Unlocking the psychopharmacology of psychedelics

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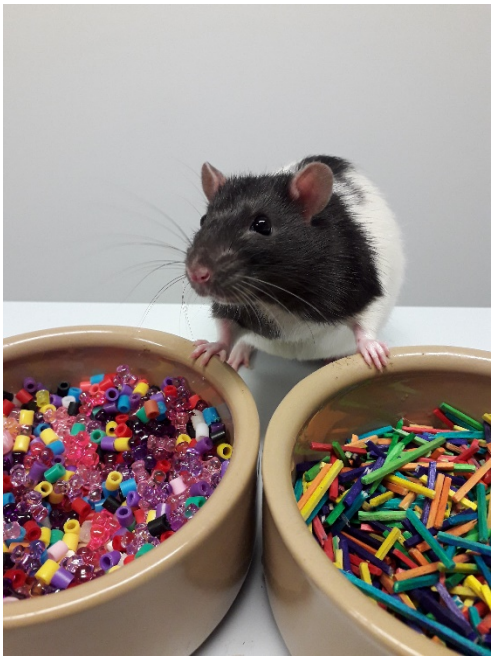
Project description:

In the last few years there has been a surge in interest in the potential clinical benefits of psychedelic drugs. This has also led to new investment not only to study the clinical effects of these drugs but also to better understand their fundamental biology. Through this work, new treatments with better tolerability and wider clinical applications may be developed. It is somewhat surprising to find that our knowledge of the fundamental biology of psychedelic drugs remains so limited. Although psychedelic effects of drugs have been exploited by humans for millennia and utilised in psychiatry up until the 1970s, much about the fundamental biology of these psychedelic drugs remains unknown. As naturally occurring substances, these drugs have a complex pharmacology and interact with multiple receptor populations. Not all psychedelics are the same and even small differences in their pharmacology may have big impacts on their behavioural effects. For example, most have activity at the 5-HT2A receptor but also act at other 5-HT receptors and it is still not known which receptors or combination of receptors contribute to the different aspects of their effects.



In this project we have established a collaboration with COMPASS Pathways who are developing psilocybin for clinical use. This project will start to address these unanswered questions using an integrated approach combining electrophysiological, behavioural and molecular pharmacology. Our initial focus will be the prefrontal cortex and the positive valence system, e.g. reward-related behaviours. We aim to establish the behavioural effects of psychedelics using behavioural tasks in normal rodents that map onto different aspects of reward processing, such as valuation, anticipation and learning. Specifically, we predict that psychedelics will have greater effects on reward learning which may contribute to their sustained effects. Recent imaging studies as well as animal data strongly support a key role for the prefrontal cortex and direct modulation of glutamate signalling. We will explore this using slice electrophysiology and look at acute drug effects in naïve tissue as well as taking samples from animals at different time points after treatment. By establishing the exact nature of changes which occur over time, we anticipate being able to integrate this with the behavioural data to better explain how and why these drugs have both acute and sustained effects. Once we have established a more substantial data set, there will also be an opportunity to use more sophisticated analytical methods.