This Week in The Journal

● Cellular/Molecular

Ubiquitination Regulates Synaptic Vesicle Release

Gina V. Rinetti and Felix E. Schweizer

(see pages 3157–3166)

Ubiquitination involves attaching the polypeptide ubiquitin to lysine residues of a target protein. The role of polyubiquitination in tagging proteins for degradation is widely recognized, but ubiquitination also has other functions, including triggering internalization and recycling of membrane proteins, assembling signaling complexes, and promoting DNA repair. In neurons, ubiquitination plays roles in axon guidance and synaptogenesis, and it regulates levels of synaptic vesicle proteins and neurotransmitter receptors. Rinetti and Schweizer found that blocking degradation in the proteasome rapidly increased the frequency of spontaneous and miniature EPSCs and IPSCs in cultured hippocampal neurons, probably by increasing synaptic vesicle release. This effect was not likely mediated by accumulation of protein that would normally be degraded, because it occurred even when protein synthesis was blocked. Blocking ubiquitination produced the same effect as blocking degradation, leading the authors to conclude that the effect of degradation results from sequestering of ubiquitin in undegraded proteins, thus preventing other ubiquitin-mediated functions.

▲ Development/Plasticity/Repair

Handedness Shapes Brain Morphology

Stefan Klöppel, Jean-Francois Mangin, Anna Vongerichten, Richard S. J. Frackowiak, and Hartwig R. Siebner

(see pages 3271–3275)

More than 90% of humans are right handed, and evidence suggests that handedness is genetic and arises before birth. Handedness is reflected in brain asymmetries: in right-handers, the left central sulcus is deeper than the right and the cortical representation of the right hand is larger than that of the left. Whether these differences drive or result from handedness is not clear. To address this question, Klöppel et al. compared brain morphology in right-handers, consistent left-handers, and "converted" left-handers who were forced to write with their right hands as children. The area of the left central sulcus in converted left-handers resembled that in right-handers and was significantly greater than that in consistent left-handers, suggesting the difference results from hand use. Interestingly, the middle part of the putamen was smaller in converted individuals than in either consistent left-handers or right-handers, and it was smallest in those converted left-handers that retained the most left hand dexterity.

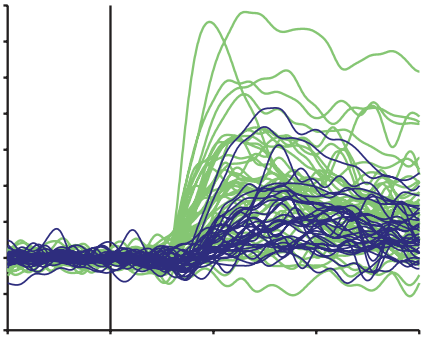
■ Behavioral/Systems/Cognitive

LIP Reflects Attention Shifts Before MT

Todd M. Herrington and John A. Assad

(see pages 3287–3296)

Detecting a subtle visual stimulus is easier if you know where to look and you attend to that spot. Directing attention is thought to increase the responsiveness of visual cortical neurons: neurons fire more when an animal is attending to the location where a stimulus is presented than if it is attending to a different location. To determine which neural pathways might drive this change in responsiveness, Herrington and Assad measured the relative timing of activity changes in two brain areas as monkeys' attention shifted. As expected, neuronal firing rate increased in both the middle temporal area (MT) and in the lateral intraparietal area (LIP)—a later stage of processing in visual cortex—when the monkey switched its attention to the recorded neuron's receptive field. The change in activity occurred sooner in LIP than in MT, however, indicating that signals related to attention may propagate from later stages to earlier ones.



Attentional modulation, measured as difference in spike rate when attention is directed in or out of a neuron's receptive field, arises sooner after attention shift (vertical line) in LIP neurons (green) than in MT neurons (blue). See the article by Herrington and Assad for details.

◆ Neurobiology of Disease

Some α-Synuclein Oligomers From Asymptomatic Mice Are Toxic

Elpida Tsika, Maria Moysidou, Jing Guo, Mimi Cushman, Patrick Gannon, *et al.*

(see pages 3409 –3418)

α-Synuclein is normally localized to synaptic terminals throughout the brain, but mutations cause it to polymerize first into oligomers and then in fibrils that aggregate in intracellular inclusions in specific classes of neurons, leading to degeneration. Whether α-synuclein oligomers are toxic at early stages of polymerization, before fibrils and inclusions form, is unclear. Tsika et al. purified α-synuclein from mice expressing a human mutant form of the protein that causes inclusions to form in spinal cord neurons. Unlike insoluble α-synuclein aggregates, which were detected only in extracts from spinal cord of symptomatic mice, soluble α-synuclein oligomers were extracted from spinal cord before symptom onset, as well as from brain regions where inclusions are never found. Although oligomers from different regions were similar in size and shared other biochemical properties, only fractions isolated from spinal cord accelerated aggregation of α-synuclein in neurons *in vitro*; fractions extracted from other regions delayed aggregation.