



Brain–Body Interactions in Human Physiology: Emerging Insights into Autonomic Regulation, Stress Responses, and Homeostasis — A Narrative Review

Dr Priyanka Samala

¹Professor of Physiology, Father Colombo Institute of Medical Sciences 506001 Orchid No: 0009000490028230

 OPEN ACCESS

Corresponding Author:

Dr Priyanka Samala

Professor of Physiology, Father
Colombo Institute of Medical
Sciences 506001 Orchid No:
0009000490028230.

drsriyanka.05@gmail.com

Received: 09-01-2025

Accepted: 04-02-2025

Published: 19-02-2025

Copyright© International Journal of
Clinical, Medical and Health Sciences

ABSTRACT

Background: Physiological stability depends on continuous communication between the brain and peripheral organs. Although autonomic, endocrine, immune, metabolic, cardiovascular, and behavioural systems are traditionally described as separate physiological domains, increasing evidence indicates that they function as interconnected components of an integrated brain–body regulatory network.

Objective: This narrative review summarizes contemporary understanding of brain–body communication, with particular emphasis on autonomic regulation, the central autonomic network, stress responses, interoception, neuroimmune communication, circadian regulation, sleep, and the maintenance of homeostasis and allostasis.

Literature Review:

A narrative literature search was conducted using PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar. Publications available from January 2000 through December 2024 were considered, with particular emphasis on literature published between 2019 and 2024. Earlier landmark studies were included where necessary to establish important physiological concepts.

Main Findings: Brain–body communication is bidirectional and occurs through local, reflex, and higher-order central regulatory mechanisms. Visceral sensory pathways continuously provide information concerning cardiovascular, metabolic, gastrointestinal, immune, and other internal states to the central nervous system. The brain integrates these signals with environmental information, previous experience, emotional state, and behavioural demands and generates coordinated autonomic, endocrine, immune, metabolic, and behavioural responses. The sympathetic–adrenomedullary system and hypothalamic–pituitary–adrenal axis are central to physiological stress adaptation. Interoception provides an important interface between internal bodily signals and higher-order neural regulation, while vagal and other neuroimmune pathways illustrate direct communication between neural and immune systems. Circadian rhythms and sleep further influence the temporal organization of autonomic, endocrine, metabolic, and immune activity.

Conclusion: Brain–body physiology is best understood as a dynamic bidirectional network rather than as a collection of isolated organ systems. Homeostatic reflexes provide rapid stabilization, whereas allostatic mechanisms enable flexible adaptation to changing demands. Dysregulated or prolonged activation may contribute to allostatic load and multisystem dysfunction. An integrated brain–body framework may therefore provide a useful physiological basis for understanding resilience, stress adaptation, and disease mechanisms.

Keywords: brain–body communication; autonomic nervous system; central autonomic network; interoception; stress physiology; hypothalamic–pituitary–adrenal axis; vagus nerve; neuroimmune communication; homeostasis; allostasis; circadian rhythm; physiological regulation.

INTRODUCTION

The human organism continuously adapts to changes in both the internal and external environment. Maintenance of cardiovascular stability, body temperature, energy availability, fluid balance, immune activity, and metabolic function

requires continuous coordination among multiple physiological systems. Traditionally, these processes have been studied as separate domains; however, modern physiological research increasingly demonstrates that the brain, autonomic nervous system, endocrine organs, immune system, and peripheral tissues operate as an interconnected regulatory network.

Brain–body communication is fundamentally bidirectional. Peripheral tissues continuously transmit information to the central nervous system, while the brain modifies peripheral physiology according to current physiological requirements, environmental circumstances, emotional state, previous experience, and anticipated demands. Recent work has conceptualized these interactions as interconnected local, reflex, and central regulatory loops, emphasizing the integrated nature of whole-organism physiology.[1]

The autonomic nervous system (ANS) is a major component of this communication network. Sympathetic and parasympathetic pathways influence cardiovascular, respiratory, gastrointestinal, metabolic, thermoregulatory, and other visceral functions. However, autonomic regulation does not operate independently of higher brain function. Brainstem nuclei, hypothalamic structures, limbic regions, insular cortex, anterior cingulate cortex, and prefrontal areas contribute to the generation and contextual modulation of autonomic responses.[2,3]

Stress physiology provides an important example of integrated brain–body regulation. Psychological or physiological challenges can activate the sympathetic–adrenomedullary system and hypothalamic–pituitary–adrenal (HPA) axis. These responses alter cardiovascular function, energy metabolism, immune activity, and behaviour to facilitate adaptation.[4–6]

The concepts of homeostasis and allostasis provide complementary frameworks for understanding these responses. Homeostasis emphasizes the maintenance of internal variables within physiologically appropriate ranges, whereas allostasis emphasizes adaptive change in response to anticipated or actual demands.[7,8] Repeated or prolonged activation of regulatory systems, however, may contribute to allostatic load and impaired physiological resilience.

