The intricate brain–body interaction in psychiatric and neurological diseases

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
D – writing the article; E – critical revision of the article; F – final approval of the article

Advances in Clinical and Experimental Medicine, ISSN 1899–5276 (print), ISSN 2451–2680 (online) *Adv Clin Exp Med*. 2024;33(4):321–326

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Funding sources
The study was supported by Next Generation EU (NGEU) and funded by the Ministry of University and Research (MUR), National Recovery and Resilience Plan (NRRP) and the MNESYS project (grant No. PE0000006): A multiscale integrated approach to the study of the nervous system in health and disease (grant No. DN. 1553 11.10.2022) granted to Simone Battaglia.

Conflict of interest
None declared

Received on February 13, 2024
Reviewed on March 1, 2024
Accepted on March 5, 2024

Published online on March 21, 2024

Cite as
Di Gregorio F, Battaglia S. The intricate brain–body interaction in psychiatric and neurological diseases. *Adv Clin Exp Med*. 2024;33(4):321–326. doi:10.17219/acem/185689

DOI
10.17219/acem/185689

Abstract

A harmonic brain–body communication is fundamental to individual wellbeing and is the basis of human cognition and behavior. In the last 2 decades, the interaction between the brain and body functioning has become a central area of study for neurologists and neuroscientists in clinical and non-clinical contexts. Indeed, brain–body axis dysfunctions occur in many psychiatric, neurological and neurodegenerative diseases. This editorial will focus on recent advances and future therapeutic perspectives for studying brain–body interactions in health and diseases.

Key words: psychiatric disorders, central nervous system, neurodegeneration, autonomic nervous system, neurological disorders

The brain–body balance

Coordinated interactions between the brain and the body are crucial for survival. The human body is a complex system of interconnected structures and functions, each playing a crucial role in maintaining brain–body homeostasis and driving behavior and cognition. However, brain–body balance disruption can lead to neurological or psychological diseases. Indeed, several psychiatric, neurological and neurodegenerative disorders present with dysregulations of brain and body functioning.[1–3] In this context, the combined assessment of brain and body functioning becomes fundamental in clinical practice, as it offers valuable insights into the relationship between brain function and body regulation.[4,5]

In this manuscript, we will delve into the profound interplay between the brain and the body, examining how disruptions in this dynamic relationship contribute to the onset and/or progression of debilitating conditions. Despite extensive research on dysfunctional brain–body interactions in neurological and psychiatric disorders, it is not currently possible to establish causative and/or hierarchical links between dysfunctional brain–body interactions and neuropsychiatric disease onset.

The onset and progression of many psychiatric and neurological diseases often involve intricate molecular, cellular and systemic changes that impact the central and autonomic nervous systems.[6] Neuronal damage, inflammation and aberrant protein accumulation can disrupt the normal flow of signals within brain networks. Such brain-level dysfunctions are linked to a cascade of symptoms and dysregulation of the autonomic nervous system while concurrently revealing the interplay between neural substrates and neuropsychiatric diseases.[6] For instance, dysfunctional cardiac activity was linked to impaired cognitive functioning in healthy and neurological populations,[7–9] and heart rate variability (i.e., a measure of cardiac functioning) was recently used as a biomarker to differentiate Alzheimer's disease from Lewy body dementia in patients with mild cognitive impairment.[10] Moreover, the degeneration of dopaminergic neurons in Parkinson's disease results in motor fluctuations and dyskinetic movements. However, relevant works have also highlighted the role of the gut microbiome in the maladaptive immune and inflammatory responses that accelerate Parkinson's pathogenesis.[11,12] Crucially, preclinical and clinical studies indicate that gut microbiome alterations may be susceptibility factors for the progression of several neurodegenerative disorders, including Alzheimer's disease and Parkinson's disease, and major psychiatric disorders.[13–17] For instance, recent findings demonstrate a consistent decrease in microbial richness in bipolar disorder patients, while differences in beta diversity were observed in major depressive disorder, schizophrenia and psychosis, compared with controls.[16] Similarly, liver diseases such as cirrhosis and hepatic encephalopathy are closely related to neurological symptoms through the liver–brain axis.[18,19]

The immune system plays a crucial role in multiple sclerosis (MS) etiology and progression.[20,21] Specifically, immunological mechanisms acting at the brain and body levels can interact through multiple pathways[22–24] and, in MS, chronic immunological dysregulations may reflect a long-term stress response to homeostatic dysregulation in the central nervous system, ultimately leading to neurodegeneration.[25] However, the role of central and peripheral immunological events in the early inflammatory phase of MS is under debate. In particular, it is unclear whether a primary immunological process occurs in the brain and extends to the periphery or vice versa, where the immune activation initiates in the periphery before transferring to the as-yet unaffected central nervous system.[26,27] Importantly, peripheral and central inflammatory processes likely play a crucial role in fatigue during MS.[27,28]

Recent advances in neuroscience and physiology have shed light on the dynamic brain–body relationship in psychiatric disorders, emphasizing the bidirectional communication between the brain and various physiological systems. Dysregulations of specific neural circuits and neurotransmitter systems and structural and functional brain changes contribute to the pathophysiology of various psychiatric disorders.[2,29–32] For instance, dysfunction in the prefrontal–limbic circuitry and alterations in neurotransmitter systems such as dopamine and glutamate are implicated in mood disorders and schizophrenia.[33–37] Moreover, epigenetic and genetic influences shape susceptibility to neuropsychiatric disorders, with genome-wide association studies identifying risk genes associated with conditions such as bipolar disorder.[31,38,39] Epigenetic modifications, including DNA methylation and histone modification, further regulate gene expression patterns linked to psychiatric phenotypes.[40,41]

