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the geometry of intelligence

Vivienne Baillie Gerritsen

All vertebrates have a skull. In which is lodged – and protected – one of the most important and complex biological tissues that exists, i.e. the brain tissue. When you compare the brains of different animals, there is one thing that stands out immediately: the amount of folds. The brain of a marmoset or mouse, for instance, seems almost smooth when put beside a sheep's, or a human's. It all has to do with available space. Human brain tissue presents such a large surface that the only way Nature has found to fit it into a rather small receptacle is to fold it many times – very much like inserting a large blanket into a small drawer. This folding has given the human brain the particular architectural characteristics it has; an architecture which – when altered – can cause severe neurological harm. Recently, scientists discovered a protein which has a direct role in folding brain tissue during brain development: TMF-regulated nuclear protein 1, or Trnp1.

by Lars Henkel (Germany)

Courtesy of the artist

The human brain begins its development at an early embryonic stage – with the differentiation, multiplication and migration of neurons – and continues well after birth, even into the sensitive and fragile period of adolescence. During the postnatal period, the brain continues its formation of synapses, followed by synaptic pruning, for months and even years. Synapses then undergo reorganisation which takes place during childhood and adolescence. Such reorganisation depends not only on genetic factors but also environmental factors. In this light, it is not hard to understand that forms of stress – such as verbal or physical abuse for instance - can alter a brain's architectural harmony, resulting in psychiatric fragility. Folding of the brain cortex – or cortical gyrification – also has its harmony. Brain tissue whose folding is hindered early on in development can have a profound influence on a brain's function and performance.

Our perception of the brain has come a long way. In the early days, the heart was believed to be the seat of intelligence and the brain was assumed to be mere "cranial stuffing". The expression "learning something off by heart" apparently stems from this ancient belief. Over the millennia, views have changed and the brain is now known to be the part of our body which incarnates intelligence. The earliest recorded reference to the brain dates back to the 17th century BC. The ancient Greeks had different views as to what a brain was for – from acting as a cooling mechanism for the blood to a place which harboured the mind. It was during the Renaissance, and the practise of cadaver dissection, that the Belgian physicist Andreas Vesalius began to jot down the structural characteristics of the brain. The advent of the microscope and, especially, the development of tissue staining towards the end of the 19th century finally revealed the structures of single neurons, and the notion grew that different parts of the brain had different functions.

These functions are defined both by neuron type and neuron connectivity, but just as importantly by brain geometry, or cortical gyrification. The geometry of a brain is defined by three axes: radial, tangential and lateral. Trnp1 has turned out to have a role in pushing the brain both upwards (radial expansion) and lengthwise (tangential expansion) during its development.

How? When the protein's expression is high, neural stem cell populations are renewed, mediating tangential growth. When Trnp1 expression is low, a surge in neuron cell numbers is observed as well as an increase in fibres that serve as guiding structures for cortex gyrification. What is more, Trnp1 is also a master regulator of radial glia fate; radial glia being populations of cells that are involved in key developmental processes, such as patterning, neuronal migration and neuron precursors.

How does Trnp1 achieve these crucial steps in brain development on the molecular level? To date, not much is known, besides the fact that Trnp1 is a nuclear transcription factor that requires an extraordinarily strong DNA interaction for its function. It is tightly associated with chromatin. In fact, the protein's sequence has a surprising number of arginines – a characteristic also found in a protein known as UTF1 which is able to affect chromatin compaction. All in all, through its interaction with DNA, Trnp1 is able to orchestrate vital steps in brain development, resulting in cell fate and cortical gyrification – in other words, the geometry of intelligence.

When the cortical architecture of our brain is hindered in any way, the consequences can be drastic. Amongst other major neurological drawbacks, it is thought that epilepsy and certain forms of autism are caused by dents in brain architecture. Harm of this nature is believed to be both of genetic origin and environmental. Surprising research has shown that physical and sexual abuse in children can cause observable harm to the developing brain, and may be the origin of long-lasting traumas and psychiatric fragility. A very intriguing study also demonstrated that there is a fair chance that chronic bullying – in other words verbal abuse – could also be at the heart of similar changes in brain structure in children, which could be the source of psychological problems later on in life. Factors such as Trnp1 are paramount in understanding brain development and architecture, and may well pave the way to novel therapies for neurological disorders caused by brain tissue which has gone askew.

Cross-references to UniProt

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