Primed microglia after acute neuroinflammation may drive an enhanced stress response

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Microglial cells become activated during acute neuroinflammation and usually they return to their basal surveillant state in a few days. However, sometimes microglia evolve towards a primed state characterized by an exacerbated response to new stimuli, which may jeopardize brain functions. Here we aimed to explore microglial priming in the hypothalamus and its consequences on the neuroendocrine regulation of the stress response. To induce priming we used a model of acute ventricular neuroinflammation by intracerebroventricular (ICV) injection of the enzyme neuraminidase (NA). Three months later, an acute stressor (consisting in forced swimming) was applied to investigate the activation of the hypothalamic-pituitary-adrenal axis and the stress response elicited, as well as the inflammatory activation of hypothalamic microglial cells. Stressed rats previously injected with NA had increased plasma levels of corticosterone compared to control rats that were equally stressed but had been ICV injected with saline. Also, qPCR studies revealed that NA-treated rats presented an increased expression of the microglial marker IBA1 and of the inflammasome protein NLRP3. Concomitantly, the morphological analysis of hypothalamic microglial cells showed a morphological bias towards a slightly activated state in microglia of NA injected rats compared to those of saline injected controls. Furthermore, in the open field test NA-treated rats displayed increased locomotor activity. These results suggest that prior neuroinflammatory episodes might result in subtle but persistent changes in microglial cells that could determine the response to future challenges such as stressful events.