This Week in The Journal

Cellular/Molecular

Nicotine Influences Stoichiometry of α3β4 Receptors

Francesca Mazzo, Francesco Pistillo, Giovanni Grazioso, Francesco Clementi, Nica Borgese, et al.

(see pages 12316–12328)

Nicotine exposure increases surface expression of several subtypes of nicotinic acetylcholine receptors (nAChRs) by facilitating receptor assembly, enhancing export of assembled pentamers from the endoplasmic reticulum (ER), and/or stabilizing assembled receptors, thus enabling more to be inserted into the plasma membrane. Most studies of the effects of nicotine on nAChRs have examined the $\alpha4\beta2$ subtype, which is most prevalent in the brain. Relatively little is known about $\alpha3\beta4$ receptors, but this subtype is highly expressed in the habenula and has recently been linked to nicotine addiction and lung cancer. Mazzo et al. found that nicotine greatly increased surface expression of $\alpha3\beta4$ nAChRs in HeLa cells, not by facilitating receptor assembly, which was efficient when nicotine was absent, but instead by enhancing ER export and slowing receptor degradation. Interestingly, both effects were attributable to nicotine-induced alteration of nAChR subunit stoichiometry: by binding to receptors during pentamer assembly, nicotine promoted recruitment of $\beta4$ rather than $\alpha3$ as the fifth subunit.

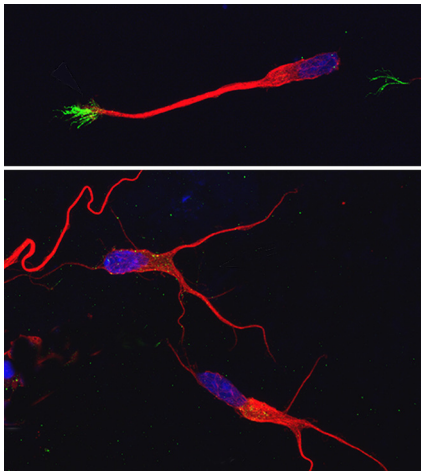
Development/Plasticity/Repair

Fascin-1 Helps Neuroblasts Migrate

Martina Sonego, Sangeetha Gajendra, Maddy Parsons, Yafeng Ma, Carl Hobbs, et al.

(see pages 12171–12185)

Before adult-born neurons can function in learning or repair, they must migrate from proliferative zones to appropriate brain areas. Sonego et al. show that fascin-1 is required for proper migration of neuroblasts from the subventricular zone (SVZ) to the olfactory bulb along the rostral migratory stream (RMS). Neuroblast migration involves extension of a leading process and adhesion of this process as the rest of the cell moves forward; Fascin-1 contributes to both of these steps. Unphosphorylated fascin-1 helps bundle actin filaments, which is necessary for process extension, but phosphorylation of fascin-1 by protein kinase C (PKC) switches its role from actin bundling to cell adhesion. Fascin-1 is highly expressed in SVZ neuroblasts, and when it was knocked out cells accumulated in the caudal portion of the RMS and migrating neuroblast chains were disorganized. As a result, fewer cells reached the olfactory bulb. In cultures, mutating the PKC phosphorylation site to either mimic or prevent phosphorylation increased branching of leading processes and slowed neuroblast migration.



Fascin-1 (green), is expressed in at the leading edge of migrating neuroblasts (top). Without fascin-1 (bottom) leading processes branch and migration is slowed. See the article by Sonego et al. for details.

Systems/Circuits

Monkeys' Dorsal Frontal Cortex Organization Resembles Humans'

Jérôme Sallet, Rogier B. Mars, MaryAnn P. Noonan, Franz-Xaver Neubert, Saad Jbabdim, et al.

(see pages 12255–12274)

Humans have unique cognitive abilities that monkeys lack, but the neural basis for this uniqueness is poorly understood. Many higher cognitive functions, such as predicting others' actions and inferring their beliefs, are thought to involve activity in the dorsal frontal cortex (DFC). How human DFC is organized and connected to other brain regions is primarily inferred from studies on macaques, which presupposes that humans have not evolved unique circuitry. To test this assumption, Sallet et al. used diffusion-weighted magnetic resonance imaging to define subregions in human DFC and used functional magnetic resonance imaging to determine how these regions were coupled to other brain areas. They then compared the coupling strength between each DFC area and its targets in humans with the coupling strength between homologous areas in macaques. Ten subregions were identified, and each was coupled with a distinct set of other brain regions. For every region, regardless of proposed function, homologous regions with similar coupling patterns were found in macaques.

Behavioral/Cognitive

Muscle Synergies Speed Adaptation to Virtual Surgery

Denise J. Berger, Reinhard Gentner, Timothy Edmunds, Dinesh K. Pai, and Andrea d'Avella

(see pages 12384–12394)

Most movements involve activation of numerous muscles that exert force on multiple joints. Rather than requiring the CNS to command movement of each muscle individually, muscles might be grouped into modules, or muscle synergies, that are activated in different combinations to produce different movements. Although EMGs recorded during behavior often demonstrate a pattern of muscle activation consistent with the synergy hypothesis, some researchers argue that the appearance of synergies results from other constraints that limit the number of activation patterns that can be produced. Berger et al. now provide stronger support for the synergy hypothesis. They first recorded EMGs from volunteers who used arm muscles to move a weighted cursor in a virtual environment. They then simulated surgical rearrangement of tendons by changing how these muscle contractions affected cursor movement. As predicted by the synergy hypothesis, participants learned more quickly to perform the task when previously used muscle synergies could be used in new combinations than when new or modified synergies were required.