Dysregulations of the neuroendocrine and immune systems have been reported in depression, anxiety and elevated stress,[42,43] with a key role for the hypothalamus–pituitary–adrenal axis (HPA).[44,45] In particular, post-traumatic stress disorder (PTSD) was related to abnormal dynamics in HPA axis activation,[46,47] which was responsible for increased cortisol levels.[48,49] This abnormal activity may lead to impairments in cognitive functions like attention, memory and cognitive control,[50–52] in PTSD patients. Moreover, dysfunctions in the heart rate, blood pressure and respiratory rate have been observed in several psychiatric disorders, including panic and generalized anxiety disorders.[53–56] The research framework highlighted the significance of heart rate variability (HRV) in the context of psychiatric disorders, adding a new dimension to our understanding of the dynamic brain–body relationship.[57] Decreased HRV has been identified as a contributing factor in heart failure patients with psychiatric conditions; furthermore, abnormal HRV has been reported in various mental disorders, emphasizing the role of the autonomic nervous system in these conditions.[58–60] Increased sympathetic activity and reduced parasympathetic tone are common findings in psychiatric disorders, highlighting the role of autonomic dysregulation in the manifestation and progression of mental health conditions, as the autonomic imbalance contributes to the resulting pro-inflammatory state of depression.[42,44,61–64] Finally, chronic inflammation, characterized by elevated levels of pro-inflammatory cytokines, has also been linked to conditions like schizophrenia.[65–67]

Diagnostic and therapeutic prospective

Integrating different markers from brain and body functioning would enhance diagnostic and prognostic accuracy across various clinical domains. Definitively, an integrative brain–body assessment approach may enable a more comprehensive understanding of the neurobiological mechanisms and help guide treatment strategies, such as selecting appropriate medications or implementing targeted interventions for personalized medical approaches.[5,68,69] As such, recent studies highlighted how combining electroencephalography (EEG) and cardiac activity may provide detailed information about the interaction between neural activity and the autonomic nervous system during cognitive processes[70] and neurological and psychiatric disorders.[71] Specifically, EEG biomarkers, such as aberrant oscillatory patterns or reduced connectivity,[37,72,73] can indicate early signs of cognitive decline, while cardiac measures may reflect autonomic dysfunction associated with neurodegenerative processes.[58,59,74,75] By integrating these measures, it is possible to improve diagnostic accuracy and track disease progression, facilitating the development of personalized treatment plans.[5,76–80]

Advancements in neuroscience and technology have opened new frontiers for treating neurological and psychiatric-related symptoms by integrating different approaches.[81–83] Neurostimulation techniques, such as deep brain stimulation, transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), transcranial electrical stimulation, and vagus nerve stimulation, are being explored as potential interventions for various neurological disorders.[84–89] These approaches aim to modulate neural activity within large neural networks, but the effects of these treatments on brain–body communication are scarcely investigated.[90]

Understanding the multifaceted interactions between the brain and the body in neurological and psychiatric diseases is essential for developing effective therapeutic approaches.[5] Current treatments often focus on mitigating symptoms, slowing disease progression or modulating specific pathways. In Parkinson's disease, for example, medications aim to target the dopaminergic system to alleviate motor symptoms.[91] However, new therapeutic approaches are becoming available for the wide range of non-motor symptoms, which are often very disabling and include neuropsychiatric, autonomic, sleep, and pain symptoms (for a review, see Foltynie et al. and Tajti et al.).[91,92] In depression, the crosstalk between inflammation, metabolic pathways and neural circuits can ultimately affect neural network activity, which is responsible for regulating behavioral and emotional responses.[63] Accordingly, several studies reported the antidepressant effects of anti-inflammatory treatments in patients with depression.[93–95] Furthermore, recent advances in exercise physiology have yielded crucial insights into the interplay between the brain and body concerning the advantageous effects of physical activity on cognition and mood in states of health and disease.[77,78,96–100] Finally, neurostimulation techniques, including TMS and tDCS, have shown efficacy in alleviating depressive symptoms when combined with psychosocial intervention.[101–103] Thus, integrated multidisciplinary approaches are generally recommended to holistically address the disease-related symptoms and ensure the best outcomes for individuals at brain and body levels.

Tip the scale

The synergistic utilization of brain and body functioning measures in clinical practice offers a multidimensional perspective on brain function and physiological regulation.[5] This integrative approach holds promise for enhancing diagnostic accuracy, treatment selection and monitoring of various neuropsychiatric and neurodegenerative conditions, ultimately improving patient outcomes and advancing the field of clinical neuroscience.[71,104] The brain–body interaction in neurological and psychiatric diseases is a complex and dynamic system that extends beyond the traditional boundaries of the nervous system,[105] including disrupted communication pathways, the influence of the immune and endocrine systems, and the role of the gut–brain axis, though our understanding of these intricate connections continues to evolve. In conclusion, unraveling dysfunctional brain–body interactions in neurological and psychiatric diseases would be the basis for innovative therapeutic interventions.[5,104] The proposal of synergistic approaches to investigating and treating brain–body communication remains at the forefront of scientific research and clinical exploration, with the potential to transform the landscape of health care in years to come. Indeed, a holistic and synergistic approach could enhance diagnostic accuracy, treatment selection, and psychological and neurological health monitoring across the lifespan.

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