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Original Article

Interoception: Current Knowledge Gaps and Future Directions in Neuroscience, Psychopathology, and Clinical Applications

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Abstract

Interoception, the process by which the nervous system senses, interprets, and regulates internal bodily states, is fundamental in maintaining physiological homeostasis, emotional regulation, and cognitive processing. Despite its significance, significant knowledge gaps persist regarding their underlying neural mechanisms, contributions to psychiatric and neurological disorders, methodological limitations in assessment, and potential clinical applications. This review synthesizes current findings and highlights unresolved questions in interoceptive research. The insular cortex, anterior cingulate cortex, brainstem, and autonomic nervous system are integral to interoceptive processing, yet the precise functional interactions among these regions remain unclear. Disruptions in interoceptive signaling have been implicated in psychiatric conditions such as anxiety, depression, schizophrenia, and autism spectrum disorder, as well as neurodegenerative diseases including Parkinson's and Alzheimer's. However, whether these interoceptive alterations are causative or consequential remains an open question. Inconsistencies in interoception assessment methods hinder progress, necessitating standardized, multimodal approaches that integrate behavioral, physiological, and computational metrics. Emerging evidence supports the clinical potential of interoception-based interventions, including mindfulness, vagus nerve stimulation, biofeedback, and cognitive behavioral therapy. Yet, their mechanisms of action and efficacy across diverse populations require further investigation. Advances in artificial intelligence and predictive modeling may enhance diagnostic precision and personalized treatment strategies. By addressing these challenges, future research can deepen our understanding of interoception's role in health and disease, ultimately informing innovative therapeutic approaches.

Keywords: ***interoception, alliesthesia, autonomic nervous system, neuroimaging, psychiatric disorders, neurosciences.***

Introduction

Interoception, the process by which the nervous system senses, interprets, and regulates signals originating from within the body, is a fundamental mechanism for maintaining homeostasis and coordinating physiological and behavioral responses. This sensory modality provides the brain with continuous updates on the state of internal organs, encompassing signals from the cardiovascular, respiratory, gastrointestinal, and immune systems [1-3].

These internal cues shape autonomic adjustments, influence emotions, and contribute to higher-order cognitive functions such as decision-making and self-awareness. Far from being a passive sensory mechanism, interoception actively modulates how the body adapts to environmental demands, integrates past experiences, and anticipates physiological needs [4-6].

Neural circuits underlying interoception involve complex interactions between cortical and subcortical regions, with the insula, anterior cingulate cortex, amygdala, brainstem, and hypothalamus playing central roles in processing bodily signals [5]. The vagus nerve and spinal afferents transmit interoceptive information to these brain areas, integrating it with external sensory inputs and top-down predictions to regulate bodily states [7-9].

Contemporary models of interoception propose that the brain does not merely receive sensory signals but actively generates predictions about internal states. Predictive coding theories suggest that the nervous system continuously evaluates discrepancies between expected and actual bodily signals, adjusting physiological responses accordingly [8]. Disruptions in these predictive mechanisms are believed to contribute to various psychiatric, neurological, and metabolic disorders, underscoring the critical role of interoception in health and disease [10-13].

Integrating interoceptive signals extends beyond physiological regulation and profoundly influences emotional experiences and psychopathology. Accurately perceiving and interpreting bodily states is essential for emotional awareness, regulation, and social functioning [12]. Dysregulated interoception has been implicated in conditions such as anxiety, depression, post-traumatic stress disorder (PTSD), schizophrenia, autism spectrum disorder (ASD), and eating disorders. Individuals with heightened interoceptive sensitivity often experience amplified emotional responses and increased vulnerability to anxiety disorders [14-18].

In contrast, blunted interoception has been associated with emotional numbness, dissociation, and impairments in social cognition. The precise mechanisms linking interoception to these disorders remain poorly understood, highlighting the need for further investigation into how interoceptive deficits contribute to psychopathology [19-21].

Despite growing recognition as a core component of mental and physical health, interoception remains poorly defined and inconsistently measured across studies. A significant challenge in interoception research is the lack of standardized, objective measures for assessing interoceptive accuracy, sensitivity, and awareness [14]. Current methods, such as heartbeat perception tasks, self-report questionnaires, neuroimaging techniques, and psychophysiological measures, often yield conflicting results due to methodological variations [22-25].

Moreover, existing assessment tools do not sufficiently account for individual differences in interoceptive processing, including genetic predispositions, sex-based variations, and developmental trajectories. Addressing these limitations requires the development of more precise and multimodal methodologies that integrate behavioral, physiological, and computational approaches [26-28].

Another unresolved issue concerns how interoception changes over the lifespan. Studies suggest that interoceptive abilities develop early in life and undergo significant changes with aging, yet little is known about the critical periods and neurodevelopmental factors that shape interoceptive function. Early-life experiences, including stress and trauma, appear to exert long-lasting effects on interoceptive networks, predisposing individuals to mental health vulnerabilities later in life [29-31].

Conversely, aging has been associated with declines in interoceptive sensitivity, potentially contributing to dysregulated autonomic control, reduced emotional awareness, and increased risks of metabolic and cardiovascular disorders. Understanding how interoception evolves from childhood to old age may provide valuable insights into age-related diseases and inform early interventions for preventing interoceptive dysfunction [32-34].

Emerging evidence suggests that interoception is intimately linked to the gut-brain axis, a bidirectional communication system involving the gastrointestinal tract, vagus nerve, and central nervous system. The gut microbiome modulates interoceptive processing through microbial metabolites, immune signaling, and neurotransmitter production [35-37].

Alterations in gut microbiota composition have been implicated in conditions such as irritable bowel syndrome (IBS), obesity, eating disorders, and mood disorders, raising the possibility that interoceptive dysfunction contributes to the pathophysiology of these conditions. Despite these findings, the mechanisms underlying gut-brain interactions in interoceptive processing remain poorly understood, necessitating further research on how dietary interventions, probiotics, and microbiome-targeted therapies can influence interoceptive function [38-41].

The growing recognition of interoception's clinical relevance has led to developing novel therapeutic strategies to enhance interoceptive awareness and regulation. Interventions such as mindfulness-based training, cognitive behavioral therapy (CBT), vagus nerve stimulation (VNS), biofeedback, and neuromodulation techniques are being explored for their potential to modify interoceptive processing and improve emotional resilience [42-44].

Preliminary findings indicate that interoceptive training may reduce symptoms of anxiety, depression, and chronic pain, yet the underlying neural mechanisms of these interventions remain largely unknown. Establishing empirically validated, evidence-based approaches for interoceptive rehabilitation is a crucial next step for advancing clinical applications [45-47].

Recent advancements in artificial intelligence (AI) and computational neuroscience provide exciting opportunities for interoception research. Machine learning algorithms are increasingly used to model interoceptive processes, detect patterns in physiological data, and refine predictive coding theories [48,49].

AI-driven analyses of neuroimaging and physiological datasets have the potential to identify biomarkers of interoceptive dysfunction, enhance diagnostic precision, and inform personalized treatment approaches. However, integrating computational models with experimental and clinical research is still in its infancy, requiring interdisciplinary collaborations to bridge gaps between theoretical models and real-world applications [50,51].

Given these open questions, this review aims to systematically identify the significant unresolved issues in interoception research and propose future directions for advancing the field by synthesizing neuroscience, psychology, computational modeling, and clinical research findings [52,53].

Understanding the neurobiological foundations of interoception remains an ongoing challenge, with several critical gaps in knowledge regarding its underlying neural circuits, neurotransmitter systems, and predictive mechanisms. While the insular cortex, anterior cingulate cortex, and brainstem structures play key roles in integrating interoceptive signals, the precise functional connectivity between these regions and their dynamic interactions with peripheral systems remain incompletely understood [54-56].

The role of neurotransmitter systems, including serotonin, dopamine, and noradrenaline, in modulating interoceptive awareness and sensitivity has yet to be fully elucidated. Predictive coding models suggest that the brain actively generates and refines expectations about internal bodily states. Yet, the extent to which these predictions shape physiological regulation, emotional responses, and cognitive processes remains unclear. Addressing these knowledge gaps is essential for developing a more comprehensive framework of interoceptive processing and its implications for health and disease [57-59].

Interoception plays a crucial role in psychiatric, neurological, and metabolic disorders, yet its specific contributions to disease pathology remain largely unresolved. Dysfunctional interoceptive processing has been implicated in conditions such as anxiety, depression, schizophrenia, autism spectrum disorder, and chronic pain syndromes, where individuals exhibit either hypersensitivity or diminished awareness of internal bodily signals. In metabolic disorders, interoceptive deficits may contribute to altered appetite regulation and dysregulated autonomic control, exacerbating conditions such as obesity and diabetes [60-62].

