use of the common NMDA receptor antagonist D,L-2-amino-5-phosphonovaleric acid (APV) to test for a link between LTP and learning in an invertebrate nervous system.

Murphy and Glanzman now show that classical conditioning of the synaptic response from sensory neurons to motor neurons is blocked by APV (see the figure). Furthermore, APV has no effects on nonassociative learning or on other facilitatory pathways that might also contribute to aspects of the behavior. Thus, the associative properties of the NMDA receptor are required for associative conditioning. Although this classical conditioning of the synaptic pathway is known to mediate the behavior of siphon withdrawal, an effect of APV on the learning of the behavior in the animal has not yet been shown. This will clearly be the next step.

The experiments described by Murphy and Glanzman provide an important test of the hypothesis that LTP-like synaptic plasticity mediates learning in a simple, well-defined task in a simple, well-defined neural circuit. It strengthens the link between Hebbian plasticity and associative learning and suggests a conservation of mechanisms among evolutionarily diverse organisms such as sea slugs and mammals. Hence, some further confidence is provided for those holding the belief that LTP equals memory.

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NEUROSCIENCE

Neocortical Neurons: Where Do They Come From?

Andrew Lumsden and Massimo Gulisano

The neocortex develops from an unpromising pair of bulges at the anterior end of the neural tube. The thin dorsal wall of each of these telencephalic vesicles produces the neocortex, whereas a bulbous swelling of the ventral wall produces the striatum—a component of the basal ganglia that receives major input from the neocortex (see the figure). Early in telencephalic morphogenesis, a prominent junction appears between the neocortical and striatal regions. Because this junction coincides with the borders of regulatory gene expression domains (*1*) and appears to segregate cells with markedly different fates (*2*), it is thought of as a boundary that partitions the telencephalon into discrete, developmentally independent compartments (*3*). Thus, the textbook view is that neocortical neurons originate exclusively from precursors that are contained within neocortical proliferative zones. This view is now challenged by Anderson *et al.* (*4*) on page 474 of this issue. They describe the origin of a subpopulation of neocortical interneurons from the developing striatum, implying that these cells migrate across the supposedly cell-tight corticostriatal junction. Significantly, this migration fails when two homeodomain transcription factors normally expressed by striatal precursor cells, DLX-1 and DLX-2, are deleted by gene targeting.

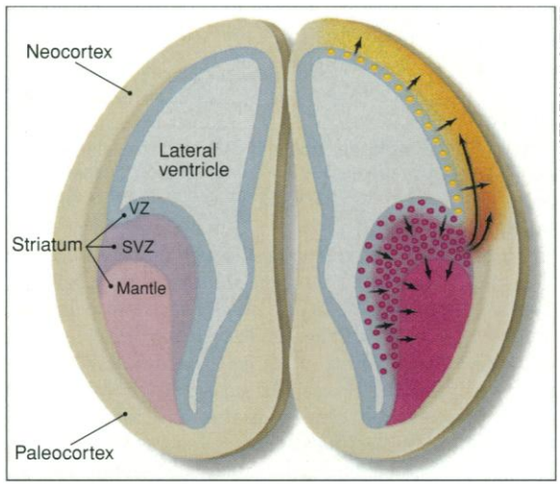

ILLUSTRATION: K. SUTLIFF

The telencephalon of an embryonic mouse. On the right, *Dlx-1*– and *Dlx-2*–expressing cells of the striatal VZ and SVZ (red) migrate into the striatal mantle and into the neocortex (arrows), where they mix with the radially migrating descendants of cortical precursors (yellow). Regions of the embryonic day 14 telencephalon shown on the left.

Most forebrain neurons are produced directly from the germinative epithelium of the ventricular zone (VZ), although some later-born neurons arise indirectly from the VZ by means of a secondary proliferative population (SPP) of nonepithelial cells that congregate in the subventricular zone (SVZ). As they differentiate, young neurons migrate out of the VZ and SVZ and into the subjacent mantle zone. Two members of the *Dlx* gene family, *Dlx-1* and *Dlx-2*, have virtually identical expression in these maturational zones of the striatum: Both genes are active (from embryonic day 9.5 in the mouse) in a subset of cells in the VZ and later in most cells of the SVZ, but the genes are switched off once the cells reach the mantle. Expression of *Dlx-1* and *Dlx-2* thus marks the transition from proliferation to differentiation (see the figure). One or the other of the genes is required for normal striatal histogenesis: In homozygous *Dlx-1/2* double knockout mice (but not in the single gene knockouts), partially differentiated neurons fail to migrate, piling up in the SVZ, and the mantle is depleted of late-born, SPP-derived neurons (*5*).

Dlx-1 and *Dlx-2* are not expressed in cortical proliferative zones, but immunopositive cells later turn up in the subventricular, intermediate, and marginal zones of the neocortex (*4*, *6*). Together with other data (*7*), these results suggested that striatal progenitors might also generate neocortical neurons—an intriguing possibility that has now been explored by Rubenstein and his colleagues (*4*). First, using vital dye labeling in slices of normal embryonic day 12.5 mouse forebrain, the authors found that cells marked in the striatal SVZ end up in the neocortex. Second, when the neocortical region is detached at its junc-

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tion with the striatum, neocortical *Dlx-1* expression is eliminated and there is a dramatic (fivefold) reduction in the number of cortical interneurons that express the inhibitory neurotransmitter γ-aminobutyric acid (GABA). Third, GABA-expressing cells in the *Dlx-1/2* double mutant neocortex are as heavily depleted as when the wild-type cortex is detached. Fourth, no cell migration from striatum into neocortex could be seen in dye-labeled slices of the double mutant forebrain.

