

Original Article

Bridging Neurological and Mental Health Paradigms in Neuropsychiatry

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Abstract: *The dividing line that has traditionally separated neurology from psychiatry is becoming harder and harder to justify, since neuroscience research keeps showing that conditions once labeled either "neurological" or "psychiatric" actually share underlying disease mechanisms. This paper brings together the existing evidence on the biological processes that connect mental health disorders with neurological conditions, looking at findings that converge across neuroimaging, immunology, neuroendocrinology, and molecular biology. The researcher examines evidence showing that mood disorders, psychotic disorders, and neurodegenerative diseases have mechanisms in common, such as neuroinflammation, disrupted hypothalamic-pituitary-adrenal axis regulation, abnormal neurosteroids, gut-brain axis dysfunction, and gene regulation mediated by microRNAs. The cerebellum, insula, and frontolimbic circuits stand out as neural substrates that cut across diagnostic categories. The paper makes the case for an integrated neuropsychiatric approach that moves beyond conventional disciplinary divisions, with consequences for diagnosis, the development of treatments, and clinical practice.*

Keywords: Neuropsychiatry, Neuroinflammation, Neuroactive Steroids, Gut-Brain Axis, Biomarkers, Transdiagnostic

I. INTRODUCTION

The conceptual division between neurology and psychiatry, formalized in the early twentieth century through the distinction between "organic" brain diseases and "functional" mental disorders, has never been entirely adequate (Hussain et al., 2026). While this nosological split may be administratively practical, it conceals the essential truth that all mental phenomena arise from brain activity and that all brain disorders express themselves to varying degrees in cognitive, emotional, and behavioral domains (Association between mood disorders and autoimmune diseases of the nervous system, 2026). Modern neuroscience has gradually dismantled this boundary, uncovering shared pathophysiological mechanisms that transcend conventional diagnostic categories (Braga-Neto et al., 2025; The psychopathology of mood disorders, 2025).

Epidemiological evidence highlights the clinical necessity for integration. Individuals with bipolar disorder have a threefold greater risk of developing dementia relative to the general population, a finding that cannot be entirely accounted for by shared risk factors or methodological artifacts (Kessing & Munkholm, 2026). Epilepsy and depression demonstrate bidirectional comorbidity rates that exceed what chance would predict, with each condition worsening the other's clinical trajectory (Gut microbiota-neuroinflammation axis, 2025). Autoimmune diseases of the nervous system, such as multiple sclerosis and myasthenia gravis, show strong associations with mood disorders in longitudinal cohort studies (Pinna et al., 2025). These patterns point not to mere coincidental co-occurrence but to shared underlying pathological processes.

The prevalence of co-occurring psychiatric and neurological disorders has been systematically documented through umbrella reviews of meta-analyses, showing that comorbidity rates considerably surpass chance expectations across virtually all diagnostic combinations examined (Fornaro et al., 2026). This comprehensive atlas of comorbidity patterns demonstrates that the boundary between mental health and neurology represents not a natural fault line in brain function but rather an artifact of historical classification practices (Chen et al., 2026).

This paper synthesizes current evidence on the biological intersections of mental health and neurology. The researcher examines convergent findings from multiple domains: neuroimaging studies that map structural and functional alterations across diagnostic boundaries (Dindarian et al., 2026); immunological research revealing the role of neuroinflammation in both psychiatric and neurodegenerative conditions (Spectrum-based integrative conceptual framework, 2026); neuroendocrinological investigations of stress axis dysfunction (Critchley et al., 2025); and emerging work on the gut-brain axis as a bidirectional communication system linking gastrointestinal function to affective and cognitive states (Wingo et al., 2025). The researcher also considers the role of neuroactive steroids as endogenous modulators of neural excitability and their therapeutic potential (Landín-Romero et al., 2024; Rakeshkumar et al., 2025).



Our central thesis is that the mind is embodied, that mental health and neurological health are manifestations of a single, integrated system whose dysregulation produces symptom profiles that cross conventional diagnostic boundaries (Andreazza et al., 2025). This recognition has profound implications for how we classify, study, and treat brain disorders (Insel et al., 2010).

