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Impaired transport in neurons triggers prion disease

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A new study shows that nervous system integrity and axonal properties may play a key role in prion diseases. The findings, from researchers at the Rudolf Virchow Center and the Institute of Virology of the University of Würzburg, expand our understanding of the development of prion disease and suggest novel targets for therapeutic and diagnostic approaches in its early stages. Details are published August 21 in the open-access journal *PLoS Pathogens*.

Despite growing awareness of prion diseases, such as bovine spongiform encephalopathy (BSE) and the human variant, Creutzfeldt-Jakob disease, the molecular mechanisms responsible for their development are still not completely understood. These diseases are associated with neuropathological symptoms that include dementia, motor system defects and amnesia, although previous observations identified molecular hallmarks in the absence of these neuropathological symptoms, creating a paradox. The recent work of Vladimir Ermolayev and colleagues helps resolve this paradox, bringing new insights into the key factors triggering the onset of the clinical disease.

Impaired axonal transport is known to be involved in the development of neurodegenerative disorders like Alzheimer's or Parkinson's diseases. Previously, prion infections were shown to cause spongiform vacuolations, axonal swellings and accumulation of amyloid protein fibrils. Impaired axonal transport had not been observed so far. To monitor the axonal transport, Ermolayev and co-authors injected special dyes into mouse motor neurons, using a combination of confocal and

novel ultramicroscopy techniques to monitor the dye delivery to the neurons and characterize the functional properties of axonal transport.

After prion injection into the brain and motor neuron system, Ermolayev and colleagues observed the described clinical symptoms. When clinical symptoms occurred, the researchers found a clearly reduced axonal transport in the neurons of two brain centers, the red nucleus and the motor cortex. Axonal transport impairments were seen in 45 per cent of neurons in the red nucleus and up to 94 per cent of motor cortex neurons.

"These results will help us to find better ways for diagnosis and treatment of prion diseases," says Dr. Vladimir Ermolayev.

More information: Ermolayev V, Cathomen T, Merk J, Friedrich M, Ha¨rtig W, et al. (2009) Impaired Axonal Transport in Motor Neurons Correlates with Clinical Prion Disease. *PLoS Pathog* 5(8): e1000558. doi:10.1371/journal.ppat.1000558

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