

Biological phenomena as psychological expression

David A. Dawson *

AMCANN, LLLP Department of Research, Murrieta, California, USA.

World Journal of Biological and Pharmaceutical Research, 2025, 09(02), 001-012

Publication history: Received on 03 September 2025; revised on 11 October 2025; accepted on 13 October 2025

Article DOI: <https://doi.org/10.53346/wjbpr.2025.9.2.0023>

Abstract

Background: Psychology has historically been conceptualized as distinct from biology, rooted in dualistic frameworks that separate mind from body. Advances in neuroscience, molecular biology, and psychoneuroimmunology now challenge that division, demonstrating that cognition, emotion, and behavior arise from biological processes. This paper advances the principle that every psychological phenomenon is an expression of biological function, framing mental disorders as molecular and cellular states manifesting through behavior and cognition.

Methods: Using a biomolecular psychology framework, four major conditions traditionally defined in psychological terms—Post-Traumatic Stress Disorder (PTSD), Attention-Deficit/Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD), and Depressive Disorders, are examined to illustrate how neural circuitry, immune signaling, and endocannabinoid modulation shape symptom expression. Each disorder is analyzed through converging evidence from neuroimaging, molecular profiling, psychoneuroimmunology, and endocannabinology.

Results: Across conditions, disruptions in glutamatergic-GABAergic balance, neurotrophic support, and cytokine signaling converge with dysregulated endocannabinoid system (ECS) activity to produce characteristic cognitive and affective phenotypes. Reduced anandamide (AEA) and 2-arachidonoylglycerol (2-AG) levels correlate with impaired emotional regulation and stress resilience, while restoration of ECS tone, through endogenous modulation or phytocannabinoid supplementation, normalizes circuit function and behavior. Emerging clinical data indicate that cannabidiol (CBD), cannabigerol (CBG), and related phytochemicals improve anxiety, attention, social reciprocity, and mood while attenuating neuroinflammation.

Conclusions: These findings position the endocannabinoid system as a central integrative mechanism linking neural, immune, and psychological domains. The biomolecular psychology framework dissolves the traditional mind-body divide, establishing mental health as a branch of biological science. Quantifying endocannabinoid tone and related molecular biomarkers offers a pathway toward precision diagnostics and nutraceutical therapeutics that restore biological equilibrium as the foundation of psychological well-being. This multidisciplinary synthesis bridges molecular neuroscience, psychoneuroimmunology, and endocannabinology to generate a unified model of mind-body interaction.

Keywords: Biomolecular Psychology; Endocannabinoid System; Psychoneuroimmunology; PTSD; ADHD; Autism Spectrum Disorder; Depression; Nutraceutical; Anandamide; Cannabidiol; Biological Psychiatry

1. Introduction

Psychology has long wrestled with its identity, positioned uneasily between philosophy, medicine, and biology. Early schools of thought typically framed the mind as distinct from the body, treating thought, mood, and behavior as phenomena separable from biology. This perspective, rooted in Cartesian dualism and reinforced by psychoanalysis and behaviorism, established psychology as an intellectual domain independent of physiology [1,2,3]. Such separation has

* Corresponding author: David A. Dawson Email: david.amcannresearch@gmail.com

become increasingly difficult to defend in light of advances in neuroscience, molecular biology, biomolecular psychology, and psychoneuroimmunology, which consistently demonstrate the interdependence of brain, body, and behavior. It has now become evident that every psychological phenomenon is rooted in biology, whether in neural networks, molecular signaling, or immunological crosstalk.

The guiding tenet of this paper is simple but far-reaching: Everything psychological has roots in the biological. This principle reframes mental health disorders not as abstract constructs but as biological states expressed through cognition and behavior. In this view, psychiatry and psychology converge with molecular and cellular sciences, yielding a truly integrative model of the human condition.

Biomolecular psychology adopts a comprehensive and integrative approach to understanding both mental and physical health. It combines principles from endocannabinology, psychopharmacology, psychoneuroimmunology, and related holistic health frameworks to examine how molecular and cellular processes influence brain function, emotional regulation, and immune responses. This perspective highlights the profound interconnectedness of the body's biological systems with mental health, emphasizing the roles of molecules, neurotransmitters, and immune factors in maintaining overall well-being and supporting a balanced mind-body connection [4,5,6,7,8].

