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ENTERIC NERVOUS SYSTEM

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Enteric Nervous System (ENS) is a system of neurons and glia cells located in the gastrointestinal tract, it is a part of the PNS that can work independently without the help of the CNS, nevertheless it can also communicate with the CNS bidirectionally via vagus nerve, sympathetic nerves and spinal nerves, hormonal and immune pathways (Dowling L. et al., 2022). ENS has 2 layers of ganglia: myenteric plexus (in the muscularis externa) and the Meissner's plexus (in the submucosa). Neurogastroenterology describes that myenteric plexus is mostly involved in control of motility including peristalsis and mixing, whereas Meissner's plexus regulates secretion, local mucosal functions and transmucosal fluid movement. Both plexuses contain sensory and motor neurons, also are interconnected via interneurons enabling local enteric reflexes.

CNS and ENS controls different areas of the GI tract at different levels. CNS through vagal afferent neurons mainly monitors the contractile activity, acid secretion and adjusts motility. By vago-vagal reflexes CNS determines movements of striated muscles of the esophagus, it also maintains defecation through spinal pathways to lumbosacral defecation centers (Furness J.B et al., 2014.). However, research also says that removal of vagal, sympathetic or voluntary connections is not life threatening.

ENS disorders can arise due to defects in development, due to infectious origin, dysfunction in neuroimmune system or neurodegenerative changes. Such disorders could be Hirschsprung disease, Chagas disease, esophageal achalasia and gastroparesis, inflammatory bowel disease and colorectal cancer (Holland A. et al., 2021). It has been found that there are vascular endothelial growth factor (VEGF) receptors in enteric neurons which can provide protective and regenerative effect for neurons, thereby these receptors may prevent neuronal damages (Hecking I. et al., 2022). This signalling can be regarded as a survival and neurovascular support pathway and aid in recovery from the above given disorders. A new scientific discovery shows that Varicella Zoster Virus (VZV) may remain hidden in ENS, and when reactivated, since there is no connection between ENS and skin innervation, they go to surrounding gut and cause painful enteric zoster, also causing meningitis and stroke, due to gut-brain axis (Rao, M., Gershon, M.D., 2016).

It was revealed that long-chain unsaturated free fatty acids (LUFFAs) from enterobacteria or diet show a chemosensory effect activating free fatty acid receptor (FFAR1/4) on nitrergic myenteric ganglia, causing calcium-dependent release of nitric oxide causing the relaxation of the smooth muscles, independent of signals from the epithelium (J. Zhang et al., 2025).

ENS also includes glial cells which play neuromodulator, immunomodulatory, provide support, modulate synaptic signalling for regulation of diverse gastrointestinal disease processes. Moreover, glial cells communicate with immune cells to maintain gastrointestinal immune homeostasis. Interaction between enteric glia and cancer stem cells regulates tumorigenesis, can modulate inflammation causing dysfunction for a long period (Seguella L. et al., 2021) These cells resemble astrocytes.

Enteroendocrine cells and the ENS serve as contributors to help interaction between gut microbiota and CNS. There's emerging evidence that microbiota has an important role in gut-brain signalling with the help of steroids (So S., 2021). Research shows that disruption of the intestinal microbiota is linked not only to diseases in the gut but also to brain symptomatology, including neurodegenerative and behavioural disorders like Parkinson disease, Alzheimer disease, autism, anxiety, and depression.

ENS is vital for life as it can autonomically control and regulate motility, secretion, blood flow, nutrient absorption and immunity of the gut. Recent work also focuses on disease treatment by exploring the natural role of ENS stem cells and investigating their potential therapeutic uses.