mRNA was translated locally in axons. Dubacq et al. show that in mice, some axonal odorant receptor mRNAs are associated with polyribosomes, suggesting local translation. Moreover, the percentage of mRNA associated with polyribosomes was elevated during development and regeneration compared to in uninjured adults. Transport of mRNAs into the axon also appeared to be elevated. Although the presence of polyribosome-associated mRNA was not definitively localized to growing axons, the results suggest that translation is higher during periods of growth, adding support to the hypothesis that axonal expression of olfactory receptors is involved in guidance.

■ Behavioral/Systems/Cognitive

Ortho- and Retro-nasal Conditioning Involve Overlapping Brain Areas

Julie Chapuis, Samuel Garcia, Belkacem Messaoudi, Marc Thevenet, Guillaume Ferreira, et al.

(see pages 10287–10298)

When animals explore food, odors reach the olfactory epithelium through the nose (orthonasally). When food is ingested, odors reach the olfactory epithelium through the nasopharynx (retronasally). Presentation of a novel odor by either pathway, if paired with gastrointestinal malaise, produces conditioned olfactory aversion. To determine whether distinct brain areas are involved in orthonasal and retronasal conditioning, Chapuis et al. measured oscillatory activity in local field potentials. In animals that developed aversion, increased beta frequency (15–40 Hz) oscillations occurred in olfactory areas, frontal areas, and amygdala upon orthonasal odor presentation, regardless of whether the odor was presented retronasally during conditioning. Rats that received retronasal conditioning showed additional increases in infralimbic and primary gustatory cortex during subsequent orthonasal stimulation. Increases in beta oscillations were proportional to the strength of aversion, did not occur in rats that did not develop aversion despite conditioning, and were eliminated by extinction training, suggesting they reflect the aversive memory.

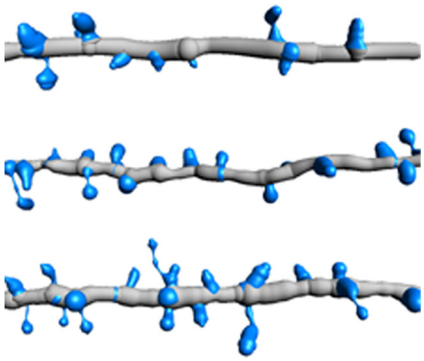
♦ Neurobiology of Disease

γ-Secretase Inhibition Reduces Spine Density

Tobias Bittner, Martin Fuhrmann, Steffen Burgold, Christian K. E. Jung, Christiane Volbracht, et al.

(see pages 10405–10409)

Alzheimer's disease (AD) is characterized by the formation of β-amyloid (Aβ) plaques, but the cognitive impairment associated with the disease is more strongly linked to soluble, toxic Aβ oligomers, which are thought to interact with synaptic proteins, leading to synaptic loss and retraction of dendritic spines. Aβ is formed by cleavage of amyloid precursor protein (APP) by the β-site APP-cleaving enzyme 1 (BACE1) and subsequent cleavage of the APP C-terminal fragment by γ-secretase. Modulating γ-secretase function to reduce production of toxic Aβ fragments has been proposed as a potential therapy for AD. But *in vivo* two-photon imaging by Bittner et al. revealed that γ-secretase inhibitors also reduced dendritic spine density in mouse cortex. The effect did not occur in mice lacking APP, indicating that spine loss resulted from cleavage of APP rather than another protein. Whether the effect of γ-secretase on spine density counteracts any benefits of reducing toxic Aβ levels has yet to be tested.



Mice lacking APP (bottom) have a greater density of thin, stubby, and mushroom-shaped dendritic spines than wild-type (top) or heterozygous (middle) mice. See the article by Bittner et al. for details.