To illustrate this framework, four conditions commonly framed in psychological terms are examined: Post-Traumatic Stress Disorder (PTSD), Attention-Deficit/Hyperactivity Disorder (ADHD), Autism Spectrum Disorder (ASD), and Depressive Disorders. The utility of this approach is best illustrated through conditions traditionally framed in psychological terms. Each serves as a case study in how biology manifests as psychology: PTSD demonstrates how trauma becomes etched in neural circuits and stress-response pathways; ADHD underscores the influence of neurotransmitter systems and cortical networks on attention and impulse control; ASD highlights the ways in which neurodevelopmental biology and immune signaling shape social and cognitive expression; and depressive disorders exemplify mood as an emergent property of monoaminergic and immunological states [4,8,9,10]. By elucidating the biological foundations of these conditions, the persistent division of “mental” from “physical” becomes untenable. In its place, a unified framework emerges—one that interprets psychological phenomena as the expression of biological processes, dissolving the mind-body divide and positioning psychology within the life sciences while advancing the promise of biomarker-driven diagnostics and therapeutics.

- PTSD: Trauma Engraved in Biology

2. Clinical Overview and Epidemiology

Post-Traumatic Stress Disorder (PTSD) is a debilitating psychiatric condition characterized by a persistent maladaptive response to severe stressors such as violent assault, natural or human-made disaster, serious accident, or combat. Core symptoms include intrusions, nightmares, panic, hypervigilance, emotional numbing, detachment, and suicidality, reflecting enduring alterations in stress-response systems and memory circuits [11,12]. Prevalence is substantial and unevenly distributed: at any given time, ~3% of adults meet diagnostic criteria, with lifetime prevalence ranging from 2–9% in the general population, doubling in conflict-affected groups, and exceeding 50% among rape survivors [13,14,15]. More recently, post-COVID cohorts have exhibited elevated trauma-related symptom profiles consistent with PTSD phenotypes [16,17]. Importantly, heterogeneity is the rule rather than the exception; mechanistic pathways vary widely between individuals, complicating one-size-fits-all approaches to treatment [18,19,20].

2.1. Limits Of Current Treatments

Despite widespread use, first-line pharmacotherapies such as selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) provide only modest and inconsistent benefit, while large proportions of patients remain symptomatic following trauma-focused psychotherapies (e.g., cognitive processing therapy, prolonged exposure) and other guideline-concordant care. Remission is achieved in only a minority of cases. Non-response rates as high as 66% have been reported in military cohorts [21,22,23,24]. This persistent therapeutic gap underscores the need for interventions grounded in biological mechanisms rather than symptom-based classifications.

2.2. Neural Circuitry and HPA-Axis Dysregulation

PTSD is characterized by imbalance within the amygdala-hippocampus-ventromedial prefrontal cortex (vmPFC) network: amygdala hyperreactivity to threat, impaired contextual discrimination and reduced neurogenesis in the hippocampus, and reduced vmPFC activation during extinction tasks [25]. Dysregulation of hypothalamic-pituitary-adrenal (HPA) axis signaling, including altered cortisol dynamics and impaired feedback sensitivity, further destabilizes

these circuits, reinforcing persistent fear memories and hyperarousal [26]. These neural abnormalities are not merely correlates but represent substrates through which traumatic experiences become biologically encoded and behaviorally expressed.

2.3. Molecular and Immune Signatures

Convergent evidence implicates disturbances in glutamatergic and GABAergic balance, altered noradrenergic and serotonergic tone, and diminished neurotrophic support such as reduced brain-derived neurotrophic factor (BDNF). A pro-inflammatory bias, characterized by elevated interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and related cytokines, alongside microglial activation, influences synaptic pruning, plasticity, and mood-anxiety phenotypes, thereby linking immune status to symptom severity [19,28,29]. Oxidative stress and mitochondrial dysfunction further sensitize neural circuits, fostering intrusive memory and hypervigilance. These molecular alterations intersect directly with endocannabinoid signaling, which in turn modulates both synaptic plasticity and immune tone.

