COPPER IN THE ALZHEIMER’S BRAIN

Biochemical studies of the brains of Alzheimer’s patients have revealed dramatic regional drops in copper levels—as much as 50 percent of the metal being lost from the hippocampus and amygdala, both critical regions for memory processing and emotions. Where that copper goes, however, remains a bit of a mystery. Copper within the cell may accumulate in some regions while leaving other areas deficient. Outside the cell, copper may accumulate as a complex with amyloid beta peptides, preventing the metal from being taken up by post-synaptic neurons and possibly leading to drops in intracellular copper. To treat such copper dysregulation, researchers are testing copper bis(thiosemicarbazone) complexes, or BTSCs, as vehicles for delivering the metal to copper-deficient locations within the cell.

Extracellular copper is imported via the CTR1 membrane transporter, then shuttled to the Golgi apparatus by the chaperone protein ATOX1.

In the Golgi, copper is packaged into presynaptic vesicles that travel the length of the axon and release their contents into the synapse during normal neuronal firing.

Some of the copper that is released from the cell may get trapped in the extracellular amyloid beta peptides, which form the plaques characteristic of Alzheimer’s.

Copper BTSCs are small planar complexes with a peptide-like backbone wrapped around copper ions, allowing them to easily cross cell membranes and bypass normal copper transport routes.