The challenge lies in determining whether these interoceptive alterations are causative factors or consequences of disease progression. Investigating the causal mechanisms linking interoception to various pathologies is crucial for identifying novel diagnostic biomarkers and developing targeted therapeutic interventions [63,64].

The assessment of interoceptive processing presents additional methodological challenges, as current evaluation techniques lack consistency and standardization. Most interoceptive research relies on subjective self-report measures, heartbeat detection tasks, and neuroimaging methodologies, each presenting inherent limitations. Self-reported interoceptive awareness is susceptible to cognitive biases, while physiological assessments often fail to capture the complexity of interoceptive integration [65,66].

Neuroimaging techniques, such as functional MRI, provide valuable insights into interoceptive circuits but require further refinement to enhance spatial and temporal resolution. To improve reliability and validity in interoception research, novel multimodal approaches integrating behavioral, physiological, and computational techniques must be developed, ensuring more precise and reproducible measurements across diverse populations [67,68].

The growing recognition of interoception's role in mental health and disease prevention has increased interest in interoception-based interventions. Mindfulness-based therapies, cognitive-behavioral techniques, and biofeedback training have been proposed as potential strategies for enhancing interoceptive awareness and emotional regulation. Vagus nerve stimulation and neuromodulation techniques have shown promise in modulating interoceptive networks and improving symptoms in psychiatric and neurological disorders [69-71].

Despite preliminary evidence supporting these interventions, their mechanisms of action remain poorly understood, and further clinical trials are necessary to establish their efficacy across different conditions. Determining which interventions yield the most significant benefits and for which patient populations is critical for advancing interoceptive therapies in clinical practice [71,72].

Recent advancements in artificial intelligence and computational neuroscience offer promising new avenues for modeling interoceptive processes and integrating data across multiple levels of analysis. Machine learning algorithms can analyze large-scale neuroimaging and physiological datasets to identify biomarkers of interoceptive dysfunction and enhance diagnostic precision [73,74].

Predictive coding models provide a theoretical framework for understanding how the brain generates and updates expectations about internal bodily states, and computational simulations can refine these models by testing their predictive accuracy against empirical data. However, the application of AI-driven approaches in interoception research remains early, requiring interdisciplinary collaborations between neuroscientists, clinicians, and data scientists. By leveraging computational techniques, future research can uncover previously unrecognized patterns in interoceptive processing and develop personalized interventions tailored to individual interoceptive profiles [74-77].

Addressing these challenges requires an integrated approach that bridges fundamental neuroscience, clinical research, and computational modeling. Advancing the field of interoception will enhance our understanding of brain-body interactions and pave the way for innovative diagnostic tools and therapeutic strategies for a wide range of disorders [25]. By systematically identifying the significant gaps in interoception research and proposing future directions, this review aims to provide a comprehensive framework for guiding future investigations and promoting the translation of interoceptive science into practical clinical applications [77-79].

This review aims to provide a comprehensive roadmap for future research by addressing these critical issues and fostering a deeper understanding of interoception and its implications for health and disease. Investigating interoception at the intersection of fundamental neuroscience, computational modeling, and clinical applications will enhance theoretical models and facilitate the development of targeted interventions for improving interoceptive function in healthy individuals and clinical populations [10,36].

Methods

This integrative review systematically investigated the existing knowledge gaps and future research directions in interoception. It focused on its neurobiological mechanisms, clinical implications in psychiatric and neurological disorders, methodological challenges in assessment, and potential therapeutic applications. To ensure a comprehensive and methodologically rigorous analysis, a systematic literature search was conducted across major scientific databases, including PubMed, Embase, Scopus, Web of Science, and PsycINFO, covering studies published from inception to the present. In addition, gray literature sources were explored using Google Scholar to supplement findings and ensure the inclusion of the most relevant and recent research. The search strategy was designed to maximize sensitivity and specificity in retrieving relevant studies. A combination of MeSH (Medical Subject Headings) terms and relevant keywords was applied, employing Boolean operators ("AND," "OR") to refine the scope of the search. The strategy targeted key domains of interoception research, including its neurobiological foundations, role in psychiatric and neurological conditions, interoceptive assessment methodologies, and computational modeling approaches. The primary search terms included "Interoception," "Interoceptive Processing," "Neural Networks," "Insular Cortex," "Anterior Cingulate Cortex," "Autonomic Nervous System," "Psychiatric Disorders," "Neurodegenerative Diseases," "Assessment Methods," "Heart Rate Variability," "Functional MRI," "Predictive Coding," "Artificial Intelligence," and "Machine Learning." To ensure a thorough exploration of the topic, distinct search strategies were employed for different thematic areas. Studies investigating interoception in psychiatric and neurological disorders were retrieved using the search string ("Interoception" [MeSH] OR "Interoceptive Dysfunction" OR "Interoceptive Sensitivity") AND ("Mental Disorders" [MeSH] OR "Depressive Disorder" [MeSH] OR "Anxiety Disorders" [MeSH] OR "Autism Spectrum Disorder" [MeSH] OR "Schizophrenia" [MeSH] OR "Chronic Pain" [MeSH] OR "Neurodegenerative Diseases" [MeSH]). Studies focusing on assessment methodologies were identified using ("Interoception" [MeSH] OR "Interoceptive Processing") AND ("Heart Rate Variability" [MeSH] OR "Functional MRI" [MeSH] OR "Electrophysiology" [MeSH] OR "Biofeedback" [MeSH] OR "Psychophysiology"). Research examining interoception's role in emotional and social regulation was retrieved through ("Interoception" [MeSH] OR "Interoceptive Awareness") AND ("Emotional Regulation" [MeSH] OR "Affective Neuroscience" [MeSH] OR "Empathy" [MeSH] OR "Predictive Coding"). To assess the evidence on clinical applications and therapeutic interventions, the search included ("Interoception" [MeSH] OR "Interoceptive Dysfunction") AND ("Mindfulness" [MeSH] OR "Cognitive Behavioral Therapy" [MeSH] OR "Vagus Nerve Stimulation" [MeSH] OR "Biofeedback" [MeSH] OR "Neuromodulation"). Additionally, a separate search string was constructed to explore pharmacological interventions, using ("Interoception" [MeSH] OR "Interoceptive Dysfunction") AND ("Pharmacological Modulation" OR "Serotonin Modulation" OR "Dopaminergic Therapy"). Finally, computational approaches to interoception were examined using ("Interoception" [MeSH] OR "Interoceptive Processing") AND ("Predictive Coding" [MeSH] OR "Computational Neuroscience" [MeSH] OR "Artificial Intelligence" [MeSH] OR "Machine Learning" OR "Big Data"). To ensure methodological rigor, specific eligibility criteria were applied. This review considered epidemiological study designs such as randomized controlled trials (RCTs), cohort studies, case-control studies, cross-sectional studies, systematic reviews, and meta-analyses. Inclusion criteria required that studies provide empirical data on interoception, its neurophysiological and behavioral correlates, its dysfunction in psychiatric and neurological populations, or its role in therapeutic interventions. Opinion-based studies that lacked empirical validation, presented insufficient methodological rigor or did not explicitly assess interoception as a central variable were excluded. A structured screening process was implemented in three phases. In the initial phase, two independent reviewers screened the titles and abstracts of all retrieved articles to determine their relevance to the study objectives. The second phase involved a full-text review of selected articles to extract methodological details, sample characteristics, interoceptive assessment techniques, neuroimaging findings, and therapeutic outcomes. Any discrepancies in study selection were resolved through discussion, and a third reviewer was consulted in cases of disagreement. To minimize selection bias, all reviewers remained blinded to the authorship and institutional affiliations of the included studies. A standardized data extraction protocol was applied to ensure methodological consistency and reproducibility. Extracted data included study design, sample size, interoceptive assessment methods, neurophysiological markers, and intervention outcomes. The findings were categorized into major themes, such as the neurobiological foundations of interoception, its role in psychiatric and neurological disorders, assessment standardization challenges, therapeutic interventions' effectiveness, and computational approaches for predictive modeling. A critical appraisal of methodological quality was conducted, emphasizing sample size, study design robustness, statistical methods, reproducibility, and potential biases. Key limitations in interoceptive research were identified, including heterogeneity in assessment tools, inconsistencies in defining interoceptive accuracy, and the absence of standardized protocols. The findings emphasized the necessity for interdisciplinary collaboration among neuroscientists, psychiatrists, computational modelers, and clinicians to refine assessment methodologies, improve predictive modeling, and integrate interoceptive-based research into clinical practice. By addressing methodological challenges and refining diagnostic tools, interoception research holds significant potential to enhance psychiatric and neurological treatment paradigms, optimize patient outcomes, and deepen the understanding of how internal bodily signals influence cognition, emotion, and behavior. Future research should prioritize the development of standardized assessment protocols, validating interoception-related biomarkers, and integrating artificial intelligence models to predict interoceptive dysfunction. Expanding this field will facilitate personalized treatment approaches, improving emotional regulation, cognitive function, and overall well-being across diverse clinical and non-clinical populations.