2.4. Endocannabinoid System: Tone, Plasticity, and Extinction

The endocannabinoid system (ECS), consisting of cannabinoid receptors (CB₁/CB₂), ligands anandamide (AEA) and 2-arachidonoylglycerol (2-AG), and the catabolic enzymes fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL), regulates stress responsivity, emotional homeostasis, and fear extinction, and functions as a therapeutic linchpin in PTSD. Preclinical studies demonstrate that enhancing ECS signaling, for example through FAAH or MAGL inhibition, facilitates extinction learning and reduces anxiety-like behavior after trauma, whereas CB₁ antagonism impairs extinction. In humans, altered circulating endocannabinoid levels and changes in CB₁ receptor availability within cortical-limbic regions have been observed in individuals with PTSD, consistent with reduced endocannabinoid tone and compensatory receptor adaptations [30,31]. Moreover, genetic variation in ECS components such as *CNR1* and *FAAH* has been linked to heightened stress reactivity and PTSD vulnerability in translational cohorts [32]. Collectively, these findings identify ECS dysregulation as a mechanistic bridge between trauma exposure and persistent symptom expression.

2.5. Psychoneuroimmunology and Nutraceutical Rationale

From a biomolecular psychology perspective, PTSD represents a convergence of disrupted neural circuits, neurotransmitter and neuromodulator imbalance, and dysregulated immune-brain communication. Psychoneuroimmunology predicts that attenuating chronic low-grade inflammation can improve mood-anxiety phenotypes, and indeed recovery trajectories often parallel normalization of cytokine profiles across treatment modalities [19,28]. Within this framework, phytocannabinoids active at the endocannabinoid system (ECS), including cannabidiol (CBD), cannabigerol (CBG), cannabichromene (CBC), and selected terpene profiles, may mitigate neuroinflammation and oxidative stress while restoring endocannabinoid tone [4,36]. Observational data in veteran cohorts (Figure 1) suggest improvements in quality of life and reductions in concurrent opioid, alcohol, and tobacco use with medicinal cannabis relative to standard antidepressant therapies, although mechanistic biomarkers are rarely collected in studies of this nature [36,37].

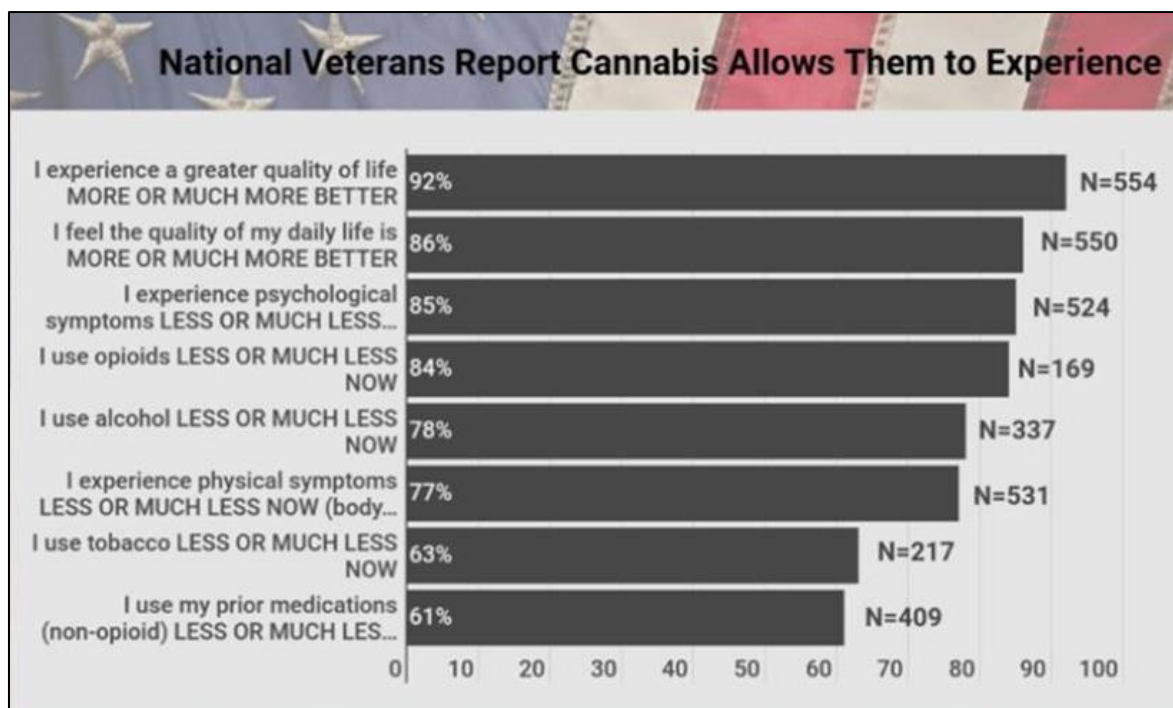


Figure 1 Data from the 2019 Veterans Health and Medical Cannabis study conducted by Dr. Marion McNabb et al

