

Peripheral infiltration and neuroinflammatory increases in the CLP + daily stress model of sepsis

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Sepsis has been increasingly linked to dementia and cognitive decline in later life. One proposed theory is that increased inflammation and immune response due to sepsis leads to blood-brain-barrier (BBB) damage and the recruitment of peripherally derived immune cells to the central nervous system (CNS). This can further increase the neuroinflammatory state of the brain and drive cognitive deficits and neurodegenerative disease development. This mechanism has been previously observed using less clinically relevant models of sepsis, such as the LPS model, however it has not been shown in clinically relevant models, such as the Cecum Ligation and Puncture (CLP) + Stress model. Using a CX3CR1^{GFP/+}/CCR2^{RFP/+} transgenic mouse, we measured peripheral infiltration using both flow cytometry and imaging techniques. We also measured the levels of proinflammatory cytokines at 7-days, 14-days, and 4-months post sepsis. The presence of CCR2+ inflammatory monocytes was increased at 7-days and 14-days post sepsis, but not long term at 4-months. Pro-inflammatory cytokines were increased at all time points when compared to navies. These findings support our hypothesis of peripheral immune cell driven inflammation; however further research must be done to identify the effects of sepsis associated changes in cognition and other neuroinflammatory changes long-term.

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