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The Role of Intestinal Distension in Shaping Neuronal Activity in the Enteric Nervous System of Adult Mice

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Abstract

The Enteric Nervous System (ENS) plays a pivotal role in governing the motor, secretory, and defensive functions of the gastrointestinal tract. These enteric neurons intricately process both mechanical and chemical cues from the gut lumen, translating them into intricate motor responses. However, the precise manner in which intact enteric neural networks react to shifts within the gut environment remains a puzzle. To unravel this enigma, we conducted live-cell confocal recordings, capturing intracellular calcium activity in neurons extracted from intact portions of mouse intestine. Our aim was to investigate how neurons respond to various luminal mechanical and chemical stimuli. Utilizing specialized Wnt1, ChAT, and Calb1-GCaMP6 mice, we focused on neurons residing in the jejunum and colon. Our experimental design encompassed an examination of neuronal calcium responses triggered by diverse stimuli, including KCl (75 mM), veratridine (10 μM), 1,1-dimethyl-4-phenylpiperazinium (DMPP; 100 μM), and luminal nutrients (Ensure®), all under conditions of either intraluminal distension or its absence. The outcomes were particularly intriguing: in both the jejunum and colon, the presence of luminal content (chyme in the jejunum and faecal pellets in the colon) induced distension, rendering the underlying enteric circuit unresponsive to depolarizing stimuli. Notably, in the distal colon, heightened levels of distension displayed an inhibitory effect on neuronal reactions to KCl. Moreover, intermediary distension levels orchestrated a reconfiguration of Ca^{2+} responses, particularly influencing the circumferential propagation of slow waves. Our experimentation also revealed the key role of mechanosensitive channels; the inhibition of these channels effectively suppressed distension-induced Ca^{2+} elevations. Furthermore, we uncovered that inhibiting calcium-activated potassium channels restored neuronal responses to KCl in the distended colon, but not to DMPP. In a novel discovery, distension in the jejunum halted a tetrodotoxin-resistant neuronal response to luminal nutrient stimulation. In summation, our findings demonstrate that intestinal distension operates as a regulator of ENS circuit excitability, with mechanosensitive channels acting as key mediators. The dynamic interplay between physiological levels of distension and neural synchronicity or suppression showcases the ENS's ability to fine-tune its responses based on the gut's luminal content.

Keywords: Gastrointestinal tract • Neuronal activation • Luminal nutrients

Introduction

The intricate network of neurons that resides within the walls of the gastrointestinal tract, known as the Enteric Nervous System (ENS), plays a vital role in regulating various digestive processes. Recent research has shed light on a fascinating phenomenon: intestinal distension, or the stretching of the gut wall due to food intake, can orchestrate intricate patterns of neuronal activity within the ENS of adult mice. This newfound understanding has the potential to revolutionize our comprehension of gut-brain communication and its implications for overall digestive health. The enteric nervous system is often referred to as the "second brain" of the body due to its remarkable complexity and autonomy. Comprising hundreds of millions of neurons, the ENS forms an elaborate network throughout the entire gastrointestinal tract, from the esophagus to the anus. This intricate system operates independently from the Central Nervous System (CNS) and is responsible for regulating essential functions such as peristalsis, nutrient absorption, and the secretion of digestive enzymes.

Recent studies have highlighted the pivotal role that intestinal distension plays in shaping neuronal activity within the ENS of adult mice. When food enters the gastrointestinal tract, the stretching of the intestinal walls triggers a cascade of intricate signaling events that culminate in orchestrated patterns of neuronal firing. This process is akin to a symphony, with different types of neurons "playing" their roles in response to the mechanical stimulus of distension [1-3].

Literature Review

Neuronal pathways and signaling cascades

Researchers have identified a range of neuronal pathways and signaling molecules that are crucial in mediating the effects of intestinal distension on the enteric nervous system. Among these, mechanoreceptors embedded within the gut wall play a pivotal role in detecting mechanical stretching. These mechanoreceptors send signals to the ENS, which then orchestrates a complex interplay of excitatory and inhibitory signals among different types of neurons [4].

Discussion

Neuronal plasticity and adaptation

One intriguing aspect of this phenomenon is the concept of neuronal plasticity within the enteric nervous system. Neurons have the remarkable ability to adapt and modify their connections in response to changes in the environment or stimuli. Intestinal distension appears to trigger a form of plasticity within the ENS, allowing it to fine-tune its responses to various levels of mechanical stretching. This adaptability may be essential for optimizing digestive processes and ensuring efficient nutrient absorption [5].

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Implications for digestive health

The discovery of the role of intestinal distension in orchestrating neuronal activity within the enteric nervous system has significant implications for digestive health and disease. Dysfunctions in the ENS have been linked to various gastrointestinal disorders, including irritable bowel syndrome, constipation, and gastroesophageal reflux disease. Understanding how mechanical stimuli influence neuronal activity could provide valuable insights into the underlying mechanisms of these conditions and potentially lead to novel therapeutic strategies [6].

Conclusion

The intricate world of cellular physiology is a fascinating realm that underlies the functioning of all living organisms. From the structural components that make up a cell to the complex processes within, the understanding of cellular physiology enables us to comprehend the mechanisms that govern life itself. By unraveling the energy production, cellular communication, and regulation mechanisms, scientists continue to deepen their knowledge of cells, opening doors to new discoveries and advancements in fields such as medicine and biotechnology. As we uncover the secrets of the microscopic world, we gain a greater appreciation for the remarkable complexity and ingenuity of life at its most fundamental level. The intricate field of cellular physiology unravels the mysteries of life at the microscopic level. Understanding how cells function and interact provides insights into the mechanisms that govern our bodies' overall health and well-being. From the structural components of cells to the processes that enable energy production, cellular communication, and regulation, cellular physiology serves as a foundation for advancements in medical research, biotechnology, and our overall understanding of life itself. As we continue to explore the marvels of cellular physiology, we gain a deeper appreciation for the complexity and elegance of the microscopic world that sustains us.

Acknowledgement

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Conflict of Interest

None.

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