

P044 Neurochemical changes associated with prion using the murine ME7 scrapie model.

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Experimentally induced prion can be used as a model of chronic degeneration. We are using the local injection of murine scrapie (ME7) into the mouse hippocampus as a model of prion induced degeneration. We have already identified a selective disruption in the organization of the stratum radiatum of the hippocampus that correlates with early behavioural dysfunction in animals undergoing ME7 induced degeneration (1). The present study builds on this earlier observation which already suggest synapses are an early target in this prion induced hippocampal degeneration. We observe the previously described disruption in synaptophysin immunostaining in the stratum radiatum and now use quantitative western blotting to show a decrease in synaptophysin content of the hippocampus during the ontogeny of ME7 induced hippocampal degeneration. In a similar way we find a selective disruption in the organization (immunocytochemistry) and absolute levels (western blotting) of other synaptic vesicle proteins over a similar time course (e.g. synaptobrevin). This contrasts a lack of change in the expression of a number of synaptic markers associated with the presynaptic membrane, the post synaptic membrane or the synaptic cytomatrix. We take our results to indicate that synapses represent an early target in the onset of this model neurodegeneration and hypothesise that prion may selectively target the synaptic vesicle compartment during the early time points of prion induced chronic degeneration. (1) Cunningham et al., 2003 *E.J.Neurosci.* 17. 2147-2155.