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EARLY LIFE STRESS AND SOCIAL HIERARCHIES: THE ROLE OF CORTICO-STRIATAL CIRCUITS

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Background: Stressful experiences during the early life period have a critical impact in brain circuits and behaviors that persist into adulthood and may increase the risk to develop maladaptive behaviors and neuropsychiatric disorders later in life.

Aims: The major aims of this study were: 1) to understand the impact of exposure to early-life stress in social interactions and social hierarchy in adult animals and 2) to identify cellular and molecular correlates of stress-related behavior changes in the medial prefrontal cortex (mPFC).

Method: Towards these goals, and in order to mimic an environment of maternal neglect, we employed a maternal separation and unpredictable stress (MSUS) paradigm, in which mouse pups were separated daily from their dams for a 3h period, between P2 and P14, while the dams were subjected to one of two stress protocols: forced swimming or restraint.

Results: Using this paradigm, we observe that early life stress (ELS) induced a submissive phenotype in male animals inserted into a social hierarchy. These animals also displayed alterations in social recognition and foraging behavior. At the circuit level, ELS mice displayed dendritic atrophy in pyramidal neurons from layer II/III of the medial prefrontal cortex and enhanced inhibitory synaptic currents. Using RNA-seq, we identified a set of genes with altered expression in the mPFC of stressed animals. From these, our findings demonstrate that the synaptic NPY receptor 1 (NPY1R) is a marker for social subordination both in ELS animals and in lower ranked wildtype mice.

Conclusions: These data illustrate the consequences of traumatic maternal separation and provide mechanistic insight into the behavioral and molecular adaptation animals undergo in the face of adverse rearing conditions. More broadly, the adaptive behavioral strategy in animals subjected to adverse rearing conditions implicates NPY1r in dominance social behaviors, identifying this receptor and inhibitory synaptic activity as targets to better understand chronic stress and the deleterious effects of persistent social subordination.

Keywords: Social subordination, Social hierarchy, Early life stress, mPFC; NPY1r

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