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The Interaction between Neurological and Immune Systems in Food Allergy: Examining Enteric Neurons and Mucosal Mast Cells

Georgios C Papadopoulos*

Institute of Clinical Neurobiology, Innsbruck Medical University, USA

Abstract

The nervous system and the immune system individually play important roles in regulating the processes necessary to maintain physiological homeostasis, respond to acute stress and protect against external threats. These two regulating systems for maintaining the living body had often been assumed to function independently. Allergies develop as a result of an overreaction of the immune system to substances that are relatively harmless to the body, such as food, pollen and dust mites. Therefore, it has been generally supposed that the development and pathogenesis of allergies can be explained through an immunological interpretation. Recently, however, neuro-immune crosstalk has attracted increasing attention. Consequently, it is becoming clear that there is close morphological proximity and physiological and pathophysiological interactions between neurons and immune cells in various peripheral tissues. Thus, researchers are now beginning to appreciate that neuro-immune interactions may play a role in tissue homeostasis and the pathophysiology of immune-mediated disease, but very little information is available on the molecular basis of these interactions. Mast cells are a part of the innate immune system implicated in allergic reactions and the regulation of host–pathogen interactions. Mast cells are ubiquitous in the body, and these cells are often found in close proximity to nerve fibers in various tissues, including the lamina propria of the intestine. Mast cells and neurons are thought to communicate bidirectionally to modulate neurophysiological effects and mast cell functions, which suggests that neuro-immune interactions may be involved in the pathology of allergic diseases.

Keywords: Enteric nervous system; Food allergy; Mucosal mast cell; Neuro-immune crosstalk; Sensory neuron

Introduction

Food allergies have become a growing concern worldwide, affecting millions of individuals across all age groups. The prevalence of food allergies has been on the rise, and scientists are constantly seeking a better understanding of the intricate mechanisms underlying these reactions. Recent research has shed light on the fascinating interplay between the nervous system and the immune system, specifically in the context of food allergies. This article explores the phenomenon of neuro-immune crosstalk, with a particular focus on the role of enteric neurons and mucosal mast cells [1-3].

The gut-brain connection

The gut, often referred to as the "second brain" due to its complex and independent nervous system, plays a pivotal role in our overall health. Enteric neurons, which are found within the walls of the gastrointestinal tract, form an intricate network that controls various aspects of digestion, including motility, secretion, and absorption. These neurons communicate with the central nervous system (CNS) but also function autonomously to regulate local gut functions. Enteric neurons are equipped with receptors and sensory fibers that can detect changes in the gut environment, including the presence of allergenic food particles. This local sensing capability is critical for maintaining gut homeostasis and responding to potential threats, such as food allergens.

Mucosal mast cells in food allergy

Mucosal mast cells, found throughout the gastrointestinal tract's mucosal lining, are key players in the immune response to food allergens. These specialized immune cells contain granules loaded with histamine and other mediators that are released when the cells are activated. In the context of food allergies, mucosal mast cells play a central role in initiating and amplifying the allergic response [4]. When a person with a food allergy ingests an allergenic substance, the immune system identifies it as a threat and triggers the release of immunoglobulin E (IgE) antibodies specific to that allergen. These IgE antibodies then bind to the surface of mucosal mast cells, sensitizing them to the allergen.

Neuro-immune crosstalk in food allergy

Recent research has revealed that enteric neurons can directly influence the behavior of mucosal mast cells in response to allergenic substances. This neuro-immune crosstalk occurs through several mechanisms:

Neurotransmitter release: Enteric neurons release neurotransmitters, such as acetylcholine, neuropeptide Y, and substance P, that can influence mucosal mast cell activation. These neurotransmitters bind to receptors on mast cells and modulate their responses.

Nerve fiber proximity: The close proximity of enteric nerve fibers to mucosal mast cells allows for rapid communication. Nerve fibers can detect allergen exposure and release signaling molecules that trigger mast cell activation.

***Corresponding author:** Georgios C Papadopoulos, Institute of Clinical Neurobiology, Innsbruck Medical University, USA, Phone: 1187421953230; E-mail: Georgios C Papadopoulos @gmail.com

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Nervous system control: The enteric nervous system can modulate gut motility, permeability, and blood flow, all of which can influence the rate at which allergenic food particles are exposed to mucosal mast cells. This control can either exacerbate or dampen the allergic response.