Interoception represents another fundamental component of brain–body communication. It involves the sensing and processing of signals arising from within the body, including mechanical, chemical, thermal, hormonal, and metabolic information.[9,10] Interoceptive information can influence autonomic activity, emotion, motivation, cognition, and behaviour.

The immune system also participates in bidirectional communication with the nervous system. Neural pathways can detect inflammatory signals, while autonomic and neuroendocrine pathways can modify immune activity.[11,12] The vagus nerve is particularly important within this framework, although the extent and consistency of anti-inflammatory effects of vagal stimulation in humans remain under investigation.[13]

Circadian rhythms and sleep further demonstrate that brain–body regulation is dependent not only on the magnitude of physiological responses but also on their timing. Circadian organization influences endocrine, autonomic, metabolic, immune, and behavioural processes and interacts closely with stress physiology.[14,15]

This narrative review therefore aims to integrate contemporary physiological concepts concerning brain–body communication and to examine the major mechanisms through which the brain coordinates autonomic, endocrine, immune, metabolic, circadian, and behavioural responses.

Literature Search Strategy

A narrative literature search was performed using **PubMed/MEDLINE, Scopus, Web of Science, and Google Scholar**.

The search covered publications available from **January 2000 through December 2024**. Particular emphasis was placed on publications from **2019 to 2024**, while earlier landmark studies were retained when they were important for establishing fundamental physiological concepts.

The principal search terms included:

- “brain–body communication”
- “brain-body physiology”
- “autonomic nervous system”
- “central autonomic network”
- “interoception”
- “stress physiology”
- “hypothalamic-pituitary-adrenal axis”
- “HPA axis”
- “vagus nerve”
- “neuroimmune communication”
- “inflammatory reflex”
- “homeostasis”
- “allostasis”
- “allostatic load”
- “circadian rhythm”

- “sleep”
- “metabolic regulation”
- “physiological stress”

Search terms were combined using Boolean operators where appropriate. Reference lists of major review articles were also screened manually to identify additional relevant publications.

The present work is a **Narrative Review** and was not designed as a systematic review or meta-analysis. Therefore, no formal risk-of-bias scoring, PRISMA flow diagram, or quantitative pooled analysis was undertaken.

Literature cutoff: 31 December 2024.

Conceptual Framework of Brain–Body Communication

Brain–body communication involves continuous information exchange between the central nervous system and peripheral organs. This interaction can be considered at three broad levels: local communication, reflex regulation, and central adaptive regulation.[1]

At the local level, sensory neurons and peripheral cells interact directly within tissues. Such mechanisms are particularly relevant to inflammation and tissue protection. At the reflex level, visceral sensory information is transmitted to brainstem and hypothalamic circuits that generate relatively rapid autonomic and endocrine responses. At the central level, higher-order brain regions integrate internal bodily information with external sensory information, emotional context, previous experience, motivation, and behavioural goals.[1,10]

These levels are not independent. Rather, they form interconnected feedback loops. Changes in peripheral physiology alter neural activity, neural activity modifies peripheral function, and the resulting physiological changes provide further feedback to the brain.

This integrated model represents a major shift from viewing physiological systems as independent units toward understanding the organism as a coordinated regulatory network.

Table 1. Major components of brain–body communication

Component	Principal physiological role	Direction of communication
Visceral sensory pathways	Detect internal organ and tissue states	Body → Brain
Nucleus of solitary tract	Integration of visceral afferent information	Body ↔ Brain
Hypothalamus	Autonomic, endocrine, metabolic and thermoregulatory regulation	Brain ↔ Body
Brainstem autonomic nuclei	Rapid cardiovascular and visceral regulation	Brain ↔ Body
Sympathetic nervous system	Cardiovascular and metabolic activation	Brain → Body
Parasympathetic/vagal pathways	Cardiac, gastrointestinal and visceral regulation	Brain ↔ Body
HPA axis	Neuroendocrine stress regulation	Brain → Body
Immune mediators	Inflammatory and metabolic signalling	Body → Brain
Cortical and limbic networks	Emotional, cognitive and behavioural regulation	Brain ↔ Body
Circadian system	Temporal organization of physiology	Brain ↔ Body

Central Autonomic Network

The central autonomic network (CAN) is a distributed functional system involved in the regulation of visceral and autonomic processes. Important components include the insular cortex, anterior cingulate cortex, amygdala, hypothalamus, periaqueductal gray, parabrachial complex, nucleus of the solitary tract, and medullary autonomic nuclei.[2,3]

The CAN should not be considered a single anatomical centre. Instead, it represents interconnected neural structures capable of coordinating cardiovascular, respiratory, gastrointestinal, endocrine, pain-related, emotional, and behavioural responses.

Visceral sensory information reaches the brain through vagal, glossopharyngeal, and spinal afferent pathways. Brainstem nuclei provide an important first stage of integration. Signals can subsequently reach hypothalamic, thalamic, limbic, and cortical networks.

The insular cortex is particularly important for integration of internal bodily signals. The anterior cingulate and prefrontal regions contribute contextual and behavioural information, allowing physiological responses to be modified according to environmental circumstances and expectations.

