Scientists find new form of prion disease that damages brain arteries

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National Institutes of Health (NIH) scientists investigating how prion diseases destroy the brain have observed a new form of the disease in mice that does not cause the sponge-like brain deterioration typically seen in prion diseases. Instead, it resembles a form of human Alzheimer's disease, cerebral amyloid angiopathy, that damages brain arteries.

The study results, reported by NIH scientists at the National Institute of Allergy and Infectious Diseases (NIAID), are similar to findings from two newly reported human cases of the prion disease Gerstmann-Straussler-Scheinker syndrome (GSS). This finding represents a new mechanism of prion disease brain damage, according to study author Bruce Chesebro, M.D., chief of the Laboratory of Persistent Viral Diseases at NIAID's Rocky Mountain Laboratories.

Prion diseases, also known as transmissible spongiform encephalopathies, primarily damage the brain. Prion diseases include mad cow disease or bovine spongiform encephalopathy in cattle; scrapie in sheep; sporadic Creutzfeldt-Jakob disease (CJD), variant CJD and GSS in humans; and chronic wasting disease in deer, elk and moose.

The role of a specific cell anchor for prion protein is at the crux of the NIAID study. Normal prion protein uses a specific molecule, glycophosphoinositol (GPI), to fasten to host cells in the brain and other organs. In their study, the NIAID scientists genetically removed the GPI anchor from study mice, preventing the prion protein from fastening to

cells and thereby enabling it to diffuse freely in the fluid outside the cells.

The scientists then exposed those mice to infectious scrapie and observed them for up to 500 days to see if they became sick. The researchers documented signs typical of prion disease including weight loss, lack of grooming, gait abnormalities and inactivity. But when they examined the brain tissue, they did not observe the sponge-like holes in and around nerve cells typical of prion disease. Instead, the brains contained large accumulations of prion protein plaques trapped outside blood vessels in a disease process known as cerebral amyloid angiopathy, which damages arteries, veins and capillaries in the brain. In addition, the normal pathway by which fluid drains from the brain appeared to be blocked.

Their study, Dr. Chesebro says, indicates that prion diseases can be divided into two groups: those with plaques that destroy brain blood vessels and those without plaques that lead to the sponge-like damage to nerve cells. Dr. Chesebro says the presence or absence of the prion protein anchor appears to determine which form of disease develops.

The new mouse model used in the study and the two new human GSS cases, which also lack the usual prion protein cell anchor, are the first to show that in prion diseases, the plaque-associated damage to blood vessels can occur without the sponge-like damage to the brain. If scientists can find an inhibitor for the new form of prion disease, they might be able to use the same inhibitor to treat similar types of damage in Alzheimer's disease, Dr. Chesebro says.

More information: B Chesebro et al. Fatal transmissible amyloid encephalopathy: A new type of prion disease associated with lack of prion protein membrane anchoring. PLoS Pathogens 6(3): e1000800. DOI:10.1371/journal.ppat.1000800 (2010).