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How the nervous system generates sensory and motor perception: linking peripheral detection, axonal cytoskeletal dynamics, and cortical representation

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Abstract

Sensory and motor perception arise from a structurally continuous and functionally integrated system that connects peripheral stimulus detection to cortical interpretation and adaptive behavior. Peripheral receptors convert physical and chemical stimuli into electrical signals that propagate along long sensory axons. The structural stability and functional reliability of these axons depend on microtubule-based cytoskeletal organization and efficient axonal transport. Dynamic regulation of microtubules and tubulin post-translational modifications sustains mitochondrial positioning, membrane turnover, and conduction fidelity. When cytoskeletal integrity is compromised, axonal transport becomes inefficient, distal axons destabilize, and ascending sensory transmission deteriorates. Signals are subsequently integrated within spinal and thalamic circuits before reaching somatotopically organized cortical maps that shape perception and motor output. Chemotherapy-induced peripheral neuropathy exemplifies how cytoskeletal perturbation can propagate from molecular dysfunction to systems-level sensory distortion, highlighting cytoskeletal integrity as a fundamental determinant of perceptual reliability.

Key words: Peripheral nervous system; sensory perception; axonal transport; neuronal cytoskeleton; cortical representation

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Introduction

Understanding how the nervous system transforms physical stimuli into meaningful perception and coordinated motor responses remains a central challenge in neuroscience. Sensory and motor functions are often studied at distinct anatomical or conceptual levels, molecular, cellular, circuit, or cortical, yet in reality they represent a continuous and interdependent biological process. Dissecting this continuum requires an integrative framework that connects peripheral receptor biology, axonal structural integrity, ascending pathway organization, cortical representation, and adaptive behavior. In this mini review, we examine how sensory and motor perception emerge from the coordinated interaction of these levels, with particular emphasis on the role of cytoskeletal dynamics and axonal transport as foundational determinants of systems-level integrity. By bridging molecular mechanisms with circuit organization and cortical processing, we propose a unified model explaining how sensation becomes perception, recognition, and action, and how disruption at any level can destabilize the entire sensory axis.

Perception as a Multilevel Systems Process. Sensory perception is frequently framed as a cortical achievement. Yet the fidelity of perception depends on a distributed and hierarchically organized system that begins in the periphery, is sustained by cytoskeletal-dependent axonal transport, and culminates in cortical interpretation and adaptive behavior. Perception is not generated by the brain in isolation; it emerges from the structural and functional continuity of a neurobiological axis extending from receptor membranes to cortical maps. The nervous system is organized into central and peripheral components. The central nervous system (CNS), comprising brain and spinal cords integrates and interprets incoming signals. The peripheral nervous system (PNS) forms the interface with the external and internal environment, detecting stimuli and transmitting encoded information centrally. Critically, the PNS lacks the structural protection afforded to the CNS and is directly exposed to systemic metabolic, inflammatory, and toxic influences. This vulnerability is amplified by the unique architecture of peripheral sensory neurons, many of which extend axons over extraordinary distances. The preservation of sensory fidelity therefore depends on the integrity of these long projections and the molecular machinery that sustains them. Understanding how sensation becomes perception requires integrating three interdependent domains: receptor specialization, cytoskeletal regulation of axonal transport, and cortical representation.

Peripheral Detection: Receptor Diversity as the Basis of Sensory Coding

All sensory processing begins with receptor transduction. Peripheral receptors convert mechanical, thermal, chemical, or photonic energy into electrical signals through modality-specific ion channels. Mechanoreceptors detect forces such as touch, vibration, and stretch, thermoreceptors respond to temperature changes, chemoreceptors monitor chemical composition in external and internal environments, photoreceptors transduce light, and nociceptors respond to potentially damaging stimuli. Receptors can also be categorized anatomically as exteroceptors, which monitor the external world, interoceptors, which survey internal physiological conditions, and proprioceptors, which encode body position and movement. Structurally, sensory receptors range from simple free nerve endings to specialized encapsulated corpuscles. Mechanoreceptors such as Merkel complexes, Meissner and Pacinian corpuscles, Ruffini endings, and proprioceptive organs including muscle spindles and Golgi tendon organs together encode tactile forces, vibration, stretch, and body position. Regions such as the fingertips contain particularly high densities of mechanoreceptors, a specialization reflected centrally by enlarged cortical representation. However, receptor diversity alone does not ensure perceptual accuracy. The transition from detection to perception requires the structural continuity of ascending pathways, a continuity fundamentally sustained by the neuronal cytoskeleton.

