How do GluD1 glutamate receptors in the hippocampal CA2 region control social behaviours and related mental health conditions?

Supervisory team:
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Project description:
The CA2 region of the hippocampus is key for everyday social behaviours, and deficits in CA2 function are associated with autism, schizophrenia and loss of social interaction. A particular glutamate receptor, called the delta ionotropic receptor (GluD1), is very highly concentrated within the CA2 region of the hippocampus. Interestingly, data from genome wide association studies have identified perturbations in GrinD1 (the GluD1 gene) to be associated with autism, schizophrenia and sociability deficits, and GluD1 knockout mice have behavioural phenotypes consistent with these mental health conditions. However, the function of GluD1 receptors in CA2 is unknown. Therefore, this project will test the novel hypothesis that GluD1 within CA2 is essential for controlling everyday social behaviours, and that this control is brought about by GluD1 regulating synaptic transmission, plasticity, neuronal and circuit activity within CA2. Furthermore, loss of GluD1 function specifically in CA2 will result in behaviours associated with schizophrenia and autism.

To understand how GluD1 exerts control over synaptic and neuronal function in the CA2 region, and how this contributes to social behaviours, conditional CA2 selective-GluD1 knockout mice will be used in ex vivo synaptic recordings, in vivo multi-unit recordings, and in assessment of social behaviours. We will also use molecular methods to acutely, and reversibly, prevent the essential interaction between postsynaptic GluD1 and its presynaptic neurexin-cerebellin partner. This method will allow additional detailed insights into the molecular mechanisms that regulate GluD1 control of synaptic transmission and plasticity in CA2.

Together, this collaborative and multi-level approach will enable the student to make advances in understanding how the CA2 region of the hippocampus brings about everyday social behaviours, and how these behaviours goes awry when GluD1 function in CA2 goes wrong. This study will therefore provide crucial insights into the mechanisms controlling mental health conditions.

The student will work within a highly collaborative grouping of Bristol and Exeter PIs, postdocs, PhD students and technicians and will gain experience in using a range of different neuroscience techniques to investigate this important and novel question. Our groups have a history of successful collaborations across a range of projects centred around understanding cellular, synaptic and network mechanisms of learned behaviours.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.