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21155 | Uncovering the microglia response during neonatal Group B *Streptococcus* meningitis

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Abstract

Group B *Streptococcus* (GBS) remains the most common bacterial cause of meningitis in neonates. Microglia, the brain resident immune cells, have a critical role in the development of neural circuits. However, the role of GBS infection on microglia activation and neurological sequelae remains poorly characterised. Here, we aimed to evaluate whether GBS induces changes in microglia profile during the acute phase of infection, using a mouse model that mimics key steps of GBS pathophysiology in humans. Female C57BL/6 mice were intra-vaginally inoculated with GBS during gestation, and CFU analysis was performed on postnatal days (P) 1, 3 and 5. Bacterial colonisation was found at all ages, peaking at P3. When analysing the status of microglia by flow cytometry in the whole brain of male pups at P3, an overall activation was observed in the infected group. Mainly, we found a significant increase in microglia frequency, as well as the mean fluorescence intensities (MFIs) of CD45, CD11b and F4/80. Additionally, we also analysed some microglial receptors that are important neuro-immune regulators with relevant functions during development. We observed increased CX3CR1 expression in microglia, whereas Sirpα and CD200r were not altered. Moreover, analysing the cortex and hippocampus, relevant regions for cognition, we found similar numbers in Iba1^{+} cells, a known microglia marker, in the hippocampus of infected pups. In contrast, a significant decrease was observed in the cortex, suggesting altered migration of these cells. Furthermore, microglia phagocytosis was increased in the cortex of infected pups but not in the hippocampus. Interestingly, quantification of neurons revealed a significant decrease in the hippocampus of infected pups while being increased in the cortex, compared with age-match controls. Altogether, our results show that GBS meningitis alters the neonatal microglia profile. Further studies will be necessary to better understand the microglia inflammatory state after GBS infection.

Keywords: Group B *Streptococcus*; neonatal meningitis; microglia.

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