Cytoskeletal Architecture and Axonal Transport: The Structural Core of Sensory Integrity

Peripheral sensory neurons are among the most structurally demanding cells in the body. Their long axons must maintain metabolic stability, membrane composition, and excitability over great distances. This is made possible by axonal transport, a microtubule-dependent system that distributes essential cargo between soma and terminals. Microtubules form polarized tracks along which kinesin and dynein motor proteins transport mitochondria, ion channels, synaptic vesicle precursors, and trophic signals. Tubulin post-translational modifications, including detyrosination, Δ2-tubulin formation, and polyglutamylation, regulate motor protein affinity and microtubule stability. In this way, cytoskeletal dynamics directly influence transport efficiency. Axonal transport is not ancillary to sensory processing; it is foundational. Proper mitochondrial positioning ensures ATP availability for maintaining ion gradients and action potential propagation. Continuous renewal of membrane proteins preserves receptor responsiveness. Retrograde transport conveys survival signals to the soma. When microtubule integrity is compromised, transport becomes inefficient, leading to distal axonal degeneration, altered conduction velocity, and corrupted signal timing. Thus, cytoskeletal stability represents a systems-level determinant of sensory reliability. Without it, ascending sensory transmission cannot preserve temporal and spatial fidelity, and cortical interpretation becomes based on degraded input.

Ascending Pathways and Cortical Interpretation

After successful peripheral transmission, sensory signals ascend through spinal and brainstem circuits to the thalamus, which functions as a critical relay and gating hub. From there, information is conveyed to primary somatosensory cortex, where somatotopic organization, the sensory homunculus, provides a spatially ordered representation of the body. Cortical magnification reflects receptor density and behavioral importance rather than anatomical size. In humans, the hands and face occupy extensive cortical territory. In rodents, whisker representation dominates sensory cortex. In primates, forelimb representation is expanded. Across species, cortical organization mirrors ecological demands, underscoring that perception is shaped by evolutionary pressures acting on both peripheral and central systems. Cortical maps are dynamic. Altered peripheral input can drive reorganization, demonstrating that cortical representation depends on the integrity of ascending transmission.

From Sensation to Recognition and Action

Sensation represents the initial encoding of stimuli at receptor and afferent levels. Perception arises when ascending signals are organized into conscious experience. Recognition assigns meaning through integration with memory and top-down processing. Visual illusions reveal that

identical sensory input can produce different perceptual outcomes depending on cortical interpretation, highlighting that perception is constructive. Once recognized, stimuli guide action. Somatic motor pathways generate voluntary movement and reflexes. Autonomic pathways regulate visceral responses. Accurate behavioral output depends on the fidelity of upstream sensory coding. Disruption at any level, receptor, axon, synapse, circuit, or cortex, alters this continuum.

Peripheral Neuropathies as Models of Cytoskeletal and Metabolic Vulnerability: Chemotherapy and Diabetes