Thus, the CAN provides an important physiological interface between automatic visceral regulation and higher-order emotional and behavioural processes.

Autonomic Regulation and Cardiovascular Homeostasis

The cardiovascular system provides a clear example of continuous brain–body feedback.

Arterial pressure is detected primarily by mechanosensitive receptors located in the carotid sinus and aortic arch. Afferent information reaches the nucleus of the solitary tract through the glossopharyngeal and vagal nerves. Brainstem circuits subsequently modify sympathetic and parasympathetic activity to regulate heart rate, myocardial contractility, vascular resistance, and cardiac output.

This baroreflex operates continuously and rapidly. Nevertheless, cardiovascular regulation also depends on higher-order influences. Exercise, posture, emotional stress, temperature, hydration, pain, and anticipated activity can all modify autonomic cardiovascular activity.

Sympathetic activation generally increases heart rate, myocardial contractility, and vascular tone, whereas parasympathetic activity, particularly through vagal pathways, contributes to cardiac slowing and recovery.

Heart rate variability (HRV) provides a non-invasive measure of beat-to-beat cardiovascular fluctuations and is frequently used in studies of autonomic regulation. However, HRV should not be interpreted as a direct and isolated measure of parasympathetic activity because it is influenced by respiratory pattern, posture, age, physical fitness, medications, circadian phase, and other factors.

The cardiovascular system therefore demonstrates how reflex mechanisms, higher brain networks, peripheral receptors, and behavioural state operate together to maintain physiological stability.

Brain–Body Interactions During Stress

Stress is a state in which physiological regulatory systems respond to actual or anticipated challenge. The response involves coordinated activation of neural, endocrine, metabolic, cardiovascular, immune, and behavioural pathways.

Two major physiological mechanisms are the sympathetic–adrenomedullary system and the HPA axis.

Sympathetic activation provides rapid responses through norepinephrine released from sympathetic nerve terminals and catecholamines released from the adrenal medulla. These changes increase cardiovascular performance and mobilize metabolic resources.

The HPA axis operates on a slower time scale. Stress-related neural activity promotes hypothalamic corticotropin-releasing hormone secretion, which stimulates pituitary adrenocorticotrophic hormone release and subsequent glucocorticoid secretion from the adrenal cortex.[4-6]

Cortisol influences glucose metabolism, cardiovascular function, immune activity, cognition, and behavioural responses. Cortisol secretion also follows pronounced circadian and ultradian rhythms, linking stress physiology with the temporal organization of the organism.[14]

The magnitude of the stress response varies according to the nature of the challenge and individual characteristics including previous experience, psychological appraisal, sleep, age, sex, physical condition, and environmental context.[5]

Acute Stress and Physiological Adaptation

The acute stress response is fundamentally adaptive. During short-term physiological or psychological challenge, increased sympathetic activity and HPA-axis activation help mobilize energy and support cardiovascular performance.

Heart rate and blood pressure may increase, glucose availability rises, and resources are redistributed toward physiological functions required for immediate adaptation.

Termination of the stress response is equally important. Parasympathetic reactivation, reduction of sympathetic activity, glucocorticoid negative feedback, and restoration of metabolic balance contribute to physiological recovery.

Consequently, a healthy stress response requires both appropriate activation and effective recovery.

Repeated activation, inadequate recovery, or prolonged exposure to stressors can gradually alter the functioning of regulatory systems and contribute to allostatic load.

Chronic Stress and Allostatic Load

Homeostasis refers to the maintenance of relatively stable internal physiological conditions. Allostasis extends this concept by emphasizing adaptive change according to environmental demands.[7,8]

Allostatic regulation permits the organism to anticipate and respond to changing circumstances. For example, cardiovascular and metabolic systems begin adapting before and during physical activity rather than waiting for severe physiological disturbance.

Allostatic responses become problematic when regulatory systems are activated excessively, repeatedly, or for prolonged periods. McEwen described allostatic load as the cumulative physiological burden associated with chronic adaptation to stress.[7]

Potential consequences include alterations in cardiovascular regulation, metabolic function, immune activity, sleep, endocrine signalling, and neural function.

Table 2. Comparison of homeostasis and allostasis

Feature	Homeostasis	Allostasis
Primary concept	Stability of internal variables	Stability through adaptive change
Main response	Correction of deviation	Anticipatory/adaptive adjustment
Example	Baroreflex regulation of arterial pressure	Cardiovascular preparation during exercise
Major systems	Neural, endocrine, renal, cardiovascular	Neural, endocrine, metabolic, immune and behavioural
Primary advantage	Internal stability	Physiological flexibility
Potential limitation	May be inadequate during major challenges	Repeated activation may contribute to allostatic load

Homeostasis and allostasis should therefore be considered complementary rather than competing concepts. Homeostatic mechanisms provide rapid correction, whereas allostatic mechanisms provide flexibility.

