This Week in The Journal

● Cellular/Molecular

Glucocorticoids, Leptin, and Endocannabinoids in the PVN

Renato Malcher-Lopes, Shi Di, Victor S. Marcheselli, Feng-Ju Weng, Christopher T. Stuart, Nicolas G. Bazan, and Jeffrey G. Tasker

(see pages 6643–6650)

Malcher-Lopes et al. provide electrophysiological and biochemical evidence for a signaling pathway that begins with glucocorticoid stimulation of endocannabinoid synthesis via a $G\alpha_s$–cAMP–PKA pathway, and which is countered by leptin via phosphodiesterase 3B-mediated reduction of cAMP levels. This action takes places in the hypothalamic paraventricular nucleus (PVN). At stake is endocannabinoid-mediated retrograde inhibition of synaptic responses onto PVN magnocellular and parvocellular neurons. The authors show that the action of glucocorticoids is rapid and nongenomic, involving a membrane receptor. The action of leptin involves the Ob-Rb leptin receptor leading through a series of kinases to activation of phosphodiesterase 3B. What are the consequences? Well, in response to fasting, for example, there is a decrease in leptin levels, an increase in glucocorticoids, and activation of CB1 cannabinoid receptors, leading to hypothalamic stimulation of feeding. The signaling pathway outlined by the authors seems well positioned to regulate energy homeostasis, fluid balance, and the stress response.

▲ Development/Plasticity/Repair

Temperament and the Response to Monetary Incentives

Amanda E. Guyer, Eric E. Nelson, Koraly Perez-Edgar, Michael G. Hardin, Roxann Roberson-Nay, Christopher S. Monk, James M. Bjork, Heather A. Henderson, Daniel S. Pine, Nathan A. Fox, and Monique Ernst

(see pages 6399–6405)

Behaviorally inhibited (shy) people have heightened behavioral and neural responses to threatening stimuli. This week, Guyer et al. tested the responses of a cohort of shy and non-shy adolescents (10–15 years of age) to a rewarding stimulus: a monetary incentive delay task. The subjects pressed a button in response to a target image to either win (20 cents to $5), or avoid losing, money. Of no surprise, subjects in both groups preferred $5 rewards to 20 cent rewards. Overall, there were no group performance differences according to valence (gain vs loss) or incentive magnitude. However, functional magnetic resonance imaging revealed different neural responses in the striatum. In the behaviorally inhibited group, striatal activation was greater than in the noninhibited group and increased with higher incentives. The caudate and nucleus accumbens were more strongly activated than the putamen. In contrast, activation of the amygdala was based on incentive value rather than behavioral inhibition status.

■ Behavioral/Systems/Cognitive

Stimulating Risk-Taking Behavior

Daria Knoch, Lorena R. R. Gianotti, Alvaro Pascual-Leone, Valerie Treyer, Marianne Regard, Martin Hohmann, and Peter Brugger

(see pages 6469–6472)

Are you the type of person that takes great risks for minimal rewards, or do you want big rewards for even minimal risk? No, this is not a survey of investment strategies, rather Knoch et al. this week offer some interesting insights into the cortical regions involved in risk-taking behavior. They used a standard gambling paradigm to assess risk-taking before and after stimulation of the dorsolateral prefrontal cortex (DLPFC) by repetitive transcranial magnetic stimulation (rTMS). Low-frequency stimulation (15 min, 1 Hz, or 900 pulses) transiently suppresses excitability in the targeted cortical regions for several minutes following rTMS. The subjects, young males in their 20s, earned greater rewards (or penalties) for higher risk choices and generated a point score after a 7 minute session. Subjects that had right, but not left, DLPFC stimulation earned fewer points and were more likely to choose the high-risk option, suggesting that right prefrontal areas affect risk-taking and that rTMS can cause short-term changes in behavior.

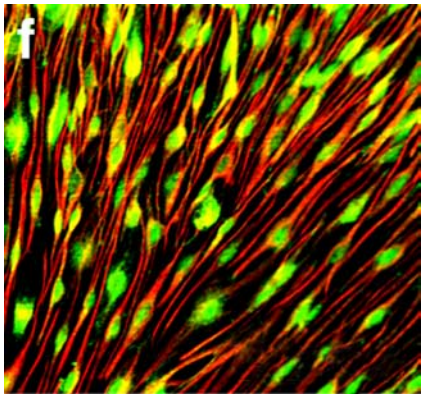
♦ Neurobiology of Disease

Making Schwann Cells from Skin Precursors

Ian A. McKenzie, Jeff Biernaskie, Jean G. Toma, Rajiv Midha, and Freda D. Miller

(see pages 6651–6660)

The hunt goes on for more accessible sources of neural stem cells. In this week's *Journal*, McKenzie et al. go to the skin as a source of neural crest precursors. When the authors treated rodent and human skin-derived precursors (SKPs) with forskolin and neuregulin-1β, some of the cells differentiated into Schwann cells. The authors then cocultured rodent SKP-derived Schwann cells, genetically labeled with yellow fluorescent protein (YFP), with dorsal root ganglion neurons from *shiverer* mice that lack myelin basic protein. After 3 weeks *in vitro*, most of the tagged Schwann cells were associated with axons, many took on a myelinating phenotype, and some proliferated, apparently in response to axon-derived cues. YFP-labeled, SKP-derived Schwann cells, transplanted into the sciatic nerve or brain of *shiverer* mice, also successfully myelinated axons. Significantly, naive human SKPs transplanted into injured peripheral nerve or neonatal mouse brain to neonatal *shiverer* mouse brains differentiated *in vivo* and formed compact myelin.



Purified cultures of SKP-derived Schwann cells were double labeled with the Schwann cell markers P0 (green) and the p75 neurotrophin receptor (red). See McKenzie et al. for details.