2.6. Endocannabinoid Deficiency and the “Entourage” Concept.

The clinical endocannabinoid deficiency hypothesis posits that inadequate signaling of anandamide (AEA) and 2-arachidonoylglycerol (2-AG) may underlie symptom clusters across multiple disorders, including PTSD. Restoring tone through phytocannabinoid supplementation or inhibition of catabolic enzymes such as FAAH and MAGL has been proposed as a corrective strategy [35,39]. In parallel, the “entourage effect”—the synergistic interaction of cannabinoids with terpenes and other plant constituents, has been suggested to broaden therapeutic windows and mitigate adverse effects relative to single-molecule interventions [39,40]. However, debate persists regarding the robustness of human clinical evidence and the challenges of standardization.

2.7. Clinical implications and future directions

A biologically anchored approach reframes PTSD treatment as the repair of disrupted circuits and systems rather than the suppression of symptoms. Priority areas include: (i) pairing exposure-based psychotherapies with endocannabinoid system-modulating agents such as FAAH/MAGL inhibitors or cannabidiol-forward formulations to enhance extinction learning; (ii) implementing biomarker-guided protocols that integrate circulating AEA and 2-AG levels, cytokine panels, PET-CB₁ binding measures, and HPA-axis dynamics; (iii) conducting rigorous clinical trials that compare nutraceutical, poly-mechanistic combinations against single-target pharmaceuticals with respect to remission, functional recovery, and safety; and (iv) stratifying patients according to mechanistic phenotype (e.g., inflammatory-high, ECS-low, HPA-dysregulated) to enable personalized interventions. In sum, PTSD exemplifies how biological processes manifest as psychological phenomena, underscoring that effective therapy must directly engage the biology that sustains the disorder.

3. ADHD: Attention as Neurochemical Expression

3.1. Clinical Overview and Epidemiology

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent neurodevelopmental condition defined by inattention, hyperactivity, and impulsiveness, frequently accompanied by emotional dysregulation, cognitive impairment, and psychiatric comorbidities [41]. Global prevalence estimates suggest ADHD affects ~5% of children and ~3% of adults, with persistence into adulthood in a substantial proportion of cases [42]. Family, twin, and adoption studies consistently show high heritability for ADHD (60–80 %) and strong familial aggregation (e.g. twin/family review, molecular genetics review) [43]. Concurrently, perinatal complications, prenatal exposures (e.g. substance, nutritional deficits,

inflammation), and psychosocial adversities contribute additional risk (prenatal risk factor meta-analysis; environmental risk review) [44,45].

3.2. Current Treatment Limitations

First-line pharmacological interventions typically involve psychostimulants such as amphetamines (e.g., Adderall) or methylphenidate (e.g., Ritalin). These compounds are effective in enhancing dopamine release but are associated with adverse cardiovascular, gastrointestinal, and psychiatric effects [46]. Furthermore, 10–30% of patients either fail to respond adequately or cannot tolerate stimulants, leading to second-line treatment with atomoxetine or, less commonly, antidepressants such as sertraline or fluoxetine, though these alternatives often provide only modest efficacy [47].

3.3. Neural Circuitry and Neurochemical Basis

Dysfunction of dopaminergic and noradrenergic signaling within prefrontal and striatal circuits is central to ADHD pathophysiology. Neuroimaging studies reveal reduced dopamine transporter activity and impaired reward processing, suggesting a “reward deficiency” framework [48]. While stimulant medications temporarily correct dopamine deficits, they do not address underlying regulatory imbalances nor long-term symptom persistence.

3.4. Endocannabinoid System and ADHD Pathophysiology

Emerging evidence implicates endocannabinoid signaling in ADHD. Human and animal studies demonstrate that the endocannabinoid system (ECS) regulates emotional homeostasis and cognition [49]. Altered anandamide degradation has been documented in ADHD patients, indicating an impaired capacity to sustain endocannabinoid tone [50]. Mechanistic studies show that dopamine release in striatal circuits is mediated by anandamide signaling, linking endocannabinoid disruption to dopaminergic dysfunction in ADHD [51]. Together, these findings suggest that the ECS not only modulates attention and impulse control indirectly through dopaminergic pathways but also functions as a direct regulatory system, whose dysregulation may contribute to core ADHD symptoms.