II. HISTORICAL AND CONCEPTUAL FOUNDATIONS

A. The Neurology-Psychiatry Divide: Origins and Consequences

The split between neurology and psychiatry arose from nineteenth-century attempts to classify mental disorders based on presumed etiology (Kendler, 2025). Conditions with identifiable brain lesions, such as strokes, tumors, and epilepsies, belonged to neurology, whereas conditions without demonstrable structural pathology were assigned to psychiatry (Berrios, 1996). This distinction was always more pragmatic than scientific; as early as the 1870s, Hughlings-Jackson noted that psychiatric symptoms could stem from neurological lesions, and conversely, that neurological disorders frequently produced behavioral and emotional disturbances (Hughlings-Jackson, 1958).

The twentieth century saw this divide institutionalized through separate training programs, research traditions, and clinical services (Martin, 2002). Yet even as the boundary hardened, clinical reality repeatedly transgressed it. Patients with Parkinson's disease experienced depression at rates far exceeding general population estimates (Reijnders et al., 2008). Individuals with schizophrenia showed progressive gray matter loss on neuroimaging (Vita et al., 2012). The discovery of antipsychotic and antidepressant medications, drugs that modulated neurotransmitter systems, further undermined the notion of a fundamental distinction between "organic" and "functional" disorders (López-Muñoz & Alamo, 2009).

The consequences of this divide have been substantial. Patients with comorbid conditions often receive fragmented care, with neurologists addressing motor and sensory symptoms while psychiatrists address emotional and behavioral symptoms, frequently without adequate communication between providers (Kanner, 2011). Research funding has followed disciplinary boundaries, with psychiatric and neurological research programs often operating in isolation despite shared scientific questions (Insel & Landis, 2013). Training programs have perpetuated the divide, producing clinicians who may lack confidence in managing conditions outside their disciplinary expertise (Benjamin et al., 2010).

B. The Transdiagnostic Turn

Recent decades have witnessed a transdiagnostic turn in neuroscientific research. Rather than studying DSM or ICD categories in isolation, investigators increasingly examine shared mechanisms across diagnostic boundaries (Cuthbert & Insel, 2013; Dalglish et al., 2020). This approach has revealed that cognitive impairments in schizophrenia, bipolar disorder, and major depression share common neurophysiological signatures (Barch et al., 2023). Neuroimaging studies find overlapping patterns of frontolimbic dysfunction across anxiety disorders, mood disorders, and obsessive-compulsive disorder (McTeague et al., 2016). Inflammatory markers are elevated across a range of psychiatric and neurological conditions, suggesting immune dysregulation as a transdiagnostic pathophysiological mechanism (Miller & Raison, 2016).

The transdiagnostic perspective does not deny the reality of symptom differences between conditions. Rather, it recognizes that categorical diagnoses may capture heterogeneous syndromes while missing underlying mechanistic commonalities (Insel, 2014). A patient with depression and a patient with Parkinson's disease may present very differently yet share fundamental biological abnormalities that could be targeted by the same treatment (Bandelow et al., 2017).

The Research Domain Criteria (RDoC) initiative represents one systematic effort to transcend categorical diagnosis by organizing research around fundamental behavioral and neural dimensions (Insel et al., 2010). Similarly, the recognition that inflammation, neurosteroid dysregulation, and gut-brain axis dysfunction cut across diagnostic categories suggests that biomarker-based stratification may identify patient subgroups more homogeneous, and more treatable, than conventional diagnoses (Fernandes et al., 2017).

C. Philosophical and Conceptual Considerations

The integration of mental health and neurology raises profound philosophical questions about the nature of mental disorders and the relationship between mind and brain (Kendler, 2016). Dualistic assumptions, that mental phenomena are fundamentally different from physical brain processes, have historically underpinned the separation of psychiatry from neurology (Zachar & Kendler, 2007). Yet contemporary philosophy of mind has largely abandoned substance dualism in favor of various forms of physicalism or emergentism (Chalmers, 1996).

The embodied mind perspective, recognizing that mental phenomena emerge from brain and body physiology, provides a conceptual foundation for neuropsychiatric integration (Varela et al., 1991). This perspective does not reduce mental health to biology but rather acknowledges that biological, psychological, and social dimensions of human experience are inextricably intertwined (Engel, 1977). Understanding how they interact across conditions and individuals represents both a scientific challenge and a clinical imperative (Bolton & Gillett, 2019).

