This Week in The Journal

● Cellular/Molecular

Postsynaptic Signaling Promotes Synapse Development in Aplysia

Jiang-Yuan Hu, Yang Chen, Joanna K. Bougie, Wayne S. Sossin, and Samuel Schacher

(see pages 8353–8366)

The establishment of functional neural circuits requires presynaptic neurons to identify the correct postsynaptic targets. This is achieved partly through bidirectional molecular communication between synaptic pairs. In *Aplysia* neuronal cultures, for example, contact with motor neuron L7 induces sensory neurons to secrete the neuropeptide sensorin—which stimulates sensory neurite growth and synapse maturation—whereas contact with motor neuron L11 has no such effect. Hu et al. found that L7-specific effects on sensory neuron growth and sensorin secretion occurred after initial synaptic contacts were made and were accompanied by accumulation of protein kinase C isoform Apl II at contact sites. These effects were reduced by removing the *Aplysia* cell adhesion molecule ApCAM specifically from L7 or by expressing dominant-negative Apl II in L7. Contact with L11 reduced sensorin expression in sensory neurons, and this effect was not altered by removal of ApCAM from L11. Therefore, target-specific intracellular signaling induces alterations in presynaptic sensory neurons to promote synaptic development.

▲ Development/Plasticity/Repair

Migration Requires Receptor Trafficking

Perrin M. Wilson, Robert H. Fryer, Yin Fang, and Mary E. Hatten

(see pages 8529–8540)

After their final division in the external granular layer, newborn cerebellar granule neurons migrate along radial glia fibers to the internal granular layer. To migrate, neurons first adhere to glial fibers and extend a leading process. Intracellular organelles, including the centrosome, move into the base of the leading process. The nucleus quickly follows the centrosome and the adhesion junction releases, allowing somatic membrane to flow forward. Complex molecular interactions between actin, microtubules, associated motors, and neuron-glial adhesion molecules [particularly astrotactin 1 (ASTN1)] drive these cyclic migratory movements. Wilson et al. demonstrate the importance of adhesion molecule cycling in mouse granule cells migrating in culture. ASTN1 accumulated at the neuron-glial adhesion site, but as the adhesion was released, ASTN1 flowed into the leading process. It then reaccumulated in front of the advancing soma. ASTN1 cycling (and migration itself) required clathrin-mediated endocytosis, and might be regulated by a related protein, ASTN2.

■ Behavioral/Systems/Cognitive

VMPFC and OFC Respond Differently to Internal vs External Cues

Sebastien Bouret and Barry J. Richmond

(see pages 8591–8601)

Ventral prefrontal cortex is thought to be involved in motivating goal-directed behaviors. The ventromedial portion (VMPFC) is heavily interconnected with limbic and autonomic structures, whereas the orbitofrontal region (OFC) is interconnected with sensory areas, suggesting that VMPFC is more important for actions driven by internal cues (e.g., thirst), whereas OFC primarily motivates actions based on external cues (e.g., water-associated stimuli). Bouret and Richmond found support for this hypothesis by recording neuronal activity while monkeys performed different tasks to receive a drink. Sometimes visual cues directed monkeys to perform the task, whereas other times monkeys performed the task *ad libitum*. Neuronal activity related to different task events (e.g., cue presentation) was correlated with the value the monkey assigned to the events as assessed using behavioral measures. Neurons in both VMPFC and OFC responded to cues and reward size, but their timing and the proportion of neurons responding varied: neurons in VMPFC were more engaged when the task was self-initiated, whereas those in OFC were more engaged when the task was cue-driven.

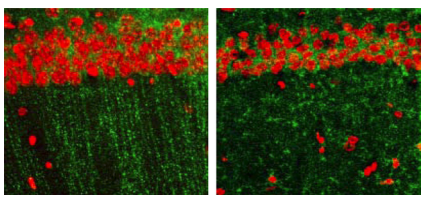
♦ Neurobiology of Disease

Presenilin Regulates ER Calcium Levels

Hua Zhang, Suya Sun, An Herreman, Bart De Strooper, and Ilya Bezprozvanny

(see pages 8566–8580)

Presenilin cleaves amyloid precursor protein to form β-amyloid, and presenilin mutations are a common cause of familial Alzheimer's disease (AD). Mutant presenilin also increases release of calcium from internal stores, suggesting that presenilin regulates either levels of stored calcium or the molecules responsible for its release. Studies in non-neural cells suggested that presenilin acts as a calcium leak channel in the endoplasmic reticulum (ER) and that AD-causing mutations disrupt this function, leading to overfilling of the calcium store. Zhang et al. support this hypothesis with data from hippocampal neurons cultured from presenilin-null and presenilin-mutant mice. An ER-specific calcium indicator revealed that calcium levels were elevated in transgenic neurons, and ionophore-mediated calcium release was greater in transgenic than in wild-type neurons. Interestingly, increased expression of ryanodine receptors, the ER calcium channel, partially compensated for loss of presenilin in mutant mice, and blocking these receptors *in vivo* increased AD pathology in transgenic mice.



Blocking ryanodine receptors *in vivo* in mutant mice (right) decreases expression of postsynaptic density protein PSD95 (green) in hippocampal neurons (red), compared with levels in untreated mutant mice (left). See the article by Zhang et al. for details.