Medical Xpress

Findings could speed the development of drugs for Parkinson's disease

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Australian scientists have significantly advanced our understanding of dopamine release from nerve cells, findings that should speed the development of more effective drugs for treating Parkinson's Disease.

People with Parkinson's Disease suffer from muscle rigidity, tremor, a slowing of physical movement and, in extreme cases, a loss of physical movement. These primary symptoms are caused by the loss of dopamine producing nerve cells in the brain.

Medicines used for treating Parkinson's either provide extra dopamine or attach to the remaining nerve cells that release dopamine and regulate its release. In the latter case, no-one understands the mechanisms involved, or how to control them.

When an electrical impulse reaches the end of a dopamine nerve cell, called a synapse, it sometimes stimulates the release of dopamine. Yet more often it doesn't. Only about 1 in 5 impulses cause dopamine release, and the release rhythm is irregular. So the cell might release dopamine 5 times in a row, then not release twice, then release once, and so on.

Neuroscientists at Sydney's Garvan Institute of Medical Research have developed a mathematical model and microscopy method that reveal the mechanisms behind synaptic dopamine release - and the factors that govern the probability of release.

These important findings, made by Drs James Daniel and Bryce Vissel, are now published online in the Journal of Neuroscience.

"While there has been an enormous amount of effort put into the development of drugs for Parkinson's Disease, very little has been known about how the dopamine releasing drugs achieve their effects, other than the fact they attach to a receptor on a dopamine nerve cell, and then something happens," said Dr Vissel.

"We know that there's an intrinsic probability of the release of a neurotransmitter, but what's really interesting is that this release probability is regulated. A neuron can make it more likely or less likely that a neurotransmitter will be released, but it can't guarantee release. For example, it becomes more likely that a neurotransmitter will be released in a nerve pathway that is used a lot."

Neurotransmitters are small molecules that are released from one nerve cell and which act on the next nerve cell. Some are excitatory, some inhibitory, some modulatory. Dopamine is a modulator. In other words, it smooths out the ups and downs of a nerve cell, effectively telling it 'not to get over excited', or 'not to get over inhibited'. All the inputs add up, and if a nerve cell gets enough plusses, it fires an impulse.

According to Vissel, we are still in the dark ages in understanding the sub-microscopic events that take place in the brain. "We have roughly 100 billion nerve cells in our brains, with up to 100,000 connections each. We're only just beginning to understand that every connection is regulated in the most extraordinarily sophisticated way," he explained.

"The surprising thing is that out of all this irregularity and complexity comes predictable or reliable function. Most of us can catch a ball that is thrown to us without dropping it, for example. When you think about the millions of nerve cell events in that simple act alone, it's remarkable.

Unfortunately, in Parkinson's disease this phenomenal ability to regulate movement is lost".

"Our work involved developing sophisticated statistical analysis protocols and mathematical models of synapses, and it helps de-mystify the part of the process that takes place at the dopamine nerve cell synapse. We believe it will help us work out how drugs currently being used to treat Parkinson's Disease are regulating dopamine release. It will also open up new avenues for pharmaceutical development."

Source: Research Australia (news : web)