This is compelling evidence that the GABA-containing, nonpyramidal interneurons of the neocortex—of which there are many—do not arise uniquely from neocortical proliferative regions; rather, there is also a significant source of these cells in the neighboring territory, from a proliferative region that also produces the GABA-containing, medium spiny neurons that populate the striatum. Equally compelling is the evidence that *Dlx-1* or *Dlx-2* homeobox gene function is required, presumably cell autonomously, for emigration from the striatal SVZ, both radially into the striatal mantle and tangentially into the neocortex.

These findings will provoke debate about the status of the cortico-striatal junction. Compartment formation presupposes the early allocation of defined assemblies of precursor cells whose borders are coextensive with the expression domains of genes involved in the acquisition of regional identity. Crucial to the compartment definition is the containment of cell polyclones at a boundary where cell mixing is restricted (*3*). Consistent with this notion is the finding that cells in the telencephalic VZ disperse tangentially, yet they never cross from neocortex to striatum (*2*). Furthermore, an adhesive difference has been shown between neocortical and striatal cells that would favor their segregation or nonmixing (*8*). However, clonal analysis has suggested extensive movement of cells between neocortex and subcortical regions (*9*), and now we see striatal precursors producing neocortical neurons. How can these apparently conflicting data be resolved?

Where there is no apparent restriction to movement, the cells involved may well be already-specified neurons that are migrating along preassigned vectors into their neighbor's territory, rather than passively stumbling into it. In the hindbrain, where a metameric series of compartments (rhombomeres) are formed, rhombomeric domains of the VZ remain completely lineage-restricted throughout neurogenesis, although inter-rhombomeric migration of cells occurs within the mantle (*10*). Lineage restriction thus exists only for the VZ (*3*), whereas the mantle is unrestricted. A similar situation may prevail in the forebrain, where no violation of the cortico-striatal junction has ever been noted for VZ cells. The adhesion properties responsible for holding incompletely specified precursor cells together would be lost as the cells acquire their regional identity and commence migration (*8*). The loss of compartment properties during differentiation may indeed be a prerequisite for organized migration, a process that would require a switch in cell-cell affinity.

How are *Dlx*-expressing cells guided into the cortex? Being orthogonal to the long axes of radial glial cells, their path is unlikely to be laid out by the glial scaffold customarily used by migrating neurons. *Dlx*-expressing cells may be guided by preexisting axon tracts (*11*): axons of cortical projection neurons do arrive in the striatum at the appropriate time (*12*). Time-lapse analysis of brain slices from *Dlx-GFP* transgenic mice might be useful here and could also show the full extent of the migratory cohort.

There are many examples of tangential migration by neurons, or their precursors, within the cortex (*13*), but the molecular regulators of migration, whether tangential or radial, are largely unknown; the particular significance of the new work by Anderson *et al.* (*4*) is the discovery that *Dlx* homeobox genes are (possibly direct) regulators of the process. With this crucial step in place, the next will be to identify downstream targets of *Dlx* and thereby the cellular machinery required for migration.

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PLANETARY SCIENCE

Lensing by Triton's Atmosphere

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During a total lunar eclipse, Earth-based observers can see the moon glowing with a coppery color as it passes through the center of Earth's umbra. An observer on the moon at the same time would see Earth's limb illuminated as a ring of refracted, reddened sunlight. On much larger spatial scales, and much more rarely, a more distant planet occults a more distant star in an alignment similar to a total lunar eclipse. In this case, when the stellar image is within a critical distance from the planet-observer line, light from the star refracts in unison around the planet's limb, forming a phenomenon known as the central flash. Central flashes have been observed during stellar occultations by Mars, Neptune, Saturn, and Saturn's largest moon, Titan. On page 436 of this issue of *Science*, Elliot *et al.* report the first observation of a central flash produced by Neptune's large and interesting moon Triton (*1*).

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When Voyager 2, so far the only spacecraft to visit Neptune, encountered that planet in 1989, investigators detected a tenuous nitrogen-rich atmosphere on Triton (*2*). They measured the density and surface pressure by observing the bending of radio waves transmitted through Triton's atmosphere to Earth as the spacecraft was occulted. The spacecraft occultation was not close to central, and no central flash could have been seen in any case because the bending was very slight (maximum of about 10^{-6} radians). The geometry of a stellar occultation by Triton as seen from Earth is vastly different. In this case, the maximum bending angle, still only about 3×10^{-7} radians, is large enough to give a deflection of one Triton radius by the time the ray gets to Earth, enough for a central flash. Bending of light into the shadow is enormously sensitive to the atmospheric structure, for it depends on spatial second derivatives of the atmospheric density. In the central flash region, the global second derivatives determining the atmosphere's projected radius of curvature become most important.