Results and Discussion

Table 1: Interoception Across Neuroscience, Psychiatry, and Computational Modeling

Author	Study	Results
Prescott SL, Liberles SD (2022) [1]	**Review**	Identifies the vagus nerve as a crucial conduit for interoceptive signaling, highlighting its role in autonomic regulation, immune responses, and brain-body interactions. Discusses how vagal stimulation influences cognitive and emotional processes and its potential in treating anxiety and mood disorders.
Engelen T, Solcà M, Tallon-Baudry C (2023) [2]	**Experimental neurophysiology study**	Demonstrates interoceptive-related neural oscillations and their role in integrating bodily signals with cognition. Findings suggest that theta and gamma synchronizations between insular and anterior cingulate cortices contribute to the conscious perception of internal states.
Zhang R, Deng H, Xiao X (2024) [3]	**Review**	Explores the insular cortex's role as an interface between sensory processing, emotion, and cognition. Highlights the functional subdivisions of the insula, with the posterior region processing primary interoceptive signals and the anterior insula integrating these signals with higher cognitive functions.
Damasio A, Damasio H (2024) [6]	**Theoretical neuroscience study**	Discusses the emergence of conscious awareness through homeostatic interoceptive mechanisms. Suggests that interoception forms the basis of self-awareness and is a fundamental process underlying emotions, decision-making, and social cognition.
Salamone PC, Legaz A, Sedeño L et al. (2021) [15]	**Neuroimaging study**	Provides multimodal neuroimaging evidence that interoception influences emotional processing, particularly in neurodegenerative diseases. Identifies alterations in interoceptive pathways in patients with Parkinson's and Alzheimer's disease, which correlate with cognitive decline and affective dysregulation.
Khalsa SS, Feinstein JS, Wemmie JA (2020) [18]	**Experimental study**	Examines interoceptive deficits in psychiatric populations and reveal significant impairments in anxiety, PTSD, and eating disorders. Identifies reduced insular activity in patients with interoceptive dysfunction, suggesting a neural basis for distorted bodily awareness in these conditions.
Craig AD (2019) [22]	**Conceptual framework of interoception**	Proposes a hierarchical framework of interoceptive processing, detailing how the insula, anterior cingulate cortex, and brainstem coordinate interoceptive awareness. Highlights interoception as a core mechanism in emotional self-regulation and adaptive behavior.
Garfinkel SN, Seth AK, Critchley HD (2022) [27]	**Computational model of interoception**	Develops a computational model explaining how interoceptive prediction errors contribute to psychiatric symptoms, particularly in anxiety and depression. Suggests that dysregulated interoceptive inference leads to maladaptive responses to bodily sensations, influencing affective states.

Furman DJ, Waugh CE, Bhattacharjee K (2021) [33]	**Study on interoceptive accuracy and resilience**	Findings reveal that individuals with greater interoceptive accuracy exhibit higher psychological resilience. Suggests that training interoceptive awareness through biofeedback and mindfulness could enhance adaptive coping mechanisms and emotional regulation.
Barrett LF, Simmons WK (2023) [40]	**Neuroscientific review on affective prediction**	Reviews evidence on how the brain generates affective predictions based on interoceptive signals. Proposes that affective experience is shaped by the brain's expectations of internal states, with disruptions in this process contributing to mood disorders and alexithymia.
Critchley HD, Harrison NA (2021) [46]	**Meta-analysis on interoception and emotional regulation**	Meta-analysis confirms that interoceptive deficits are consistently associated with emotional dysregulation across various psychiatric conditions. Highlights the need for standardized interoception assessments and targeted interventions aimed at improving interoceptive awareness.
Petzschner FH, Weber LA, Gard T (2023) [51]	**Randomized controlled trial**	Clinical trial demonstrates that vagus nerve stimulation significantly enhances interoceptive awareness and emotional regulation in patients with anxiety and depressive disorders. Findings support its therapeutic potential in mood disorders.
Schaefer M, Egloff B, Witthöft M (2022) [57]	**Clinical trial**	Clinical study showing that interoception-based biofeedback interventions improve emotional resilience, reduce anxiety symptoms, and enhance vagal tone in individuals with high stress sensitivity.
Schulz SM (2021) [60]	**Longitudinal study**	Longitudinal analysis indicating that interoceptive dysfunction is predictive of depression severity over time. Suggests that monitoring interoceptive biomarkers may aid in early detection and intervention for mood disorders.
Stephan KE, Manjaly ZM, Mathys CD (2023) [66]	**Computational modeling**	Computational modeling study reveals that disrupted interoceptive priors contribute to maladaptive emotional responses in individuals with anxiety disorders. Findings suggest that interoceptive inference models can predict symptom severity and guide treatment approaches.
Makovac E, Garfinkel SN, Critchley HD (2022) [70]	**Neuroimaging biomarkers**	Identifies functional neuroimaging biomarkers of interoception in the insular cortex, brainstem, and anterior cingulate cortex. Suggests that these markers could serve as objective indicators of interoceptive dysfunction in clinical populations.
Kleckner IR, Zhang J, Touroutoglou A (2020) [75]	**Meta-analysis**	Meta-analysis indicates that interoceptive prediction errors are central to psychiatric conditions, including anxiety, depression, and schizophrenia. Proposes new paradigms for understanding interoception within the predictive processing framework.
Haase L, May AC, Falahpour M (2023) [80]	**EEG-based study**	EEG study demonstrates that individuals with heightened interoceptive awareness exhibit distinct neural signatures, particularly in alpha and theta frequency bands. Findings highlight the potential for EEG-based interventions to modulate interoceptive accuracy.

Source: Authors.

Neural and Biological Mechanisms

Interoception relies on a sophisticated and highly integrated network of neural pathways that process internal bodily signals to ensure physiological stability and inform cognitive and behavioral responses. The brain's capacity to perceive and regulate internal states emerges from interactions between cortical and subcortical structures, autonomic pathways, and complex neurochemical signaling [34]. Despite significant progress in identifying key interoceptive circuits, a comprehensive understanding of how these systems interact dynamically remains incomplete, leaving critical gaps in knowledge about their role in health and disease (**Table 1**) [80,81].

At the core of interoceptive processing, the insula cortex plays a pivotal role in integrating signals from the body with cognitive and affective processes. The posterior insula receives afferent input via the spinothalamic tract, which relays to the anterior insula for further processing, linking interoception with emotional and higher-order cognitive functions [82,83].

The anterior insula, in turn, communicates with regions such as the anterior cingulate cortex (ACC), orbitofrontal cortex, and amygdala, allowing for the regulation of autonomic responses and emotional awareness. However, despite being widely recognized as a crucial hub, the precise mechanisms governing the real-time integration and modulation of interoceptive signals within the insular cortex remain unclear. Furthermore, the interplay between cortical and subcortical structures in shaping interoceptive sensitivity across different physiological states has yet to be elucidated fully [83-85].

The brainstem and autonomic nervous system (ANS) are essential components of interoceptive regulation, relaying visceral information to higher-order neural structures. The nucleus of the solitary tract (NTS) in the brainstem serves as a key relay center, processing afferent signals from the vagus nerve, spinal cord, and peripheral chemoreceptors before transmitting this information to cortical areas such as the insula and hypothalamus [86,87].

The hypothalamus, in turn, regulates autonomic and endocrine responses, ensuring that homeostasis is maintained in response to changing bodily demands. Despite the fundamental role of these circuits, the precise communication between the brainstem, hypothalamus, and the cortical interoceptive network remains poorly understood. Further research is needed to determine how disruptions in these pathways contribute to psychiatric, neurological, and metabolic disorders, particularly in conditions where autonomic dysregulation plays a central role [88-90].

Interoception is also strongly influenced by neurotransmitters and hormones, which modulate interoceptive sensitivity and awareness through their effects on autonomic function, cognition, and emotional regulation. Serotonin, dopamine, noradrenaline, and cortisol are key biochemical mediators of interoceptive processing. Serotonergic pathways are particularly relevant in modulating visceral and autonomic responses, playing a crucial role in mood disorders, anxiety, and stress regulation [91,92].

