Mechanism explains complex brain wiring

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How neurons are created and integrate with each other is one of biology's greatest riddles. Researcher Dietmar Schmucker from VIB-KU Leuven unravels a part of the mystery in Science magazine. He describes a mechanism that explains novel aspects of how the wiring of highly branched neurons in the brain works. These new insights into how complex neural networks are formed are very important for understanding and treating neurological diseases.

Neurons, or nerve cells

It is estimated that a person has 100 billion neurons, or nerve cells. These neurons have thin, elongated, highly branched offshoots called dendrites and axons. They are the body's information and signal processors. The dendrites receive electrical impulses from the other neurons and conduct these to the cell body. The cell body then decides whether stimuli will or will not be transferred to other cells via the axon.

The brain's wiring is very complex. Although the molecular mechanisms that explain the linear connection between neurons have already been described numerous times, little is as yet known about how the branched wiring works in the brain.

The connections between nerve cells

Prior research by Dietmar Schmucker and his team lead to the identification of the Dscam1 protein in the fruit fly. The neuron can create many different protein variations, or isoforms, from this same

protein. The specific set of isoforms that occurs on a neuron's cell surface determines the neuron's unique molecular identity and plays an important role in the establishment of accurate connections. In other words, it describes why certain neurons either come into contact with each other or reject each other.

Recent work by Haihuai H and Yoshiaki Kise from Dietmar's team indicates that different sets of Dscam1 isoforms occur inside one axon, between the newly formed offshoots amongst each other. If this was not the case, then only linear connections could come about between neurons. These results indicate for the first time the significance of why different sets of the same protein variations can occur in one neuron and it could explain mechanistically how this contributes to the complex wiring in our brain.

Clinical impact

Although this research was done with fruit flies, it also provides new insights that help explain the wiring and complex interactions of the human brain and shine a new light on neurological development disorders such as autism. Thorough knowledge of nerve cell creation and their neural interactions is considered essential knowledge for the future possibility of using stem cell therapy as standard treatment for certain nervous system disorders.

More information: "Cell-intrinsic requirement of Dscam1 isoform diversity for axon collateral formation." Haihuai He, Yoshiaki Kise, Azadeh Izadifar, Olivier Urwyler, Derya Ayaz, Akhila Parthasarthy, Bing Yan, Maria-Luise Erfurth, Dan Dascenco, and Dietmar Schmucker. *Science* 6 June 2014: 344 (6188), 1182-1186.Published online 15 May 2014. DOI: 10.1126/science.1251852

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