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Lack of metal in mouse plaques points to a link to neurodegeneration in human Alzheimer's disease

Amyloid beta ($A\beta$) is the primary component of Alzheimer's disease (AD) plaques, a key pathological feature of the disease. Metal ions of zinc, copper, iron, and calcium are elevated in human plaques and are thought to be involved in the death of certain brain cells – a process called neurodegeneration. Mouse models of AD also develop plaques, but do not show the high degree of neurodegeneration observed in humans. In this study, we examined the zinc, iron, copper, and calcium distribution in a transgenic mouse model representing end-stage AD and compared them to plaques in human AD. We found that the mouse plaques contained only a 29% increase in zinc and there was actually *less* copper, iron, and calcium in the plaque compared to the surrounding tissue. These findings were in stark contrast to the high metal content observed in human AD plaques, further implicating the role of metal ions in human AD pathology. Since metal binding to $A\beta$ is thought to result in damage to neurons, the reduced metal binding in the mice is consistent with the lack of neurodegeneration in these animals.