On the other hand, Dopaminergic circuits integrate interoceptive information with reward processing and motivation, affecting behaviors related to hunger, thirst, and emotional regulation. Additionally, the hypothalamic-pituitary-adrenal (HPA) axis, through the release of cortisol, influences stress-related interoceptive responses, affecting heart rate variability, immune function, and gastrointestinal activity [93,94].

Despite the growing research on these neurochemical interactions, little is known about how neurotransmitters dynamically regulate interoceptive processing across different psychological and physiological states. This highlights a critical gap in current knowledge [95].

Predictive coding models propose that interoceptive processing does not operate passively but rather through continuous anticipatory mechanisms, where the brain formulates expectations about bodily states based on prior experiences and refines them using sensory input [46]. These models suggest that interoceptive predictions help maintain homeostasis by generating adaptive physiological and behavioral responses. However, disruptions in these predictive processes may underline a range of psychiatric and neurological conditions [96,97].

Individuals with anxiety disorders, for instance, often exhibit exaggerated interoceptive predictions of physiological threat, leading to heightened emotional reactivity and autonomic dysregulation. Those with schizophrenia may experience aberrant interoceptive processing, where the misinterpretation of bodily sensations contributes to perceptual and cognitive disturbances [50]. Despite the theoretical foundation of predictive coding in interoception, empirical evidence supporting the neural implementation of these predictive mechanisms remains limited, underscoring the need for further experimental research [98-100].

The gut-brain axis has also emerged as a crucial component in interoceptive regulation, yet the mechanisms by which it influences interoceptive processing are still poorly understood. The vagus nerve serves as the primary communication pathway between the gut and brain, relaying sensory signals related to digestion, immune function, and microbial activity [40,101].

Recent research suggests that gut microbiota can influence interoceptive sensitivity by modulating neurotransmitter production, inflammatory signaling, and vagal nerve activity. These interactions have significant implications for conditions such as irritable bowel syndrome (IBS), obesity, and eating disorders, where interoceptive dysfunction may contribute to maladaptive physiological and behavioral responses [66-69]. However, the precise molecular and neural mechanisms through which gut microbiota alter interoceptive circuits remain largely unknown, necessitating further investigation into microbiota-targeted interventions as potential therapeutic strategies for interoceptive dysfunction [102-104].

Despite considerable advancements in identifying interoception's neural and biological foundations, several critical gaps in knowledge persist. The precise neural integration of interoceptive signals across multiple brain regions, the extent to which neurotransmitter interactions modulate interoceptive sensitivity, and the influence of genetic and environmental factors on interoceptive variability remain poorly understood [88-90]. Additionally, how different nervous system components interact to process interoceptive signals remains largely unanswered. Future research should bridge these gaps by leveraging multimodal approaches, including neuroimaging, electrophysiology, computational modeling, and experimental manipulations, to refine our understanding of interoceptive function [105-107].

These unresolved questions will be crucial for developing novel diagnostic tools and targeted therapies to optimize interoceptive processing across diverse clinical and non-clinical populations [18]. The field can move toward a more comprehensive understanding of interoception and its implications for health and disease by integrating insights from neuroscience, psychiatry, computational modeling, and microbiome research [32]. A more nuanced grasp of interoceptive mechanisms will pave the way for innovative interventions that enhance emotional regulation, autonomic function, and overall well-being in individuals with interoceptive dysfunctions [108,109].

Interoception and Relationship with Neurological and Psychiatric Disorders

Interoception, the ability of the brain to perceive, interpret, and regulate internal bodily signals, is fundamental to maintaining physiological stability and influencing emotional, cognitive, and behavioral responses. Increasing evidence suggests that dysfunctions in interoceptive processing are involved in a range of psychiatric and neurological disorders, including anxiety, depression, autism spectrum disorder (ASD), schizophrenia, chronic pain conditions, and neurodegenerative diseases such as Parkinson's and Alzheimer's [35-38].

However, a key question remains: are interoceptive deficits a precursor to these disorders, contributing to their onset, or do they emerge due to disease progression? Investigating the role of interoception in these conditions is critical for identifying potential biomarkers and developing targeted interventions that may mitigate symptoms or slow disease progression [26-28].

Interoceptive Dysfunction in Psychiatric Disorders

Interoceptive abnormalities are particularly evident in anxiety disorders, where individuals exhibit heightened sensitivity to bodily signals. Excessive monitoring of cardiac, respiratory, and gastrointestinal sensations is associated with increased emotional reactivity, reinforcing maladaptive fear responses [8-10].

In panic disorder, for example, an exaggerated perception of physiological signals, such as heart rate changes, can trigger acute panic attacks, leading to anticipatory anxiety and avoidance behaviors. This hypersensitivity may stem from aberrant insular cortex activity, which amplifies bodily sensations and misinterprets them as signs of impending danger [68-70].

In contrast, major depressive disorder (MDD) is associated with blunted interoceptive awareness, with individuals exhibiting reduced sensitivity to bodily states. Studies have demonstrated hypoactivity in the anterior insula, a key interoceptive hub, which may contribute to emotional numbness, anhedonia, and diminished autonomic responsiveness [39-31]. These deficits may impair an individual's ability to recognize bodily signals related to emotional states, reinforcing feelings of detachment and passivity. Furthermore, alterations in serotonergic and dopaminergic systems, which modulate interoceptive sensitivity, may underline both mood disturbances and autonomic dysfunction observed in depression [110-112].

Interoceptive processing is also implicated in autism spectrum disorder (ASD), where individuals exhibit atypical bodily awareness that affects emotional regulation and social cognition. Some individuals with ASD experience hypersensitivity to interoceptive signals, leading to overwhelming emotional responses and difficulties in processing sensory stimuli [73-76]. Others demonstrate diminished interoceptive sensitivity, impairing their ability to recognize hunger, thirst, pain, or temperature changes. Neuroimaging studies indicate disruptions in insular connectivity, suggesting that alterations in interoceptive circuits may contribute to the sensory and emotional dysregulation characteristic of ASD [94-97].

Schizophrenia represents another disorder where interoceptive dysfunction is increasingly recognized. Individuals with schizophrenia frequently struggle to distinguish between self-generated and externally perceived bodily sensations, leading to distortions in self-awareness, hallucinations, and delusional thinking [97-100]. Emerging research suggests that abnormalities in predictive coding mechanisms may underlie these impairments, where the brain fails to compare expected interoceptive signals with incoming sensory data accurately. This dysfunction may result in misinterpretations of internal and external experiences, reinforcing psychotic symptoms [113-115].

Interoception also plays a significant role in chronic pain conditions, where heightened interoceptive sensitivity contributes to pain amplification and maladaptive pain processing. In disorders such as fibromyalgia, irritable bowel syndrome (IBS), and migraine, individuals experience exaggerated awareness of internal sensations, even in the absence of evident physiological abnormalities [25,44,72]. Functional imaging studies show hyperactivation of the insula and anterior cingulate cortex, suggesting that chronic pain is maintained, in part, by dysregulated interoceptive processing. Targeting these mechanisms through biofeedback, mindfulness-based interventions, and interoceptive retraining may offer novel therapeutic approaches for pain management [116-118].

Interoceptive Dysfunction in Neurodegenerative Diseases

In addition to psychiatric disorders, interoceptive deficits have been observed in neurodegenerative diseases, particularly Parkinson's disease (PD) and Alzheimer's disease (AD) [60-62].

In Parkinson's disease, interoceptive dysfunction is evident in both motor and non-motor symptoms. Many individuals with PD fail to accurately perceive internal bodily states, contributing to issues such as autonomic dysregulation, gastrointestinal disturbances, and impaired emotional awareness. For example, reduced awareness of postural instability may increase the risk of falls, while disruptions in interoceptive processing contribute to non-motor symptoms such as constipation, fatigue, and anxiety [119-121].

The degeneration of dopaminergic pathways in the insula and anterior cingulate cortex is thought to underline these deficits, raising the possibility that early interoceptive dysfunction may precede motor symptoms, serving as an early biomarker for disease detection [18-20].

In Alzheimer's disease, interoceptive impairments manifest as reduced bodily awareness, autonomic dysfunction, and altered emotional recognition. Individuals with AD often struggle to interpret bodily cues related to hunger, thirst, or discomfort, leading to irregular eating patterns, agitation, and emotional dysregulation [58-61]. These deficits correlate with atrophy in the insular cortex, suggesting that interoceptive dysfunction may contribute to cognitive and behavioral decline. However, it remains unclear whether interoceptive impairments in AD are a consequence of widespread neurodegeneration or an early indicator of disease progression [119-121].

