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Cerebrovascular hypothesis of stress-induced behavioral alterations

ABSTRACT:

Stress is a contributing factor to several mood disorders, including depression and anxiety, which are associated with significant changes in behavioral and cellular domains. Additionally, sex differences in the prevalence of these neuropsychiatric disorders are well established. Emerging evidence suggests that stress is linked to cerebrovascular diseases and that blood-brain barrier (BBB) dysfunction contributes to the development and exacerbation of neuropathology and neuroinflammation. Despite these interesting findings, very little attention has been given to the effect of both acute and chronic stress (unpredictable chronic mild stress-uCMS) on the link between behavioral and BBB alterations.
In this study, we used the open field and forced swimming tests (FST) to evaluate locomotor activity, anxiety- and depressive-like behaviors, in male and female Wistar rats. Western blotting or ELISA was used to quantify the levels of different proteins related to BBB components and neuroinflammation in the prefrontal cortex. We found that acute stress induced anxiety only in males, whereas uCMS had no effect. Additionally, acute stress decreased immobility time in the FST, pointing to a coping strategy in both sexes. In contrast, uCMS increased immobility time only in males, indicating depressive-like behavior. Additionally, both types of stress had no major impact on TNF-α, GFAP, and C3/C3aR proteins. Nevertheless, acute stress significantly reduced occludin and VEGF protein levels in both sexes, highlighting significant alterations in the neurovasculature. Concerning uCMS, there was an upregulation in claudin-5 protein levels only in females, suggesting a possible compensatory mechanism of the BBB in response to a prolonged situation of stress. In conclusion, acute and uCMS induce distinct behavioral and biochemical profiles, particularly affecting BBB proteins.

Keywords

Acute stress, Unpredictable chronic mild stress, Behaviour, Neuroinflammation, Blood-brain barrier

Published Work:

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