

S001 Glutamate receptors in hippocampus-dependent learning and memory

David M Bannerman

*Department of Experimental Psychology,
University of Oxford*

Hippocampal dysfunction is a key component of several psychiatric disorders including schizophrenia, depression and anxiety. Experimental lesions of the hippocampus impair learning on a range of spatial memory tasks. The development of transgenic mice in which specific glutamate receptor subunits can be selectively deleted has revealed different patterns of deficits and sparing across these spatial memory tests, suggesting that there are multiple memory mechanisms within the hippocampal formation that would not have been identified with lesion studies. Various AMPA, NMDA and metabotropic glutamate receptor subunit knockout mice have been generated, resulting in very different behavioural phenotypes. For example, deletion of NR2A and NR2B NMDAR subunits may have very different effects on behaviour. Furthermore, it is also now possible to delete individual glutamate receptor subunits from specific hippocampal subfields. Deletion of the NR1 NMDAR subunit has very different behavioural consequences depending on which hippocampal subfields are affected. Studies with transgenic mice have revealed the presence of two distinct learning mechanisms: (i) a short-term memory mechanism that underlies performance on win-shift, spatial working memory tasks, and (ii) a long-term memory mechanism that supports spatial reference memory tasks. Under certain conditions these two memory processes compete with one another such that mice with impaired short-term memory, as a result of certain glutamate receptor deficiencies in the hippocampus, can actually display superior long-term memory. These findings may have important implications for various clinical disorders.