NMDA receptor subunit 1 hypomorphic mice show impaired hippocampal LTP, stereotypical behaviour and deficits in spatial learning tasks

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The constitutive mouse mutant with 90% reduced expression of the NMDA receptor subunit 1 (NR1) has been widely investigated as a putative mouse model of impaired glutamatergic signaling in schizophrenia. Phenotyping of these mutants mainly focused on specific behavioral and neurophysiological tests that are thought to be of relevance as putative endophenotypes of this disorder. To date, data is missing regarding the phenotype of the NR1 mutants in hippocampal long-term potentiation (LTP) and many traditional behavioral tests. We find reduced LTP in NR1 mutants compared to controls, both with high-frequency tetanic, as well as theta-burst stimulation in the CA1 region. The mutants showed increased open sector activity on the O-maze and impaired habituation in the open field test. Escape time in the water-maze was massively prolonged in the mutants. Their performance was the second worse ever tested in a database covering 107 different mutations. Indexes of working memory in the 8-arm radial maze were significantly impaired in the mutant group. However, in both memory tests, NR1 mutants showed increased measures of stereotypical behavior and altered movement patterns, representing a major confounding factor for analyzing specific memory impairments. The present data imply impairments in the NR1 mutants in multiple brain systems. However, no conclusive statement can be made regarding memory deficits in spatial learning tasks, due to stereotyped movement patterns in these mutants.

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