EVIDENCE OF A MYENTERIC PLEXUS BARRIER AND ITS MACROPHAGE-DEPENDENT DEGRADATION DURING MURINE COLITIS

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Neuroinflammation in the gut is associated with many gastrointestinal (GI) diseases, including inflammatory bowel disease. In the brain, neuroinflammatory conditions are associated with blood-brain barrier (BBB) disruption and subsequent neuronal injury. We sought to determine whether the enteric nervous system (ENS) is similarly protected by a physical barrier and whether that barrier is disrupted in colitis. We identified a blood-myenteric barrier (BMB) consisting of ECM proteins (agrin and collagen-4) and glial end-feet, reminiscent of the BBB, surrounded by a collagen-rich periganglionic space (PGS). The BMB is impermeable to the passive movement of 4 kDa FITC-dextran particles.

A population of macrophages is present within enteric ganglia (intraganglionic macrophages, IGMs) and exhibits a distinct morphology from muscularis macrophages (MMs), with extensive cytoplasmic vacuolization and mitochondrial swelling, but without signs of apoptosis. IGMs can penetrate the BMB in physiological conditions and establish direct contact with neurons and glia. DSS-induced colitis leads to BMB disruption, loss of its barrier integrity, and increased numbers of IGMs in a macrophage-dependent process. In intestinal inflammation, macrophage-mediated degradation of the BMB disrupts its physiologic barrier function, eliminates the separation of the intra- and extra-ganglionic compartments, and allows inflammatory stimuli to access the myenteric plexus.

This suggests a potential mechanism for the onset of neuroinflammation in colitis and other GI pathologies with acquired enteric neuronal dysfunction.