This Week in The Journal

● Cellular/Molecular

Stress-Induced SP1 and p75NTR Transcription

Alberto Ramos, Wai Chi Ho, Stephanie Forte, Kathleen Dickson, Jacqueline Boutilier, Kristy Favell, and Philip A. Barker

(see pages 1498–1506)

The p75 neurotrophin receptor (p75NTR), normally expressed at low levels in adult tissue, springs to life in times of crisis, such as brain injury, ischemia, and seizures, and facilitates neuronal apoptosis. Ramos et al. this week examined how the stress of cell swelling, induced by hypo-osmolarity, triggers p75NTR expression. The authors focused on a proximal promoter region shared by the human, rat, and mouse p75NTR genes. The conserved GC-rich region contained several putative binding sites for the zinc-finger transcription factor Sp1. In human embryonic kidney 293 cells and primary cultures of mouse cortical neurons, p75NTR expression was significantly and reversibly elevated by hypo-osmotic solutions. When Sp1 activity was reduced by overexpression of a dominant-negative Sp1, RNA interference, or inhibitors, the effect on p75NTR was diminished. Six hours of hypotonic solution stabilized the normally rapid degradation of SP1, suggesting that changes in SP1 turnover may regulate p75NTR expression in response to stress.

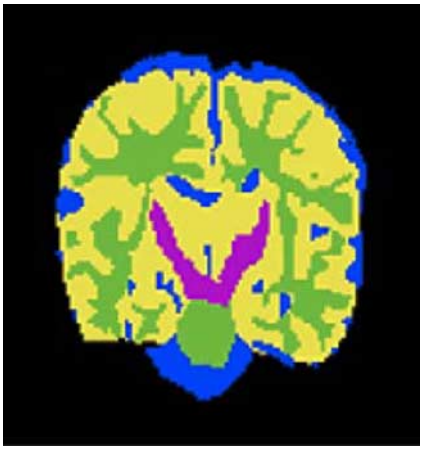
▲ Development/Plasticity/Repair

Sexually Dimorphic Brain Development in Infants

John H. Gilmore, Weili Lin, Marcel W. Prastawa, Christopher B. Looney, Y. Sampath K. Vetsa, Rebecca C. Knickmeyer, Dianne D. Evans, J. Keith Smith, Robert M. Hamer, Jeffrey A. Lieberman, and Guido Gerig

(see pages 1255–1260)

This week, Gilmore et al. examined the growth of gray and white matter during the first weeks of life. The authors performed magnetic resonance imaging (MRI) on 74 neonates and created an MRI atlas as a template to estimate gray, white, and CSF volumes. As in children and adults, neonatal male brains were slightly larger than in females, by ~9%. Males also had slightly more cortical gray matter, cortical white matter, and subcortical gray matter. Neonates of both sexes had more left than right hemisphere gray matter, the opposite of older children and adults. Occipital asymmetry, left larger than right, matched the pattern in adults, but the neonatal pattern differed from adults in prefrontal regions. The scans revealed tremendous early gray matter growth, particularly in occipital regions, and indicate that sexual dimorphic brain size exists at birth, but certain asymmetries develop later.



MRI images of human infants were automatically segmented into CSF (blue), gray matter (yellow), unmyelinated white matter (green), and myelinated white matter (pink). See the article by Gilmore et al. for details.

■ Behavioral/Systems/Cognitive

Male Sweat as a Possible Chemosignal

Claire Wyart, Wallace W. Webster, Jonathan H. Chen, Sarah R. Wilson, Andrew McClary, Rehan M. Khan, and Noam Sobel

(see pages 1261–1265)

Human pheromones likely do exist, but one criterion has yet to be satisfied by putative chemosignals: that the substance influences the hormonal state of the responder. This week, Wyart et al. test androstadienone (AND), a component of male sweat. Heterosexual women took 20 sniffs from vials containing AND or a control odor with similar qualities, in this case yeast. Subjects were wired to measure nine physiological indicators. After odor exposure, the subjects watched videos designed to heighten emotional state, answered a series of questions about their mood, and provided samples of saliva. As expected, AND heightened mood, physiological arousal, and subjective sexual arousal compared to control subjects. In addition, cortisol levels were higher in the saliva of women who smelled AND, consistent with an effect of this chemosignal on hormonal state. Seems male sweat might just have a use after all.

♦ Neurobiology of Disease

Isoflurane-Induced Apoptosis

Zhongcong Xie, Yuanlin Dong, Uta Maeda, Robert D. Moir, Weiming Xia, Deborah J. Culley, Gregory Crosby, and Rudolph E. Tanzi

(see pages 1247–1254)

The volatile anesthetic isoflurane can boost apoptosis and amyloid-β (Aβ) accumulation *in vitro*. This week, Xie et al. used cell lines to unravel the underlying mechanism. Treatment of naive human H4 neuroglioma cells with 2% isoflurane increased caspase-3 activation and decreased cell viability without affecting secreted Aβ. In APP-overexpressing cells, however, isoflurane increased APP processing, Aβ production, and caspase-3 activation, all of which were attenuated by a caspase inhibitor. Isoflurane also increased the amyloid precursor protein (APP) cleavage enzymes, β-site APP-cleaving enzyme, and γ-secretase. Inhibition of Aβ aggregation with iAβ5 or clioquinol dampened isoflurane-induced caspase-3 activation. The authors suggest that isoflurane triggers a cycle of apoptosis, increased Aβ generation and aggregation, and then additional apoptosis. Although these studies were all *in vitro*, the events occurred at a clinically relevant concentration of isoflurane (2%), albeit for a long period (6 h). Thus, patients with elevated aβ levels could be vulnerable to this anesthetic side effect.