New insights into the gut-brain axis in Parkinson's disease

There is growing evidence that Parkinson's disease may begin in the gut, with aggregates of the protein alpha-synuclein arising in the gut, playing a key role in the development of the disease. This study published in *Brain* journal shows that both brain and gut injections of extracted α-synuclein aggregates have the ability to initiate and extend the neurodegenerative process, demonstrating the bidirectional long-distance propagation of α-synuclein pathology between the brain and the gut in non-human primates.

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There is growing evidence that Parkinson's disease (PD) may begin in the gut, with aggregates of the protein alpha-synuclein arising in the gut, playing a key role in the development of the disease. In experiments in non-human primates, a team of Spanish and French researchers say they have found additional evidence that brain alpha-synuclein can also travels down to the gut. This study offers a new invaluable primate data exploring the role of the gut-brain axis in the initiation and propagation of PD pathology.

Parkinson's disease is characterized by the cell death of a specific neuronal population and by the buildup of a misfolded protein, called alpha-synuclein, in the cells of the brain. The research about the gut-brain axis emerged in 2003 when a neuroanatomists team spotted alpha-synuclein inclusions within the enteric nervous system of people who had died with PD. They proposed a staging scheme in which α-synuclein pathology spread from the gut to the brain. However, the intestinal origin of PD has not been proved in nonhuman primates and the bidirectional travel of alpha-synuclein is still under investigation.

Recent data show that extracted α-synuclein aggregates of brains of dead patients have the ability to initiate and extend the neurodegenerative process that typifies Parkinson's disease in mice and primates.

The study conducted in non-human primates shows that injection of extracted α-synuclein aggregates from PD patients have the ability to induce:

1- Two years after administration, injected monkeys displayed neurodegeneration regardless of the injection site, in the brain or in the gut.
2- Alpha-synuclein deposits of the pathological form of the protein was observed both in the enteric system and in the brain. We can observe a high α-synuclein level in enteric neurons correlated with the progressive destruction of the nigrostriatal pathway.
3- When the aggregates were injected into the brain, pathologic form of alpha-synuclein was observed both in the brain and in the enteric system and vice-versa.

These results indicate that both brain and gut injections of aggregates can induce α-synuclein pathology in the enteric system, demonstrating the bidirectional long-distance propagation of α-synuclein pathology between the brain and the gut in the non-human primate.

Although further experiments are necessary, the study also suggests that the transmission of α-synuclein pathology does not go through the vagus nerve as it was previously suggested, but through a possible systemic mechanism, in which the general circulation would act as a route for long-distance bidirectional transmission of endogenous α-synuclein" explained Dr. Dehay, strengthening the predictive role of alpha-synuclein as a biomarker.

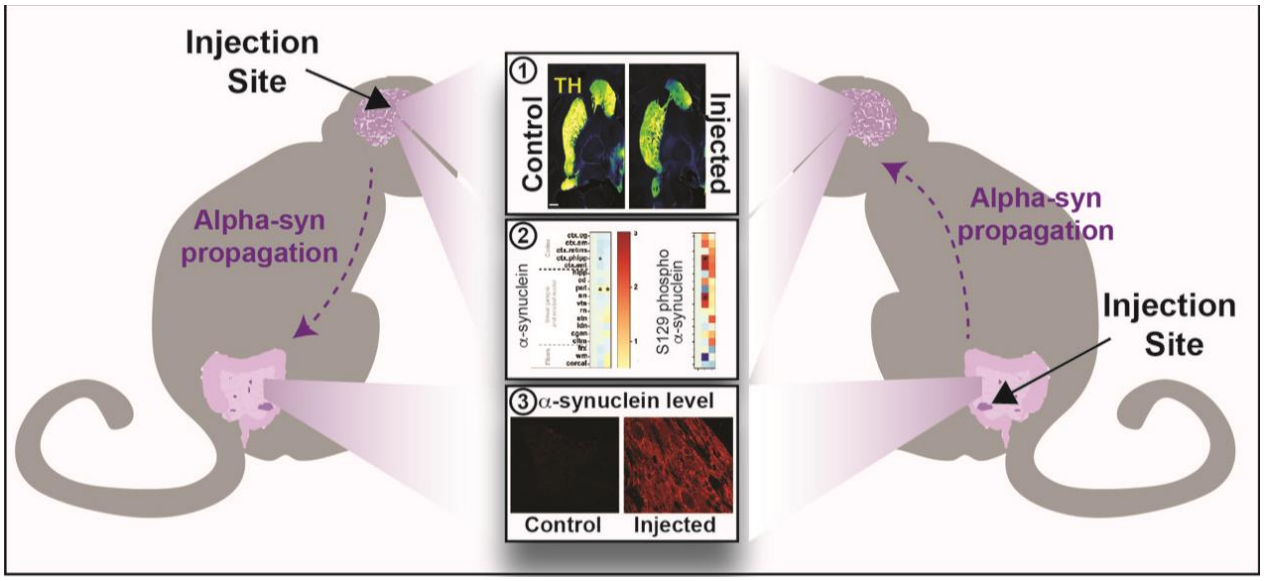

***Figure** Caption:* Both, brain and gut injections of enriched fraction of human aggregates alpha-synuclein induce: **1** nigro-striatal degeneration, **2** alpha-synuclein pathology in the central nervous system, and **3** alpha-synuclein pathology in the enteric system.

To know more:

Bidirectional gut-to-brain and brain-to-gut propagation of synucleinopathy in non-human primates.
Arotcarena ML, Dovero S, Prigent A, Bourdenx M, Camus S, Porras G, Thiolat ML, Tasselli M, Aubert P, Kruse N, Mollenhauer B, Damas IT, Estrada C, Garcia-Carrillo N, Vaikath NN, El-Agnaf OMA, Herrero MT, Vila M, Obeso JA, Derkinderen P, Dehay B, Bezard E.
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