III. SHARED NEUROBIOLOGICAL MECHANISMS

A. Neuroinflammation as a Common Pathway

Neuroinflammation has become arguably the most convincing shared mechanism connecting psychiatric and neurological disorders. Microglia, the brain's resident immune cells, drive inflammatory responses that can disrupt synaptic function, impair neuroplasticity, and eventually cause neuronal damage (Yirmiya et al., 2011). Positron emission tomography studies using TSPO ligands, which mark microglial activation, have documented heightened neuroinflammation in major depressive disorder, schizophrenia, bipolar disorder, and Alzheimer's disease (Setiawan et al., 2015).

The inflammatory cascade entails intricate crosstalk between the peripheral and central immune systems. Peripheral immune cells, such as macrophages and T cells, release cytokines including interleukin-6 and tumor necrosis factor-alpha that are able to cross the blood-brain barrier and affect central nervous system function (Dantzer et al., 2008). This peripheral-to-central signaling route offers a mechanistic account of the well-established link between systemic inflammatory conditions and psychiatric symptoms (Raison et al., 2013). The kynurenine pathway serves as a particularly significant interface between immune activation and neurotransmitter function. Inflammatory stimuli boost the conversion of tryptophan into kynurenine, which is then metabolized into neuroactive compounds such as quinolinic acid (an NMDA receptor agonist with neurotoxic effects) and kynurenic acid (an NMDA receptor antagonist with neuroprotective effects) (Schwarcz et al., 2012). An imbalance between these metabolites, favoring quinolinic acid production, has been implicated in the pathophysiology of depression, schizophrenia, and neurodegenerative conditions (Erhardt et al., 2017).

Recent research has identified a spectrum-based integrative framework linking immune dysregulation to microglia-related brain dysfunction across major depressive disorder, bipolar disorder, and schizophrenia (Spectrum-based integrative conceptual framework, 2026). This framework proposes that shared immune mechanisms contribute to the overlapping cognitive and affective symptoms observed across these conditions, suggesting that immunomodulatory treatments might have transdiagnostic efficacy (Miller et al., 2024).

B. Neuroactive Steroids and Neural Homeostasis

Neuroactive steroids, encompassing both peripherally derived hormones and neurosteroids synthesized within the central nervous system, form a fundamental homeostatic system whose dysregulation appears central to many brain disorders (Pinna et al., 2025). These compounds, produced in both glutamatergic and GABAergic neurons, act on specific neuronal receptors to regulate excitability, synaptic integration, and network dynamics (Belelli & Lambert, 2005).

Allopregnanolone, a potent positive allosteric modulator of GABA-A receptors, has drawn particular attention. Reduced allopregnanolone levels have been documented in major depressive disorder, post-traumatic stress disorder, and premenstrual dysphoric disorder (Bäckström et al., 2014). The therapeutic efficacy of renanolone (a synthetic allopregnanolone formulation) in postpartum depression provides proof-of-concept that targeting neurotropic pathways can produce rapid and robust antidepressant effects (Meltzer-Brody et al., 2018). More recently, zuranolone, an orally available neuroactive steroid, has demonstrated efficacy in major depressive disorder, further validating this therapeutic approach (Deligiannidis et al., 2023).

The neurosteroid system's relevance extends beyond mood disorders. Alterations in neurosteroid levels have been documented in schizophrenia, autism spectrum disorder, epilepsy, Alzheimer's disease, Parkinson's disease, and multiple sclerosis (Pinna, 2020). This broad involvement reflects the fundamental role of neurosteroids in maintaining neural homeostasis, regulating inhibitory tone, modulating inflammatory signaling, and shaping synaptic plasticity (Rupprecht & Holsboer, 1999).

The therapeutic potential of neuroactive steroids extends to neurological conditions. In epilepsy, neurosteroid dysregulation may contribute to seizure susceptibility, and neurosteroid-based treatments have shown anticonvulsant properties (Reddy, 2010). In neurodegenerative conditions, neurosteroids may exert neuroprotective effects through modulation of inflammation and excitotoxicity (Melcangi et al., 2008). These findings suggest that neurosteroid-based therapies may have applications across the diagnostic spectrum (Schüle et al., 2011).

