Pathological differences observed in the presubiculum and entorhinal cortex in post-mortem Alzheimer's disease brain tissue

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Introduction: Previous observations indicate that the presubiculum accumulates amyloidogenic proteins in a range of diseases, but only minimal neurofibrillary degeneration is seen. However, in the neighbouring entorhinal cortex and subiculum severe neuronal loss and deposition of amyloid plaques is observed. Using post-mortem brain samples from AD cases, we aimed to characterise the protein deposits and determine the level of microglial activation in both the presubiculum and the neighbouring areas.
Materials and Methods: Immunohistochemistry was performed on sporadic AD (n=19) and familial AD (n=11) cases in order to visualise the presubiculum and the entorhinal cortex. The density of amyloid, tau and microglial staining present in both areas was assessed. Amyloid deposits from the presubiculum and the entorhinal cortex were laser captured for biochemical analysis.
Results: Significantly less tau and microglial activation was observed in the presubiculum compared to the entorhinal cortex in both AD groups. Neurofibrillary tangles were absent in the presubiculum. However, resting microglial levels were closer to equal in both areas in both groups. Mass spectrometry analysis revealed there were less N-terminally truncated and pyro-glutamate modified amyloid peptides in the presubiculum compared to the entorhinal cortex.
Conclusion: We have shown that the presubiculum has different pathological characteristics in a number of AD cases compared to the entorhinal cortex. The differences detected could be due to a number of different tissue factors. Understanding why this region has less truncated forms of Aβ peptides and less microglial activation may provide insight into the disease mechanism of Alzheimer's disease and other neurodegenerative disorders.