Interoception and Internal Bodily Signalling

Interoception refers to the sensing and processing of internal physiological signals. These signals may include cardiovascular, respiratory, gastrointestinal, thermal, hormonal, metabolic, and inflammatory information.[9,10]

Interoceptive pathways transmit information through vagal and spinal afferents, with subsequent processing through brainstem, thalamic, insular, cingulate, and somatosensory networks.

The coding of interoceptive signals is complex. Different internal signals may be represented through distinct combinations of peripheral receptors, sensory neurons, brainstem circuits, and higher cortical networks.[10] Contemporary physiological research increasingly views interoception as a dynamic network process rather than the function of one isolated brain region.[17]

Interoceptive information can influence autonomic regulation, motivation, emotional state, cognition, and behaviour. Conversely, behavioural and cognitive processes can modify physiological state.

This bidirectional relationship provides a physiological basis for understanding how bodily states and mental processes influence one another.

Vagus Nerve and Neuroimmune Communication

The vagus nerve is a major communication pathway between the brain and thoracic and abdominal organs. Vagal afferents convey information concerning visceral mechanical, chemical, metabolic, and inflammatory conditions to the brainstem.

Vagal efferent activity influences cardiac, gastrointestinal, and other visceral functions. The vagus nerve has also become an important component of neuroimmune physiology.

The concept of the inflammatory reflex proposes that inflammatory signals can activate sensory pathways and central regulatory circuits, followed by efferent neural modulation of immune responses.[11,12]

Experimental work has demonstrated that cholinergic mechanisms can influence inflammatory cytokine production. These observations have stimulated interest in vagus nerve stimulation and other neuromodulatory approaches.

However, mechanistic evidence should not be equated with established clinical efficacy. A 2024 systematic review and meta-analysis reported no consistent evidence for a reliable anti-inflammatory effect of vagus nerve stimulation across human studies.[13] Therefore, further controlled clinical research is required to determine the therapeutic significance of these pathways.

Neuroimmune Integration

The immune system is an important component of whole-organism physiological regulation.

Inflammatory mediators can influence the nervous system through neural, humoral, and cellular pathways. These signals can affect sleep, appetite, temperature regulation, motivation, fatigue, and behaviour.

During acute infection or tissue injury, such changes may be adaptive because they redirect physiological and behavioural resources toward recovery.

Conversely, neural pathways can influence immune function. The inflammatory reflex illustrates how neural activity can modulate inflammatory responses.[11,12]

Recent brain–body frameworks have also emphasized **immunoception**, referring broadly to neural detection and integration of immune-related physiological information.[1]

This concept strengthens the view that immune regulation is not exclusively peripheral but is integrated with neural and behavioural physiology.

Metabolic Regulation and Brain–Body Communication

Energy homeostasis requires continuous communication between the brain and peripheral metabolic organs.

The hypothalamus integrates information concerning energy availability from hormones, nutrients, gastrointestinal signals, and neural pathways. Insulin, leptin, gastrointestinal peptides, glucose, and other metabolic signals contribute to central regulation of feeding and energy expenditure.

Autonomic pathways influence hepatic metabolism, pancreatic activity, gastrointestinal function, adipose tissue physiology, and energy utilization.

Conversely, peripheral metabolic status influences brain function and behaviour. Energy deficiency can stimulate food-seeking behaviour, whereas adequate energy availability activates satiety-related mechanisms.

Therefore, appetite and metabolic behaviour represent outputs of an integrated brain–body regulatory system rather than isolated psychological phenomena.

Circadian Regulation of Brain–Body Physiology

Physiological regulation is strongly dependent on time.

The suprachiasmatic nucleus functions as a central circadian pacemaker and coordinates biological rhythms with the light–dark cycle. Peripheral tissues also possess molecular clocks, creating a distributed temporal regulatory system.

The HPA axis demonstrates pronounced circadian organization. Cortisol secretion varies across the day and contributes to metabolic, immune, cognitive, and behavioural regulation.[14]

Circadian disruption caused by shift work, irregular sleep, insufficient sleep, or abnormal light exposure may alter the temporal coordination of physiological systems.

The interaction between circadian rhythms and stress is particularly important because stress responses vary according to circadian phase. Persistent disruption may contribute to altered HPA-axis activity and reduced physiological resilience.[14,15]

Sleep and Brain–Body Regulation

Sleep is an active physiological state characterized by coordinated changes in autonomic, endocrine, metabolic, immune, and neural activity.

During normal sleep, cardiovascular activity, autonomic balance, hormonal secretion, thermoregulation, and metabolic processes undergo characteristic changes. Sleep therefore contributes to physiological recovery and recalibration rather than representing simply a period of reduced consciousness.

Sleep deprivation may disturb autonomic and endocrine responses to subsequent stress. A 2024 systematic review found substantial variability in autonomic and cortisol responses following total sleep deprivation, emphasizing the complex relationship between sleep loss and stress physiology.[18]

These observations support the concept that adequate sleep is an important component of brain–body resilience.

