Introduction

Stress is highly present and appears to be increasing in our modern and demanding society. Different studies have shown that prolonged exposure to stress, apart from affecting our health, has significant consequences in certain brain areas. Although research has been mainly focused on the impact of stress on the hippocampus, more recently the influence of chronic stress on the prefrontal cortex (PFC) has been exhaustively investigated due to its important role in cognitive and emotional processes.

The aims of this review are:
- To describe the stress-induced cellular changes in prefrontal cortical pyramidal neurons.
- To analyze the impairment of prefrontal-dependent cognitive functions induced by chronic stress.
- To study the potential implication of stress-induced changes in the PFC in the pathology of some neuropsychiatric illnesses.

Theoretical framework

Chronic stress

When the brain perceives an experience as stressful, it activates a coordinated response to cope with that challenge or stressor. This so-called stress response is crucial to adapt to the changing environment, but its prolonged activation may have negative effects on brain and many other organs.

Prefrontal cortex

The PFC, which is our most evolved brain region, constitutes the highest level of the cortical hierarchy dedicated to the representation and execution of actions.

Stress-induced cellular changes in the prefrontal cortex

Stressful experiences have a profound impact on neuronal plasticity in the PFC. The most remarkable effects occur on pyramidal neurons, which are the most abundant neuronal population of the PFC.

Changes in dendritic morphology and spine density

- Reduction of the length of apical dendrites
- Increase in dendritic branching of distal apical dendrites
- Basal dendrites remain unaffected

Prolonged stress may impact the axosomatic synaptic input into the PFC and this could be reflected in functional impairments

Changes in glutamate receptors expression

1. Exposure to chronic stress increases GC levels, enhancing the activation of GR.
2. GR activate the E3 ubiquitin ligases Fbx2 and Nedd4-1 which ubiquitinate NMDAR and AMPARs.
3. Enhancement of the proteasome-mediated degradation of these receptors.

Decreased surface expression of different subunits of glutamate receptors in the PFC:
- AMPAR: GluA1, GluA2, GluA3
- NMDAR: GluN1, GluN2A, GluN2B

Altered glutamatergic transmission can have detrimental effects on PFC-dependent functions

Stress-related mental illnesses

Stress is a well-established risk factor for the development of many neuropsychiatric illnesses, such as depression, post-traumatic stress disorder (PTSD) and anxiety disorders, among others.

PFC under chronic stress conditions

Further exploration of the relationship between altered plasticity in the PFC after stress and pathology of stress-related mental illnesses

References