This Week in The Journal

● Cellular/Molecular

Segregation of Kainate and AMPA Synapses

Neil J. Bannister, Timothy A. Benke, Jack Mellor, Helen Scott, Esra Gürdal, John W. Crabtree, and John T. R. Isaac
(see pages 5259–5271)

Kainate receptors have long been the poor stepchildren of the ionotropic glutamate receptor family. First, they were named for an agonist that also activates AMPA receptors. Then, even after molecular cloning established their unique composition, their small conductance and the lack of selective antagonists hampered study. However, their presynaptic and postsynaptic function is now well established in several brain regions, including layer IV of the barrel cortex. There, glutamatergic transmission abruptly switches from kainate- to AMPA receptor-mediated transmission during the first postnatal week. This week, Bannister et al. report that this developmental switch is associated with total segregation of these receptors, indicating that individual synapses use either kainate or AMPA receptors, but not both. The authors used strontium to evoke single quantal events. Kainate receptor-mediated events had small quantal amplitude, slow kinetics, and large charge transfer, whereas AMPA-mediated transmission had larger quanta, fast kinetics, and small charge transfer. The slow kainate receptor kinetics could not be attributed to an extrasynaptic localization.

▲ Development/Plasticity/Repair

A Pathway for Retrograde Signaling by Neurotrophin

Gregorio Valdez, Wendy Akmentin, Polyxeni Philippidou, Rejji Kuruvilla, David D. Ginty, and Simon Halegoua
(see pages 5236–5247)

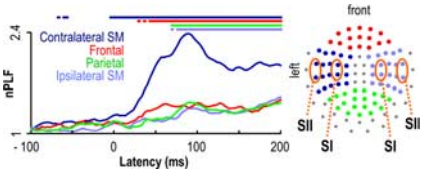
Signaling of neurotrophins requires uptake of their activated receptors at axonal and dendritic membranes, followed by retrograde transport to the nucleus. This week, Valdez et al. identify a clathrin-independent pathway that mediates endocytosis of Trk receptor tyrosine kinases in peripheral and central neurons. The internalization pathway appears to be an intermediate between macropinocytosis and receptor-mediated endocytosis and required a membrane trafficking protein, appropriately named Pincher. Superior cervical ganglion neurons expressed Pincher, often colocalized with phosphorylated TrkA (P-TrkA), the receptor for NGF. A dominant-negative Pincher prevented cytoplasmic accumulation of P-TrkA, and Pincher RNA interference reduced TrkA internalization. Pincher also mediated internalization of TrkB receptors after BDNF binding. This novel endocytic mechanism involves the formation of macroendosomes from plasma membrane ruffles. The macroendosomes are refractory to lysosomal degradation and thus sorted to multivesicular bodies containing Trk vesicles, apparently ready for the ride along microtubules to the nucleus.

■ Behavioral/Systems/Cognitive

Detecting Perception by t = *30 ms*

Satu Palva, Klaus Linkenkaer-Hansen, Risto Näätänen, and J. Matias Palva
(see pages 5248–5258)

It seems like a conscious perception should require some time for network processing after a sensory stimulus first arrives in the cortex. Well, maybe not. In this week's *Journal*, Palva et al. examine the differences between neural responses to consciously perceived and unperceived somatosensory stimuli. The two stimuli are thought to elicit the same response in the first 100 ms, whereas later components diverge. Subjects received near-threshold electrical shocks to a fingertip, during which neuromagnetic [magnetoencephalography (MEG)] responses were recorded. The authors found that perceived stimuli were associated with evoked cortical activity earlier than previously thought. Even at 30 ms, cortical activity was phase-locked to the subsequently perceived stimulus in somatosensory, frontal, and parietal cortical regions. Unperceived stimuli, in contrast, evoked weaker phase-locked activity, primarily in the somatosensory cortex. Oscillations in all frequency ranges were locked to the consciously perceived stimulus, but the α-frequency oscillations appeared most influential in sensory awareness.



Phase locking to the detected stimuli averaged across MEG gradiometer selections over the somatosensory, frontal, and parietal regions, in response to somatosensory stimulation of the contralateral fingertip. Each gradiometer pair is shown with a correspondingly colored dot in the topography (right). SM, Sensorimotor cortex; nPLF, normalized phase-locking factor. See the article by Palva et al. for details.

◆ Neurobiology of Disease

Running Wheels, Play Tubes, and Cognitive Decline

Joanna L. Jankowsky, Tatiana Melnikova, Daniel J. Fadale, Guilian M. Xu, Hilda H. Slunt, Victoria Gonzales, Linda H. Younkin, Steven G. Younkin, David R. Borchelt, and Alena V. Savonenko
(see pages 5217–5224)

Mounting evidence suggests that an enriched environment, in the form of cognitive activity for humans or toys for mice, can stave off the clinical progression of Alzheimer's disease (AD). In this week's *Journal*, Jankowsky et al. test the performance of transgenic AD mice raised in an enriched environment. Female mice reared with running wheels and colorful toys performed better in radial and Morris water maze assays. The performance of the AD mice in the enriched environment improved to the level of control mice raised in standard housing. Surprisingly, the improved performance occurred despite increased steady-state levels of endogenous and transgene-derived amyloid-β (Aβ). In contrast, Lazarov et al. [Lazarov O, Robinson J, Tang YP, Hairston IS, Korade-Mirnics Z, Lee VM, Hersh LB, Sapolsky RM, Mirnics K, Sisodia SS (2005) Cell 120:701–713] reported that Aβ declined in male transgenic mice reared in an enriched environment, perhaps indicative of a sexually dimorphic response to the environment. In any case, as in humans, environmental factors appear to slow behavioral deficits in AD mice.