Thermoregulation as an Example of Integrated Brain–Body Control

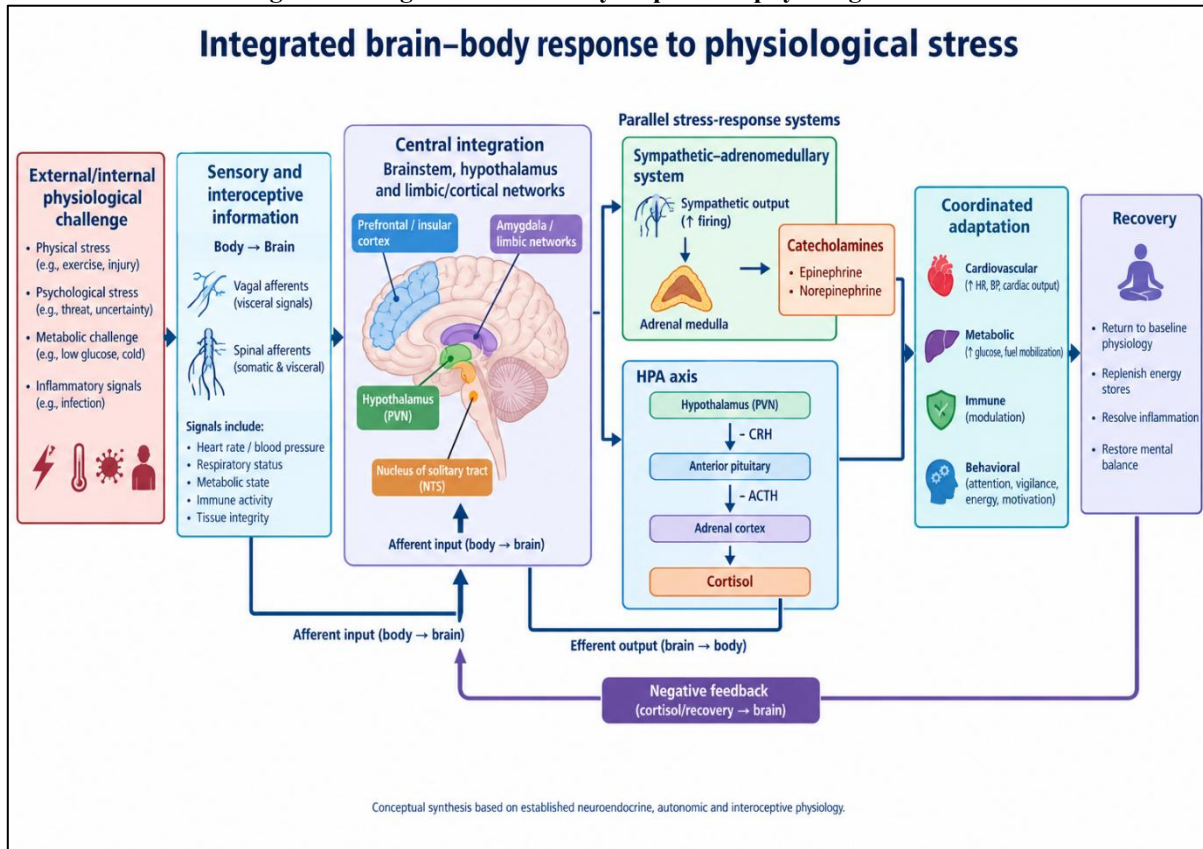
Thermoregulation provides a classic example of integrated physiological regulation.

Thermal information is detected by peripheral and central sensory mechanisms and transmitted to hypothalamic and other regulatory circuits. The resulting responses include changes in skin blood flow, sweating, metabolic heat production, shivering, and behaviour.

Thermoregulatory behaviour may also be anticipatory. Individuals may seek shade, warmth, fluids, or altered clothing before substantial changes in core temperature occur.

