This Week in The Journal

● Cellular/Molecular

Adenosine Bidirectionally Regulates Astrocytic GABA Uptake

Sofia Cristóvão-Ferreira, Gemma Navarro, Marc Brugarolas, Kamil Pérez-Capote, Sandra H. Vaz, et al.

(see pages 15629–15639)

A_1 adenosine receptors (A_1Rs) are usually coupled to $G_{i/o}$ proteins that inhibit adenylase cyclase activity, whereas A_{2A}Rs, which have a lower affinity for adenosine than A_1Rs, are coupled to G_s proteins that stimulate adenylase cyclase. Despite their opposing effects, however, Cristóvão-Ferreira et al. show that A_1Rs and A_{2A}Rs can form heterotetrameric receptors that couple to both $G_{i/o}$ and G_s. These receptors bidirectionally regulate GABA uptake by rat cortical astrocytes. Low concentrations of an adenosine analog inhibited GABA uptake, as did A_1R agonist. In contrast, higher adenosine analog concentrations facilitated GABA uptake, as did A_{2A}R agonist. Both A_1R- and A_{2A}R-specific agonists caused internalization of both A_1Rs and A_{2A}Rs. Interestingly, the effect of either agonist was blocked by antagonists of either A_1Rs or A_{2A}Rs, as well as by inhibiting either $G_{i/o}$ or G_s. Because ATP coreleased with GABA is extracellularly hydrolyzed to adenosine, concentration-dependent regulation of heterotetrameric receptors might serve to increase GABA uptake when synaptic activity is high.

▲ Development/Plasticity/Repair

Prospero Regulates Expression of CO_2 Receptors

Marion Hartl, Laura Loschek, Daniel Stephan, K. P. Siju, Christiane Knappmeyer, et al.

(see pages 15660–15673)

Mosquitoes are attracted to CO_2 expired from hosts. The olfactory receptor neurons (ORNs) responsible for CO_2 detection are located on maxillary palps near mosquitoes' mouths, and they project to medial olfactory glomeruli associated with gustatory stimuli. In contrast, CO_2 repels *Drosophila*; their CO_2-sensitive ORNs are located on the antennae rather than the maxillary palps, and the ORNs project to ventral olfactory glomeruli. *MicroRNA-279* (*miRNA-279*) influences CO_2 receptor expression in *Drosophila* ORNs, and loss of *miRNA-279* results in expression of CO_2 receptors in supernumerary maxillary palp ORNs that project to both ventral and medial olfactory glomeruli. Hartl et al. found that mutations in the transcription factor Prospero produce a phenotype similar to loss of *miRNA-279* and that Prospero normally promotes expression of *miRNA-279*. Their results suggest that Prospero and *miRNA-279* reduce expression of two transcription factors that induce expression of CO_2 receptors in maxillary palp ORNs. Misexpression did not make CO_2 attract flies, however.

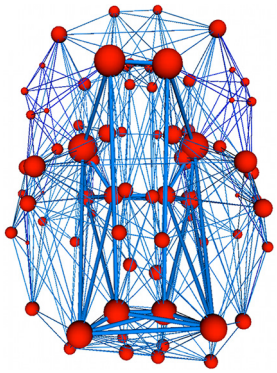
■ Behavioral/Systems/Cognitive

Main Hubs in Human Brain Are Highly Interconnected

Martijn P. van den Heuvel and Olaf Sporns

(see pages 15775–15786)

Human brains are complex networks comprising many interconnected nuclei and cortical regions. After structural and/or functional imaging identifies brain regions (nodes) and their connections, graph theory can be used to quantify various network characteristics, such as how many connections each node has, how interconnected a group of neighboring nodes is, and the extent to which nodes cluster into independent modules. These characteristics describe how interconnected the network is and identify hubs—nodes that have many connections—that are particularly important for communication between modules. van den Heuvel and Sporns used diffusion tensor imaging to map connections among 82 cortical and subcortical regions in human brains, and subsequent graph theoretical analysis identified 12 highly interconnected bilateral hubs in the hippocampus, thalamus, and putamen, and in precuneous, superior frontal, and superior parietal cortices. The high interconnectivity might minimize the effects of local damage and suggests that the hubs function as an integrated unit.



Connections (blue lines) among 82 cortical and subcortical regions (red circles). Circle size indicates the relative number of other nodes each region is connected to. Thick blue lines indicate connections among hubs. See the article by van den Heuvel and Sporns for details.

♦ Neurobiology of Disease

Inhibiting Striatal Interneurons Produces Dystonia and Tics

Aryn H. Gittis, Daniel K. Leventhal, Benjamin A. Fensterheim, Jeffrey R. Pettibone, Joshua D. Berke, et al.

(see pages 15727–15731)

The basal ganglia are involved in selecting appropriate actions and inhibiting inappropriate actions. Excitatory inputs from thalamus and cortex enter the basal ganglia via the striatum, which transmits information to output structures via direct and indirect inhibitory projections of medium spiny neurons (MSNs). Approximately 95% of striatal neurons are MSNs; the remainder includes cholinergic, persistent low-threshold spiking, and fast-spiking interneurons (FSIs). Although much is known about the molecular, electrophysiological, and synaptic properties of MSNs, how circuits within the striatum process information is poorly understood. To investigate the function of FSIs, Gittis et al. exploited the fact that these are the only striatal neurons that require activation of GluA2-lacking AMPA receptors to reach spike threshold. Blocking these receptors caused mice to exhibit twisted postures and jerky movements. Because disruption of striatal GABAergic signaling is thought to underlie human hyperkinetic movement disorders such as tics and dystonias, these data suggest that FSI dysfunction contributes to these disorders.