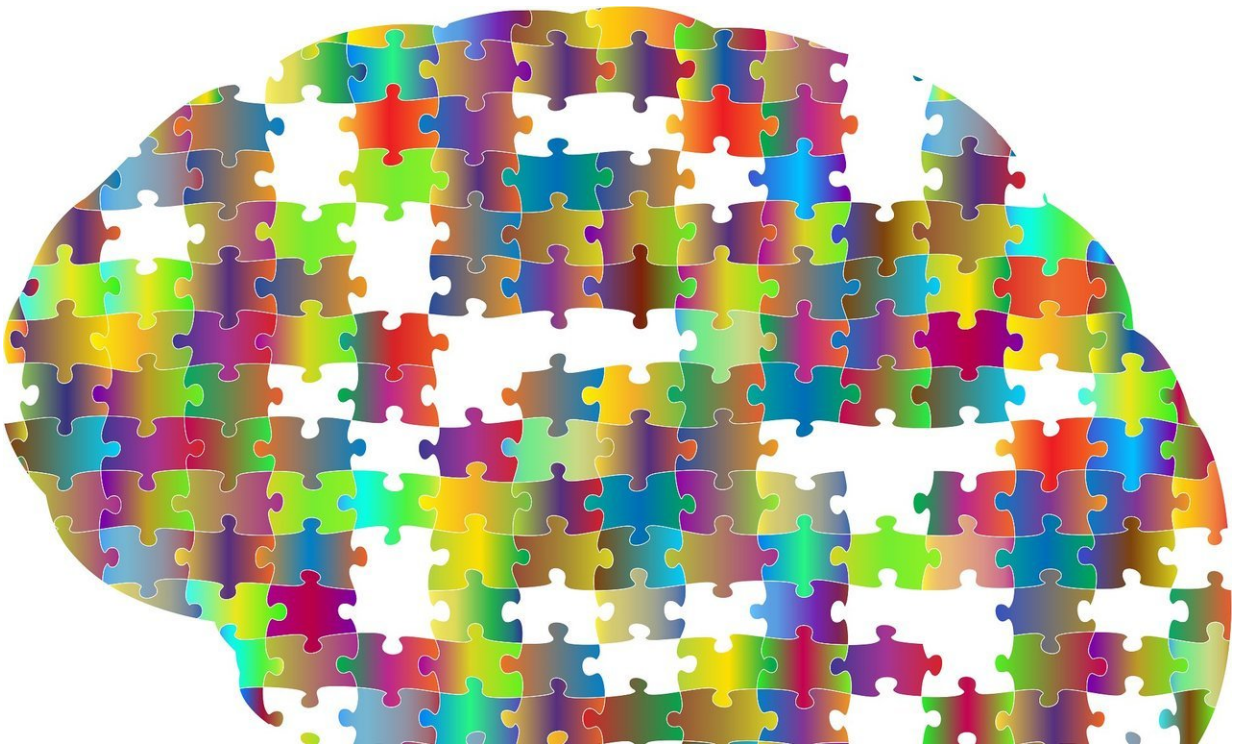


Neuronal 'barcodes' shape complex networks in the brain

July 6 2018



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The brain is an enormously complex organ. Understanding how billions of brain cells make precise connections is a major challenge for neuroscientists. Professor Joris de Wit and his team (VIB-KU Leuven) have unraveled a molecular code that determines the shape, location and function of connections between individual neurons. These findings

could help researchers better understand brain disorders such as autism and schizophrenia.

The human [brain](#) contains billions of neurons that form highly specialized and complex networks regulating thoughts, emotions, memory and muscle movements. Signals are transmitted along these networks from one neuron to another at designated points of contact called synapses.

In order to get this many neurons connected in an organized and meaningful way, it is critical that synapse formation be tightly regulated. Professor Joris de Wit (VIB-KU Leuven) wants to know how, when and where these signal-transmitting connections arise: "How do neurons recognize their appropriate partners? How do they know which type of synapse needs to be where? These are very basic questions, highlighting how much we still need to learn about the brain."

Adhesion molecules

De Wit's team went looking for answers by studying [adhesion molecules](#). These [molecules](#) can be found on the cell surface, where they physically connect neurons to one another. Neurons express large and diverse sets of [adhesion](#) molecules, but it is not clear why they would need so many different adhesion molecules.

Therefore, the team set out to study how a set of three different adhesion molecules, present in the same neurons in the hippocampus (the area of our brain responsible for memory), regulates neuronal connectivity.

"We first analyzed the distribution of these adhesion molecules in great detail, as the [hippocampal neurons](#) that we study form lots of different synapses with other [brain cells](#)," explains Anna Schroeder, one of the researchers in de Wit's laboratory. "With the help of our imaging

experts, we used a combination of light and electron microscopy to examine the architecture of the different synapses. We also took advantage of electrophysiology in order to investigate changes in synaptic [function](#)."

A barcode at the synapse

The scientists found that while one of the adhesion molecules controls the number of connections, the other two affect signal transmission instead—one positively and the other negatively. In combination, the three adhesion molecules precisely define how synapses look and function.

"Think of it as a zip code or barcode for brain cells," explains Schroeder. "The adhesion molecules are digits with a specific function, but in combination they determine a more complex pattern that shapes the connection between two neurons. In other words, they define the identity of that connection."

In this way, the many different adhesion molecules found in [neurons](#) across the brain allow for precise fine-tuning of the different connections they make.

Connections and brain disease

All three adhesion molecules under investigation have been associated with neurodevelopmental and neuropsychiatric disorders, such as autism and schizophrenia. Understanding their role in brain connectivity is thus of vital importance, says de Wit:

"Now that we understand that these adhesion molecules not only shape the number, but also the architecture and function of synapses, this may

lead to a better understanding of how disease-associated mutations in the genes that encode these molecules affect circuit connectivity and function."

More information: A modular organization of LRR protein-mediated synaptic adhesion defines synapse identity, Schroeder et al. *Neuron* 2018.

Provided by VIB (the Flanders Institute for Biotechnology)

Citation: Neuronal 'barcodes' shape complex networks in the brain (2018, July 6) retrieved 10 May 2024 from <https://medicalxpress.com/news/2018-07-neuronal-barcodes-complex-networks-brain.html>

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