

- P067** Increased IGF-1 receptor levels, decreased IGFBP-2 levels, and defects in normal IGF-1 and insulin receptor signalling are associated with the pathogenesis of Alzheimer's disease. Rebecca Griffin¹, Aileen Moloney¹, Mary Kelliher¹, Janet A. Johnston², Rivka Ravid³, Rosemary O'Connor¹, Cora O'Neill¹
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Accumulating data indicates a potential role of the insulin like growth factor 1 receptor (IGF-1R) and the insulin receptor (IR) in the pathogenesis of Alzheimer's disease (AD). However, in depth analysis of the status of IGF-1R/IR and their signalling pathways in AD is lacking. For the first time this study examined the levels of IGF-1R and IR proteins in AD brains compared to matched non-disease control brains. Results detected a significant increase in the levels of IGF-1R in the temporal cortex of AD cases compared to controls. This was accompanied by a significant decrease in levels of IGFBP-2, one of the major IGF binding proteins in brain. Together, this indicates an attempt to increase signalling through the IGF-1R that links to the pathogenesis of AD. Levels of IR were not found to be significantly different in AD compared to control temporal cortex. Immunohistochemical analysis showed IGF-1R to be predominantly expressed throughout the neuronal cell soma in control brain. In AD, IGF-1R levels were significantly up-regulated in astrocytes, and IGF-1R localisation was concentrated towards the plasma membrane of pyramidal neurons. IGF-1R immunoreactive cells were frequently found to surround neuritic plaques. Further examination of components of the IGF-1R/IR signalling pathway including, IRS1/2, p85 α and PDK1 detected significant decreases in levels of these proteins in AD compared to control brain. Together these results point to deregulation of normal brain IGF-1R/IR signalling in AD.