# The Impact of Gut-Brain Interactions on Brain Development in Premature Infants

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Although the gastrointestinal system and the central nervous system are not anatomically intertwined, there is a growing body of literature (Niemarkt et al., 2019; Pammi et al., 2017) suggesting that there are potent interactions between the microbiome of the gastrointestinal tract, systemic inflammation and the central nervous system. Necrotizing enterocolitis, a gastrointestinal disease of premature infants, is one such example.

Premature infants have an immature gastrointestinal tract which is susceptible to dysbiosis of the microbiome. As a consequence, a localized infectious process within the gastrointestinal system can evolve into a systemic inflammatory response and sepsis characteristic of NEC. It is well-established in the clinical literature that infants who have had NEC in the neonatal period are at an increased risk of neurodevelopmental impairment (Niemarkt et al., 2019). NEC results in white matter changes on brain imaging of these patients as well. Although several inflammatory markers and receptors, such as IL-6 and the toll-like receptor family, have been identified as mediators in this cascade, it is unclear exactly how they affect neuronal development to cause future cognitive issues.

While the gastrointestinal and inflammatory aspects of NEC have been studied in animal models, the brain-gut-inflammatory axis has just started to be explored. Gastrointestinal inflammation results in decreased neuronal density within the hippocampus more than cortical regions. This proposal would augment this knowledge base by examining the neuronal changes seen in the hippocamps of a murine model of NEC. Specifically, we will be i) examining which specific neuronal populations are affected by NEC ii) evaluating how these changes affect the physiological function and health of these neurons.