This Week in The Journal

● Cellular/Molecular

External Tufted Cells Synchronize Mitral Cell Bursts

Didier De Saint Jan, Daniela Hirnet, Gary L. Westbrook, and Serge Charpak

(see pages 2043–2052)

Olfactory sensory neurons project to glomeruli in the olfactory bulb, where they form synapses with mitral cells (the output neurons of the olfactory bulb) and with excitatory interneurons called external tufted (ET) cells. Odors elicit synchronous, rhythmic bursting in populations of mitral cells that project to a single glomerulus. Although this bursting is entrained to the respiratory rhythm, it persists *in vitro*, suggesting that it can be intrinsically generated. De Saint Jan et al. now report that ET cells, which have intrinsic pacemaker properties, synchronize the bursting activity of mitral cells. In olfactory bulb slices, mitral cell oscillations were temporally correlated with ET cell bursts, and electrical stimulation of a single ET cell induced synchronous bursting in mitral cells. ET and mitral cells within a glomerulus are extensively electrically coupled, but whether these electrical connections, hitherto undescribed chemical synapses, or a combination are responsible for synchronization remains to be determined.

▲ Development/Plasticity/Repair

STAT5 Mediates Protective Effects of Methylprednisolone

Jan Xu, Shawei Chen, Hong Chen, Qingli Xiao, Chung Y. Hsu, Drew Michael, and Jianxin Bao

(see pages 2022–2026)

Methylprednisolone (MP), a synthetic glucocorticoid, is widely used to protect myelin after spinal cord injury and in multiple sclerosis. Xu and colleagues have been unraveling the molecular pathways that produce this effect. They previously found that MP binds to glucocorticoid receptors and increases transcription of bcl-X_L, an anti-apoptotic protein. In other cell types, the transcriptional effects of glucocorticoids are determined by whether the activated receptor binds directly to glucocorticoid response elements in promoters or first interacts with other transcription factors and bind to those factors' response elements. Xu et al. now show that when oligodendrocytes are activated by MP, glucocorticoid receptors interact with the signal transducer and activator of transcription STAT5. Together, these bind to the STAT5-binding site in the promoter of bcl-X_L. Overexpression of constitutively active STAT5 protected oligodendrocytes from apoptosis, and knockdown of STAT5 blocked the protective effects of MP, demonstrating the importance of STAT5 in this pathway.

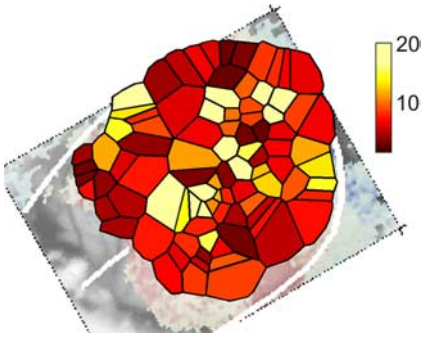
■ Behavioral/Systems/Cognitive

Auditory Cortex Shows Limited Functional Specialization

Jennifer K. Bizley, Kerry M. M. Walker, Bernard W. Silverman, Andrew J. King, and Jan W. H. Schnupp

(see pages 2064–2075)

Some regions of auditory cortex show tonotopic organization, but the extent to which other features of sound—e.g., timbre and pitch—are processed in specialized regions of cortex is uncertain. To definitively answer this question, Bizley et al. have examined the responsiveness of neurons in five regions of ferret auditory cortex to sounds that varied systematically in timbre, pitch, and apparent spatial location. Using innovative statistical methods, they determined how much of the variance in a neuron's post-stimulus temporal spike pattern could be explained by each of the three parameters. Most neurons throughout auditory cortex were modulated by more than one parameter. Although different cortical areas had some degree of specialization, processing was distributed throughout the cortex, such that every region contained clusters of neurons that were sensitive to pitch, timbre, and/or azimuth. Therefore, the auditory system, unlike the visual system, does not appear to process different characteristics of sensory input in separate streams.



Voronoi tessellation map showing the average proportion of variance explained by pitch for all neurons recorded at each electrode penetration across the auditory cortex. See the article by Bizley et al. for details.

◆ Neurobiology of Disease

Neprilysin Reduces Amyloid Load, But Doesn't Restore Memory

William J. Meilandt, Moustapha Cisse, Kaitlyn Ho, Tiffany Wu, Luke A. Esposito, Kimberly Scearce-Levie, Irene H. Cheng, Gui-Qiu Yu, and Lennart Mucke

(see pages 1977–1986)

Abnormal accumulation of amyloid β (Aβ) protein is widely believed to cause memory impairments in Alzheimer's disease (AD), and increasing evidence suggests that aggregates of soluble trimers are especially detrimental. Neprilysin is an endogenous protease that degrades Aβ, and thus could potentially halt cognitive decline. Unfortunately, results by Meilandt et al. suggest otherwise. The authors overexpressed neprilysin in transgenic mice that expressed an aggregation-prone human mutant form of amyloid precursor protein. Although neprilysin overexpression reduced plaque formation and decreased overall soluble Aβ levels by $>$50%, it did not reduce the levels of Aβ trimers or Aβ*56, a soluble Aβ assembly that was previously shown to induce cognitive deficits in rats. Moreover, neprilysin overexpression did not improve spatial learning, and it did not reduce abnormal hyperexploratory behaviors. These data are consistent with the hypothesis that soluble Aβ oligomers, rather than plaques, cause cognitive impairments in AD, and suggest that AD treatments should target these oligomers.