C. The Hypothalamic-Pituitary-Adrenal Axis and Stress Response

Dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis represents another shared mechanism across psychiatric and neurological conditions (Pariante & Lightman, 2008). The HPA axis coordinates the body's response to stress through a cascade of hormonal signals culminating in cortisol release from the adrenal glands. Chronic stress and HPA axis dysfunction have been implicated in depression, anxiety disorders, post-traumatic stress disorder, and, importantly, in the exacerbation of neurological conditions including epilepsy and multiple sclerosis (Zunszain et al., 2011).

Corticotropin-releasing hormone (CRH) and its receptor CRHR1 play central roles in mediating stress responses. CRHR1 is widely distributed throughout the brain and interacts with glutamatergic, serotonergic, and dopaminergic systems, neurotransmitter networks critically involved in mood regulation (Reul & Holsboer, 2002). Genetic polymorphisms and epigenetic modifications in the CRHR1 gene have been associated with increased depression risk, and CRHR1 has been linked to synaptic plasticity, neuroinflammation, and gut dysbiosis (Rakeshkumar et al., 2025). These findings position CRHR1 as a potential therapeutic target bridging stress biology and mood pathology (Holsboer & Ising, 2008).

The relationship between HPA axis dysfunction and neurological conditions is bidirectional. Recurrent epileptic seizures exacerbate HPA axis dysfunction and gut dysbiosis, while stress and HPA axis abnormalities increase seizure susceptibility, forming a vicious cycle that maintains both conditions (Gut microbiota–neuroinflammation axis, 2025). Similar bidirectional relationships have been documented in multiple sclerosis, where stress exacerbates disease activity and inflammatory processes further dysregulate HPA axis function (Gold et al., 2005).

Novel molecular insights into CRHR1 function have revealed its involvement in neuroplasticity, inflammatory signaling, and metabolic regulation (Rakeshkumar et al., 2025). These findings suggest that CRHR1 antagonists might have therapeutic applications beyond depression, potentially including anxiety disorders, substance use disorders, and neurodegenerative conditions (Zorrilla & Koob, 2004).

D. The Gut-Brain Axis

The gut microbiota, the trillions of microorganisms inhabiting the gastrointestinal tract, has emerged as a critical regulator of brain function and behavior (Cryan et al., 2019). The gut-brain axis encompasses multiple communication pathways including vagal nerve signaling, immune system modulation, microbial metabolite production, and HPA axis regulation (Mayer et al., 2011).

Dysbiosis, disruption of normal gut microbial composition, has been documented in major depressive disorder, bipolar disorder, schizophrenia, autism spectrum disorder, Parkinson's disease, and Alzheimer's disease (Valles-Colomer et al., 2019). Mechanistically, gut microbiota influence brain function through production of short-chain fatty acids, modulation of neurotransmitter metabolism, and regulation of inflammatory responses (Dinan & Cryan, 2017). Specific probiotic strains, including *Lactobacillus* and *Bifidobacterium* species, have demonstrated antidepressant and anxiolytic effects in both animal models and human studies (Wallace & Milev, 2017). Fecal microbiota transplantation (FMT) has shown therapeutic promise across a range of neuropsychiatric conditions. In animal models of post-stroke depression, FMT reduced neuroinflammation and restored neurotransmitter levels (Gut microbiota–neuroinflammation axis, 2025). Clinical case reports describe improvement in both seizure frequency and affective symptoms in epilepsy patients receiving FMT for other indications (He et al., 2021). These findings suggest that targeting the gut microbiome may offer a novel therapeutic approach for conditions at the intersection of neurology and psychiatry (Sampson & Mazmanian, 2015).

The gut-brain axis has particular relevance for understanding comorbidity between epilepsy and depression (Kanner, 2011). Research has identified a gut microbiota–neuroinflammation axis that may underlie this comorbidity, with dysbiosis promoting both seizure susceptibility and depressive symptoms through shared inflammatory mechanisms (Gut microbiota–neuroinflammation axis, 2025). This mechanistic understanding suggests that interventions targeting the gut microbiome might simultaneously address both conditions (Dahlin & Prast-Nielsen, 2019).

E. MicroRNAs and Gene Regulation

MicroRNAs, small non-coding RNA molecules that regulate gene expression, have recently emerged as potential contributors to both psychiatric and neurodegenerative disorders (Wingo et al., 2025). A landmark study analyzing post-mortem brain tissue from 604 donors identified specific microRNAs associated with major depression, bipolar disorder, schizophrenia, post-traumatic stress disorder, and Parkinson's disease (Wingo et al., 2019).

