Microglial and neurogenic alterations in hypothalamus due to acute stress

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Microglial cells are an important glial population known to be involved in several biological processes such as stress response. These cells engage an activated state following a stress insult that may lead to nervous tissue damage, including new cell generation impairment. This has been widely studied in regions with notable neurogenesis such as de hippocampus, however, the effect in other regions with fewer yet relevant neurogenesis remains partially unknown. One of them is the hypothalamus, a key vegetative control center playing an important role in stress response. Moreover, most of the stress models studied concern neuroinflammatory and neurogenic changes due to a chronic stressor but not a single stress event. Given the repercussion of these processes alone, it would be interesting to elucidate the relationship between microglial response, hypothalamic neurogenesis, and acute stress.

Therefore, this project focuses on studying acute stressed C57BL/6J mice, both at the histological and molecular level. An intense stressor combining water immersion and movement restriction was performed. Using immunohistochemical and molecular analysis with Luminex, we could analyze microglial distribution and morphology, neurogenesis, and inflammatory environment in the hypothalamic parenchyma. Three regions related to stress were studied: the paraventricular, ventromedial and arcuate nucleus.

Results pointed to a more active microglial morphology near the Arcuate nucleus, particularly in the ventromedial region. This state was enhanced by acute stress, but not in stress priming. Regarding newborn cells, despite overall proliferation being decreased, cell survival was not significantly different. Moreover, changes in young

neuron (DCX+) presence were not observed in the aforementioned hypothalamic nucleuses but it was highly decreased in the periventricular zone. As a matter of fact, these changes were microglia-mediated according to a mediation analysis. A possible explanation to this could be the peak in IL-6 levels within the hypothalamus observed 1 h after stress treatment, which returned to basal levels after 24 h. Other inflammation chemokines were not affected, and further stress priming did not affect the parameters studied.

As a conclusion, this study supported the particularly relevant effect of acute stress in hypothalamic microglia, which leads to a reduction in cell proliferation, probably due to inflammatory chemokine release into the parenchyma.

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