Team decodes neuron signals

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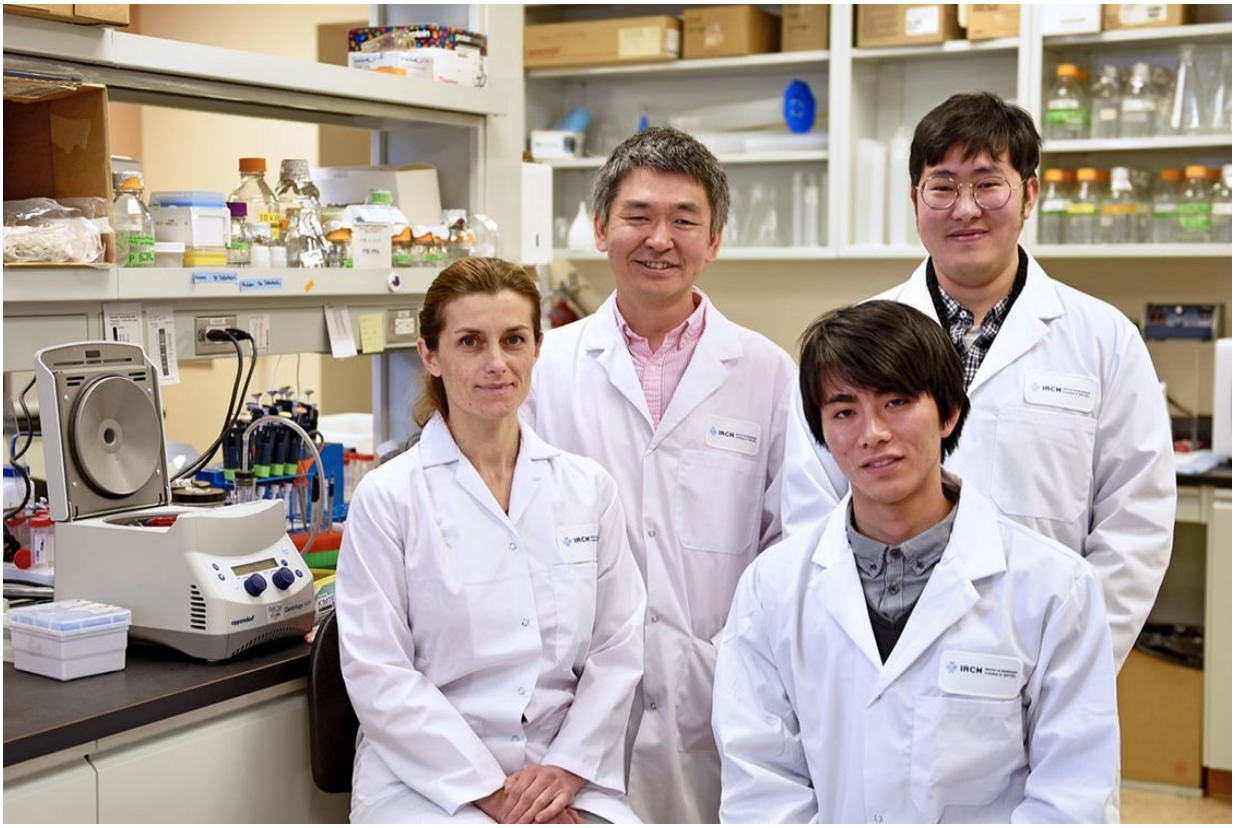

Credit: University of Montreal

Did you know that your body is made up of a hundred billion nerve cells, which, like little computers, receive, process and transmit crucial information? These machines are neurons, the foundation of your nervous system. Thanks to neurons, your brain transforms information provided by the retina into images and your mood adapts to the situation

you're in.

Hideto Takahashi, a researcher at the Montreal Clinical Research Institute (IRCM) and professor at Université de Montréal's Faculty of Medicine, is like a computer specialist, but for neurons. By studying signals transmitted by these "biological processors," Takahashi and his team have identified a gene that may be linked to certain neuropsychiatric disorders, such as schizophrenia. The discovery was recently published in *Nature Communications*.

Neurons and memes behave in the same way

Neurons have an elongated shape, varying from one millimetre to over one metre in length. They're real chatterboxes, too—constantly talking to each other.

Takahashi is particularly interested in the ends of these cells, which allow them to communicate. These junction points, called synapses, allow chemical signals containing information to pass from neuron to neuron, just like a meme that goes viral on your friends' Facebook timelines.

Synapses can both amplify the signal transmitted to the next neuron (excite) and reduce or even delete it (inhibit). These two states may seem to be in competition, but they are both necessary, depending on the circumstances. "It's all about balance," said Takahashi, who is also director of the IRCM Synapse Development and Plasticity Research Unit. "Excitatory and inhibitory synapses are essential to the body's functioning. They ensure that information flows to the right place at the right time."

When the delicate balance of signals is disturbed, the brain may be affected. For one thing, studies have shown that abnormally excited

neurons may be linked to neuropsychiatric disorders.

But what influences these different types of signals? Scientists are looking for the answer in our genes. Up until now, 70 to 80 per cent of genes have been identified as "exciters." The others are hybrid in nature—they activate some synapse receptors and inhibit others at the same time. Exclusively inhibitory genes have been fairly rare until now, although there are many different types of inhibitory synapses in the brain. This observation intrigued Dr. Takahashi.

A selective gene

While screening genes that could have this property in mice, the IRCM team identified a second inhibitory gene that stood out from the rest: IgSF21. The team showed that IgSF21 binds to a protein located on the surface of synapses: neurexin2α. This connection allows an inhibitory neurotransmitter (GABA) to move around.

"We were surprised by these observations," recalled Takahashi. "Neurexins occur in six different forms, neurexin2α being just one of them. Normally, genes can interact with several forms of neurexin at the same time. This characteristic shows that IgSF21 is a highly selective gene, which could explain why it behaves in an exclusively inhibitory manner."

Takahashi and his team also established that the presence of IgSF21 is essential to the development of inhibitory synapses in mice. "In mice without the IgSF21 gene, we observed behaviour similar to that observed in neuropsychiatric disorders related to low inhibitor levels such as schizophrenia," explained Takahashi. "It makes sense. Without IgSF21, it is impossible for neurexin2α to inhibit signals. These results support previous studies, which had established the link between mutations in neurexin and schizophrenia."

What's the next step in Dr. Takahashi's research? To try to find IgSF21's and neurexin2α's human cousins, then determine whether there are mutations of these two genes that could prevent their inhibitory effect on neurons in people with neuropsychiatric disorders. If that's possible, a way might be found to reprogram the interaction of IgSF21 with neurexin2α to balance the signals between synapses – one more puzzle to solve in the incredibly complex world of neural research.

More information: Yuko Tanabe et al. IgSF21 promotes differentiation of inhibitory synapses via binding to neurexin2α, *Nature Communications* (2017). DOI: 10.1038/s41467-017-00333-w

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