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Elevated levels of copper in amyloid plaques associated with neurodegeneration in mouse models of AD

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Metals such as iron, copper, and zinc are important for many biological processes. In recent years, studies have shown that these nutritionally-essential metals are elevated in human Alzheimer's disease (AD) brains and some animal models of AD. Scientists are now exploring whether these metals are causing the neurodegeneration seen in AD or are indicative of other ongoing pathologic processes.

In a new study, investigators used synchrotron x-ray fluorescence microscopy to image metal ions in the brain, focusing on the amyloid plaques that are the hallmark of AD. They found that, in two AD mouse models that exhibit neurodegeneration, the plaques contained about 25% more copper than an AD mouse model that shows little neurodegeneration. Looking at other metals, they found that none of the mouse models had significant increases in iron and very little increases in zinc. Metal content was not related to the age of the plaque. The study is reported in the current issue of *Biomedical Spectroscopy and Imaging*.

"Since excess copper should not be 'free' in the brain to bind to the plaques, these data suggest that the cellular control of copper is altered in AD, which may lead to toxic reactions between free copper ions and neurons," comments lead investigator Lisa M. Miller, PhD, a biophysical chemist in the Photon Sciences Directorate at Brookhaven National Laboratory. In previous work, Dr. Miller's group found very high levels of copper in human AD plaques.

Since elevated iron in the AD brain is well documented in both human brains and AD mouse models, the researchers measured iron content in the cortex of all three mouse models. They found that iron content was doubled in all AD mouse model cortices compared to controls, whether or not the models showed neurodegeneration. Upon further investigation, spectroscopic data revealed that the excess iron was present in the ferric (oxidized) state and consistent with the iron storage protein ferritin. "The increase in iron may be a reflection of changes in metalloprotein content and metal storage within the brain that is not well understood," says Dr. Miller.

Nevertheless, since iron in ferromagnetic and detectable through MRI, Dr. Miller suggests that in the future iron may be used as a biomarker for AD at early stages of disease, even before plaques are formed.

More information: "Elevated copper in the amyloid plaques and iron in the cortex are observed in mouse models of Alzheimer's disease that exhibit neurodegeneration," by Megan W. Bourassa, Andreana C. Leskovjan, Ryan V. Tappero, Erik R. Farquhar, Carol A. Colton, William E. Van Nostrand, and Lisa M. Miller. *Biomedical Spectroscopy and Imaging*, Volume 2/Issue 2. DOI: 10.3233/RNN-120303

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