Keep an eye on the prion – the spreading pathology of MSA

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Over the last 50 years the origin of prion diseases has become more secure even if the mechanism by which the abnormal protein accumulation kills cells is still unresolved. These disorders include genetic conditions such as Gerstmann-Straussler-Scheinker disease as well as sporadic diseases such as CJD. Of late there has been a great deal of interest in whether other, more common, neurodegenerative disorders of the CNS may have a similar basis – namely that the pathogenic protein that lies at the core of the condition can act in a prion like disease. This has been explored in most detail with tau and alpha synuclein and are the subject of two papers from the Pruisner lab that have just been published in PNAS.

These studies involve in vitro studies using human embryonic kidney cells along with the in vivo work involving the Tgm83 +/- mice that express alpha synuclein (A53T). In each case the cells/animals are "inoculated" with "prions" purified from the brains of patients dying with PSP, MSA or PD. In the first study they show that both MSA and PSP brains can infect cells in vitro, while PD brain extracts did not display such behaviour. This was then confirmed in the second paper with respect to MSA versus PD synuclein extracts in the mouse model. The authors therefore conclude that "alpha synuclein is the first human prion to be identified, to our knowledge, since the discovery a half century ago that CJD was transmissable".

This is a bold statement although fits with an emerging literature showing that alpha synuclein can spread from cell to cell and seed pathology in some instances. Thus this finding adds to that existing literature, although does draw a distinction between the alpha synuclein "strains" found in PD and MSA which again has been suggested by other studies (e.g. Peelaerts et al Nature 2015). Thus these papers are of great interest to those working in this field, although as far as I know, it has still not been shown that anyone has developed an alpha synucleinopathy from exposure to "infected" human tissue as has been the case for CJD.

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