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Maternal separation and cerebellum: a study of psychological and neuronal vulnerability to early life stress.

In 1995 the Center for Diseases Control provided strong scientific evidence that childhood adversity, i.e. emotional neglect and physical abuse, increases the risk of neuropsychiatric conditions such as anxiety and depression in adulthood (Felitti et al., 1998).

Exposure to early life stress (ELS) activates the hypothalamic-pituitary axis, which signals adrenal glands to secrete cortisol. Cortisol has widespread impacts on brain areas such as hippocampus, amygdala, and the prefrontal cortex, which play a central role in emotional responses to stress (Malave et al, 2022).

During the first 2 weeks of life in rodents a proper maternal care ensures a quiescent stress response in the pup, the so-called stress hyporesponsive period, characterized by low basal ACTH and corticosteroids levels (Čater and Majdič, 2021). Indeed, maternal separation (MS) early in life elicits a stress response in offspring that may lead to neuropsychiatric disorders.

A brain region that may be particularly vulnerable to ELS is the cerebellum as it shows the greatest increase in size of any brain region during the postnatal period. This brain structure has also a high density of glucocorticoid receptors during development and plays a critical role in mediating stress response (Pavlík and Buresová, 1984). However, only few studies have examined the effect of ELS on the cerebellum, with an MRI study reporting small cerebellar lobe volumes and reduced functional cerebellar activity children who experienced early deprivation (Bauer et al, 2009).

The aim of our PhD proposal is to examine in mice the effects of MS on cerebellum at cellular, molecular and network level using electrophysiological, imaging and molecular analyses. Behavioral tests will be also performed to assess the neuropsychiatric phenotypes in adolescent and adult MS offspring.

The analysis of cerebellar alterations associated with MS in mice might provide new insights into the neurobiological mechanisms by which ELS affects brain development resulting in altered behavior later in life.

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