This Week in The Journal

● Cellular/Molecular

Neuron, Astrocyte, and Oligodendrocyte Transcriptomes

John D. Cahoy, Ben Emery, Amit Kaushal, Lynette C. Foo, Jennifer L. Zamanian, Karen S. Christopherson, Yi Xing, Jane L. Lubischer, Paul A. Krieg, Sergey A. Krupenko, Wesley J. Thompson, and Ben A. Barres

(see pages 264-278)

In this issue, Cahoy et al. describe a comprehensive database of quantitative gene expression data from neurons, astrocytes, and oligodendrocytes isolated from mouse forebrain at different developmental stages. To do this, the authors first developed a novel purification strategy, involving immunopanning and fluorescence-activated cell sorting, to obtain nearly pure samples of each cell type, including mature astrocytes. They then profiled the expression of >20,000 genes using GeneChip arrays. Besides providing a wealth of quantitative gene enrichment data for the neuroscience community, their analysis revealed that the transcriptomes of astrocytes and oligodendrocytes are as different from each other as they are from neurons and that cultured astrocytes are substantially different from mature astrocytes (the former may be more akin to reactive astrocytes). In addition, a new, highly specific, broadly expressed astrocyte marker, aldhL1, was identified. Finally, analysis of molecular pathway genes suggested that phagocytosis may be a major function of astrocytes.

▲ Development/Plasticity/Repair

Extended Period of Retinocollicular Synaptic Plasticity in $\beta2^{-/-}$ Mice

Ruchir D. Shah and Michael C. Crair

(see pages 292-303)

Spontaneous retinal waves, mediated by cholinergic synapses during the first postnatal week, are thought to drive refinement of the retinotopic map in the superior colliculus. This week, Shah and Crair use mice lacking the nicotinic acetylcholine receptor $\beta2$ subunit ($\beta2^{-/-}$) to investigate mechanisms of synaptic plasticity in retinocollicular synapses. In normal mice, the AMPA/NMDA receptor ratio and the amplitude of AMPA currents increased from postnatal day 3 (P3) to P7, while the proportion of silent synapses decreased. These changes also occurred in $\beta2^{-/-}$ mice but only after the second postnatal week, when glutamate-mediated retinal waves occur. The delay in maturation of retinocollicular synapses in $\beta2^{-/-}$ mice was paralleled by an extended period in which long-term potentiation (LTP) could be elicited: a stimulation paradigm that mimicked retinal wave bursts elicited LTP in a majority of synapses in P3–P4 control mice, but not P6–P7 controls, whereas this stimulation produced LTP in $\beta2^{-/-}$ mice at both ages.

■ Behavioral/Systems/Cognitive

Antimanic Drugs and AMPA Receptors

Jing Du, Thomas K. Creson, Long-Jun Wu, Ming Ren, Neil A. Gray, Cynthia Falke, Yanling Wei, Yun Wang, Rayah Blumenthal, Rodrigo Machado-Vieira, Peixiong Yuan, Guang Chen, Min Zhuo, and Husseini K. Manji

(see pages 68-79)

Although lithium and valproate have long been used to treat manic disorder, the mode of action of these structurally dissimilar treatments is not fully understood. Du et al. now suggest that these drugs reduce trafficking of AMPA receptor GluR1/GluR2 tetramers to synapses. Chronic treatment of rats with therapeutic doses of lithium or valproate reduced levels of GluR2 in hippocampal synaptosomes, as had been shown previously for GluR1. The overall expression level of GluR2 in hippocampus was unchanged, however, suggesting that the reduction in membrane expression may result from decreased receptor trafficking. This hypothesis was supported by chronically treating rats with a fusion peptide that specifically blocks PKA phosphorylation of GluR1 at Ser 845, a site necessary for insertion of GluR1/2 tetramers into membranes. The treatment mimicked the effects of lithium and valproate on GluR1 and GluR2 localization, and it also decreased amphetamine-induced hyperactivity, a common model of mania.

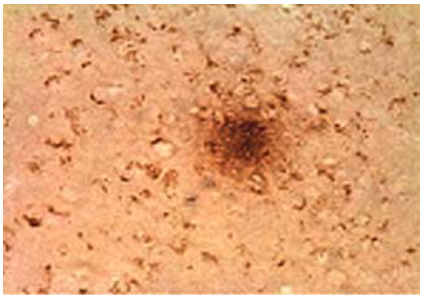
◆ Neurobiology of Disease

Environmental Trigger for Alzheimer's Disease

Jinfang Wu, Md. Riyaz Basha, Brian Brock, David P. Cox, Fernando Cardozo-Pelaez, Christopher A. McPherson, Jean Harry, Deborah C. Rice, Bryan Maloney, Demao Chen, Debomoy K. Lahiri, and Nasser H. Zawia

(see pages 3-9)

Early exposure to environmental toxins can lead to diseases much later in life. This week, Wu et al. report that primates exposed to lead as infants showed Alzheimer's disease (AD)-like pathology years later. From birth to 400 d of age, monkeys were exposed to lead levels that produced no obvious sign of toxicity. Although by young adulthood blood lead levels in exposed monkeys were indistinguishable from those of controls, when examined at approximately 23 years of age, the brains of lead-exposed monkeys exhibited many hallmarks of AD, including Aβ plaques and neurofibrillary tangles, as well as increased expression of Aβ precursor protein (APP) and Sp1, a transcription factor that regulates APP expression. DNA methyl transferase I activity was reduced in lead-exposed monkeys, whereas oxidative damage to DNA was increased. These results indicate that lead exposure early in life can predispose animals to later neurodegenerative disease, possibly through alterations in DNA methylation and oxidation.



AD-like pathology in forebrain section of 23-year-old monkeys exposed to lead as infants. Anti-Aβ antibody staining reveals granular and intracellular staining and plaques. See the article by Wu et al. for details.