Trauma, excessive stress, and childhood maltreatment may lead to maladaptive responsiveness to stressful situations, strongly associated with anxiety disorders and post-traumatic stress disorder (PTSD). Stress and anxiety related disorders occur both in children and adults, and their consequences include significant suffering and disability, yet only one third of the affected patients receive drug treatment, and it is estimated that only half of the cases of stress and anxiety disorders have been recognized. Importantly, anxiety disorders are the most common neuropsychiatric conditions nowadays, affecting up to 34% of the population. The core of PTSD and many anxiety disorders pathophysiology, are deficits in the processing of contextual information related to emotional memory and fear extinction. An important neuronal mechanism underlying the development of PTSD comprise impaired pattern separation, process that reduces overlap between patterns of neuronal activity representing similar experiences. Yet the mechanisms and neural circuits involved in control of anxiety remain elusive. Consequently, available therapies treat observable symptoms, rather than known neuronal mechanisms. Therefore, exploring neuronal circuits and interactions involved in the control of anxiety and stress responses is of highest importance and may lead to the development of improved treatments for related neurological and psychopathologies.

Brain structure implicated as a principal component of the circuit controlling emotional behaviour, stress response and anxiety is ventral hippocampus, and recent study indicated existence of ‘anxiety cells’ in ventral, but not dorsal hippocampus, that are activated by anxiogenic factors. At the same time, ventral, but not dorsal hippocampus is enriched with fibres containing relaxin-3 (RLN3) neuropeptide, however the origin of this innervation as well as the influence of RLN3 on hippocampal neurons remain unknow.

The main source of RLN3 in the brain in nucleus incertus (NI), highly stress sensitive structure, localised in the brainstem. It was previously shown that the NI is a key structure in contextual memory formation, but its role in shaping vHipp activity and possible involvement of NI-vHipp pathway in anxiety related behaviours remain unknown.

Therefore, to answer the question about the role NI innervation in shaping ventral hippocampus activity, in the current project, the most modern experimental techniques in neuroscience will be used, including opto- and chemogenetics and electrophysiological recordings from genetically modified animals, expressing fluorescent protein in GABAergic hippocampal neurons. Inputs to hippocampus from the NI will be analysed at the cellular, neural network and behavioural levels. It is anticipated that data from the proposed studies will contribute to a better understanding of the role of brainstem-vHipp pathway in anxiety behaviours. The proposed research studies have a high level of inherent scientific interest and will address the societal need to understand the aetiology and physiology of anxiety related disorders.