Key to the development of fundamental treatment methods for Parkinson's disease

January 12 2016

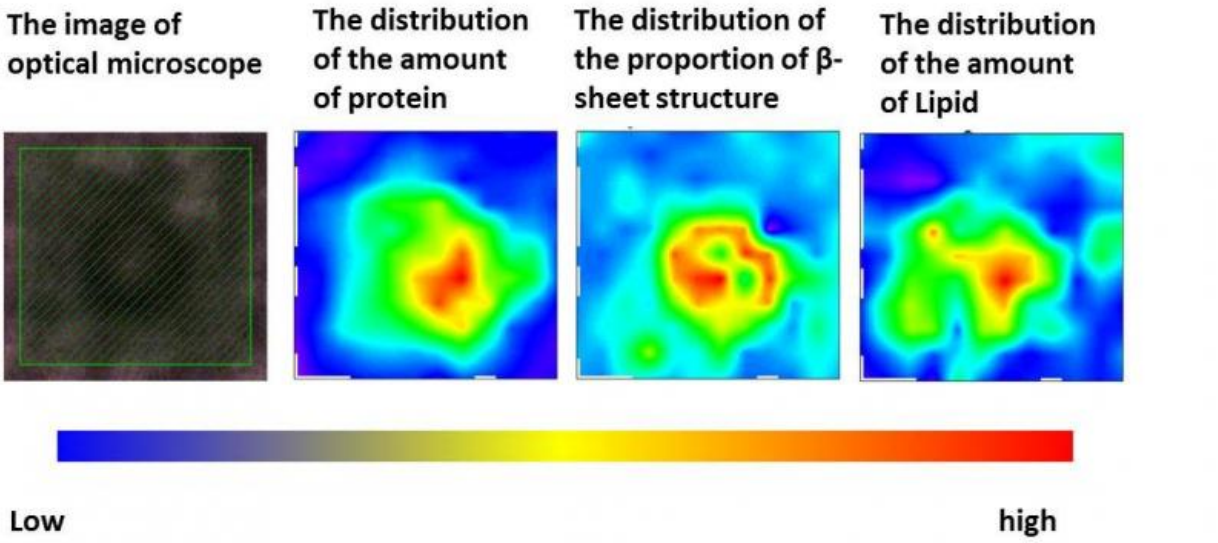

Fig. 1 - The analysis results for typical Lewy bodies: The central region (core) contains a large amount of proteins (second from left) and lipids (fourth from left). In contrast, the content of the β sheet structure (third from left) is higher in the peripheral region (halo) than in the core.

A group of researchers at Osaka University in cooperation with the Japan Synchrotron Radiation Research Institute (JASRI), succeeded in elucidating the secondary structure of Lewy bodies in the brain of Parkinson's disease patients for the first time with synchrotron Fourier transform infrared micro-spectroscopy (FTIRM).

Lewy bodies are considered to be a key element of pathogenesis for Parkinson's disease. Although structural analysis for Lewy bodies with an electron microscope had been performed, it had no secondary structural information of proteins, which is important for the development of drugs.

In recent years, many researchers have focused on new treatment to inhibit the formation of abnormal protein aggregates, which can delay the onset and progression of Parkinson's disease. The results and methods of this research may provide important clues to the development of epoch-making treatment for Parkinson's disease.

Parkinson's disease is the most common progressive neurodegenerative disorder after Alzheimer's disease, and there is no basic treatment to control the development of the disease. It had been known for quite some time that Lewy bodies, abnormal protein aggregates, are formed in the brain of Parkinson's disease patients, and it is thought that Lewy bodies play an important role in the onset of the disease. However, the structural analysis of Lewy bodies has made no progress other than observation with an electronic microscope in the last 20 years. Information on proteins required for developing treatment drugs has been unavailable from electron microscopic observation.

A group of researchers led by Hideki Mochizuki, Professor and Katsuya Araki, Clinical Fellow at the Department of Neurology, Graduate School of Medicine, Osaka University, in cooperation with Dr. Naoto Yagi, JASRI, analyzed proteins by synchrotron Fourier transform infrared micro-spectroscopy with the infrared beamline BL43IR at the SPring-8 synchrotron radiation facility and succeeded in obtaining structural information which had not been obtained from the electronic microscopy.

In experiments by this group, it was necessary to make measurements

while irradiating infrared beams of a few micrometers in diameter on a Lewy body of with a 10 micrometer diameter. For that purpose, radiation light at the SPring-8, the brightest in the world, played a great role.

The experiment showed that Lewy bodies in the brain of Parkinson's disease patients had many β sheet structures. This supports the validity of in-vitro studies in the past. It was also found that the rate of β sheet structures was higher in the halo of a Lewy body than in the core of a Lewy body and the core was lipid-rich. These findings will lead to the elucidation of the mystery of the formation of Lewy bodies.

This research was featured in the electronic version of *Scientific Reports* on Tuesday, December 1, 2015.

β sheet structure

The β sheet structure is one of the typical secondary structures of proteins and has a stable plane structure due to hydrogen bonding between a stretch of polypeptide chain and either parallel or antiparallel extended polypeptide chains. Another typical secondary structure is α-helix, a spiral conformation.

More information: Katsuya Araki et al. Synchrotron FTIR micro-spectroscopy for structural analysis of Lewy bodies in the brain of Parkinson's disease patients, *Scientific Reports* (2015). DOI: 10.1038/srep17625

Provided by Osaka University

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