Peripheral neuropathies provide powerful translational models illustrating how molecular and metabolic perturbations destabilize the entire sensory axis. Among these conditions, chemotherapy-induced peripheral neuropathy (CIPN) and diabetic peripheral neuropathy (DPN) represent two clinically prevalent and mechanistically informative disorders that affect both humans and animal species. Although distinct in etiology, one pharmacologically induced, the other metabolically driven, both converge on a common pathophysiological pathway centered on cytoskeletal disruption, impaired axonal transport, and distal axon degeneration. CIPN arises from exposure to microtubule-targeting agents such as paclitaxel and vincristine, which directly perturb microtubule polymerization dynamics, or platinum compounds such as oxaliplatin, which induce mitochondrial dysfunction and oxidative stress that secondarily disrupt cytoskeletal organization. Because peripheral sensory neurons rely heavily on microtubule-dependent axonal transport to maintain distal axonal integrity, even subtle perturbations of microtubule stability can produce profound length-dependent degeneration. The resulting “dying-back” neuropathy reflects the high transport demand imposed by long sensory axons. Animal models of CIPN reproduce characteristic clinical features, including mechanical allodynia, thermal hypersensitivity, and cold intolerance, and demonstrate microtubule disorganization, altered tubulin post-translational modification profiles, mitochondrial trafficking deficits, and reduced intraepidermal nerve fiber density. Similarly, diabetic peripheral neuropathy, one of the most common complications of metabolic disease in both humans and companion animals, exemplifies how chronic hyperglycemia and metabolic dysregulation compromise axonal integrity. In humans, DPN is characterized by progressive sensory loss, dysesthesia, and pain, often following a distal symmetrical pattern. In veterinary medicine, diabetic neuropathy is well documented in cats and increasingly recognized in dogs. At the molecular level, hyperglycemia induces oxidative stress, mitochondrial dysfunction, advanced glycation end-product accumulation, and microvascular impairment. These metabolic stressors destabilize cytoskeletal organization and impair axonal transport, leading to distal axonopathy. Thus, although diabetes does not directly target

microtubules pharmacologically, it converges on similar structural and transport-related mechanisms that ultimately degrade ascending sensory transmission. In both CIPN and diabetic neuropathy, axonal transport failure precedes overt structural degeneration. Impaired mitochondrial distribution reduces local ATP availability, compromising ion gradient maintenance and conduction velocity. Altered tubulin post-translational modifications further disrupt motor protein interaction with microtubules, amplifying transport inefficiency. As distal axons degenerate, sensory signal timing and amplitude become distorted, degrading the fidelity of ascending transmission to spinal and thalamic circuits. Electrophysiological techniques provide critical functional validation of these molecular and structural alterations. Nerve conduction studies (NCS) consistently demonstrate reduced sensory nerve action potential amplitudes and slowed conduction velocities in both CIPN and DPN models. Electromyography (EMG) reveals signs of denervation or altered motor unit recruitment when motor fibers are involved, particularly in advanced stages. Importantly, electrophysiological abnormalities often precede visible axonal degeneration, underscoring their sensitivity as early biomarkers of cytoskeletal and transport dysfunction. In animal models, longitudinal EMG and NCS recordings allow dynamic monitoring of disease progression and therapeutic intervention, bridging molecular findings with systems level phenotypes. Chronic aberrant peripheral input in both disorders can induce spinal sensitization and cortical reorganization. Altered afferent signaling reshapes somatosensory cortical maps and modifies nociceptive processing, reinforcing the concept that peripheral cytoskeletal and metabolic disturbances propagate through ascending pathways to alter perception and behavior at the cortical level. Taken together, CIPN and diabetic neuropathy demonstrate that peripheral metabolic and cytoskeletal stressors converge on a shared mechanistic endpoint: impaired axonal transport, distal axon vulnerability, and degraded sensory reliability. These conditions underscore the fundamental dependence of perception on cytoskeletal integrity and metabolic homeostasis.

Conclusion Cytoskeletal and Metabolic Integrity as Foundations of Sensory and Motor Perception

Sensory and motor perception emerge from a structurally continuous and dynamically regulated neurobiological axis linking peripheral receptors to cortical networks. Peripheral detection initiates encoding, cytoskeleton-dependent axonal transport sustains transmission, ascending circuits integrate signals, and cortical maps interpret and translate them into adaptive motor and autonomic responses. CIPN and diabetic neuropathy illustrate that when cytoskeletal dynamics or metabolic stability are disrupted, this continuum becomes unstable. Impaired axonal transport compromises conduction fidelity, distorted afferent input reshapes central circuits, and perception

itself becomes unreliable. Thus, the neuronal cytoskeleton, and the metabolic systems that sustain it, constitutes a foundational determinant of sensory and motor function.

Understanding how perception is generated therefore requires bridging molecular neurobiology, metabolic regulation, circuit organization, and cortical representation within a unified framework. Sensory experience is not solely a cortical phenomenon; it is the emergent output of an integrated system whose reliability depends fundamentally on cytoskeletal stability and metabolic resilience across the entire sensory axis

Conflicts of Interest: the Author declares no conflict of interest

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