The Microbiome: A Key Regulator of the Gut-Brain Axis in Visceral Pain

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A growing body of preclinical and clinical evidence supports a relationship between the complexity and diversity of the microorganisms that inhabit our gut and health status. Under normal homeostatic conditions this microbial population helps maintain intestinal peristalsis, mucosal integrity, pH balance, immune priming and protection against invading pathogens. Furthermore, these microbes can influence centrally regulated emotional behaviour through mechanisms including microbially derived bioactive molecules (amino acid metabolites, short-chain fatty acids, neuropeptides and neurotransmitters), mucosal immune and enteroendocrine cell activation, as well as vagal nerve stimulation. The microbiota-gut-brain axis comprises a dynamic matrix of tissues and organs including the brain, autonomic nervous system, glands, gut, immune cells and gastrointestinal microbiota that communicate in a complex multidirectional manner to maintain homeostasis and resist perturbation to the system. Changes to the microbial environment, as a consequence of illness, stress or injury, can lead to a broad spectrum of physiological and behavioural effects locally including a decrease in gut barrier integrity, altered gut motility, inflammatory mediator release as well as nociceptive and distension receptor sensitisation. Centrally mediated events including hypothalamic-pituitary-adrenal (HPA) axis, neuroinflammatory events and neurotransmitter systems are concomitantly altered. Thus, both central and peripheral pathways associated with pain manifestation and perception are altered as a consequence of the microbiota-gut-brain axis imbalance. In this lecture the involvement of the gastrointestinal microbiota in visceral pain will be discussed focusing on the anatomical and physiological nodes whereby microbiota may be mediating pain response, and address the potential for manipulating the microbiome as a therapeutic target for visceral pain disorders such as Irritable Bowel Disorder.