Schizophrenia is a complex brain disease which affects around 1% of the population. The disease is characterised by hallucinations, delusions, muddled thoughts and changes in behaviour. Although many important advances have been made to try and understand, and eventually treat, schizophrenia, the underlying causes of the disease are still very poorly understood. The olfactory regions of the brain have been classically associated with processing smells. However, there is good reason to believe that olfactory regions are involved in much more than smell and are associated with the fundamental disease processes in schizophrenia. Since the early 1970's to today abnormal olfaction has been thought to be an early warning sign for schizophrenia. Olfactory regions are also connected to a number of regions thought to be involved in schizophrenia and therefore abnormal activity in olfactory would lead to changes in these target structures. Despite the potential role that altered activity of olfactory structures may play in schizophrenia relatively few studies have directly investigated this possibility.

Our previous work has identified and comprehensively studied abnormal brain activity in one brain region implicated in schizophrenia, the nucleus accumbens. Recently, we have carried out a series of pilot studies and identified that a related abnormal activity can be recorded in olfactory areas. Our initial findings, using a well-establish rodent model of schizophrenia, showed this signal may in fact be generated by specific areas in the olfactory system. The purpose of the grant proposal is to investigate this activity in more detail. In this study, we will use state-of-the-art electrodes and introduce a more advanced form of brain recording which will enable us to investigate neuronal activity in detail. We will record oscillatory activity from large groups of neurons (to provide a broad index of the pattern of activity from a neuron ensemble) and single-unit activity (to determine how individual neurons change their activity). These techniques will enable us to investigate exactly where in the brain the abnormal signals found in a model of schizophrenia are coming from and get clues about the underlying network or circuits that generate the activity. We already know that a more distant structure in the brain stem (ventral tegmental area) plays a role in the generation of the abnormal brain signals we record and the second aspect of this study is to investigate precisely how this structure influenced brain activity in olfactory regions. Some experiments will be carried out under anaesthesia.

These findings may be quite significant since it would appear that a previously unrecognized activity is generated in olfactory regions and is directly related to animal models of a brain disease. This work is a direct extension of our previous studies and will be important to others working in related fields as it should help explain and resolve competing interpretation about the generation of this abnormal brain signal. The work also has clear societal impact, since localising and understanding the ways in which abnormal brain signal are generated provides new routes for therapy. This can be by targeting previously unrecognised brain circuits or by using the abnormal signals as a biomarker of a disease state to determine the effectiveness of drug treatments.