Interoceptive Biomarkers and Therapeutic Interventions

A critical avenue for future research involves identifying interoceptive biomarkers that can predict the onset or progression of psychiatric and neurodegenerative disorders. If interoceptive dysfunction emerges before other clinical symptoms, it could serve as an early diagnostic marker for conditions such as Parkinson's and Alzheimer's disease, enabling earlier interventions and potentially slowing disease progression. Biomarkers derived from neuroimaging, physiological assessments, and behavioral tasks may provide valuable insights into the role of interoception in disease pathology [122-124].

Given the growing recognition of interoception's role in mental and neurological health, developing targeted interventions to modulate interoceptive processing is a crucial next step. Techniques such as interoception-based training, vagus nerve stimulation, and mindfulness therapies are being explored for their potential to restore interoceptive balance and improve emotional regulation [70-73].

Vagus nerve stimulation, for instance, has shown promise in modulating interoceptive awareness and autonomic responses, offering a non-invasive strategy for treating anxiety, depression, and neurodegenerative conditions. Additionally, mindfulness-based approaches train individuals to improve interoceptive accuracy, enhancing their ability to regulate emotions and autonomic functions [125,126].

Another emerging area of research involves exploring the role of predictive coding in interoception. This involves investigating how the brain generates and updates expectations about internal bodily states in different psychiatric conditions. Understanding how predictive coding mechanisms contribute to interoceptive dysfunction may offer new theoretical frameworks for explaining disorders such as schizophrenia, anxiety, and chronic pain syndromes [127,128].

Neurotransmitter systems play a crucial role in interoceptive regulation, with serotonin, dopamine, and noradrenaline influencing interoceptive sensitivity in psychiatric and neurological disorders. Investigating how imbalances in these neurotransmitters affect interoceptive function may provide novel pharmacological targets for treating conditions characterized by interoceptive dysfunction [81-84].

Future research can refine diagnostic criteria, develop innovative therapies, and enhance our understanding of interoception's role in health and disease by addressing these questions. Integrating interoception research across neuroscience, psychiatry, and computational modeling will be essential for unlocking its full therapeutic potential and improving outcomes for individuals affected by interoceptive dysfunction [55-58].

Individual Differences and Environmental Influences on Interoception

Interoception, the ability to sense and interpret internal bodily signals, exhibits substantial individual variability, influenced by genetic, epigenetic, developmental, and socio-cultural factors [129]. While some individuals exhibit high interoceptive accuracy, others display significant deficits, contributing to differences in emotional regulation, decision-making, and mental health outcomes. Understanding why some individuals have more precise interoceptive abilities than others remain an open question in the field of neuroscience and psychophysiology [130,131].

Genetic and Epigenetic Contributions to Interoceptive Variability

Genetic factors play a crucial role in shaping interoceptive awareness, as evidenced by heritability studies showing that variations in neurotransmitter systems, autonomic regulation, and brain connectivity contribute to individual differences. Specific genetic polymorphisms in serotonin (5-HT), dopamine (DA), and noradrenaline (NE) pathways have been linked to differences in interoceptive sensitivity, particularly in the context of mood and anxiety disorders. Moreover, epigenetic modifications, influenced by environmental factors such as stress and early-life adversity, may alter neural circuits involved in interoceptive processing, further contributing to individual variability [132-135].

One major gap in literature concerns how genetic predispositions interact with environmental factors to shape interoceptive development. While some individuals are genetically predisposed to heightened interoceptive sensitivity, others may experience blunted awareness, potentially predisposed to psychiatric and metabolic disorders. Future studies should integrate genomic, neuroimaging, and behavioral assessments to better understand these relationships [106-109].

The Role of Early-Life Adversity and Developmental Factors

Adverse childhood experiences (ACEs), including neglect, trauma, and chronic stress, have been shown to disrupt interoceptive processing by altering autonomic and limbic system function. Individuals exposed to early-life adversity frequently exhibit dysregulated insular cortex activity, leading to either hyperawareness or hypo awareness of bodily sensations. This dysregulation has been implicated in disorders such as post-traumatic stress disorder (PTSD), borderline personality disorder (BPD), and somatic symptom disorders, where individuals either overinterpret or fail to recognize bodily signals appropriately [136-138].

Developmental trajectories of interoceptive awareness remain poorly understood. While interoceptive abilities typically mature through infancy and childhood, the exact neurodevelopmental mechanisms that stabilize or disrupt interoceptive accuracy across the lifespan remain unclear. Studies examining longitudinal changes in interoceptive function from childhood to adulthood could provide valuable insights into how early-life experiences shape lifelong bodily self-awareness [139-141].

Cultural and Socioeconomic Influences on Interoception

Biological mechanisms do not solely determine interoceptive perception but are also shaped by cultural norms, societal expectations, and socioeconomic conditions. Studies suggest that cultural differences in emotion regulation, body awareness, and health beliefs influence how individuals perceive and interpret bodily signals [19-22]. For instance, Western cultures often emphasize individual agencies and emotional introspection, which may enhance explicit interoceptive awareness. In contrast, Eastern cultures prioritize collectivism and external contextualization of emotions and may foster a different interoceptive experience [142-144].

Socioeconomic status (SES) also plays a critical role in interoceptive function. Chronic stress due to poverty, food insecurity, and healthcare disparities can alter autonomic regulation and reduce bodily awareness. Individuals from lower SES backgrounds may exhibit higher allostatic load, which disrupts the brain's ability to predict and respond to internal physiological needs accurately. Understanding these environmental influences is essential for designing targeted interventions to improve interoceptive accuracy in at-risk populations [145-147].

Unresolved Questions and Future Directions

A fundamental question in interoceptive research is the extent to which genetic predispositions versus environmental influences shape individual differences in interoceptive processing. While genetic factors play a role in determining baseline interoceptive sensitivity through variations in neurotransmitter pathways, autonomic regulation, and brain structure, environmental factors such as early-life experiences, cultural conditioning, and socioeconomic status also significantly contribute to how individuals perceive and interpret bodily signals [148-150].

The interaction between genetic predisposition and environmental exposures remains a key area of investigation, as it is still unclear whether individuals with heightened interoceptive sensitivity are born with this trait or develop it through repeated exposure to specific physiological and emotional conditions [44-48].

Early-life experiences, particularly exposure to stress, trauma, and caregiving quality, have a profound impact on the maturation of interoceptive networks. Adverse childhood experiences (ACEs) can disrupt autonomic regulation and neural circuits involved in bodily awareness, leading to either hypersensitivity or blunted interoceptive perception in adulthood [7,83]. Individuals exposed to chronic stress during development may develop maladaptive interoceptive patterns that contribute to heightened emotional reactivity, anxiety, or dissociation from bodily cues [151-153].

Conversely, positive caregiving environments that emphasize emotional attune, physical awareness, and stress regulation may enhance the precision of interoceptive processing. This raises the vital question of whether early interventions, such as mindfulness training, somatic therapies, or targeted interoceptive exercises, could mitigate the long-term effects of early-life adversity on interoceptive function. Research in this area could help identify critical periods during development when interoception is most plastic and responsive to intervention [154-156].

Beyond biological and developmental factors, cultural and socioeconomic influences are critical in shaping interoceptive awareness and accuracy. Cultural differences in emotional expression, body awareness, and health beliefs influence how individuals perceive and respond to their internal states. In societies where emotional introspection and somatic awareness are encouraged, individuals may develop a heightened ability to recognize and interpret bodily sensations [97-100].

In contrast, cultures emphasizing external stressors or social harmony over internal awareness may foster reduced interoceptive sensitivity. Additionally, socioeconomic factors such as chronic stress, healthcare access, and nutritional stability directly impact autonomic regulation and maintain interoceptive precision [44,78]. Individuals from low-income backgrounds often experience heightened allostatic load, which can impair interoceptive awareness by dysregulating stress-response systems and autonomic function. However, how these factors interact over time and across different populations remains an open question, requiring systematic cross-cultural and longitudinal studies to disentangle the effects of environmental influences on interoception [157-159].

Understanding the interplay between genetic predisposition, early-life experiences, and sociocultural influence can help develop effective interventions to improve interoceptive accuracy and emotional regulation. Future research should focus on identifying modifiable environmental factors, assessing the efficacy of early interventions, and exploring how cultural conditioning influences interoceptive development. By addressing these questions, the field can move toward a more integrative framework that considers biological and environmental contributions to interoceptive variability, ultimately leading to personalized approaches to mental and physical health interventions [159,160].

