

This Week in The Journal

● Cellular/Molecular

Getting Vesicles Ready for Release

Ira Milosevic, Jakob B. Sørensen, Thorsten Lang, Michael Krauss, Gábor Nagy, Volker Haucke, Reinhard Jahn, and Erwin Neher
(see pages 2557–2565)

Secretion of large dense core vesicles in chromaffin cells depends on the phospholipid phosphatidylinositol-4,5-bisphosphate (PI(4,5)P₂). Previous studies have suggested two possible steps in secretion that might be affected: that PI(4,5)P₂ is necessary either in the priming of vesicles or in the release process itself. Both processes are ATP dependent, as is the synthesis of PI(4,5)P₂. Milosevic et al. manipulated PI(4,5)P₂ expression levels in bovine chromaffin cells to examine this issue. They monitored PI(4,5)P₂ levels in plasma membrane “sheets” with a specific fluorescent probe. In intact chromaffin cells, they monitored catecholamine release by amperometry and monitored exocytosis by measuring changes in membrane capacitance. Both long- and short-term increases in PI(4,5)P₂ increased the levels in the plasma membrane and stimulated release of vesicles, whereas depletion of available phospholipid blocked exocytosis. Based on their kinetic analysis, the authors conclude that PI(4,5)P₂ levels increase the readily releasable vesicular pool but do not affect vesicle fusion.

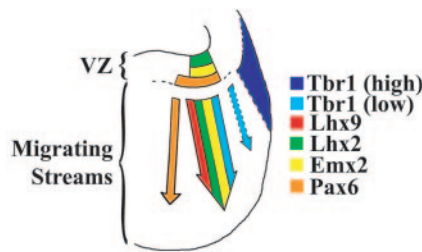
▲ Development/Plasticity/Repair

Pax6 and Specification of the Amygdala

Shubha Tole, Ryan Remedios, Bhaskar Saha, and Anastassia Stoykova
(see pages 2753–2760)

Fitting its name and its role in brain function, the developmental origin of the amygdala is indeed complex. In this week's *Journal*, Tole et al. examined the influence of two transcription factors, *Pax6* and *Emx2*, on the formation of the amygdala. During development, the telencephalic neuroepithelium consists of pallial and subpallial domains that have

different developmental fates according to transcription factor expression gradients. “Interface” nuclei, such as the amygdaloid complex, arise from the pallium–subpallium boundary (PSB) and undergo substantial spatial rearrangements with development. The authors first identified the expression patterns of *Pax6*, *Emx2*, and other transcription factors in migrating “streams” of cells emerging from the PSB. In mutant mice lacking *Pax6*, a particular subset of nuclei in the amygdaloid complex was missing or indistinguishable, whereas other parts were unaffected. In *Emx2*-deficient mutants, however, these *Pax6*-dependent structures appeared to form normally. This pattern is in contrast to the cortex, in which *Pax6* and *Emx2* have complementary roles based on their opposing expression gradients.



Distinct streams of cells emerge from the PSB and extend toward the amygdaloid complex. The schema shows the expression of different transcription factor markers in the ventricular zone and migrating streams. See the article by Tole et al. for details.

■ Behavioral/Systems/Cognitive

Marmosets Listening to Their Twitter Call

Steven W. Cheung, Srikanth S. Nagarajan, Christoph E. Schreiner, Purvis H. Bedenbaugh, and Andrew Wong
(see pages 2490–2503)

Although the songbird has been crucial to an understanding of auditory cortical plasticity, less is known about the higher-order processes of the primary auditory cortex (AI) in primates. This week, Cheung et al. focus on the response of AI

neurons to the “twitter” call of the marmoset. AI neurons altered their response properties after the monkey's larynx was surgically altered, thus lowering the frequency of their twitter, a complex vocalization composed of a series of frequency modulation (FM) sweeps, or phrases. Months later, the authors made extracellular multiunit recordings in AI. The altered twitters activated neurons that normally would have responded only weakly to the normal vocalization. AI neurons still displayed normal tonotopic organization and responses to pure tones, but fast responses to complex sounds were compromised. The changes in response properties reflect a form of cortical plasticity involved in more complex sounds, such as species-specific vocalizations.

◆ Neurobiology of Disease

Counting Brain Cells Made Simple

Suzana Herculano-Houzel and Roberto Lent
(see pages 2518–2521)

Cell counts in the brain generally require stereological methods that are limited to discrete, homogenous brain areas of known volume. Now comes a method for cell counting for the geometrically challenged neuroscientist, and say the authors, it's fast, quick, and cheap. Herculano-Houzel and Lent devised what they call the isotropic fractionator method, a way to count neurons and glia from the whole brain or large dissected areas. They dissociated fixed rat brain tissue to produce a homogenous suspension of cell nuclei. To calculate total cell number, they stained nuclei with the fluorescent DNA-specific dye 4',6-diamidino-2-phenylindole dihydrochloride (DAPI) and counted nuclear density in aliquots of the suspension. They used neuronal nuclear antigen immunohistochemistry to obtain the fraction of cells that were mature neurons. The rat brains contained ~330 million cells, of which 60% were neurons. Sorry, glial biologists, it seems there are more neurons than glia in the brain.