Identification of unfolded protein response, apoptosis and autophagy markers in human AD

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Research Abstract

During ageing, a decline in vital neuronal function leaves brain cells vulnerable to the activation of damaging cellular pathways, a process interwoven with accumulation of Alzheimer’s disease (AD) related proteins (amyloid and tau). Mis-folded and toxic proteins trigger an adaptive response known as the ‘unfolded protein response (UPR)’, a process common in a wide range of brain disorders and recently proposed as a break-through key therapeutic target. Whilst initially beneficial, under prolonged stress cells must activate pathways for protein degradation,

inflammation and ultimately cell death. In AD these adaptive responses may be hijacked leading to accelerated accumulation of toxic proteins. To confirm the role of this pathway in dementia, we propose to study human brain tissue using protein quantification and visualisation techniques to determine markers for URP and subsequent cellular events. Cellular pathways will be examined in relation to the stage of the dementia, the documented score of pre-mortem cognition, and established AD protein markers. Correlations between these adaptive responses and the stage of AD is critical to confirm their causative role since data so far have been based on experimental models. Deciphering cellular pathways and their role in degenerative processes will be key to develop future therapeutic strategies.

Further information available at:

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