Parkinson's disease: the fragility of neurons, a question of ion channels?

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The degeneration of the dopaminergic neurons located in the substantia nigra is a hallmark of Parkinson's disease. However, dopaminergic neurons located in another adjacent region of the brain are not as susceptible to this degeneration. Researchers at GIGA-Neurosciences of the University of Liege have shown that the density of a particular class of ion channels on these neurons differs between these two regions. Their results were published on July 7th in the Journal of Neuroscience.

Nerve cells producing dopamine, called dopaminergic neurons, occupy a part of the brain called the mesencephalon or "mid-brain". More precisely, these neurons are found in the substantia nigra and in the ventral tegmental area of the mesencephalon where they play very different roles. The former are involved in motor control, the initiation of voluntary movements. The latter are involved in the reward circuit and therefore in the motivation to carry out a task, as well as in certain cognitive processes.

The dysfunction or degeneration of these dopaminergic neurons located in distinct regions of the brain have different consequences for the organism. For example, we have known for a long time that a massive loss of neurons of the substantia nigra is observed in individuals suffering from Parkinson's disease. The dopaminergic neurons of the ventral tegmental area, on the other hand, are involved in conditions such as addictions and other psychiatric disorders.

Why do the dopaminergic neurons of the substantia nigra become fragile in the case of Parkinson's, whereas those of the ventral tegmental area do not? Given that these neurons have very similar physiological properties, the question has haunted researchers. The team of Vincent Seutin and Dominique Engel (GIGA-Neurosciences) has focused its attention on the question by quantifying the density of ion channels that are found in these neurons. Ion channels are transmembrane proteins that enable the passage of ions from the interior to the exterior of cells and vice versa. It is the movement of ions through these channels that enables phenomena such as transmission of nerve impulses, the heartbeat and muscle contraction. There are several
kinds of ion channels which enable cells to perform their different roles. Likewise, several types of channels can exist for the same ion. This is the case for calcium, for example. One category of voltage-dependent channels permeable to calcium, known as "L" channels, have attracted the attention of Fabian Philippart, a doctoral student in the laboratory. The researchers from Liege have discovered that this type of channel is present in greater density on the cell bodies of the dopaminergic neurons of the substantia nigra than on the cell bodies of the neurons in the ventral tegmental area.

The results of this study have been published in the *Journal of Neuroscience* on Thursday July 7th. They suggest that there could be a correlation between the greater presence of these ion channels and a "weakening" of the dopaminergic neurons of the substantia nigra, leading to the development of Parkinson's disease. The scientists now intend to try to understand why this difference in density of the L calcium channels predisposes the dopaminergic neurons of the substantia nigra to degenerate. The researchers at GIGA-Neurosciences would also like to quantify the density of other ion channel species in order to build a mathematical model which would reflect the physiological properties of these two groups of neurons.

(1) *Differential somatic Ca2+ channel profile in midbrain dopaminergic neurons*, Fabian Philippart et al. *Journal of Neuroscience*, 2016.