

P014 Neurochemical Changes Associated with Prion Disease Using the ME7 Murine Scrapie Model

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Prion disease affects the mammalian nervous system, resulting in typical neuropathology characterised by vacuolation of the grey matter, gliosis and neuronal cell death. The disease is caused by the conformational change of the normal cellular prion protein (PrP^c) to an infectious PrP^{Sc} form, which aggregates within the brain. There is a body of evidence indicating that prion-induced degeneration is likely to begin at the synapse and progress via retrograde degeneration towards the cell body. Our investigation into the synaptic pathogenesis of prion disease focuses specifically on the early pathology within hippocampal synapses. The expression of a selected number of synaptic proteins representative of each synaptic sub-compartment was profiled to determine if specific components were more susceptible to degeneration than others. Initial investigation showed that there was a time-dependent disruption of pre-synaptic proteins prior to post-synaptic proteins primarily within the CA1 region of the hippocampus. More specifically, the intensity of a number of synaptic vesicle proteins and their associated co-chaperones decreased more significantly than other synaptic proteins. Additional studies of synaptic ultra-structure have lead to a hypothesis of a targeted effect at the synapse, culminating with disruption of normal protein chaperoning and vesicle trafficking.