New treatment targeting versatile protein may protect brain cells in Parkinson's disease

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In Parkinson's disease (PD), dopamine-producing nerve cells that control our movements waste away. Current treatments for PD therefore aim at restoring dopamine contents in the brain. In a new study from Lund University, researchers are attacking the problem from a different angle, through early activation of a protein that improves the brain's capacity to cope with a host of harmful processes. Stimulating the protein, called Sigma-1 receptor, sets off a battery of defence mechanisms and restores lost motor function. The results were obtained in mice, but clinical trials in patients may not be far away.

By activating the Sigma-1 receptor, a versatile protein involved in many cellular functions, levels of several molecules that help nerve cells build new connections increased, inflammation decreased, while dopamine levels also rose. The results, published in the journal *Brain*, show a marked improvement of motor symptoms in mice with a Parkinson-like condition that had been treated with a Sigma-1-stimulating drug for 5 weeks.

This treatment has never before been studied in connection with Parkinson's disease. However, various publications linked to stroke and motor neurone disease have reported positive results with drugs that stimulate the Sigma-1 receptor, and a biotech company in the US will soon begin clinical trials on Alzheimer's patients. The fact that substances stimulating this protein are already available for clinical use is a major advantage, according to Professor M. Angela Cenci Nilsson, head of the research team at Lund University.

"It is a huge advantage that these substances have already been tested in people and approved for clinical application. It means that we already know that the body tolerates this treatment. Clinical trials for Parkinson's disease could theoretically start any time". Boosting the brain's in-built defence mechanisms with approaches like this is a rather new idea in Parkinson's research. Professor Cenci Nilsson, however, believes that the number of targets for future treatments is increasing as we learn more and more about the complex effects of PD on many different types of cells in the brain.

"The motor improvements we have seen in mice are disproportionately large compared to the recovery of dopamine levels. We believe this is because the treatment has protected the brain against a series of indirect consequences triggered by the Parkinson-like lesion. For example, we know today that a loss of dopamine causes the target neurons to lose synapses, and also alters both neural pathways and non-neuronal cells in the brain. Since the Sigma-1 receptor is widely expressed in many cell types, the treatment could intervene in many of these damaging processes ".

The treatment was shown to be significantly more effective when started at the beginning of the most aggressive phase of dopamine cell death. As a future potential therapy for Parkinson's disease, this treatment would therefore need to be started as soon as possible after diagnosis in order to deliver maximum impact.

"In order to accelerate a possible clinical translation of our findings, we will now seek further evidence in support of this type of treatment. We are now discussing various opportunities with different collaborating partners, and we will try to procure funding for clinical studies in Parkinson´s disease as soon as possible", concludes M. Angela Cenci Nilsson.

Provided by Lund University