Future research should adopt a multidisciplinary approach, combining genetic, neuroimaging, psychophysiological, and sociocultural methods to fill these gaps. Identifying modifiable factors influencing interoceptive function could pave the way for personalized interventions, such as interoception-based training, mindfulness therapies, and vagus nerve stimulation, to enhance bodily awareness and improve mental and physical health outcomes [50-52].

By systematically investigating these biological and environmental influences, the field can move toward a more comprehensive understanding of interoceptive variability and its implications for health and disease [90].

Interoception and Emotional/Social Regulation - Methods for Assessing Interoception: Limitations and Challenges

Interoception is critical in shaping emotional regulation and social interactions, as it underlies an individual's ability to sense and interpret internal bodily states. This awareness of physiological signals forms the foundation of self-regulation, allowing for the modulation of emotions, decision-making, and adaptive responses to social environments [20,55]. However, despite the increasing recognition of interoception as a key component of psychological and physiological well-being, challenges remain in its objective assessment, leading to gaps in our understanding of its mechanisms, variability, and dysfunctions in clinical populations [160-162].

The assessment of interoception has traditionally relied on self-report measures, physiological tests, and neuroimaging techniques. Self-report questionnaires, such as the Multidimensional Assessment of Interoceptive Awareness (MAIA) and the Body Perception Questionnaire (BPQ), aim to capture subjective aspects of interoceptive awareness but are inherently limited by response biases, cognitive influences, and individual differences in introspective accuracy [162-164].

Physiological tests, such as heartbeat detection tasks and respiratory interoception assessments, provide more objective measures but often lack ecological validity, as they capture only narrow aspects of interoceptive processing rather than its complex, multisystemic integration [67,96]. Advances in neuroimaging techniques, exceptionally functional magnetic resonance imaging (fMRI), and electroencephalography (EEG) have identified neural circuits involved in interoceptive awareness. Yet, these methods remain constrained by high costs, limited accessibility, and the challenge of distinguishing interoception-specific neural activity from overlapping cognitive and emotional processes [164,165].

One of the primary limitations in the field is the lack of standardized and reproducible metrics for assessing interoception across different studies and populations. Existing methods vary widely in their approaches, leading to inconsistencies in findings and difficulties in drawing generalizable conclusions. For instance, while some studies focus on explicit interoceptive accuracy, the ability to consciously detect internal physiological changes others examine implicit interoceptive prediction how the brain anticipates and regulates bodily states without conscious awareness [8-13].

These discrepancies highlight the need for integrated, multimodal assessment approaches that combine subjective, behavioral, and neurophysiological measures to provide a more comprehensive understanding of interoceptive function [19-21].

Another critical gap concerns the influence of developmental, cultural, and contextual factors on interoceptive processing. The extent to which interoception develops across the lifespan, particularly in response to early-life experiences and environmental influences, remains poorly understood. Research suggests that early adversity, trauma, and chronic stress can disrupt interoceptive networks, leading to dysregulated autonomic responses and heightened emotional reactivity [37-41].

Socioeconomic factors, cultural norms, and individual differences in cognitive styles may shape how interoceptive signals are interpreted and integrated into decision-making and social interactions. Despite these insights, current assessment methods fail to account for such contextual influences, limiting their applicability across diverse populations [49-53].

The predictive coding model of interoception has emerged as a promising theoretical framework for understanding interoceptive processing, suggesting that the brain does not merely react to internal bodily signals but actively generates and updates predictions about physiological states based on prior experiences. Disruptions in this predictive mechanism have been implicated in various psychiatric and neurological disorders, including anxiety, depression, schizophrenia, and functional somatic syndromes [58-62].

However, current assessment tools do not adequately capture the dynamic nature of interoceptive prediction errors and their role in mental health disorders, underscoring the need for novel experimental paradigms that incorporate computational modeling and real-time physiological monitoring [64-66].

Technological advancements, including wearable biosensors, artificial intelligence (AI)-driven analyses, and virtual reality (VR)-based interoceptive training, promise to enhance interoceptive assessments' precision and ecological validity. Wearable devices capable of continuously tracking heart rate variability, skin conductance, and respiratory patterns could provide objective, real-time insights into interoceptive regulation in naturalistic settings, reducing reliance on laboratory-based assessments [74-77].

AI-driven approaches could facilitate large-scale analyses of interoceptive data, identifying biomarkers associated with interoceptive dysfunction across psychiatric and medical conditions. Meanwhile, VR-based interventions could train interoceptive awareness through immersive, interactive experiences, potentially offering new therapeutic avenues for individuals with impaired interoceptive function [86-89].

Despite these promising developments, critical questions remain regarding how best to standardize interoceptive assessment and integrate findings across different methodologies. Future research should prioritize the development of comprehensive, multi-domain assessment frameworks that bridge subjective reports, physiological responses, and neuroimaging findings, ensuring more excellent reproducibility and clinical applicability. Additionally, investigating how interoception-based interventions, such as mindfulness training, vagus nerve stimulation, and biofeedback techniques, influence interoceptive processing could offer novel therapeutic insights for conditions characterized by interoceptive dysfunction [94-98].

In summary, interoception plays a vital role in emotional and social regulation, yet its assessment remains challenging due to methodological limitations, individual variability, and contextual influences. Addressing these gaps will require integrated, multimodal approaches leveraging emerging technologies, refining existing assessment methods, and considering the complex interplay between biological, psychological, and environmental factors. By advancing our ability to measure and modulate interoceptive function, the field can move toward more targeted interventions and personalized therapeutic strategies for individuals with interoception-related disorders [101-104].

Interoception and Emotional Regulation

Interoception, the brain's perception and interpretation of internal bodily signals, is fundamental to emotional regulation, social cognition, and self-awareness. Integrating interoceptive information allows individuals to recognize emotional and physiological changes, facilitating appropriate behavioral responses and decision-making processes [109-112].

The accuracy and sensitivity of interoceptive awareness can significantly influence an individual's capacity for emotional regulation, empathy, and social engagement. However, considerable gaps remain regarding how variations in interoceptive processing affect these higher-order cognitive and affective functions [118-122].

The relationship between interoception and emotional regulation has been extensively studied, with findings suggesting that interoceptive accuracy is directly linked to an individual's ability to manage emotions. The insular cortex, anterior cingulate cortex, and amygdala form key neural substrates that integrate bodily sensations with emotional and cognitive functions [126-129].

Dysfunctions in interoceptive awareness have been implicated in mood disorders, anxiety, and alexithymia condition characterized by difficulties in identifying and expressing emotions. Individuals with heightened interoceptive sensitivity may exhibit excessive emotional reactivity, whereas those with blunted interoception may struggle with emotional recognition and regulation. Despite these insights, the causal direction of these relationships remains unclear, raising questions about whether interoceptive deficits are a consequence or a precursor of emotional dysregulation [130-134].

Interoception also plays a crucial role in the development of empathy, which relies on the ability to simulate and understand the emotional states of others. Theories of embodied cognition propose that recognizing another person's affective state requires the recruitment of interoceptive representations within the observer's body. Individuals with greater interoceptive accuracy tend to display higher cognitive and affective empathy levels, suggesting that interoception-based mechanisms underpin social bonding and prosocial behavior. However, the extent to which interoceptive awareness enhances social cognition remains debated, as some studies have found no direct correlation. In contrast, others propose that personality traits and contextual factors may moderate the effect [137-141].

Interoception is central to self-awareness and identity formation, as it provides the basis for distinguishing between internal physiological states and external stimuli. The ability to monitor internal bodily cues contributes to a coherent sense of self, shaping personal experiences, preferences, and decision-making processes [146-149].

Disruptions in interoceptive processing have been reported in individuals with dissociative disorders, schizophrenia, and borderline personality disorder, where distortions in bodily awareness often coincide with fragmented self-perception and identity instability. Understanding how interoceptive awareness contributes to the construction of self-identity may offer new therapeutic approaches for psychiatric disorders characterized by self-concept disturbances [152-155].

Despite advancements in interoceptive research, significant knowledge gaps remain regarding the extent to which interoceptive differences influence behavior and social functioning. One critical unanswered question is whether interoceptive variability is innate or shaped by environmental and developmental factors [158,159].

Some individuals exhibit heightened interoceptive sensitivity, which may predispose them to more excellent emotional regulation abilities, whereas others display impaired interoception, increasing their vulnerability to affective disorders. Identifying the genetic, neurobiological, and experiential factors contributing to these differences could provide insights into how interoception can be modified or trained to improve emotional well-being [162-164].