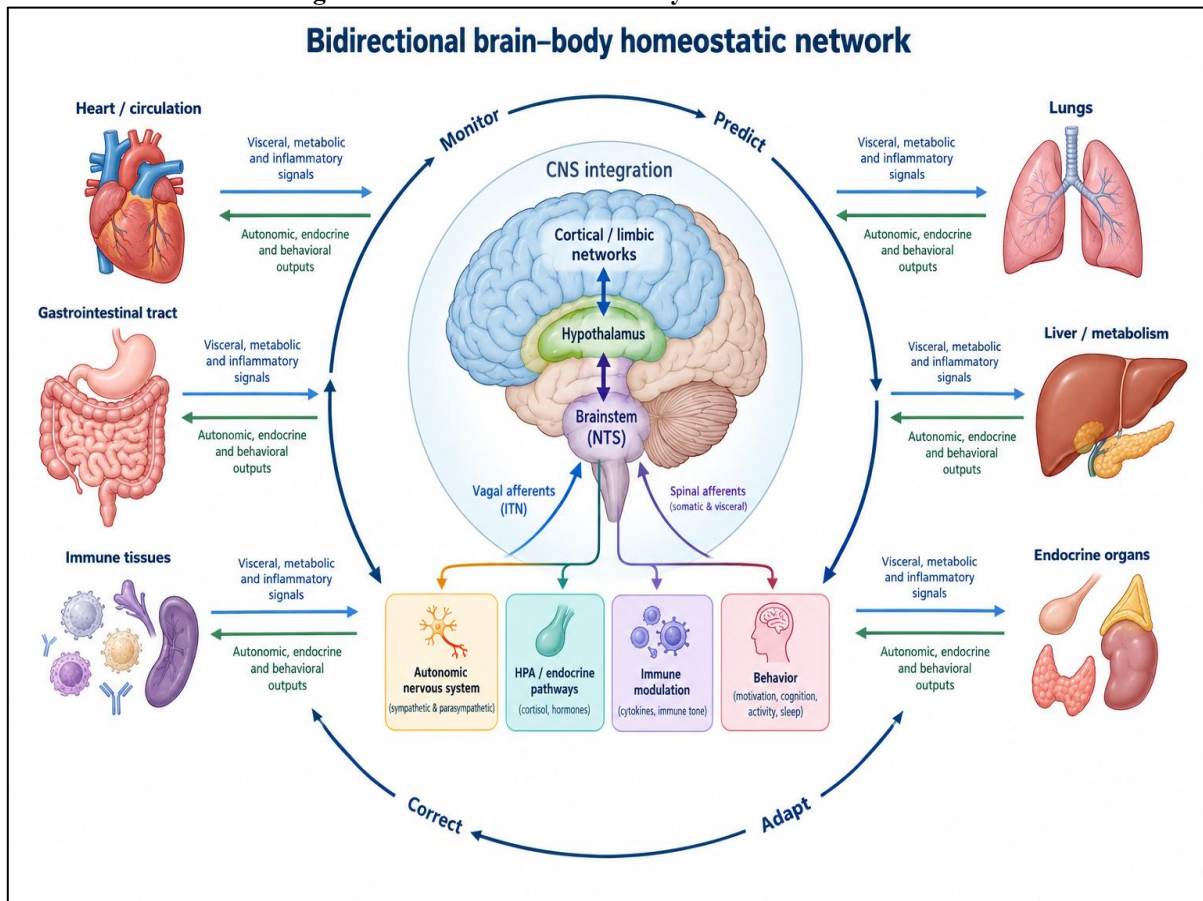
Thus, thermoregulation combines sensory detection, autonomic control, endocrine and metabolic responses, and behaviour within a coordinated regulatory system.

Figure 1. Integrated brain–body response to physiological stress



The integrated model demonstrates that physiological stress is not mediated by a single pathway. Instead, peripheral information is processed at multiple levels and produces coordinated autonomic, endocrine, immune, metabolic, and behavioural responses.

Figure 2. Bidirectional brain–body homeostatic network



This model emphasizes that brain–body communication is bidirectional. Peripheral organs provide information about internal physiological conditions, while central networks coordinate responses designed to preserve or adapt physiological function.

Principal Brain–Body Regulatory Pathways

Table 3. Principal regulatory pathways involved in brain–body physiology

Regulatory pathway	Major physiological signal	Principal function
Visceral afferent–brainstem pathway	Mechanical and chemical visceral signals	Autonomic reflex regulation
Baroreflex	Arterial pressure	Heart rate and vascular regulation
Sympathetic–adrenomedullary pathway	Sympathetic activity/catecholamines	Cardiovascular and metabolic activation
HPA axis	CRH–ACTH–cortisol	Stress and metabolic adaptation
Vagal pathway	Visceral neural signals	Cardiac, gastrointestinal and neuroimmune regulation
Interoceptive pathways	Internal bodily signals	Homeostatic and behavioural regulation
Neuroimmune reflexes	Cytokines/inflammatory signals	Modulation of inflammation
Circadian system	Light and temporal cues	Temporal organization of physiology
Cortical–limbic autonomic pathways	Cognitive/emotional context	Context-dependent autonomic regulation

Clinical and Physiological Relevance

Understanding brain–body interactions has increasing relevance to clinical physiology and translational research.

Autonomic measurements such as HRV, blood pressure variability, respiratory patterns, and skin conductance can provide information concerning physiological regulation and recovery. However, such variables should be interpreted within their broader physiological context rather than as isolated biomarkers.

Stress-related disorders may involve interactions among autonomic, endocrine, immune, metabolic, and behavioural systems. A brain–body framework may therefore provide a more comprehensive explanation for clinical symptoms that cross conventional organ-system boundaries.

The neuroimmune interface also provides a potential target for neuromodulatory therapies. Vagus nerve stimulation is an important example, although the evidence for consistent anti-inflammatory effects in humans remains inconclusive.[13]

Circadian biology and sleep physiology may provide additional opportunities for improving physiological resilience. Regular sleep–wake schedules, appropriate light exposure, physical activity, and behavioural interventions may influence several regulatory systems simultaneously.

Emerging bioelectronic technologies may further permit monitoring and modulation of brain–body circuits. Nevertheless, translation into routine clinical use requires rigorous validation of physiological biomarkers, reproducibility, safety, and clinical benefit.

