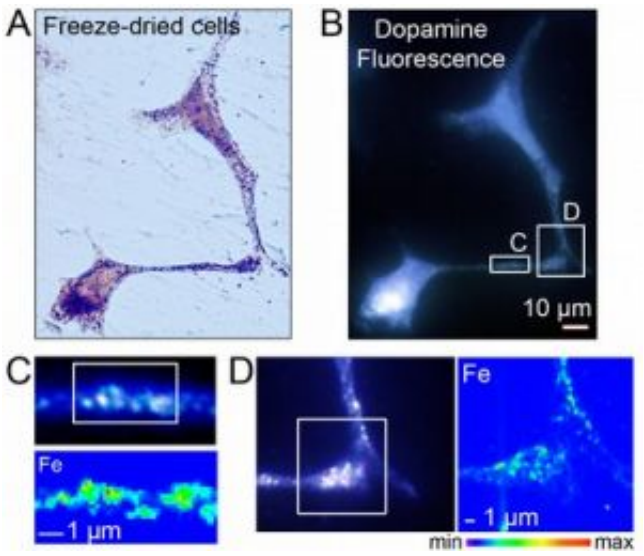
Scientists spot sneaky 'neurodegenerative' iron at the European synchrotron

October 10 2007



Iron is localized within dopamine neurovesicles. Visible light microscopy of freeze-dried cells (A), and epifluorescence microscopy of the same freeze-dried cells (B) enable the identification of dopamine distribution, while synchrotron X-ray fluorescence nano-imaging reveals the distribution of iron (C, D). Panels C and D represent comparison of the same region imaged in a fluorescent mode to visualize dopamine and with X-ray fluorescence to localize iron. Dopamine and iron are co-located within 200 nm structures characteristic of dopamine neurovesicles as identified by epifluorescence microscopy. A large number of iron and dopamine neurovesicles are found in neurite outgrowths (C) and distal ends (D). Min-max range bar units are arbitrary. Scale bars = 1 µm.

Scientists suspect that iron accumulation plays a role in

neurodegenerative processes such as Parkinson's disease, but its distribution in neurons has never been observed because of the lack of techniques to do so. Until today.

Researchers from CNRS at the University of Bordeaux (France), University of Sevilla (Spain), INSERM Grenoble Institute of Neurosciences (France) and ESRF have studied the iron distribution in an in vitro model of neuronal cells that produce dopamine.

Dopamine is a neurotransmitter, a chemical messenger between nerve cells in the mammalian brain. Because dopamine can form stable complexes with iron, Richard Ortega from the cellular chemical imaging group in Bordeaux, believed that dopamine may exert a protective effect by buffering iron in dopaminergic neurons and that this system might be at fault in Parkinson's disease.

With the aim of testing this hypothesis, the team used the new nanoprobe imaging experimental station recently developed at the European Synchrotron Radiation Facility to study the distribution of elements in cells. The resolution of 90 nanometres allowed scientists to visualize the elements distribution in the neurotransmitter vesicles. The nanoprobe excites the sample with a strongly focused X-ray beam and collects the characteristic fluorescence signal that is re-emitted. This allows showing the different trace elements in a point, and then the sample is scanned point by point to form a complete multi-element image of the cells.

The team shows that iron is stored within dopamine vesicles inside the neuronal cells. This is the first evidence of iron-dopamine co-localization in neuro-vesicles. The results also explain that when dopamine production is obstructed, the iron in the vesicles drastically decreases. This new function of dopamine vesicles in iron storage is of critical importance to understand the molecular mechanisms involved in

Parkinson's disease. In this neurological disorder, dopamine vesicular storage has been found impaired. According to these results, this would increase the levels of highly toxic iron-dopamine complexes in the neurons. The results are published in PLoS ONE on September 26.

The synchrotron nano-imaging station offers a new tool for researchers involved not only in the study of neurodegenerative diseases but also in many other fields where the determination of metal ions distribution at the subcellular level is important such as: metal toxicology, chemical carcinogenesis, and cellular pharmacology of inorganic compounds. This is one of the reasons why the team decided to submit their results in an open access journal such as PLoS ONE: " We want the different scientific communities to know that this machine is available, and the best way is by letting everyone have access to the results", explains Peter Cloetens, in charge of the station at ESRF.

Reference: Ortega R., Cloetens P., Devès G., Carmona A., Bohic S. (2007) Iron storage in neurovesicles revealed by chemical nano-imaging. PLoS ONE (September 26, 2007)(www.plosone.org/doi/pone.0000925).

Source: ESRF