What are the relationships between Sensory Processing Differences and Innate and/or Adaptive Immunity?

Sensory neurons bidirectionally regulate innate and adaptive immunity, while sensory processing differences in ASD link to immune dysregulation

Sensory neurons detect pathogens, allergens, and tissue damage through ion channels and pattern recognition receptors, then release neuropeptides that directly modulate immune cell function — establishing a bidirectional neuroimmune axis (Foster et al., 2017; Kim & Artis, 2025; Crosson et al., 2025). In parallel, sensory processing differences in autism spectrum disorder (ASD) co-occur with chronic innate immune dysregulation and adaptive immune abnormalities, suggesting shared neurodevelopmental pathways (Leisman et al., 2026; Hughes et al., 2022; Leisman et al., 2026).

Sensory Neuron Modulation of Innate Immunity

Sensory neurons activate or suppress innate host defense in a tissue- and pathogen-dependent manner, with seemingly paradoxical effects that depend on local microbial and inflammatory cues (Deng et al., 2024; Saraiva-Santos et al., 2024). *Staphylococcus aureus* directly activates sensory neurons via N-formylated peptides and pore-forming toxins, triggering pain and modulating downstream immune responses (Kim & Artis, 2025). Distinct sensory neuron subtypes — such as TRPV1+ and Mrgprd+ populations — differentially regulate immune cells in the skin, demonstrating functional specialization (Deng et al., 2024; Crosson et al., 2025).

- Sensory neurons suppress neutrophil-mediated bacterial and fungal clearance during acute single-dose infections by inhibiting **Th1 and Th17 cytokine release** (Aguilar et al., 2024).
- Calcitonin gene-related peptide (CGRP) and substance P act on multiple innate immune cell types — including macrophages, dendritic cells, and mast cells — to shape inflammatory outcomes across tissues (Kim & Artis, 2025; Deng et al., 2024; Crosson et al., 2025).
- Nociceptors drive **type 2 but not type 1** adaptive immunity in airway inflammation models, illustrating context-dependent neuroimmune regulation (Foster et al., 2017).

Sensory Neuron Regulation of Adaptive and Humoral Immunity

Sensory neurons are required for B-cell recruitment and antibody production in both bacterial infection and allergic asthma models, with the specific neuropeptide released determining the downstream immunoglobulin class (Aguilar et al., 2024). During *Streptococcus pneumoniae* infection, sensory neurons preferentially release vasoactive intestinal polypeptide (VIP), which stimulates plasma cells via the VIP1 receptor to promote IgG production and neutrophil activation (Aguilar et al., 2024). Conversely, during allergic asthma, sensory neurons release substance P, which drives IgE production and eosinophilic and mast cell responses (Aguilar et al., 2024).

Immune Stimulus	Neuropeptide Released	Target Cells	Antibody/Outcome
S. pneumoniae infection	VIP	B cells, plasma cells (VIP1R)	↑ IgG, ↑ neutrophil activity (Aguilar et al., 2024)
Alternaria asthma	Substance P	B cells, ILC2s, DCs	↑ IgE, ↑ eosinophilia (Aguilar et al., 2024)

Immune Stimulus	Neuropeptide Released	Target Cells	Antibody/Outcome
Acute bacterial/fungal (single-dose)	Various	Th1, Th17 cells	↓ Cytokine release, ↓ neutrophil clearance (Aguilar et al., 2024)
Papain allergen (skin)	Substance P	Dermal DC2s (MRGPRA1)	Th2 priming, cutaneous inflammation (Deng et al., 2024)

FIGURE 1 Stimulus-dependent neuropeptide release by sensory neurons and their differential effects on adaptive immune outcomes.

Depletion of sensory neurons reduces B-cell populations and antibody levels in both infection and allergy models, confirming their necessity for humoral immunity (Aguilar et al., 2024). B cells express neurotransmitter receptors for substance P, VIP, noradrenaline, and neuropeptide Y, and select neuropeptides can induce IgE, IgG, and IgA release in vitro (Aguilar et al., 2024).

Sensory Processing Differences and Immune Dysregulation in ASD

Atypical sensory processing — encompassing hyperresponsivity, hyporesponsivity, and sensory-seeking behaviors — is a core feature of ASD, affecting 82–97% of autistic individuals across multiple sensory modalities (Leisman et al., 2026; Dellapiazza et al., 2018; Kojovic et al., 2019). Chronic low-grade systemic inflammation and neuroinflammation have emerged as key pathophysiological mechanisms underlying sensory dysregulation in ASD, with meta-analyses showing persistent elevations of pro-inflammatory cytokines (IL-6, IL-1β, TNF-α, IFN-γ) alongside reduced anti-inflammatory mediators (IL-10, IL-1Ra) (Vergara Serpa & Verbel, 2026; Hughes et al., 2022).

These inflammatory alterations are associated with **central sensory network dysfunction** and peripheral sensory receptor sensitization, constituting the neurobiological substrate of sensory crises (Vergara Serpa & Verbel, 2026). Blood-brain barrier disruption, microglial pro-inflammatory activation, and reactive astrogliosis further compound excitatory-inhibitory imbalance linked to sensory processing atypicalities (Vergara Serpa & Verbel, 2026; Hughes et al., 2022). A proposed psychoneuroimmunoendocrine model integrates chronic neuroinflammation and dysautonomia as central organizing axes of the sensory phenotype in ASD (Vergara Serpa & Verbel, 2026).

Adaptive immune abnormalities also contribute to ASD phenotypic variability: Th17 cells and elevated IL-17A are associated with symptom severity, while B-cell autoantibody generation and altered mucosal immunity suggest disrupted immune-neural interactions in ASD subgroups (Leisman et al., 2026). Functional polymorphisms in macrophage migration inhibitory factor (MIF), which affects both innate and adaptive immunity, have been associated with ASD severity (Leisman et al., 2026). Maternal immune activation during gestation produces ASD-like behavior and altered innate immune function in offspring, linking prenatal immune perturbation to downstream sensory and neurodevelopmental differences (Hughes et al., 2022; Leisman et al., 2026).

Synthesis and Caveats

The evidence spans two largely distinct literatures: mechanistic animal studies demonstrating that sensory neurons directly regulate innate and adaptive immune cells via stimulus-dependent neuropeptide release, and clinical research linking sensory processing differences in ASD to systemic immune dysregulation. The former establishes causal circuitry; the latter is predominantly associative, with most human findings derived from observational and cross-sectional designs (Leisman et al., 2026; Dellapiazza et al., 2018). Whether the neuroimmune mechanisms identified in peripheral tissues directly account for sensory processing differences in neurodevelopmental conditions remains an open question, and the field would benefit from studies bridging these two levels of analysis.

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