A urine test for Creutzfeldt-Jakob Disease may be possible

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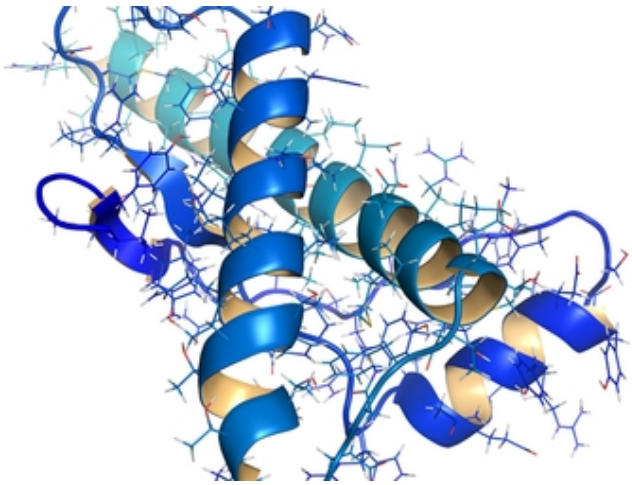

Credit: Medical Research Council

Researchers at the MRC Prion Unit at UCL have found that it may be possible to determine whether or not a person has sporadic Creutzfeldt-Jakob Disease (sCJD) by testing their urine for the presence of abnormal prion proteins.

Prions are infectious agents that cause invariably fatal brain diseases such as CJD in humans, scrapie in sheep and BSE (bovine spongiform encephalopathy or 'mad cow disease') in cattle. They are a rare but important cause of dementia and it is increasingly recognised that the fundamental process involved in these diseases – prion proteins changing

shape and sticking together to form fibres or polymers that damage the brain – is also what happens in the much more common dementias such as Alzheimer's disease, Parkinson's disease and other neurodegenerative diseases.

CJD is a degenerative neurological disease that is currently incurable. Variant CJD (vCJD) was identified in 1996 and is linked to the consumption of meat infected with bovine spongiform encephalopathy (BSE). There are also inherited forms of human prion disease linked to mutations of a prion protein gene and cases caused by infection via medical or surgical treatments (iatrogenic CJD). Sporadic CJD is the most common form of the disease and represents about 85% of all CJD cases. In the UK the lifetime risk for sCJD is around 1 in 5000 the cause of which remains unclear.

Currently, the only ways to determine in life whether or not a patient has sCJD are complex and may include MRI scans, brain biopsy and sampling of cerebrospinal fluid. These procedures are usually only performed when there is already a high likelihood that a patient has the disease, and sadly, the patient may have just weeks to live by the time the diagnosis is confirmed.

In all forms of CJD, abnormal infectious prion proteins accumulate through a mechanism of 'misfolding'. While previous work has shown that the abnormal proteins can be detected in the blood of patients with vCJD, the process was unable, until now, to detect them in patients with the sporadic form of the disease.

In this study, published in the journal *JAMA Neurology*, the researchers used a modification of a test developed for blood samples to test the urine of patients known to have CJD. They analysed anonymised samples from 162 people - 91 'controls' (patients known not to have the disease), 34 patients with non-prion neurodegenerative disease, and 37

patients with prion disease, 20 of whom had sCJD. The results showed a very high specificity for the prion target, and correctly identified 40% of sCJD cases.

The researchers hope to be able to increase the performance of the test by isolating the molecule or molecules in urine that are present in patients with sCJD.

Dr Graham Jackson from the MRC Prion Unit and lead author of the study, said: "Although there is currently no cure for this disease, an accurate and early diagnosis is extremely important for patients and their families. In the future, as trials of potential therapies become available, the earlier a patient can be diagnosed the more effective any treatment is likely to be.

"This test could be a critical step forward in being able to identify disease sufferers early using a simple test, perhaps at the first signs of being unwell or even as part of routine screening. By studying the nature of these disease-specific forms of the prion protein we hope to be able to improve the reliability and speed of the test to a point where it could one day be routinely used by clinicians including GPs to detect all forms of CJD."

Dr Nathan Richardson from the MRC, which funded the study, said: "Although we currently have no cure for CJD, or for other neurodegenerative diseases such as Alzheimer's, understanding the early biomarkers for these can be extremely important in identifying targets for the eventual development of drugs treatments."

Provided by Medical Research Council