The study identified four microRNAs with particularly strong evidence for disease contribution: miR-499a-5p (bipolar disorder and schizophrenia), miR-92b-3p (Parkinson's disease), miR-190b-5p (post-traumatic stress disorder), and miR-1908-5p (bipolar disorder and major depression) (Wingo et al., 2025). Notably, several microRNAs contributed to risk for multiple conditions, suggesting shared molecular mechanisms. miR-499a-5p's association with both bipolar disorder and schizophrenia, and miR-1908-5p's association with both bipolar disorder and major depression, point to common genetic regulatory pathways underlying these clinically distinct syndromes (Wingo et al., 2025).

Separate research has identified a conserved microRNA-inflammatory axis connecting Parkinson's disease, depressive disorder, and gastrointestinal dysfunction (A molecular convergence in the triad of Parkinson's disease, depressive disorder and gut health, 2025). This study found significant downregulation of miR-199a-5p and miR-219a-5p and upregulation of miR-200a-3p in the brains of both Parkinson's disease and depression patients, associated with increased expression of TNF α , IFN- γ , and NF κ B1 (A molecular convergence in the triad of Parkinson's disease, depressive disorder and gut health, 2025). The same microRNA pattern was replicated in the brains and intestines of mouse models, providing direct evidence for a shared molecular mechanism spanning the gut-brain axis (A molecular convergence in the triad of Parkinson's disease, depressive disorder and gut health, 2025).

These findings suggest that microRNA-based therapeutics might have applications across diagnostic boundaries (O'Connor et al., 2012). By targeting specific microRNAs involved in inflammatory signaling, it may be possible to modulate disease processes shared across psychiatric and neurological conditions (Issler & Chen, 2015).

IV. NEURAL SYSTEMS AND CIRCUITS

A. The Cerebellum Beyond Motor Control

The cerebellum, long regarded primarily as a center for motor coordination, has come to be recognized as a key node in the neural circuitry underlying psychiatric disorders (Braga-Neto et al., 2025). Structural and functional abnormalities of the cerebellum have been documented in schizophrenia, bipolar disorder, depression, anxiety disorders, attention-deficit/hyperactivity disorder, and autism spectrum disorder (Schmahmann et al., 2007). The cerebellum's involvement in psychiatric conditions stems from its extensive connectivity with cortical and subcortical regions that support cognitive, emotional, and behavioral functions. Cerebellar-thalamic-cortical circuits regulate executive function, working memory, and emotional regulation, domains typically impaired across psychiatric disorders (Andreasen & Pierson, 2008). The cerebellum also takes part in social cognition and reward processing, functions mediated through its connections with the amygdala and prefrontal cortex (Buckner, 2013).

Post-mortem and neuroimaging studies have identified cerebellar gray matter reductions in schizophrenia and bipolar disorder, with some evidence pointing to progressive changes over the course of illness (Laidi et al., 2015). These findings suggest that cerebellar pathology may contribute not only to motor symptoms, where it has long been recognized, but also to the cognitive and affective disturbances that characterize psychiatric syndromes (Phillips et al., 2015). The cerebellum's role in psychiatric disorders carries therapeutic implications. Cerebellar transcranial direct current stimulation (tDCS) has shown promise in modulating cognitive and affective symptoms in schizophrenia and autism spectrum disorder (Grimaldi et al., 2016). These findings suggest that the cerebellum may represent a novel target for neuromodulation interventions across psychiatric conditions (Ferrucci et al., 2012).

B. The Insula and Interoception

Interoception, the perception of internal bodily states, has emerged as a foundational concept linking bodily physiology to emotional experience and psychiatric symptoms (Critchley et al., 2025). The insula serves as the primary cortical hub for interoceptive processing, integrating signals from the cardiovascular, respiratory, and gastrointestinal systems into conscious representations of bodily state (Craig, 2002).

Perturbations in interoceptive processing have been documented in anxiety disorders, depression, autism spectrum disorder, and dissociative conditions (Paulus & Stein, 2010). These alterations may contribute to characteristic symptoms: heightened interoceptive awareness in panic disorder, blunted interoception in depersonalization, and atypical interoceptive processing in autism (Garfinkel et al., 2016). The insula's role in interoception also connects to emotional regulation, decision-making, and social cognition, domains impaired across psychiatric conditions (Critchley & Garfinkel, 2017).

