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Finding brings scientists one step closer to Parkinson's drug

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Van Andel Institute announces that researchers at Lund University in Sweden have published a study detailing how Parkinson's disease spreads through the brain. Experiments in rat models uncover a process previously used to explain mad cow disease, in which misfolded proteins travel from sick to healthy cells. This model has never before been identified so clearly in a living organism, and the breakthrough brings researchers one step closer to a disease-modifying drug for Parkinson's.

"Parkinson's is the second most common neurodegenerative disorder after Alzheimer's disease," said Patrik Brundin M.D., Ph.D., Jay Van Andel Endowed Chair in Parkinson's Research at Van Andel Research Institute (VARI), Head of the Neuronal Survival Unit at Lund University and senior author of the study. "A major unmet medical need is a therapy that slows disease progression. We aim to better understand how Parkinson's pathology progresses and thereby uncover novel molecular targets for disease-modifying treatments."

Previous research demonstrates that a misfolded protein known as alpha-synuclein protein gradually appears in healthy young neurons transplanted to the brains of Parkinson's patients. This discovery gave rise to the group's hypothesis of cell-to-cell protein transfer, which has since been demonstrated in laboratory experiments.

In the current study, published this week in the PLoS ONE, researchers for the first time were able to follow events in the recipient cell as it accepts the diseased protein by allowing it to pass its outer cell

membrane. The experiments also show how the transferred proteins attract proteins in the host cell leading to abnormal folding or "clumping" inside the cells.

"This is a cellular process likely to lead to the disease process as Parkinson's progresses, and it spreads to an increasing number of brain regions as the patient gets sicker," said Elodie Angot, Ph.D., of Lund University's Neuronal Survival Unit, and lead co-author of the study.

"In our experiments, we show a core of unhealthy human alpha-synuclein protein surrounded by alpha-synuclein produced by the rat itself. This indicates that this misfolded protein not only moves between cells but also acts as a "seed" attracting proteins produced by the rat's brain cells," said Jennifer Steiner, Ph.D., of Lund University and Van Andel Institute's Center for Neurodegenerative Science, the study's other lead author.

These findings are consistent with results from previous laboratory cell models and for the first time extend this observation into a living organism. However, it remains unclear exactly how alpha-synuclein gains access from the extracellular space to the cytoplasm of cells to act as a template for naturally occurring alpha-synuclein, causing the naturally-occurring protein to, in turn, misfold. Further studies are needed to clarify this important step in the process.

The discovery does not reveal the root of Parkinson's disease, but in conjunction with disease models developed by Lund University researchers and others, could enable scientists to develop new drug targets aimed at mitigating or slowing the effects of the disease, which currently strikes more than 1% of people over the age of 65.

More information: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0039465

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