Imaging technique uncovers protein abnormality in motor neuron disease

August 8 2024

Pathological abnormalities associated with motor neuron disease have been identified using a new technique developed at the University of Birmingham.
The method will help scientists better understand the changes in the brain that lead to motor neuron disease (MND) and could eventually yield insights that will help with the development of new treatments. The abnormalities were identified in a collaboration between the University of Birmingham and the University of Sheffield, and published in *Nature Communications*.

Motor neuron disease, also known as *amyotrophic lateral sclerosis* or ALS, is a muscle wasting condition caused by messages from the brain's motor neurons not reaching the muscles, causing them to weaken. Around 5,000 people in the UK have the disease at any one time, and currently there is no cure.

At the University of Birmingham, researchers have developed a technique that enables them to examine specific proteins in their native state, directly from brain and spinal cord tissue samples. Called native ambient mass spectrometry (NAMS), the tool enables the structure of proteins to be studied in relation to their location within the tissue in greater detail than ever before.

Working with colleagues at the University of Sheffield, the researchers were able to identify a metal deficiency in a specific protein, known as SOD1, and show that it accumulates in specific regions of the brain and spinal cord in mice with MND.

SOD1 has previously been implicated in motor neuron disease, but this is the first time that detailed molecular imaging has been able to show how versions of the protein with missing metal ions accumulate in the affected mice.

Lead researcher Helen Cooper, of Birmingham's School of Biosciences, said, "This approach is the first to show that this form of SOD1 correlates with the pathology of motor neuron disease. It's a very early
step towards finding treatments for MND and is also an exciting new route for understanding the molecular basis of other diseases in unprecedented detail."

Richard Mead from the Sheffield Institute for Translational Neuroscience said, "We were very excited to apply this fantastic methodology, which Helen's team has developed, to gain new insights into the biology of MND and we look forward to using the technology further to explore why motor neurons die and find new interventions for those affected by MND."

The next steps for the researchers will be to test to see if the same imbalances are present in human tissue samples, and to try to treat the imbalance in the mice using available drug compounds.

**More information:** Oliver J. Hale et al, Mass spectrometry imaging of SOD1 protein-metal complexes in SOD1G93A transgenic mice implicates demetalation with pathology, *Nature Communications* (2024). DOI: 10.1038/s41467-024-50514-7, [www.nature.com/articles/s41467-024-50514-7](https://www.nature.com/articles/s41467-024-50514-7)

Provided by University of Birmingham


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