Title

Untangling the complexity of neuropeptidergic signalling in stress and anxiety

Summary

Stress and anxiety are two very common ailments of modern society. While mild forms can be relieved by non-pharmacological interventions, more severe cases require the use of drugs which, unfortunately, are still not fully effective in treating the mental conditions and have several unwanted side-effects. To develop more precise and effective therapeutic strategies, we first need to better understand the brain mechanisms responsible for regulating stress and anxiety. The goal of this project is to do so by revealing the basic principles regulating the functioning of neuronal circuits which use neuropeptidergic signalling as a way of neuronal communication.

Main text

Neuronal circuits eliciting stress responses evolved to help animals to cope with adverse environmental conditions. Responses to mild short-term stress are beneficial to the individual, since adverse physical and psychological events, known as stressors, activate adaptive reactions essential for survival, such as avoidance of potential threats. The same circuits, when not functioning properly, can also induce emergence of maladaptive behaviors. In humans, dysregulation of stress circuits is associated with debilitating psychiatric conditions, including anxiety. Better understanding of functioning of neuronal circuits controlling stress and anxiety, especially identification of common and divergent mechanisms, would not only advance our knowledge of basic principles regulating the functioning of circuits controlling defensive behavior, but also potentially contribute to the development of new therapeutic strategies to treat mental illness.

Many of the circuits controlling stress and anxiety reside in the hypothalamus, a brain structure situated very deep in the brain. Because of its difficult accessibility due to its location, it is challenging to study the role of the hypothalamus in stress in mammals. To overcome this limitation, we will use the zebrafish larva as a model organism. Zebrafish has several characteristics that make it ideal for the purpose of this project. In its larval stage, the zebrafish brain is relatively small and translucent, properties that allow us to use advanced microscopy methods to monitor and modify activity of specific groups of neurons in the hypothalamus labeled with molecular genetic techniques. Moreover, zebrafish has been used as a model to study stress and stress-related psychiatric conditions, including anxiety-like behavior, and the hypothalamic neuronal circuits and molecular pathways regulating stress responses in zebrafish are very similar to the ones present in mammals. Many of these circuits use small proteins–neuropeptides–as neurotransmitters to communicate with each other.

Our main goal is to understand how neuropeptidergic signaling in the hypothalamus modulate stress and anxiety. We will concentrate our attention on a small population of neurons producing the neuropeptide Galanin, which we previously showed to be involved in stress regulation in zebrafish. We will use these neurons as entry points to dissect the complex mechanisms regulating a neuropeptide's functions in behaviors not only important for an animal's survival, but also extremely relevant to human mental wellbeing.