DEVELOPMENT

Evolving ideas about migration

In the developing mammalian brain, neurons are highly migratory, and their final destinations are often far from their sites of origin in the proliferative zones. Their migration pathways have been extensively mapped in laboratory animals, but as Letinic and Rakic report in *Nature Neuroscience*, it might not always be appropriate to extrapolate these findings to humans. The authors have identified a migration pathway, from the telencephalon to the dorsal thalamus (DT), that seems to be unique to the human brain, and that might have contributed to the expansion of certain brain regions during evolution.

The DT arises from the diencephalon, yet in the human brain it undergoes considerable growth after proliferation has ceased in this region, indicating that cells are being imported from elsewhere. Previous studies in fixed tissue provided evidence for a migratory stream between the telencephalic ganglionic eminence (GE) and the DT, but nobody had seen it in action. Letinic and Rakic labelled GE cells with the lipophilic marker DiI and tracked their migration in brain slices from human fetuses. They showed that cells from the medial portion of the GE migrate to the DT. The origin of the migrating cells was further confirmed by immunohistochemistry; they produce the inhibitory neurotransmitter GABA (γ-aminobutyric acid) and the DLX1 and DLX2 homeodomain proteins, all of which are characteristic of GE-derived cells.

This migration pathway has not been identified in any other mammals, even in primates that are closely related to humans, such as the macaque monkey. So, what is different about the human brain in this region? In explant cultures, Letinic and Rakic showed that human DT tissue is attractive to human GE cells. Mouse DT tissue, on the other hand, neither attracts nor repels mouse GE cells, but they are repelled by the subthalamus, which lies between the GE and the DT. By contrast, human subthalamic tissue has no effect on GE cell migration *in vitro*, so it presumably presents no barrier to migration *in vivo*. On the basis of these experiments alone, it is not clear whether it is the adhesive properties of the GE cells or of the GE–DT migratory pathway that have changed in the human brain. This issue might be resolved by cross-species grafting experiments, and by identifying the molecular cues that mediate the attractive and repulsive activities.

During evolution, the acquisition of higher cognitive ability in humans has been attributed to enlargement of the association areas of the cortex and the thalamic nuclei that connect to these regions. This study shows that the proliferative zone of the developing human telencephalon not only contributes more cells to the cortex, but also provides a source of GABA-producing cells that migrate the DT. This migratory link between the telencephalon and the thalamus might provide the key to understanding how these regions could have evolved in tandem.

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References and links

ORIGINAL RESEARCH PAPER Letinic, K. & Rakic, P. Telencephalic origin of human thalamic GABAergic neurons. *Nature Neurosci.* **4**, 931–936 (2001)

FURTHER READING Rao. Y. & Wu, J. Y. Neuronal migration and the evolution of the brain. *Nature Neurosci.* **4**, 860–862 (2001)

WEB SITE

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IN BRIEF

NEUROLOGICAL DISORDERS

A novel action of Alzheimer's amyloid-β-protein (Aβ): oligomeric Aβ promotes lipid release.

Michikawa, M. *et al. J. Neurosci.* **21**, 7226–7235 (2001)

The authors found that oligomeric Aβ stimulates the release of lipids, including cholesterol and phospholipids, from neurons and astrocytes in culture. Monomeric and fibrillar Aβ did not have the same effect. Lipid release was blocked by inhibition of protein kinase C and by addition of Congo red, which stabilizes Aβ monomers. So, the stimulation of lipid release from cell membranes and the disruption of lipid homeostasis might be an additional factor that contributes to the neuronal dysfunction observed in Alzheimer's disease.

NEUROLOGICAL DISORDERS

Genetic suppression of seizure susceptibility in *Drosophila*.

Kuebler, D. *et al. J. Neurophysiol.* **86**, 1211–1225 (2001)

Kuebler and his colleagues advocate the use of *Drosophila* as a model system to study seizure susceptibility. They studied flies that are particularly prone to electric-shock-induced seizures — the so-called 'bang-sensitive mutants' — and looked for factors that could suppress the increased susceptibility. They performed crosses between the bang-sensitive mutants and flies with mutations in Na^+, K^+ and gap-junction channels, and identified double mutants with reduced seizure susceptibility. These findings set the scene for larger-scale screens to search for additional seizure-related candidate genes.

SYNAPTIC PHYSIOLOGY

Glutamate-induced transient modification of the postsynaptic density.

Dosemeci, A. *et al. Proc. Natl Acad. Sci. USA* **98**, 10428–10432 (2001)

Rapid formation and remodeling of postsynaptic densities in developing dendrites.

Marrs, G. S. *et al. Nature Neurosci.* 27 August 2001 (10.1038/nn717)

Two new studies emphasize the dynamic nature of the postsynaptic density — the specialized complex of receptors, signal transduction molecules and other proteins found on the postsynaptic membrane. Dosemeci *et al.* found that the postsynaptic density thickens during synaptic activity induced by glutamate or brief depolarization of the presynaptic neuron. They also show that the thickening is reversible and results, at least in part, from translocation of calcium/calmodulin-dependent protein kinase II (CaMKII) to the postsynaptic density. This transient thickening could allow the postsynaptic density to adjust itself in response to changing synaptic activity. Marrs *et al.* investigated the formation and remodelling of the postsynaptic density in developing hippocampal neurons, and found that it was structurally dynamic: postsynaptic densities could appear or disappear within less than 15 minutes, grow, shrink or move. Such plasticity could enable rapid changes in synaptic connections in the developing brain.