



OPERA (www.oxfordpsychosis.com) undertakes translational research to understand the mechanisms underlying psychosis and develop more effective, personalised treatments. Our work spans multimodal neuroimaging, neurophysiology, experimental medicine, clinical trials and computational modelling.

We welcome enquiries from prospective DPhil students interested in the projects below. The precise questions and methods would be tailored to the student's interests and background.

Understanding treatment mechanisms in early psychosis using multimodal neuroimaging

Cognitive impairment and negative symptoms are major determinants of functional outcome in psychosis, but they respond poorly to conventional dopamine D2/3 receptor-blocking treatments. New treatments targeting muscarinic receptors may act through different neural mechanisms and offer opportunities to understand—and potentially improve—these outcomes.

This project will use longitudinal data from FOCUS, a randomised mechanistic trial comparing xanomeline–trospium with conventional D2/3 receptor antagonist treatment in people with early psychosis. FOCUS combines detailed cognitive and clinical assessment with multimodal MRI, magnetic resonance spectroscopy and electrophysiology.

Potential questions include:

- how muscarinic and dopaminergic treatments differentially alter cortical excitation–inhibition balance, brain-network dynamics and subcortical function;
- whether changes in these measures explain improvements in cognition, negative symptoms or broader functioning;
- whether baseline neurobiological features can predict response to different treatments; and
- how information across imaging, electrophysiological, cognitive and clinical measures can be integrated to identify mechanistically distinct patient profiles.

Depending on the student's interests, the project could focus on a particular modality or develop a multimodal analysis. Relevant existing datasets, including data from the PEACE experimental-medicine study, could provide preliminary analyses while FOCUS recruitment and follow-up continue.

The student would gain experience in clinical neuroscience, longitudinal and trial-based analysis, neuroimaging and computational methods.

All projects potentially suitable for both full or part-time study

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