

Proteins in migration

A new animal model gives insights into mechanisms

Bonn, Germany, May 24th, 2013 – In Parkinson’s disease, the protein alpha-synuclein becomes progressively affected as the disease develops and advances. Scientists at the Institute for Neurodegenerative Diseases (DZNE) in Bonn have developed a new animal model for brain spreading and provides important clues on the mechanisms of disease progression in the lower rat brain and were able to trace the spreading of this protein. The results are published in the scientific journal “EMBO Molecular Medicine”.

Parkinson’s disease is a disorder of the nervous system. It typically manifests itself in uncontrollable trembling of the limbs, as well as non-motor symptoms, including depression and cognitive impairment.

At the present, no cure exists for Parkinson’s disease, although symptomatic treatment with dopamine agonists, can alleviate patients’ motor impairment. Parkinson’s is the second most common neurodegenerative disease after Alzheimer’s disease; it is estimated that 100,000 to 300,000 patients are affected worldwide.

In a small percentage of cases, Parkinson’s disease is due to genetic mutations. In the majority of patients, however, the cause of the disease remains unknown. It is believed that sporadic Parkinson’s disease is likely promoted by both environmental and genetic risk factors. The characteristic pathology of Parkinson’s disease is the progressive accumulation of intracellular protein aggregates. These aggregates, named after the German neurologist, Friedrich Lewy, and are therefore called Lewy bodies.

“A major discovery in the late 90’s was that Lewy bodies are formed when alpha-synuclein aggregates. This was first shown by Dr. Salvatore Di Monte. “Since then, it was also found that aggregates of alpha-synuclein are present in the brains of Parkinson’s patients’ brains during the course of the disease”.

Pathology studies from human brains show that the deposits usually start in the brainstem, a region of the brain named “medulla oblongata”. In subsequent disease stages, alpha-synuclein aggregates spread to other parts of the brain.

(more rostral) brain regions, including the midbrain and cortical areas.

“This spreading appears to follow a typical pattern based on anatomical hypotheses that alpha-synuclein or abnormal forms of it can be transported there was no way of targeting the medulla oblongata to reproduce this neuronal passage of the protein or its aggregates. We have now developed

From the neck into the brain

The researchers' concept is based on reproducing alpha-synuclein spreading in the brain. The blueprint was transported by specifically engineered viral particles. The protein passed along these fibres into the medulla oblongata, where transport

“We have good reasons to believe that the medulla oblongata is a primary site for alpha-synuclein specifically in this part of the brain. The medulla oblongata is difficult to access. This is a long nerve stretching from the abdomen via the neck to the medulla oblongata,” Di Monte explains.

A migrating protein

The researchers monitored the production and localization of human alpha-synuclein particles. As predicted, the exogenous protein was synthesized only with human alpha-synuclein was observed also in brain areas more and more distant from the site of passage of the protein along specific nerve tracts and was accompanied by alpha-synuclein.

The study, sponsored in part by the Blanche A. Paul Foundation, bears witness to the progressive spreading of pathological alpha-synuclein in Parkinson's disease. The study shows that alpha-synuclein within a specific brain region.

“Overproduction of alpha-synuclein accompanies a variety of conditions including Parkinson's disease.” concludes Di Monte. “Thus, our results suggest a link between alpha-synuclein protein and its pathological accumulation.”

Insight into the early stages of Parkinson's

The new model mimics events that likely occur in the early stages of al manifestations. "It will therefore become a valuable tool to investigate e intervention would have a greater probability to prevent or halt the spre

Original publication

Caudo-rostral Brain Spreading of α -Synuclein through Vagal Connection
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Abstract

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