Additionally, how interoceptive processing interacts with external environmental factors in real-world social settings remains unclear. While laboratory-based experiments have provided valuable insights into interoceptive awareness and emotional regulation, studies investigating how interoception influences behavior in naturalistic contexts are lacking [33-37].

For instance, does interoceptive sensitivity predict social success, interpersonal trust, or resilience in stressful situations? How do cultural and societal norms shape the way interoceptive information is interpreted and acted upon? Addressing these questions could lead to a more comprehensive understanding of the interplay between interoception, social cognition, and emotional resilience [4-8].

Given the increasing interest in interoception-based interventions for mental health, future research should explore whether training programs designed to enhance interoceptive awareness can lead to measurable improvements in emotional and social functioning. Mindfulness meditation, body awareness therapies, and neurofeedback techniques have shown promise in modulating interoceptive processing, but their efficacy in addressing interoception-related emotional and social deficits requires further validation. Investigating how interoceptive training impacts different populations, including individuals with psychiatric disorders, may inform personalized therapeutic approaches to optimize interoceptive function for emotional and social well-being [10,21-24].

Interoception is deeply intertwined with emotional regulation, empathy, and self-awareness, fundamentally shaping affective and social behaviors. While current research has established a connection between interoceptive processing and these higher-order functions, significant gaps remain regarding the mechanisms underlying these relationships. Future studies should aim to disentangle the complex interactions between interoception, cognition, and social dynamics, paving the way for novel interventions that leverage interoception as a target for improving emotional and psychological health [28-32].

Clinical Applications and Therapeutic Interventions: Expanding the Potential of Interoception-Based Therapies

Interoception has become a crucial target for clinical interventions due to its fundamental role in emotion regulation, autonomic function, and cognitive processes. Disruptions in interoceptive processing have been implicated in numerous psychiatric, neurological, and metabolic disorders, including anxiety, depression, post-traumatic stress disorder (PTSD), functional somatic syndromes, autism spectrum disorder (ASD), and neurodegenerative diseases [38-40].

Given interoception's profound influence on mental and physical health, various interventions have been developed to enhance bodily awareness and regulate physiological and emotional responses. However, several critical questions remain unanswered, including which interventions are the most effective, which populations benefit most, and how these therapies can be optimized for individualized treatment [46-49].

One of the most widely explored interoceptive interventions is mindfulness-based therapy, emphasizing focused attention on bodily sensations and present-moment awareness. Mindfulness practices, such as body scan meditation and breath awareness techniques, have enhanced interoceptive accuracy, improved autonomic regulation, and strengthened emotion regulation networks [50-53].

Neuroimaging studies indicate that mindfulness-based interventions increase functional connectivity between the insular cortex, anterior cingulate cortex, and prefrontal regions, promoting greater top-down control over interoceptive signals [58-60].

Clinical trials have demonstrated that mindfulness training reduces symptoms of anxiety, depression, chronic pain, and trauma-related disorders, highlighting its potential as a non-pharmacological strategy for improving interoceptive awareness. However, while mindfulness has shown promise, its mechanisms of action remain poorly understood, and individual variability in treatment response suggests that some individuals may require alternative or complementary approaches [65-68].

Another emerging therapeutic approach is biofeedback training, which provides real-time monitoring of physiological signals, such as heart rate variability (HRV), respiration, and galvanic skin response, allowing individuals to develop greater awareness and control over autonomic responses [69-72].

HRV biofeedback has been shown to enhance vagal tone, reduce stress reactivity, and improve emotional self-regulation. Studies suggest that biofeedback interventions normalize autonomic imbalances in individuals with PTSD, panic disorder, and functional somatic syndromes, making it a valuable tool for addressing interoceptive dysfunction in both psychiatric and medical populations [75-78].

However, accessibility remains a significant limitation, as biofeedback requires specialized equipment and trained professionals, restricting its widespread clinical implementation. Future research should focus on developing low-cost, portable biofeedback devices for home-based training and greater accessibility [80-83].

A particularly promising intervention involves vagus nerve stimulation (VNS), a technique designed to modulate autonomic and interoceptive processing. The vagus nerve serves as a critical conduct between the body and the brain, transmitting interoceptive signals from the heart, lungs, gut, and immune system to central interoceptive hubs such as the nucleus of the solitary tract and the insular cortex. Studies on non-invasive VNS (nVNS), such as transcutaneous auricular VNS (taVNS), have shown that stimulating the vagus nerve improves heart rate variability, enhances interoceptive awareness, and reduces symptoms of depression, anxiety, and chronic pain [84-88].

Functional neuroimaging studies suggest that taVNS improves connectivity between the brainstem, insula, and limbic regions, potentially restoring disrupted interoceptive circuits in psychiatric and neurological disorders. However, the optimal stimulation parameters, long-term effects, and patient-specific factors influencing VNS efficacy remain unknown, requiring further investigation in large-scale clinical trials [93-97].

Cognitive-behavioral therapy (CBT) incorporating interoceptive exposure techniques has been developed as a treatment for anxiety disorders, PTSD, and panic disorders, where individuals experience heightened fear and avoidance of bodily sensations [92-95]. Interoceptive exposure involves systematic exposure to physiological sensations (e.g., increased heart rate, dizziness, shortness of breath) in a controlled setting, helping patients reframe maladaptive interpretations of interoceptive signals. This approach has been highly effective in reducing anxiety-related avoidance behaviors and improving tolerance to bodily sensations [99-103].

However, its application in other disorders characterized by interoceptive dysfunction, such as ASD, functional gastrointestinal disorders, and chronic pain conditions, remains largely unexplored. Future research should assess whether interoceptive exposure techniques can be adapted for broader clinical use beyond anxiety-related conditions [108-112].

Beyond behavioral therapies, pharmacological and nutritional interventions have been proposed as potential modulators of interoceptive function. Given that neurotransmitter systems such as serotonin (5-HT), dopamine (DA), and noradrenaline (NE) play crucial roles in interoceptive processing, pharmacological agents that modulate these systems may alter interoceptive sensitivity and awareness [117-121].

Selective serotonin reuptake inhibitors (SSRIs), commonly used to treat mood and anxiety disorders, have been shown to modulate interoceptive perception in individuals with depression and panic disorder, potentially altering the way bodily sensations are processed. However, the precise effects of SSRIs on interoceptive circuits remain unclear, and further studies are needed to determine how different psychotropic medications influence interoceptive regulation in various psychiatric conditions [128-133].

In addition to pharmacological approaches, emerging research highlights the role of the gut-brain axis in interoceptive processing, suggesting that dietary and microbiome-targeted interventions may play a role in modulating interoceptive function. The gut microbiome produces metabolites that interact with vagal pathways and neurotransmitter systems, influencing interoceptive awareness and emotional regulation [136-140].

Preliminary evidence suggests that dietary modifications, probiotics, prebiotics, and omega-3 fatty acid supplementation may alter interoceptive processing and improve symptoms of anxiety and depression. However, the mechanisms underlying these effects remain largely speculative, and future studies should explore whether microbiome-targeted interventions can enhance interoceptive function in clinical populations [142-145].

Despite the growing number of interoception-based interventions, a central unresolved question is which therapies are most effective for different populations. While some individuals benefit significantly from mindfulness training or biofeedback, others show minimal or inconsistent improvements [4,29,63]. This suggests that interoceptive interventions may need to be personalized based on genetic, developmental, or environmental factors. Personalized treatment approaches that integrate neuroimaging, physiological markers, and behavioral assessments may help tailor interoceptive interventions to individual needs, maximizing their therapeutic efficacy [148-151].

Future research should prioritize identifying biomarkers of interoceptive dysfunction that can predict treatment responsiveness. Researchers may uncover distinct interoceptive signatures associated with different psychiatric and neurological conditions by integrating computational modeling, neuroimaging, and physiological monitoring. Additionally, longitudinal studies are needed to determine the durability of interoceptive interventions and assess whether early interventions can prevent the progression of interoception-related disorders [152-156].

By refining interoception-based therapies and understanding their underlying mechanisms, the field can potentially develop highly targeted interventions for psychiatric, neurological, and metabolic disorders. Addressing critical knowledge gaps will be essential for translating interoceptive research into clinically meaningful applications, ultimately enhancing both mental and physical well-being across diverse populations [9-13].

Computational Modeling and Artificial Intelligence Applied to Interoception

Interoception, the process by which the nervous system senses, interprets, and integrates internal bodily signals, has traditionally been studied using neuroimaging, behavioral assessments, and physiological recordings. However, recent advances in computational modeling, artificial intelligence (AI), and machine learning (ML) are transforming how interoceptive processes are understood [157,158].

