Research shows that a human protein may trigger the Parkinson's disease

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A research led by the Research Institute Vall d'Hebron (VHIR), in which the University of Valencia participated, has shown that pathological forms of the α-synuclein protein present in deceased patients with Parkinson's disease are able to initiate and spread the neurodegenerative process that typifies this disease in mice and primates. The discovery, published in the March cover of *Annals of Neurology*, opens the door to the development of new treatments that stop the progression of Parkinson's disease, aimed at blocking the expression, the pathological conversion and the transmission of this protein.

Recent studies have shown that synthetic forms of α-synuclein are toxic for neurons, both in vitro (cell culture) and in vivo (mice), which can spread from one cell to another. However, until now it was not known if this pathogenic protein synthetic capacity could be extended to the pathological human protein found in patients with Parkinson's and, therefore, whether it was relevant for the disease in humans.

In the present study, led by Doctor Miquel Vila, from the group of Neurodegenerative Diseases of the VHIR and CIBERNED member, the researchers extracted α-synuclein aggregates from brains of dead Parkinson's-afflicted patients to inject them into the brains of rodents and primates.

Four months after the injection into mice, and nine months after the injection into monkeys, these animals began to present degeneration of dopaminergic neurons and intracellular cumulus of α-synuclein

pathology in these cells, as occurs in Parkinson's disease. Months later, the animals also showed cumulus of this protein in other brain remote areas, with a pattern of similar extension to that observed in the brains of patients after years of disease evolution.

According to Doctor Vila, these results indicate that "the pathological aggregates of this protein obtained from patients with the Parkinson's disease have the ability to initiate and extend the neurodegenerative process that typifies Parkinson's disease in mice and primates," a discovery that, he adds, "provides new insights about the possible mechanisms of initiation and progression of the disease and opens the door to new therapeutic opportunities."

Therefore, the next step is to find out how to stop the progression and spread of the disease, by blocking the cell-to- cell transmission of of α-synuclein, as well as regulating the levels of expression and stopping the pathological conversion of this protein.

Parkinson's disease

Parkinson's disease is the second-most common neurodegenerative disease after Alzheimer's disease. It is characterized by progressive loss of neurons that produce dopamine in a brain region (the substantia nigra of the ventral midbrain) and the presence in these cells of pathological intracellular aggregates of α-synuclein protein, called Lewy bodies. The loss of brain dopamine as a consequence of neuronal death results in the typical motor manifestations of the disease, such as muscle stiffness, tremors and slow movement.

The most effective treatment for this disease is the levodopa, a palliative drug that restores the missing dopamine. However, as the disease progresses, the pathological process of neurodegeneration and accumulation of α-synuclein progressively extends beyond the ventral

midbrain to other brain areas. As a result, there is a progressive worsening of the patient and the emergence of non-motor clinical manifestations unresponsive to dopaminergic drugs. There is currently no treatment that avoids, delays or halts the progressive evolution of the neurodegenerative process.

More information: Ariadna Recasens, Benjamin Dehay, Jordi Bové, Iria Carballo-Carbajal, Sandra Dovero, Ana Pérez-Villalba, Pierre-Olivier Fernagut, Javier Blesa, Annabelle Parent, Celine Perier, Isabel Fariñas, José A. Obeso, Erwan Bezard and Miquel Vila. "Lewy body extracts from Parkinson disease brains trigger α-synuclein pathology and neurodegeneration in mice and monkeys." *Annals of Neurology* Volume 75, Issue 3, March 2014, Pages: 351–362. DOI: 10.1002/ana.24066