

P002 NMDA receptor-dependent translocation and activation of Rac is associated with memory formation in the mouse hippocampus

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The hippocampus is a brain area that exhibits robust forms of synaptic plasticity such as long-term potentiation (LTP) and is required for the acquisition of memories. It has been demonstrated that the formation of NMDA receptor-dependent LTP coincides with changes in dendritic morphology. GTPases such as Rac are potential mediators of LTP-associated changes in dendritic morphology in the hippocampus. We have begun investigations to determine whether NMDA receptor activation can regulate Rac in the hippocampus. We found that NMDA receptor activation causes association of Rac with the NR1 subunit of the receptor, thereby increasing the membrane-association and activation of Rac in hippocampal area CA1. These observations led us to hypothesize that membrane translocation and activation of Rac is critical for LTP and hippocampus-dependent memory. To test this hypothesis, we determined whether Rac membrane translocation and activation was associated with contextual fear conditioning in mice. In our preliminary experiments we observed an increase in membrane-associated activated Rac in hippocampal area CA1 of mice exposed to contextual fear conditioning. Taken together, these data suggest that NMDA receptor activation alters Rac localization and function and that similar alterations are associated with hippocampus-dependent learning and memory.