The interoceptive framework has therapeutic implications. Biofeedback interventions targeting cardiac and respiratory function have shown promise in anxiety and stress-related conditions, potentially operating through modulation of insular interoceptive representations (Lehrer & Gevirtz, 2014). Mindfulness-based interventions may also operate partly through effects on interoceptive processing, suggesting a mechanism for their transdiagnostic efficacy (Farb et al., 2015).

C. Frontolimbic Circuits and Transdiagnostic Dysfunction

Neuroimaging research has consistently identified frontolimbic circuit dysfunction as a transdiagnostic feature of psychiatric disorders (Dindarian et al., 2026). The prefrontal cortex, anterior cingulate cortex, amygdala, and hippocampus form interconnected circuits that regulate emotional reactivity, cognitive control, and stress responses (Etkin et al., 2007).

Structural and functional alterations in these circuits have been documented in major depressive disorder, schizophrenia, bipolar disorder, autism spectrum disorder, obsessive-compulsive disorder, and generalized anxiety disorder (McTeague et al., 2016). While the specific pattern of alteration varies by condition, common themes include prefrontal hypoactivity (impaired cognitive control of emotion), amygdala hyperactivity (heightened emotional reactivity), and disrupted connectivity between these regions (Hamilton et al., 2008).

These frontolimbic alterations are not confined to psychiatric conditions. Behavioral variant frontotemporal dementia, a neurodegenerative disorder, produces profound changes in personality, social behavior, and emotional regulation that overlap substantially with psychiatric presentations (Dindarian et al., 2026). The convergence of psychiatric and neurodegenerative conditions on frontolimbic circuits underscores the inadequacy of categorical boundaries (Piguet et al., 2011).

Neuroradiological features across major psychiatric disorders and behavioral variant of Alzheimer's disease reveal overlapping patterns of frontolimbic involvement (Dindarian et al., 2026). These findings suggest that neuroimaging biomarkers might identify shared pathophysiological processes across conditions currently classified as either psychiatric or neurological (Dindarian et al., 2026).

D. Cognitive Impairments Across Diagnostic Boundaries

Cognitive impairment, once considered characteristic of neurological conditions but not psychiatric disorders, is now recognized as a transdiagnostic feature of both (Hussain et al., 2026). A systematic review mapping cognitive domains to mental and neurological disorders identified impairments in complex attention, learning and memory, language, executive function, social cognition, and perceptual-motor function across schizophrenia, bipolar disorder, major depression, Alzheimer's disease, Parkinson's disease, and autism spectrum disorder (Hussain et al., 2026).

Neurophysiological biomarkers provide objective evidence of these cognitive impairments. Event-related potential abnormalities, including diminished P300 and N1 amplitudes in major depressive disorder, reflect disruptions in attention and memory processing (Hamilton et al., 2019). EEG band power alterations, including decreased alpha power and increased theta and delta power, have been documented across multiple conditions (Newson & Thiagarajan, 2019). These biomarkers offer potential for improving diagnostic accuracy and developing targeted treatments based on specific cognitive profiles rather than categorical diagnoses (Hussain et al., 2026).

The recognition of transdiagnostic cognitive impairments has implications for treatment development. Cognitive remediation interventions, originally developed for schizophrenia, have shown efficacy in bipolar disorder, major depression, and attention-deficit/hyperactivity disorder (Wykes et al., 2011). These findings suggest that cognitive impairments may represent a treatment target that transcends diagnostic boundaries (Hussain et al., 2026).

E. Neuroimaging Transdiagnostic Signatures

Advances in neuroimaging have enabled the identification of transdiagnostic signatures, patterns of structural or functional alteration that appear across multiple diagnostic categories (Dindarian et al., 2026). Multimodal neuroimaging studies combining structural MRI, functional MRI, diffusion tensor imaging, and positron emission tomography have revealed shared alterations in frontolimbic, default mode, and salience networks across psychiatric and neurological conditions (Dindarian et al., 2026). Machine learning approaches applied to neuroimaging data have identified dimensional axes of brain dysfunction that cut across traditional diagnostic boundaries (Dindarian et al., 2026). These approaches may ultimately yield biomarkers that stratify patients by underlying pathophysiology rather than surface symptomatology, enabling more precise and effective treatment selection (Dindarian et al., 2026).

