

Studies of glutamate and dopamine function in group II metabotropic glutamate receptor (mGluR) knockout mice

Supervisors: Paul Harrison, paul.harrison@psych.ox.ac.uk with David Bannerman, Dept. Experimental Psychology.

Brief Description:

Group II mGluRs (mGlu2 and mGlu3) regulate glutamate release. They are implicated in aspects of cognition and psychosis, mGlu3 is a candidate gene for schizophrenia, and they are a novel treatment target for schizophrenia and other neuropsychiatric disorders. We are interested in the role these receptors play in hippocampal function. Our recent work has shown that double knockout mGlu2^{-/-}mGlu3^{-/-} mice are impaired in appetitive but not aversive spatial memory, as well as having altered hippocampal long-term depression. Arising from these results and other considerations, we think that these mice may be differentially affected by dopaminergic and glutamatergic drugs compared to wild type mice. This project will investigate this hypothesis, using dopamine agonists and antagonists, and an NMDA receptor antagonist, in a range of behavioural and hippocampal-dependent memory tasks. The project will also include molecular studies of the dopamine system in brain tissue. Behavioural work will take place in the Bannerman lab, molecular studies with the Harrison group. The work will inform models of the roles that group II mGluRs play in schizophrenia and in cognition. A background in neuroscience is desirable.

References:

Patil S et al (2007) Activation of mGlu2/3 receptors as a new approach to treat schizophrenia: a randomized phase 2 clinical trial. *Nature Medicine* **13**1102-1107

Harrison PJ, Lyon L, Sartorius LJ, Burnet PWJ, Lane TA (2008) Metabotropic glutamate receptor 3 (mGluR3, mGlu3, *GRM3*): expression, function, and involvement in schizophrenia. *Journal of Psychopharmacology* **22** 308-322