Emerging Directions in Brain–Body Physiology

Network physiology

Future research is likely to move increasingly from isolated physiological variables toward integrated network models. Simultaneous assessment of autonomic, endocrine, immune, metabolic, and neural variables may provide a more comprehensive representation of physiological state.

Individualized autonomic phenotyping

Individuals can demonstrate markedly different physiological responses to similar stressors. Age, sex, fitness, sleep, previous stress exposure, medications, genetics, and environmental conditions may all contribute to this variability.

Individualized physiological phenotyping may therefore improve interpretation of autonomic and endocrine measurements.

Advanced interoceptive research

Improved neuroimaging, electrophysiological techniques, and peripheral physiological monitoring may clarify how internal bodily signals are encoded and integrated by the brain.

Neuroimmune modulation

Neuroimmune pathways represent an important area for future therapeutic research. However, mechanistic plausibility must be supported by reproducible clinical evidence before broad therapeutic implementation.

Circadian and temporal medicine

Physiological responses vary according to circadian phase. Future studies may therefore consider the timing of medication, exercise, sleep interventions, and behavioural therapies as an important component of individualized treatment.

Multimodal physiological monitoring

Wearable devices can increasingly measure heart rate, HRV, sleep, activity, temperature, and other variables. Integration of these measurements with laboratory and clinical data may provide new approaches to monitoring physiological resilience and recovery.

LIMITATIONS

This article is a narrative review and therefore does not employ the quantitative methodology of a systematic review or meta-analysis.

The literature search was designed to identify major physiological concepts and contemporary evidence rather than to calculate pooled effect estimates. Consequently, selection of literature may have been influenced by the conceptual focus of the review.

The subject is inherently broad and encompasses neuroscience, autonomic physiology, endocrinology, immunology, metabolism, sleep physiology, and circadian biology. It is therefore not possible to provide an exhaustive synthesis of every relevant publication.

CONCLUSION

Brain–body communication is a fundamental principle of human physiology. The brain does not regulate the body through one-directional commands; rather, physiological stability and adaptation emerge from continuous bidirectional communication between the central nervous system and peripheral organs.

The autonomic nervous system provides rapid regulation of visceral function, while the HPA axis contributes endocrine adaptation to stress. Interoceptive pathways continuously inform the brain about internal physiological conditions, enabling autonomic, endocrine, behavioural, and metabolic responses to be modified according to current and anticipated demands.

The vagus nerve and neuroimmune pathways demonstrate that immune activity is also integrated within neural regulatory networks. Circadian rhythms and sleep further demonstrate that physiological regulation depends not only on the intensity of a response but also on its timing and recovery.

Homeostasis and allostasis should therefore be regarded as complementary components of physiological regulation. Appropriate activation and termination of adaptive responses promote resilience, whereas persistent or dysregulated activation may contribute to allostatic load and multisystem dysfunction.

An integrated brain–body framework provides a useful foundation for modern physiology and may support future research into autonomic biomarkers, neuroimmune regulation, circadian medicine, physiological resilience, and individualized approaches to health and disease.

Ethical Statement

Ethical approval was **not applicable**, because this article is a literature-based narrative review and involved no recruitment of human participants, animal experimentation, identifiable personal data, or collection of biological samples.

Funding

No external funding was received for the preparation of this review.

Conflict of Interest

The author(s) declare no conflict of interest.

Author Contributions

The author(s) contributed to the conception of the review, literature search, interpretation of evidence, manuscript preparation, critical revision, and approval of the final manuscript.

Data Availability Statement

No original dataset was generated or analyzed for this narrative review. The evidence discussed was derived from previously published scientific literature.

REFERENCES

1. Sammons M, Popescu MC, Chi J, Liberles SD, Gogolla N, Rolls A. Brain-body physiology: local, reflex, and central communication. *Cell*. 2024;187(21):5877-5890. doi:10.1016/j.cell.2024.08.050.
2. Benarroch EE. The central autonomic network: functional organization, dysfunction, and perspective. *Mayo Clin Proc*. 1993;68(10):988-1001. doi:10.1016/S0025-6196(12)62272-1.
3. Thayer JF, Lane RD. Claude Bernard and the heart-brain connection: further elaboration of a model of neurovisceral integration. *Neurosci Biobehav Rev*. 2009;33(2):81-88. doi:10.1016/j.neubiorev.2008.08.004.
4. Ulrich-Lai YM, Herman JP. Neural regulation of endocrine and autonomic stress responses. *Nat Rev Neurosci*. 2009;10(6):397-409. doi:10.1038/nrn2647.