V. CLINICAL IMPLICATIONS

A. Rethinking Diagnostic Boundaries

The evidence reviewed above calls into question the validity of rigid distinctions between neurological and psychiatric disorders (Fornaro et al., 2026). Conditions classified in different diagnostic manuals, and managed by different specialists, share fundamental pathophysiological mechanisms. This recognition carries implications for nosology: instead of organizing

classification systems around traditional disciplinary boundaries, a mechanism-based or dimension-based approach may better capture the underlying biology (Insel et al., 2010).

The Research Domain Criteria (RDoC) initiative represents one effort to transcend categorical diagnosis by organizing research around fundamental behavioral and neural dimensions (Insel et al., 2010). Similarly, the recognition that inflammation, neurosteroid dysregulation, and gut-brain axis dysfunction cut across diagnostic categories suggests that biomarker-based stratification may identify patient subgroups more homogeneous, and more treatable, than conventional diagnoses (Fernandes et al., 2017).

B. Transdiagnostic Treatment Targets

Identifying shared mechanisms opens possibilities for transdiagnostic therapeutic development (Pinna et al., 2025). If neuroinflammation contributes to both depression and neurodegeneration, anti-inflammatory interventions might benefit both conditions. If neurosteroid dysregulation underlies mood episodes and seizure susceptibility, neurosteroid-based treatments might address both (Pinna et al., 2025).

Several therapeutic approaches illustrate this potential. Targeting the gut microbiota through probiotics, prebiotics, or fecal microbiota transplantation may ameliorate symptoms across conditions as diverse as depression, epilepsy, and Parkinson's disease (Gut microbiota–neuroinflammation axis, 2025). Modulating CRHR1 signaling might address stress-related pathology across mood and anxiety disorders while also influencing seizure thresholds (Rakeshkumar et al., 2025). Neuroactive steroids have demonstrated efficacy in postpartum depression and are under investigation for other conditions (Pinna et al., 2025).

The development of biomarkers to guide treatment selection represents a critical priority. Rather than treating all patients with a given diagnosis identically, a biomarker-informed approach would match interventions to underlying pathophysiology, an approach already transforming oncology and beginning to influence psychiatry (Fernandes et al., 2017).

C. Integrated Care Models

The clinical implications of neuropsychiatric integration extend beyond treatment development to service delivery. Patients with comorbid psychiatric and neurological conditions frequently experience fragmented care, with neurologists addressing "organic" symptoms and psychiatrists addressing "functional" ones, a division that may impede comprehensive assessment and integrated treatment planning (Fornaro et al., 2026). Integrated care models that bring neurological and psychiatric expertise together have shown promise in conditions such as epilepsy with comorbid depression, Parkinson's disease with cognitive impairment, and dementia with behavioral symptoms (Kanner, 2011). These models recognize that brain disorders affect the whole person and require approaches that address cognitive, emotional, and behavioral dimensions simultaneously (Fornaro et al., 2026).

D. Implications for Clinical Training

The integration of mental health and neurology has implications for clinical training. Traditional training programs separate psychiatric and neurological education, potentially producing clinicians who lack confidence in managing conditions outside their disciplinary expertise (Benjamin et al., 2010). Integrated training programs that provide comprehensive education in brain disorders may better prepare clinicians for the complex patients they will encounter in practice (Benjamin et al., 2010).

VI. FUTURE RESEARCH

Future research must tackle the ongoing difficulty of creating and validating biomarkers that are clinically useful for psychiatric and neurological conditions. This task is complicated by diagnostic heterogeneity, overlapping symptoms, and the need for longitudinal validation. Multimodal approaches that combine neuroimaging, electrophysiology, inflammatory markers, and molecular measures offer a promising path forward. A key priority will be grouping patients according to underlying pathophysiology rather than surface diagnosis. Such markers include neuroinflammatory indicators, neurosteroid profiles, gut microbiome signatures, and microRNA patterns that cut across traditional diagnostic boundaries. Validation will require large, comprehensive longitudinal cohorts.

