

P021 Degradation of APP during the early phase of long-term memory consolidation

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Amyloid precursor protein (APP) is required for memory formation however its functional significance is unknown. We now demonstrate learning-dependent degradation of APP in the rat hippocampal dentate gyrus to be an essential feature of memory consolidation. Neuron-specific APP695, the dominant form in the brain, expression became reduced 2-4 hours post-passive avoidance training and this was also observed in the cerebrospinal fluid. Co-immunoprecipitation studies revealed APP695 to be associated with the adaptin protein (AP) 1 and, separately, that AP1 increased its association with AP180 in the 2-4h post-training period. Collectively, these observations suggested APP695 to be internalised for degradation by clathrin-coated pits. Glial-specific APP, containing the Kunitz protease inhibitor (APP-KPI), also became internalised in the 2-4h post-training period but, by contrast to APP695, appeared to become internalised by association with the low-density lipoprotein receptor-related protein (LRP). This latter suggestion is based on the observation that the receptor antagonist protein (RAP), when administered at 3h following training, resulted in task amnesia and prevented APP-KPI internalisation. APP degradation was not observed in the CA regions and may have a role in synaptic restructuring of the perforant path input.

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