Consequences of overexpressing NAB2, a corepressor of the transcription factors EGR1, EGR2, and EGR3, on learning and memory in transgenic mice

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Both in invertebrates and vertebrates, *de novo* gene expression is important for learning and long-term memory. In addition, gene transcription and protein synthesis are necessary in *in vitro* models of memory formation, i.e., for long-lasting long-term potentiation (L-LTP) in hippocampal slices. The first genes induced upon neuronal stimulation are immediate early genes (IEGs). The zinc-finger transcription factors EGR1, EGR2 and EGR3 are typical IEGs and are upregulated in the hippocampus after induction of LTP. This upregulation suggested that EGR proteins may play a role in L-LTP and memory formation. To test this hypothesis, we generated transgenic mice with neuron-specific overexpression of NAB2, an inducible corepressor molecule that blocks the activity of EGR1, EGR2, and EGR3, but not EGR4. NAB2 overexpression in the brain of transgenic mice was confirmed by Western blot analysis. NAB2 overexpression, however, did not affect learning and memory in watermaze, conditioned taste aversion, and fear conditioning experiments. These data indicate that the function of EGR1, EGR2, and EGR3 is not required for learning and memory. To examine possible compensatory mechanisms (e.g., upregulation of EGR4), we are now quantifying the endogenous expression levels of EGR1, EGR2, EGR3, EGR4, and of specific EGR target genes.
Supported by: Swiss National Science Foundation

Tuesday, Nov. 7, 2:00 PM - 3:00 PM 565.6 Poster NN-37