

# Emerging roles of the unfolded protein response (UPR) in the nervous system: A link with adaptive behavior to environmental stress?

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### Abstract

Stressors elicit a neuroendocrine response leading to increased levels of glucocorticoids, allowing the organism to adapt to environmental changes and maintain homeostasis. Glucocorticoids have a broad effect in the body, modifying the activity of the immune system, metabolism, and behavior through the activation of receptors in the limbic system. Chronic exposition to stressors operates as a risk factor for psychiatric diseases such as depression and posttraumatic stress disorder. Among the cellular alterations observed as a consequence of environmental stress, alterations to organelle function at the level of mitochondria and endoplasmic reticulum (ER) are emerging as possible factors contributing to neuronal dysfunction. ER proteostasis alterations elicit the unfolded protein response (UPR), a conserved signaling network that re-establish protein homeostasis. In addition, in the context of brain function, the UPR has been associated to neurodevelopment, synaptic plasticity and neuronal connectivity. Recent studies suggest a role of the UPR in the adaptive behavior to stress, suggesting a mechanistic link between environmental and cellular stress. Here, we revise recent evidence supporting an evolutionary connection between the neuroendocrine system and the UPR to modulate behavioral adaptive responses.

### Keywords

**KeyWords Plus:** [ENDOPLASMIC-RETICULUM STRESS](#); [HEAT-SHOCK RESPONSE](#); [PERIPUBERTAL-JUVENILE PERIOD](#); [BOX-BINDING PROTEIN-1](#); [SYNAPTIC PLASTICITY](#); [ER STRESS](#); [TRANSLATIONAL CONTROL](#); [CAENORHABDITIS-ELEGANS](#); [IRE1-ALPHA PATHWAY](#); [PREFRONTAL CORTEX](#)

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