Learning disorders and Parkinson's disease: Tremor predicts effects of medication

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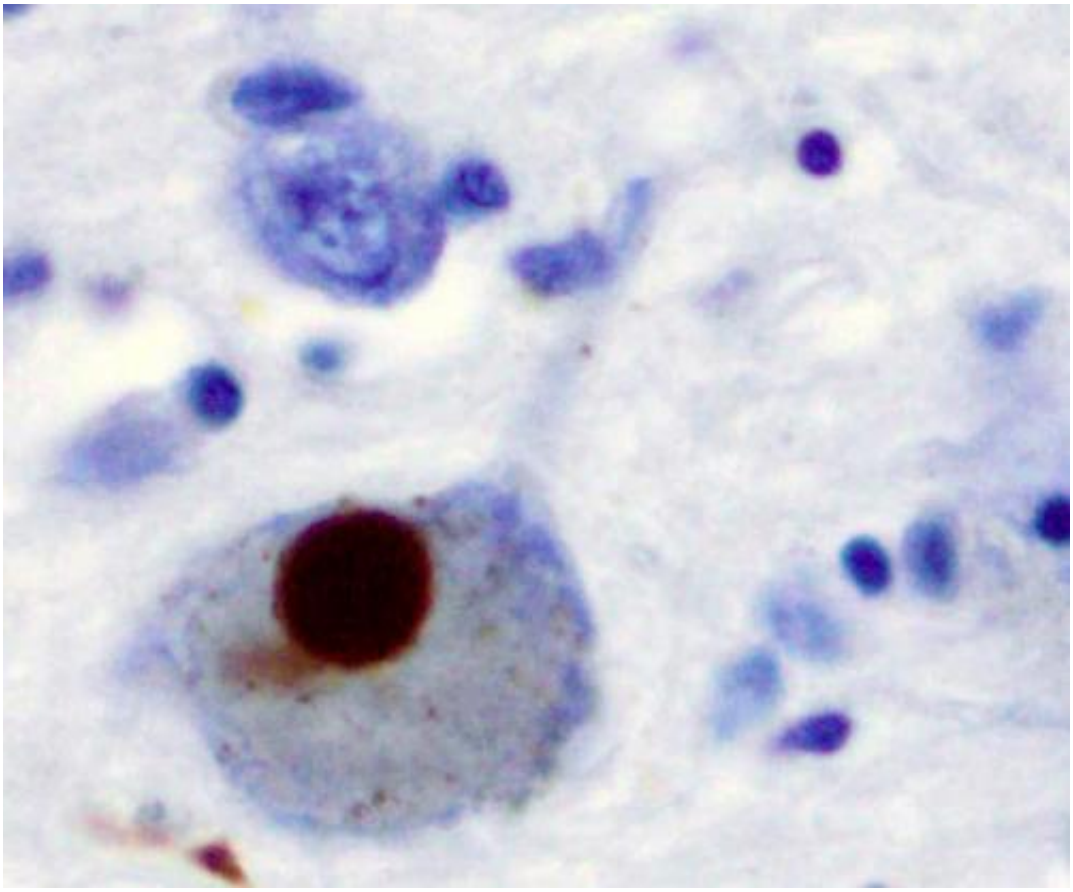

Immunohistochemistry for alpha-synuclein showing positive staining (brown) of an intraneural Lewy-body in the Substantia nigra in Parkinson's disease. Credit: Wikipedia

The effect of dopaminergic medication on the learning abilities of

patients with Parkinson's disease turns out to be linked to the presence of tremor symptoms. In patients who do not experience tremor, dopaminergic medication improves the ability to learn from rewards (reinforcement learning). Remarkably, the medication brings no benefit in reward learning to patients who do exhibit tremor. These were the results from a new study by brain researchers at the Donders Institute of Radboud University and Radboud university medical center, published on 6 November in the scientific journal *Brain*.

"It is somewhat surprising that until now, studies of cognition in Parkinson's disease never assessed the distinction between patients who exhibit tremor and those who do not," says Hanneke den Ouden, brain researcher at Radboud University. "Our study shows that there is a link between problems with motor skills and problems with cognition in patients with Parkinson's disease."

Learning abilities and Parkinson's disease

Most patients with Parkinson's disease experience tremor—shaking in an arm or leg. Only one in four patients does not experience these symptoms. In addition, many patients experience mental issues. Due to a decrease in dopamine, a chemical messenger molecule that occurs in the brain, patients with Parkinson's disease become less sensitive to learning through rewards.

A large number of prior studies have shown that this learning disorder can be remedied by administering dopaminergic medication. It remained a mystery, however, why medication had no effect in many patients. The study of the Radboud researchers reveals that this improvement through medication only occurs in patients who experience tremor.

Presence and absence of tremor

"We observed that with medication, patients without tremor got better at a task in which they had to learn to push a button in order to receive a reward (points). This result fully agrees with prior research. However, remarkably enough, patients with tremor would exhibit an opposite effect," Den Ouden says. "Importantly, patients without tremor generally exhibit a faster deterioration of the cognitive abilities and are more likely to develop dementia, for example. The fact that we only observe results from earlier studies in patients without tremor suggests that prior studies only included with these patients. This would make sense, as it is easier for patients without tremor to participate in an experiment. However, it is important to realize that three out of four patients actually do experience tremor, and our study shows that the medication has a different effect on these patients. We see this as a major warning: Always be aware of the diversity of patients in your study, as you might otherwise draw the wrong conclusions."

Predictive value

According to the researchers, it is crucial to improve our understanding of such patient diversity. "This study tells us that the dopamine systems of Parkinson's disease patients with and without tremor are affected in different ways, and that this goes beyond the level of just motor problems, affecting cognition as well," according to co-author Rick Helmich, neurologist at Radboud university medical center. "Whether someone experiences tremor or not might therefore potentially have a significant predictive value regarding the effectiveness of medication in the cognitive domain. However, more and larger studies are needed before this can be confirmed."

More information: Annelies J van Nuland et al, Effects of dopamine on reinforcement learning in Parkinson's disease depend on motor phenotype, *Brain* (2020). DOI: 10.1093/brain/awaa335