Exchange of NMDA receptor subunits NR2C by NR2B in mutant mice

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Using homologous recombination we have exchanged the subunits NR2C by NR2B of the murine N-methyl-D-aspartate (NMDA) receptor in mice. Homozygous animals develop subtle motor deficits due to age dependent down regulation of the endogenous NR2A subunit in the cerebellum and also exhibit developmental changes in the micro architecture of the cerebellum (Schlett et al. 2004). In learning and memory tasks, however, exchange mice showed improved performance compared to non-mutant litter mates but reduced long term potentiation most likely due to mutant NR2B over expression in hippocampal interneurons which leads to stronger excitation of GABAergic neurons and thus stronger inhibition of pyramidal neurons of the CA1 region (Matsushita et al., 2004). Despite these phenotypes NMDA receptor exchange mice also have increased levels of acetylcholine in the frontal cortex and amygdala. In our present study we want to explore if increased acetylcholine levels in the prefrontal cortex and the amygdala are due to NR2B expression in, and thus due to increased excitability of cholinergic neurons of the nucleus basalis. Using biotin and digoxigenin labeled anti sense RNA probes for the mutant mRNA and choline acetyl transferase (CHAT), we want to determine if the mutant gene is also expressed in the nucleus basalis by double immunofluorescence staining.

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