

The evolution of brain wiring: Navigating to the neocortex

March 23 2011

A new study is providing fascinating insight into how projections conveying sensory information in the brain are guided to their appropriate targets in different species. The research, published by Cell Press in the March 24 issue of the journal *Neuron*, reveals a surprising new evolutionary scenario that may help to explain how subtle changes in the migration of "guidepost" neurons underlie major differences in brain connectivity between mammals and nonmammalian vertebrates.

The [neocortex](#) (the "new" [cortex](#)) is a brain area that is unique to mammals and plays a central role in cognition, motor behavior, and sensory perception. A deeper brain region, called the thalamus, sends sensory information to the neocortex via a major highway called the internal capsule. As might be expected given the differences in brain anatomy, thalamic projections vary tremendously among [vertebrates](#), with paths in [reptiles](#) and birds taking a completely different route than that seen in mammals.

"What controls the differential path-finding of thalamic axons in mammals versus nonmammalian vertebrates and how these essential projections have evolved remains unknown," explains senior study author, Dr. Sonia Garel from Ecole Normale Supérieure in Paris. "We examined how thalamic axons, which constitute the main input to the neocortex, are directed internally to their evolutionarily novel target in mammals, while they follow an external path to other targets in reptiles and birds."

Using a series of comparative and functional studies, Dr. Garel and colleagues observed species-specific differences in the migration and positioning of well-characterized "corridor guidepost" neurons. The researchers went on to show that a protein called Slit2, previously implicated in cell migration and axon guidance, was critical for local positioning of mammalian guidepost cells and functioned as a kind of switch to reroute thalamic axons from the default external route to an internal path to the neocortex.

"Taken together, our results show that minor differences in the positioning of conserved guidepost [neurons](#), which is controlled by Slit2, plays an essential role in the species-specific pathfinding of thalamic [axons](#), thereby providing a novel framework to understand the shaping and evolution of a novel and major brain projection," concludes Dr. Garel. "Furthermore, our study opens the possibility that changes in cell migration may more generally control the evolution of brain connectivity, particularly the formation of other mammalian-specific tracts. Since an increase in cell migration has participated in the morphogenesis of the neocortex itself, these novel findings reveal that cell migration can be considered as a general player in the evolutionary changes that led to the emergence of the mammalian brain."

Provided by Cell Press

Citation: The evolution of brain wiring: Navigating to the neocortex (2011, March 23) retrieved 25 April 2024 from

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