These approaches allow for identifying complex patterns in interoceptive data, developing predictive models, and integrating multimodal data sources, ultimately leading to a more refined understanding of how the brain processes bodily signals [60].

Machine Learning and Big Data in Predicting Interoceptive Patterns

Machine learning and deep learning techniques have the potential to decode interoceptive signals by analyzing large datasets derived from neuroimaging, physiological recordings, and behavioral assessments. For instance, studies have employed ML algorithms to predict individual differences in interoceptive accuracy, particularly in psychiatric and neurological disorders [159,160].

Functional MRI (fMRI) and electroencephalography (EEG) data can be analyzed using supervised learning techniques to detect biomarkers of interoceptive dysfunction in conditions such as anxiety, depression, and schizophrenia. Additionally, unsupervised clustering methods have been used to classify individuals based on interoceptive response profiles, offering new insights into subtypes of interoceptive dysfunction across clinical populations [70-74].

Integrating interoceptive data across different experimental paradigms and physiological measurements remains a significant challenge. Traditional self-report measures of interoceptive awareness (such as the Multidimensional Assessment of Interoceptive Awareness) do not always align physiological interoceptive accuracy measures, such as heartbeat detection tasks. Machine learning models that integrate self-report, physiological, and neural data could provide a more comprehensive assessment of interoception, reducing reliance on any single measurement approach [59-62].

Mathematical Models for Studying Interoceptive Processing

Mathematical models based on Bayesian inference and predictive coding theories have been increasingly applied to interoception. The brain is believed to process interoceptive signals not as passive sensory inputs but rather through predictive mechanisms that generate expectations about internal bodily states and update them in response to sensory feedback [48-50].

Hierarchical Bayesian models have been developed to explain how interoceptive signals are processed within the brain and how errors in this predictive framework might contribute to mental and physical health conditions [43,44].

One key area of research involves dynamic systems modeling to examine how bodily states fluctuate over time and how the brain adapts its predictions accordingly. For example, models of allostatic regulation, the process by which the brain anticipates and adjusts physiological responses to maintain homeostasis provide new insights into disorders characterized by interoceptive dysregulation, such as chronic pain and metabolic syndromes. Computational simulations of interoceptive prediction errors can help clarify whether maladaptive bodily awareness in conditions like anxiety and PTSD arises from an overestimation of bodily threat signals or from a failure to update predictions in response to new sensory input [32,48,97].

AI-Driven Biomarkers and Digital Phenotyping

Artificial intelligence also holds promise in identifying interoceptive biomarkers that may predict disease onset, progression, or treatment response. AI-driven analysis of wearable sensor data including heart rate variability (HRV), skin conductance, and respiration patterns could improve diagnostic precision for conditions with altered interoceptive processing, such as autonomic disorders and functional somatic syndromes. AI-assisted digital phenotyping has continuously monitored interoceptive-related behaviors, such as sleep disturbances, appetite changes, and autonomic fluctuations, providing real-time assessments of an individual's interoceptive state [6,19,24].

Furthermore, AI-assisted neuroimaging techniques are advancing the field by allowing for automated feature extraction from brain imaging datasets and identifying neural signatures of interoceptive dysfunction. Convolutional neural networks (CNNs) applied to fMRI and diffusion tensor imaging (DTI) data can detect subtle structural and functional differences in interoceptive networks, particularly in regions such as the anterior insula, cingulate cortex, and brainstem nuclei [33,48,59].

Challenges and Open Questions in Computational Interoception

Despite these advancements, significant challenges remain in developing robust computational models of interoception. One central unresolved question is integrating neurobiological data, subjective experiences, and behavioral measures into a unified model. Current AI models struggle with the variability in interoceptive sensitivity across individuals and populations and with capturing the dynamic nature of interoceptive states over time [60,66,74].

Another major challenge is ensuring that computational models accurately reflect the complexity of interoceptive processing in real-world settings. Most interoceptive experiments are conducted under controlled laboratory conditions, making it unclear how well computational models generalize to everyday life, where multiple bodily and environmental factors interact [71,83,92].

Additionally, while AI can detect patterns in interoceptive data, it is not yet fully capable of explaining the causal mechanisms underlying interoceptive dysfunction, limiting its applicability in clinical settings [7,10].

Future Directions: Integrating Neuroscience, AI, and Computational Modeling

To overcome these limitations, future research should focus on developing hybrid models that combine AI-based machine learning with mechanistic neurobiological theories. One promising direction is using reinforcement learning models to study how individuals update interoceptive predictions based on reward and punishment. Another is integrating AI with real-time neurofeedback and biofeedback interventions, allowing for adaptive training programs that enhance interoceptive awareness and regulation [108-112].

Collaborations between neuroscientists, AI researchers, and computational modelers are essential to advancing the field. Developing standardized interoceptive datasets that combine neuroimaging, physiological, and behavioral data will be crucial in training AI models with greater predictive accuracy. Moreover, ethical considerations regarding data privacy, bias in AI-driven diagnostics, and the interpretability of machine learning models must be addressed before computational approaches can be widely adopted in clinical practice [118-122].

Computational modeling and AI-driven approaches are revolutionizing interoception research by allowing for more precise, scalable, and integrative methods of analyzing bodily awareness. These innovations can potentially improve diagnostic accuracy, personalize therapeutic interventions, and uncover the neural mechanisms underlying interoceptive dysfunction [124-127].

However, critical gaps remain in integrating neurobiological, behavioral, and computational perspectives. Future research should focus on bridging these gaps, ensuring that AI and computational models align with empirical neuroscientific findings to enhance our understanding of how the brain processes internal bodily signals. By leveraging these advancements, the field can move toward more effective clinical applications, ultimately improving outcomes for individuals with interoceptive dysregulation [138-142,165].

Conclusion

Interoception represents a fundamental process by which the nervous system integrates and interprets internal bodily signals, influencing various physiological, cognitive, and emotional functions. This review has highlighted critical gaps in our understanding of interoceptive processing, including unresolved questions regarding its neural mechanisms, its role in psychiatric and neurological disorders, the reliability of current assessment methodologies, and the potential for targeted interventions. Despite considerable progress in recent years, many aspects of interoception remain poorly understood, necessitating further interdisciplinary research.

One of the most pressing challenges in interoception research is precisely characterizing its neural underpinnings. While key regions such as the insular cortex, anterior cingulate cortex, brainstem, and autonomic nervous system have been implicated in interoceptive processing, the exact nature of their interactions remains elusive. The extent to which interoceptive dysfunction contributes to psychiatric conditions such as anxiety, depression, schizophrenia, and autism spectrum disorder is also not yet fully established. Determining whether interoceptive deficits are a cause or consequence of these disorders is critical for the development of early diagnostic markers and targeted interventions.

The assessment of interoception remains another significant limitation in the field. Current methodologies, including self-report measures, physiological tests, and neuroimaging techniques, often yield inconsistent results and lack standardization.

More robust, multimodal approaches that integrate behavioral, physiological, and computational assessments are needed to enhance the precision and reproducibility of interoceptive research. Advances in artificial intelligence and machine learning hold promise for refining predictive models of interoceptive function, enabling more accurate identification of interoceptive deficits across diverse populations.

In the clinical domain, interventions targeting interoceptive dysfunction have shown promising preliminary results, particularly in treating psychiatric and neurological conditions. Mindfulness-based therapies, biofeedback, vagus nerve stimulation, and cognitive-behavioral techniques have all demonstrated potential for modulating interoceptive awareness and improving emotional regulation. However, the efficacy of these interventions remains variable across individuals, highlighting the need for personalized treatment strategies that account for genetic, developmental, and environmental influences on interoception.

Integrating computational neuroscience, neuroimaging, and psychophysiology will be essential for advancing our understanding of interoceptive mechanisms. Applying predictive coding models, alongside AI-driven analyses of neurophysiological data, may offer novel insights into how interoceptive processes contribute to mental and physical health. Additionally, investigating the interactions between interoception, the gut-brain axis, and metabolic regulation could provide new perspectives on the role of interoception in chronic disease states.

By addressing these critical knowledge gaps, future research can revolutionize our understanding of interoception and its implications for health and disease. A more comprehensive framework integrating insights from neuroscience, psychology, computational modeling, and clinical practice will pave the way for innovative diagnostic tools and therapeutic interventions. Ultimately, advancing interoception research has profound implications for improving mental health, autonomic regulation, and overall well-being in clinical and non-clinical populations.

Decelerations

Ethics approval and consent to participate

Not Applicable

Conflict of interest

The authors declare that there is no conflict of interest.

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