5. Russell G, Lightman S. The human stress response. *Nat Rev Endocrinol*. 2019;15(9):525-534. doi:10.1038/s41574-019-0228-0.
6. Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, Makinson R, et al. Regulation of the hypothalamic-pituitary-adrenocortical stress response. *Compr Physiol*. 2016;6(2):603-621. doi:10.1002/cphy.c150015.
7. McEwen BS. Stress, adaptation, and disease. Allostasis and allostatic load. *Ann N Y Acad Sci*. 1998;840:33-44. doi:10.1111/j.1749-6632.1998.tb09546.x.
8. Sterling P. Allostasis: a model of predictive regulation. *Physiol Behav*. 2012;106(1):5-15. doi:10.1016/j.physbeh.2011.06.004.
9. Craig AD. How do you feel? Interoception: the sense of the physiological condition of the body. *Nat Rev Neurosci*. 2002;3(8):655-666. doi:10.1038/nrn894.
10. Wang RL, Chang RB. The coding logic of interoception. *Annu Rev Physiol*. 2024;86:301-327. doi:10.1146/annurev-physiol-042222-023455.
11. Tracey KJ. Reflex control of immunity. *Nat Rev Immunol*. 2009;9(6):418-428. doi:10.1038/nri2566.
12. Pavlov VA, Tracey KJ. The vagus nerve and the inflammatory reflex—linking immunity and metabolism. *Nat Rev Endocrinol*. 2012;8(12):743-754. doi:10.1038/nrendo.2012.189.
13. Schiweck C, Sausmekat S, Zhao T, Jacobsen L, Reif A, Thanarajah SE. No consistent evidence for the anti-inflammatory effect of vagus nerve stimulation in humans: a systematic review and meta-analysis. *Brain Behav Immun*. 2024;116:237-258. doi:10.1016/j.bbi.2023.12.008.
14. Rao R, Androulakis IP. The physiological significance of the circadian dynamics of the HPA axis: interplay between circadian rhythms, allostasis and stress resilience. *Horm Behav*. 2019;110:77-89. doi:10.1016/j.yhbeh.2019.02.018.
15. Focke CMB, Iremonger KJ. Rhythmicity matters: circadian and ultradian patterns of HPA axis activity. *Mol Cell Endocrinol*. 2020;498:110552.
16. McEwen BS. Protective and damaging effects of stress mediators. *N Engl J Med*. 1998;338(3):171-179. doi:10.1056/NEJM199801153380307.
17. Candia-Rivera D, Engelen T, Babo-Rebello M, Salamone PC. Interoception, network physiology and the emergence of bodily self-awareness. *Neurosci Biobehav Rev*. 2024;165:105864. doi:10.1016/j.neubiorev.2024.105864.
18. Messa RM, Benfica MA, Ribeiro LFP, Williams CM, Davidson SRE, Alves ES. The effect of total sleep deprivation on autonomic nervous system and cortisol responses to acute stressors in healthy individuals: a systematic review. *Psychoneuroendocrinology*. 2024;168:107114. doi:10.1016/j.psyneuen.2024.107114.
19. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. *Nat Rev Neurosci*. 2008;9(1):46-56. doi:10.1038/nrn2297.
20. Critchley HD, Harrison NA. Visceral influences on brain and behavior. *Neuron*. 2013;77(4):624-638. doi:10.1016/j.neuron.2013.02.008.
21. Barrett LF, Simmons WK. Interoceptive predictions in the brain. *Nat Rev Neurosci*. 2015;16(7):419-429. doi:10.1038/nrn3950.
22. Porges SW. The polyvagal perspective. *Biol Psychol*. 2007;74(2):116-143. doi:10.1016/j.biopsycho.2006.06.009.
23. Chrousos GP. Stress and disorders of the stress system. *Nat Rev Endocrinol*. 2009;5(7):374-381. doi:10.1038/nrendo.2009.106.
24. McEwen BS. Central effects of stress hormones in health and disease: understanding the protective and damaging effects of stress and stress mediators. *Eur J Pharmacol*. 2008;583(2-3):174-185. doi:10.1016/j.ejphar.2007.11.071.
25. Rosas-Ballina M, Tracey KJ. The neurology of the immune system: neural reflexes regulate immunity. *Neuron*. 2009;64(1):28-32. doi:10.1016/j.neuron.2009.09.039.
26. Oke SL, Tracey KJ. The inflammatory reflex and the role of complementary and alternative medical therapies. *Ann N Y Acad Sci*. 2009;1172:172-180. doi:10.1196/annals.1393.013.
27. Craig AD. Interoception: the sense of the physiological condition of the body. *Curr Opin Neurobiol*. 2003;13(4):500-505. doi:10.1016/S0959-4388(03)00090-4.
28. Thayer JF, Åhs F, Fredrikson M, Sollers JJ 3rd, Wager TD. A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. *Neurosci Biobehav Rev*. 2012;36(2):747-756. doi:10.1016/j.neubiorev.2011.11.009.
29. McEwen BS, Gianaros PJ. Stress- and allostasis-induced brain plasticity. *Annu Rev Med*. 2011;62:431-445. doi:10.1146/annurev-med-052209-100430.
30. Dhabhar FS. Effects of stress on immune function: the good, the bad, and the beautiful. *Immunol Res*. 2014;58(2-3):193-210. doi:10.1007/s12026-014-8517-0.