

Novel brain network linked to chronic pain in Parkinson's disease

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Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

Scientists have revealed a novel brain network that links pain in

Parkinson's disease (PD) to a specific region of the brain, according to a report in the journal *eLife*.

The research reveals why a subset of neurons in part of the brain called the subthalamic [nucleus](#) is a potential target for [pain relief](#) in PD, as well as other diseases such as dementia, [motor neuron disease](#) and Huntington's, and certain forms of migraine.

People with PD often report unexplained pain such as burning, stabbing, aching, itching or tingling sensations that are not directly related to their other PD symptoms. Treatment with [deep brain stimulation](#) in the subthalamic nucleus can help with the movement-related symptoms of PD, but recent studies have shown it also reduces pain. The way it does this, however, is currently unclear.

"In this study, we set out to determine whether the subthalamic nucleus is involved in translating a harmful stimulus such as injury into pain, and whether this information transmission is altered in PD," explains lead author Arnaud Pautrat, Ph.D. Student at Grenoble Institut des Neurosciences (Inserm, National Institute for Health and Medical Research/University Grenoble Alpes), France.

The team started by using electrophysiology to measure the firing of electrical signals in nerve cells in the subthalamic nucleus of rats given a shock to their back paw. Nerve cells were indeed temporally activated by this stimulation. They also found that the neurons fell into three response groups, showing an increase, decrease or no change in their baseline firing rate.

They next looked at whether these responses caused a change in brain function. Rats with a damaged subthalamic nucleus took much longer to show signs of discomfort than healthy rats. When they expanded their study to rat models of PD, the team found that [nerve cells](#) in the

subthalamic nucleus had higher firing rates and the responses to pain were bigger and longer than in the healthy animals. Taken together, this suggests that dysfunctional pain-processing pathways in the subthalamic nucleus are the cause of PD-related pain.

To understand where the pain signals to the subthalamic nucleus were coming from, the team looked at two brain structures known to be important in relaying damage signals from the spinal cord: the superior colliculus and the parabrachial nucleus. Blocking their activity revealed that both structures play a crucial role in transmitting pain information to the subthalamic nucleus, and that a direct communication pathway exists between the parabrachial nucleus and the subthalamic nucleus. As a result, the team believes this pathway is likely to be involved in the beneficial effects of deep brain stimulation on pain in PD and that these novel insights could help to target stimulation to specific parts of the brain to make it more effective as a pain reliever.

"We have found evidence that the [subthalamic nucleus](#) is functionally linked to a pain-processing network and that these responses are affected in Parkinsonism," concludes senior author and Inserm researcher Veronique Coizet, Ph.D. "Further experiments are now needed to fully characterise the effects deep brain stimulation on this [brain](#) region in our experimental models, with a view to finding ways to optimise it as a treatment for [pain](#) caused by Parkinson's and other neurological diseases."

More information: Arnaud Pautrat et al, Revealing a novel nociceptive network that links the subthalamic nucleus to pain processing, *eLife* (2018). [DOI: 10.7554/eLife.36607](https://doi.org/10.7554/eLife.36607)

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