Building on this, mechanistic research should continue to explore processes shared across diagnostic boundaries. The microRNA-inflammatory axis linking Parkinson's disease, depression, and gut dysfunction exemplifies this approach. The role of neuroactive steroids in regulating neural excitability and immune signaling also deserves further investigation. Such work should examine developmental trajectories. Do neuroinflammatory abnormalities precede symptom onset? Can early intervention targeting shared mechanisms prevent or delay multiple conditions? These questions demand longitudinal designs that span traditional boundaries.

Recognizing this heterogeneity and overlap, personalized, biomarker-guided interventions will be necessary. This requires predictive biomarkers, clinical trials that stratify by mechanism rather than diagnosis, and treatment algorithms adapted to individual pathophysiological profiles. Oncologists use tumor genetics to guide treatment selection. Similarly, psychiatrists and neurologists may eventually use biomarkers to match patients with interventions most likely to benefit them.

Consequently, the identification of shared mechanisms points to novel therapeutic targets. These include anti-inflammatory agents, neurosteroid modulators, gut microbiome interventions, and microRNA-based therapeutics. Neuromodulation approaches also hold promise. Transcranial magnetic stimulation, transcranial direct current stimulation, and deep brain stimulation may have transdiagnostic applications if targeted to shared circuit abnormalities. Translating these advances into practice will require implementation and health services research. This includes studies of clinical effectiveness, cost-effectiveness, and implementation strategies that account for organizational, financial, and cultural barriers to integration.

VII. DISCUSSION

This synthesis of contemporary research shows that the conventional divide between mental health and neurology cannot be sustained scientifically. Shared mechanisms, neuroinflammation, neurosteroid dysregulation, HPA axis abnormalities, gut-brain axis dysfunction, and microRNA-mediated gene regulation, operate across conditions classified in different diagnostic systems and treated by different specialties. Neural systems including the cerebellum, insula, and frontolimbic circuits show transdiagnostic alterations that correlate with cognitive, emotional, and behavioral symptoms regardless of categorical diagnosis.

The clinical implications of this recognition are substantial. Diagnostic systems organized around historical disciplinary boundaries may obscure underlying biological similarities and exaggerate differences. Treatment development that targets mechanisms rather than diagnoses may yield interventions effective across a broader range of conditions. Service delivery models that integrate neurological and psychiatric expertise may better address the complex needs of patients whose conditions defy traditional categorization.

The evidence reviewed here also highlights significant gaps. Most studies remain cross-sectional, limiting causal inference. Biomarkers identified in research settings have not been validated for clinical use. Therapeutic approaches targeting shared mechanisms remain largely experimental. Future research should prioritize longitudinal designs, biomarker validation, and clinical trials that stratify patients by mechanism rather than diagnosis.

The embodied mind perspective, recognizing that mental phenomena emerge from brain and body physiology, provides a conceptual foundation for neuropsychiatric integration. This perspective does not reduce mental health to biology but rather acknowledges that biological, psychological, and social dimensions of human experience are inextricably intertwined. Understanding how they interact across conditions and individuals represents both a scientific challenge and a clinical imperative.

VIII. CONCLUSION

The evidence brought together in this paper supports a fundamental rethinking of how mental health and neurology relate to one another. Conditions historically split between these two fields share pathophysiological mechanisms such as neuroinflammation, neuroactive steroid dysregulation, HPA axis abnormalities, gut-brain axis dysfunction, and microRNA-mediated gene regulation. Neural systems including the cerebellum, insula, and frontolimbic circuits show transdiagnostic alterations that cross categorical boundaries. This recognition carries implications for diagnosis, treatment, and service delivery. Diagnostic systems built around disciplinary boundaries may need revision toward mechanism-based or dimension-based approaches. Treatment development should prioritize transdiagnostic mechanisms over categorical diagnoses. Clinical services should bring together neurological and psychiatric expertise to meet the complex needs of patients with comorbid conditions.

Integrating mental health and neurology is not merely an academic exercise but a clinical necessity. Patients whose conditions span traditional boundaries deserve approaches that acknowledge the fundamental unity of brain function and dysfunction. As research continues to uncover shared mechanisms across diagnostic categories, the case for integration becomes increasingly compelling. The future of brain health lies not in preserving disciplinary boundaries but in moving beyond them.

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