Researchers discover an essential genetic mechanism of cerebral cortex development

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The cerebral cortex is the most complex and vital structure in our brain. It is the nerve centre for those "higher" functions that characterise our species, such as language and abstract thought. The nerve cells – or neurons – which comprise the cortex are key elements in ensuring its functions effectively. They are also targeted by numerous neurological and psychiatric illnesses (epilepsy, mental retardation, autism, Alzheimer´s).

Specifically, the complex functions of the cortex depend upon the precise alignment of nerve cells or neurons, which are arranged in "layers" and "columns" (Figure 1A). This precise structure provides the fundamental basis for cortical functions. Nerve cells are arranged in layers and columns during embryonic development. If the process is disrupted, various illnesses can occur (epilepsy, mental retardation and especially autistic syndromes). Whilst there is an increasing understanding of the mechanisms involved in the construction of cortical layers, those that control the formation of the columns remain a mystery.

The work of a research team, led by Pierre Vanderhaeghen and Jordane Dimidschstein (ULB, WELBIO, IRIBHM and the ULB Neuroscience Institute (UNI)), offers new perspectives on the cortical structure´s development. The team discovered a mechanism underlying the arrangement of cortical neurons in columns. This work is to be published on 18 September 2013 in the prestigious journal *Neuron*.

Using the mouse cerebral cortex as a model, researchers at the Université libre de Bruxelles (ULB, School of Medicine) initially discovered that a nerve cell signalling factor, called ephrin-B1, can act as a guide, helping nerve cells from the cortex to form columns (Figure 1B). The researchers subsequently observed that the ephrin-B1 signal acts at a very early stage in embryonic development, when the newly-produced cortical nerve cells actively move throughout the brain to reach the cerebral cortex. The researchers made the interesting finding that it is the level of ephrin signal that influences the way in which cells are arranged in a columnar fashion (Figure 1C). An increase in the ephriB signal will force the nerve cells to migrate in a "tight formation", which makes the cortical columns narrower. A reduction in the ephrin-B signal, on the other hand, will enable nerve cells to migrate more broadly, thus producing more sparsely-grouped columns.

These advances have significant implications. On a fundamental level, this research will enable us to gain a greater understanding of an essential, yet little known, aspect of cortex development: the construction of the cortical columns. Cortical column anomalies were reported in several different neurological and psychiatric diseases. Identifying genes involved in this process thus offers new perspectives for improving our understanding of these conditions.

More information: Dimidschstein, J. et al. Ephrin-B1 Controls the Columnar Distribution of Cortical Pyramidals by Restricting Their Tangential Migration, *Neuron* 79, 1–13, September 18, 2013. dx.doi.org/10.1016/j.neuron.2013.07.015

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