This Week in The Journal

● Cellular/Molecular

Impaired Stress Response in Old Mice

Nirinjini Naidoo, Megan Ferber, Monali Master, Yan Zhu, and Allan I. Pack

(see pages 6539 – 6548)

Elderly mice manage protein misfolding less efficiently than young mice, report Naidoo et al. this week. Because protein misfolding can lead to protein aggregation and neurodegeneration, cells initiate the "unfolded protein response" when unfolded proteins begin to accumulate in the endoplasmic reticulum (ER). If ER stress continues, an ER-induced apoptosis pathway is activated. Naidoo et al. previously showed that sleep deprivation activates the unfolded protein response in young mice: the chaperone BiP (which helps ensure proper folding) is upregulated, and the translation initiation factor eIF2α is inactivated by phosphorylation. The authors now show that baseline levels of BiP and phosphorylated eIF2α were lower in aged mice than in young, and the levels were not altered by sleep deprivation. Furthermore, baseline levels of pro-apoptotic proteins were higher in aged mice and were further elevated by sleep deprivation in aged mice, but not young mice, suggesting that a deficient unfolded protein response increases apoptosis.

▲ Development/Plasticity/Repair

Neuronal Activation by Astrocytic Calcium

Eiji Shigetomi, David N. Bowser, Michael V. Sofroniew, and Baljit S. Khakh

(see pages 6659 – 6663)

Increases in intracellular calcium cause astrocytes to release glutamate, but evidence that this glutamate produces currents in neurons has been contradictory. Shigetomi et al. now present convincing evidence that astrocytic glutamate release only sometimes stimulates neurons, which helps to explain previous results. In mouse hippocampal slices, the time course (but not the amplitude) of astrocytic calcium elevation differed when triggered by activation of different endogenous receptors: PAR-1 or $P2Y_1$. More importantly, only PAR-1 activation, which produced slower and longer-lasting calcium elevation, increased the frequency of slow inward currents in neurons. These currents are mediated by activation of extrasynaptic NMDA receptors. The authors' previous work suggests that PAR-1 and $P2Y_1$ receptors activate different forms of glutamate exocytosis, which could explain the differential effects on neurons. The results demonstrate that the mechanism and/or dynamics of calcium elevation is a critical determinant of whether subsequent glutamate release activates neuronal receptors.

■ Behavioral/Systems/Cognitive

Task-Dependent Attention Mechanisms

Chad M. Sylvester, Anthony I. Jack, Maurizio Corbetta, and Gordon L. Shulman

(see pages 6549 – 6556)

Attention modulates the activity of sensory areas by both increasing the activity in regions responding to attended stimuli and reducing activity in other regions. It is unclear, however, whether neural mechanisms of attention vary with perceptual requirements. To answer this question, Sylvester et al. measured prestimulus preparatory brain activity while subjects performed nearly identical visual tasks. One task (threshold detection) used low-contrast stimuli that were easily distinguishable from each other but difficult to distinguish from background, whereas the other task (discrimination) used high-contrast stimuli that were difficult to distinguish from each other. As expected, in both tasks, prestimulus activity increased in visual cortical regions representing the attended area and decreased in nontarget areas. But in the threshold detection task, activity was lower in nontarget areas, particularly the peritarget area, compared to in the discrimination task, suggesting that attention mechanisms vary depending on task requirements.

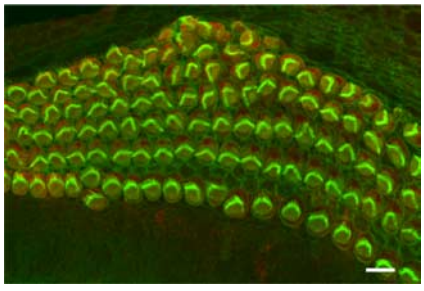
♦ Neurobiology of Disease

Novel Deafness Gene

Zheng Chen, Mireille Montcouquiol, Rene Calderon, Nancy A. Jenkins, Neal G. Copeland, Matthew W. Kelley, and Konrad Noben-Trauth

(see pages 6633– 6641)

Jackson circler mice have a recessive mutation that causes deafness and circling behavior due to defective development of the inner ear. Chen et al. have identified the gene containing this mutation, *Jxc1*, and report that elongation and patterning of the cochlea was greatly disrupted in mutants. Fewer rows of hair cells were present in some regions, whereas extra rows appeared in others. In addition, mutant cochlea had a mirror-image duplication of the tunnel of Corti and inner hair cells, and ectopic, vestibular-like hair cells were present. The vestibular system was also abnormal: the utricles and saccules were significantly thicker in mutants, and their surface areas were smaller. The sequence of *Jxc1* indicates that it has two phenylalanine-cysteine-serine-type zinc-finger domains, suggesting that it is a transcriptional silencing factor. The protein is normally expressed in the nucleus, but the mutant protein, which is a truncated form, also appears in the cytoplasm.



Confocal image of organ of Corti surface preparation shows four rows of outer hair cells at the midapical region and up to six rows at the more apical region. See the article by Chen et al. for details.