Binge eating disorder (BED) is a disease characterized by recurring, often stress triggered, episodes of compulsive consuming of an unusually large quantity of highly palatable food relative to what is biologically required. The pathophysiology of BED has been linked to childhood neglect and maltreatment. BED is associated with chronic physical conditions, including obesity as well as neuropsychiatric disorders and despite the fact that eating disorders has reached epidemic proportions in today's society, the neuronal mechanisms underlying food intake abnormalities are still obscure. Binge eating behaviour may also be observed in animal models. Experimental evidence from human and animal research indicates the mesocorticolimbic dopaminergic system, which originates in the ventral tegmental area (VTA), as particularly sensitive to early life stress. Malfunctioning of the mesocorticolimbic system, which regulates motivation for food intake, is well documented in BED. An important regulatory input to VTA dopamine (DA) neurons is provided by orexin neurons of the lateral hypothalamus (LH). However, despite earlier studies highlighting an important role for aberrant DA and orexin signalling in the pathophysiology of food intake abnormalities, the cellular mechanisms underlying compulsive feeding behaviour are far from being understood.

Maternal separation (MS) of rat pups is a widely used animal model to study the mechanisms underlying the effects of early adversity on the adult organism. The proposed project is aimed at verifying the hypothesis that in rats MS stress increases the proneness of rats to acute stress-induced binge eating, through major alterations in functioning of the mesocorticolimbic system and its reactivity to orexins. We hypothesize that MS stress affects the development and activity of dopaminergic the DA system as well as the orexins signalling within the VTA and these alternations contribute to increased vulnerability to binge eating behaviour in adulthood. We also hypothesize that MS-induced dysregulation of the feeding behaviour will be ameliorated by the treatment of MS adolescent rats with a tricyclic antidepressant, imipramine.

In order to characterise the influence of maternal separation stress on acute stress induced abnormalities in feeding behaviour in later life, as well as neuronal mechanisms underlying this influence, in particular the involvement of the orexinergic and dopaminergic systems, electrophysiological, immunohistochemical and behavioural experiments will be performed.

The proposed research project will broaden the knowledge about the mechanism of early life stress related changes in functions of the mesocorticolimbic DA system and its modulation by the orexin system. We believe that the results of proposed project will constitute a basis for future research aimed at developing effective treatment of stress-related eating disorders. The proposed research studies have a high level of inherent scientific interest and will address the societal need to understand the etiology and physiology of appetite control and eating disorders.