This Week in The Journal

● Cellular/Molecular

Blood Flow Is Not Always Linked to Synaptic Activity

Natalya Jukovskaya, Pascale Tiret, Jérôme Lecoq, and Serge Charpak

(see pages 1579–1582)

Synaptic activity consumes large amounts of energy and demands increased oxygen influx to replenish ATP supplies. Delivery of oxygen is ensured because synaptic activity is coupled to changes in cerebral blood flow. Because changes in blood volume and oxygenation can be detected with magnetic resonance imaging, these measures are widely used to infer changes in neuronal activity; but how accurately such changes reflect neuronal activity continues to be debated. Jukovskaya et al. conclude that blood flow is not always correlated with excitatory synaptic activity. They previously showed that calcium signals in presynaptic terminals of rat olfactory receptor neurons accurately reflect glutamate release onto glomeruli. They now show that although calcium signals induced by moderate odor intensities were correlated with blood flow, prolonged stimulation produced adaptation, which decreased calcium signals while blood flow remained high. Additionally, when a glomerulus was strongly activated, blood flow increased around adjacent glomeruli where presynaptic calcium signals were unchanged.

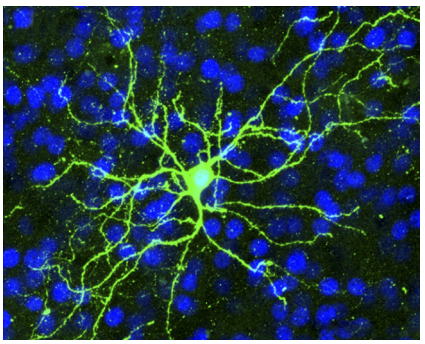
▲ Development/Plasticity/Repair

Morphogens Induce Specific Fates in Cultured Stem Cells

Teruko Danjo, Mototsugu Eiraku, Keiko Muguruma, Kiichi Watanabe, Masako Kawada, et al.

(see pages 1919–1933)

The telencephalon develops in several stages defined by patterned expression of transcription factors induced by gradients of secreted molecules. First, Sonic hedgehog (Shh), a molecule secreted at the ventral midline, distinguishes dorsal (pallium) and ventral (subpallium) telencephalon by downregulating a dorsal transcription factor in ventral regions. The pallium then divides into anterolateral and posteromedial regions that produce glutamatergic neurons of the cortex, hippocampus, and amygdala, while the subpallium splits into medial, lateral, and caudal ganglionic eminences (MGE, LGE, and CGE) that produce GABAergic neurons of the cortex, striatum, and caudate nucleus. Danjo et al. found that stimulating embryonic stem cells with moderate or high levels of Shh agonist promoted LGE or MGE/CGE fate, respectively. Subsequent treatment of the latter with fibroblast growth factor 8 (FGF8) promoted MGE fate, whereas treatment with FGF15/18 promoted CGE fate. Thus, stem cells could be directed to different fates and to differentiate into specific neuron types when transplanted into mice.



Embryonic stem cells directed toward LGE fate (green) differentiate into medium spiny neurons when injected into mouse striatum. See the article by Danjo et al. for details.

■ Behavioral/Systems/Cognitive

Anterior Piriform Cortex Detects Amino Acid Deficiency

John B. Rudell, Adam J. Rechs, Todd J. Kelman, Catherine M. Ross-Inta, Shuzhen Hao, et al.

(see pages 1583–1590)

Many amino acids cannot be synthesized by vertebrates and must be obtained in the diet. When any of these indispensible amino acids is depleted, its associated tRNA is left uncharged. Uncharged tRNA activates a kinase that phosphorylates a translation initiation factor and thus inhibits protein synthesis. Animals can sense if a food is deficient in any amino acid and stop eating it; given a choice, they select foods that have a balanced amino acid content. Behavioral responses to amino acid insufficiency do not require taste or smell, but require the primary olfactory cortex (anterior piriform cortex, APC), in which EPSP amplitude increases shortly after ingestion of inadequate food. Rudell et al. show that EPSP amplitude increased in APC slices after an indispensible amino acid was removed from the medium. Restoring the amino acid restored EPSP amplitude to control levels. Therefore, the APC can detect and respond to amino acid insufficiency without input from other brain regions.

◆ Neurobiology of Disease

Maternal Viral Infection Produces Schizophrenia-Like Effects in Mice

José L. Moreno, Mitsumasa Kurita, Terrell Holloway, Javier López, Richard Cadagan, et al.

(see pages 1863–1872)

Schizophrenia is a complex disease caused by interactions between multiple genetic mutations and environmental triggers, which cause abnormal development in many brain areas, dysfunction of several neurotransmitter systems, and diverse cognitive and behavioral symptoms, including hallucinations, social withdrawal, and working memory deficits. This complexity has impeded investigation of how the disease develops. Nonetheless, as more is learned about molecular and anatomical changes that occur in schizophrenics, the ability to link potential causes to similar changes in mice has increased. Hence, Moreno et al. examined the effects of maternal influenza infection—which increases schizophrenia risk in humans—in mice. Compared to control mice, those born to infected mothers had higher levels of 5-HT_{2A} serotonin receptors and lower levels of mGluR2/3 metabotropic glutamate receptors in the frontal cortex. Similar changes have been detected in untreated schizophrenics. Moreover, exposed mice had stronger behavioral responses to a hallucinogen, and this change, like schizophrenia, did not appear until after puberty.