Application number/Title: 35944 - Exploring the genetic basis of inhibition in the brain

Applicant PI: Dr Charlotte Stagg

Application Institution: University of Oxford, UK

Keywords provided by the Applicant PI to describe the research project:
comt, gaba, mri, plasticity, resting-state

Application Lay Summary:

Neurons communicate with one another either by causing excitation, one neuron making the next more likely to fire, or inhibition, making its firing less likely. Maintaining the balance of excitation and inhibition in the brain is crucial to allow normal brain functioning, but modulating the excitatory-inhibitory balance is necessary for plasticity, learning and recovery after stroke. Understanding how the excitatory-inhibitory balance influences the brain's ability to change should allow us to develop new interventions to improve recovery after stroke.

Excitation and inhibition are controlled through two chemicals; Glutamate and GABA. Production and transport of these neurotransmitters is controlled by enzymes including GAD67, GAD65, vGAT, BDNF and COMT. Small changes (known as single nucleotide polymorphisms- SNPs) in the genes coding for these enzymes show associations with disorders such as post traumatic seizures (Darrah et al., 2013), schizophrenia (Straub et al., 2007), and epilepsy (Sperk et al., 2012).

We will examine how SNPs in these genes relate to differences in individual's brain function using resting-state functional magnetic resonance imaging (rs-fMRI). Measures from rs-MRI correlate with inhibition (Bachtiar et al., 2015a), and we will look for relationships between the SNPs in the genes mentioned above, and rsMRI measures. This research will allow us to learn more about how these genetic factors affect brain activity. We hope to use our findings from this study to inform future experiments examining the genetic basis of individual differences in other measures of excitation and inhibition.

We will use all UK Biobank participants for whom there is both genetic data and brain MRI data, and for whom we do not have data from a close genetic relative (3rd cousin or closer). The project will last 6 months in first instance.