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Neurology

A woman with her hands on her head, looking distressed, with a brain image overlaid at the bottom.

Looking into the future:

Epilepsy: can seizures be predicted?

Dementia: identifying who is at risk

Does copper have a role in ALS?

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Neuronal damage in familial amyotrophic lateral sclerosis (ALS) may not be copper dependent after all, according to research done by Philip Wong and colleagues (Johns Hopkins University School of Medicine, Baltimore, Maryland, USA). "ALS researchers will sit up and pay attention to these new findings by Wong and his colleagues. This is going to force the field to rethink ALS", says Harry Orr (University of Minnesota Medical School, Minneapolis, MN, USA).

Up to 10% of cases of ALS are familial. About 25% of these familial ALS cases are linked to a mutation in the superoxide dismutase (SOD1) gene. Since SOD1 contains copper, researchers have long considered copper to be implicated in the motor-neuron degeneration seen in ALS. Indeed, previous work done in vitro supported a role for copper in the pathophysiology of the disease. Wong's results, however, which used a genetically-modified mouse model of familial ALS, suggest that the neuronal damage may not be copper-dependent but rather that a lethal function unrelated to the normal protective antioxidant role of SOD1 is a more likely cause of cell death.

In their experiments, Wong and colleagues built a second defect into a commonly-used mouse model of familial ALS. For copper to reach its intracellular target protein (in this case SOD1), it needs a carrier called a "copper chaperone". When the copper chaperone was inactivated in the genetically-modified mice, the researchers found that although the amount of copper-loaded mutant SOD1 was reduced, disease symptoms remained.

These data will "focus research toward other possible mechanisms involved in the cause of ALS", says Wong. "This experiment will hopefully solidify in other researchers' minds that we need to concentrate on alternative theories." However, Wong admits that uncovering the mechanism by which mutation of SOD1 causes ALS remains a complex and challenging problem. The answer may lie within the mitochondria, or in the protein aggregates seen in motor neurons in ALS. Protein aggregates exist in other neurological disorders like Huntington's, Parkinson's, and Alzheimer's. "A second gene could be involved, too", says Wong, "that intercepts with the SOD1, or another pathway, to affect motor neuron degeneration. We've learned from the Alzheimer's field that different genes converge into one common biochemical pathway to cause pathology. Similar events could be occurring in ALS."