Immune system in the intestine

The intestinal mucosa serves crucial physiological functions, including digestion, absorption, and secretion. To accommodate these dynamic roles, the mucosal surface features a delicate and permeable barrier composed of a monolayer of epithelial cells. Notably, the mucosal lining boasts the most extensive surface area of any organ in the body, dwarfing even the skin's surface by approximately 200 times. This expansive and vulnerable mucosal surface acts as a critical interface between the host organism and the external environment. Consequently, it represents the primary gateway for potential pathogen infiltration. The interaction between the nervous system and the immune system in peripheral tissues is a complex and finely tuned relationship. It involves a network of communication and regulatory mechanisms that allow the two systems to coordinate their responses to various challenges and threats in the body. This interaction plays a crucial role in maintaining homeostasis and responding to infections, injuries, and other immune-related events. Here's an overview of the key aspects of this interaction:

Neurotransmitters and immune cells: Neurotransmitters and neuropeptides released by nerves can directly influence immune cells within peripheral tissues[5-7]. For example, nerve endings can release substances like norepinephrine and acetylcholine, which can bind to receptors on immune cells. This interaction can modulate the activation and behavior of immune cells.

Innervation of lymphoid tissues: Peripheral tissues, including lymphoid organs like the spleen and lymph nodes, are innervated by autonomic nerves (sympathetic and parasympathetic). Nerve fibers in these tissues can release neurotransmitters that affect the immune responses occurring in those areas.

Immune responses to stress: The nervous system's stress response, often referred to as the "fight-or-flight" response, can impact immune function in peripheral tissues. Stress hormones like cortisol and adrenaline can suppress certain immune responses while enhancing others, depending on the context.

Pain and inflammation: Nerve endings in peripheral tissues can sense and transmit pain signals to the central nervous system in response to inflammation or tissue damage. This helps alert the body to potential threats and initiates appropriate immune responses.

Neuro-immune reflexes: Some peripheral tissues exhibit neuro-immune reflexes, where sensory nerves detect tissue damage or infection and trigger local immune responses. This is a rapid and localized way of coordinating immune defense.

Immune-mediated nerve damage: In certain autoimmune diseases, the immune system can mistakenly target and damage peripheral nerves. This can lead to conditions like Guillain-Barré syndrome or chronic inflammatory demyelinating polyneuropathy, where the immune system's actions directly affect the nervous system.

Neuroendocrine communication: The hypothalamus-pituitary-adrenal (HPA) axis and the hypothalamus-pituitary-thyroid (HPT) axis are part of the neuroendocrine system. They can influence immune responses by releasing hormones like cortisol and thyroid hormones, which have immunomodulatory effects on peripheral tissues.

Peripheral neuropathies: Certain infections or inflammatory conditions can lead to peripheral neuropathies, where damage to nerves in peripheral tissues occurs. This can disrupt the normal interaction between the nervous and immune systems in these regions.

Therapeutic interventions: Researchers are exploring ways to harness the interaction between the nervous and immune systems for therapeutic purposes. For example, neuromodulation techniques, like vagus nerve stimulation, are being investigated for their potential to modulate inflammatory responses in conditions like rheumatoid arthritis and inflammatory bowel disease.

In summary, the interaction between the nervous system and the immune system in peripheral tissues is a dynamic and intricate process that has far-reaching implications for health and disease. Understanding this interplay is essential for developing therapies that target both systems to effectively treat a wide range of conditions, from autoimmune diseases to chronic inflammatory disorders [8]. In response to this constant threat from pathogens, the mucosal immune system has evolved into the largest and most intricate immune system within the body. Remarkably, it houses roughly 70% of the body's immune cells, forming a formidable defense against invading pathogens.

Implications for food allergy research and treatment

Understanding the intricate crosstalk between enteric neurons and mucosal mast cells in the context of food allergies has significant implications for research and treatment strategies:

Targeted therapies: Researchers are exploring ways to manipulate this neuro-immune crosstalk to develop targeted therapies for food allergies. Modulating the activity of enteric neurons or mucosal mast cells could potentially reduce allergic reactions.

Early intervention: Identifying the early signals of a food allergy response, which may involve enteric neurons, could lead to earlier intervention strategies that prevent severe allergic reactions.

Gut health: Maintaining a healthy gut environment, including the balance of enteric neurons and mucosal mast cells, may be essential in preventing food allergies from developing in the first place.

Conclusion

The intricate interplay between the nervous system and the immune system, specifically involving enteric neurons and mucosal mast cells, holds promise in unlocking new insights into the mechanisms of food allergies [9,10]. This knowledge has the potential to revolutionize food allergy research and treatment, offering hope to the millions of individuals living with this condition and their families. As our understanding of neuro-immune crosstalk continues to grow, so too does our ability to develop more effective strategies for managing and eventually preventing food allergies.

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