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Neuroplastic effects of psychedelics on emotional memory circuits

Background

Psychedelic compounds are currently attracting major interest in neuroscience and psychiatry because of their potential to produce long-lasting changes in mood, cognition, and emotional processing, including ability to treat treatment-resistant depression. Classic psychedelics such as psilocybin primarily act through 5-HT2A receptors, whereas so-called non-classic psychedelics such as ketamine and MDMA act via different mechanisms. Despite their different pharmacology, both classes of compounds have been suggested to promote neuroplasticity and to reorganise functional interactions between brain regions.

However, the neural mechanisms underlying these effects remain poorly understood. Most current evidence comes from human neuroimaging studies, which provide important insights into large-scale brain activity but cannot resolve changes occurring at the level of individual neurons or synapses. Animal models therefore provide an essential bridge for understanding how psychedelic compounds influence neural circuits at a cellular level.

Aims and Methods

This project will investigate **how psychedelic compounds influence neuroplasticity in neural circuits involved in emotional learning and memory**. Using **electrophysiology in mouse brain slices**, the student will examine whether **compounds such as psilocybin, ketamine or MDMA trigger lasting changes in synaptic transmission or neuronal excitability**.

Depending on the scope and duration of the project, the work may also be complemented by **behavioural experiments in mice**. For example, fear conditioning tasks could be used to examine whether neuroplastic changes correspond to alterations in emotional memory processes.

Relevance

This project sits at the interface of cellular neuroscience, neuropharmacology and behavioural neuroscience. It addresses fundamental questions about how psychedelic compounds act in the brain to trigger lasting changes in emotion and cognition. This is relevant both for basic neuroscience and for understanding the mechanisms of emerging psychiatric treatments

Training

The candidate will receive training in a range of experimental and analytical approaches used in modern neuroscience. These may include brain slice electrophysiology, analysis of neuroplasticity and behavioural assays of emotional learning in rodents. The project will also provide experience in experimental design, data analysis, and scientific communication.

The research will take place within the Neuromodulation of Cognition Lab at Durham University and will offer exposure to interdisciplinary collaborations across groups and departments via the Learning and Memory Processes Centre and the Biophysical Sciences Institute.

Suitable for

PhD students.

References and further reading

Carhart-Harris, R. L., & Friston, K. J. (2019). REBUS and the anarchic brain: Toward a unified model of the brain action of psychedelics. *Pharmacological Reviews*, 71, 316–344.

Siegel, J. S., et al. (2024). Psilocybin desynchronizes the human brain. *Nature*, 632, 131–138.

Agorelli, C., et al. (2025). Neuroplasticity and psychedelics: A comprehensive examination of classic and non-classic compounds in pre and clinical models. *Neuroscience & Biobehavioral Reviews*, 172, 106132.