3.5. Pharmaceutical versus Nutraceutical Approaches

Conventional pharmacotherapy targets dopamine exogenously via psychostimulants, while synthetic FAAH inhibitors were designed to raise endogenous anandamide levels. However, the tragic BIA 10-2474 Phase I trial highlighted severe neurological side effects and mortality, likely due to off-target toxicity and impaired degradation of synthetic FAAH inhibitors [52]. In contrast, nutraceutical approaches utilize phytocannabinoids and natural FAAH inhibitors with safer biomolecular profiles. Phytocannabinoids such as cannabidiol (CBD), cannabigerol (CBG), and cannabichromene (CBC), alongside natural FAAH inhibitors like biochanin A, offer multimodal actions, including FAAH inhibition, antioxidant activity, and anti-inflammatory effects, that may restore endocannabinoid tone without the risks associated with synthetic compounds [53].

3.6. Biochanin A and Natural FAAH Inhibitors

Biochanin A, an isoflavone derived from red clover, exemplifies a promising nutraceutical FAAH inhibitor. Unlike synthetic analogues, it is efficiently metabolized, reducing the risk of toxic accumulation. Beyond FAAH inhibition, Biochanin A demonstrates antioxidant, anti-inflammatory, estrogen-mimetic, and neuroprotective properties [54]. Such pleiotropic effects position Biochanin A as a candidate for multimodal support in ADHD and related endocannabinoid deficiency disorders. While limited by low oral bioavailability, strategies such as nanoparticle formulations, liposomal carriers, or combination approaches may enhance its clinical utility, making it a compelling subject for translational research.

3.7. Clinical Implications and Future Directions

The convergence of genetic, neurobiological, and ECS evidence reframes ADHD as, in part, an endocannabinoid deficiency disorder. Nutraceutical interventions targeting endocannabinoid tone, particularly phytocannabinoids and natural FAAH inhibitors, offer the potential for safer, multimodal symptom relief compared to existing pharmacotherapies. However, rigorous biomarker-guided clinical trials remain necessary to validate efficacy, optimize dosing, and stratify ADHD subtypes most likely to benefit. Incorporating endocannabinoid measures into diagnostic frameworks could not only clarify individual variability in treatment response but also advance ADHD toward a more precise, biologically anchored model of care.

4. Autism Spectrum Disorder

4.1. Clinical Overview and Epidemiology

Autism spectrum disorder (ASD) is a heterogeneous neurodevelopmental condition characterized by persistent deficits in social communication and interaction, alongside restricted and repetitive behaviors. Global prevalence estimates suggest ASD affects 1–2% of the population, with symptoms emerging early in life and frequently persisting into adulthood [55]. Considerable heterogeneity exists in both symptom expression and severity, reflecting contributions from genetic, neurobiological, immune, and environmental influences.

4.2. Current Treatment Limitations

Available treatments for ASD primarily target secondary symptoms rather than the core social and communication deficits. Behavioral interventions such as applied behavior analysis (ABA) can improve adaptive functioning but are labor-intensive and variably effective [56]. Pharmacotherapies, including risperidone and aripiprazole, are approved for irritability and aggression, yet carry risks of metabolic, neurological, and endocrine adverse effects [57]. Critically, no existing pharmacological treatment addresses the underlying biological mechanisms of ASD, underscoring the need for novel therapeutic frameworks.

4.3. Neural Circuitry and Neurobiological Underpinnings

Neuroimaging and electrophysiological studies implicate disrupted connectivity between the prefrontal cortex, amygdala, and superior temporal sulcus—networks essential for social cognition and emotional regulation [58,59]. In addition, atypical excitatory–inhibitory balance, particularly involving glutamatergic and GABAergic systems, has been observed and is thought to contribute to sensory hypersensitivity and altered information processing [60]. These findings support a view of ASD as a network-level disorder shaped by developmental alterations in both synaptic signaling and broader circuit integration.

4.4. Molecular and Immune Signatures

Molecular investigations reveal altered expression of synaptic proteins, neurotrophic factors, and monoaminergic signaling pathways in individuals with ASD [61,62]. Immune dysregulation is also prominent, with elevated pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α), along with evidence that maternal immune activation during pregnancy increases offspring risk [63,64]. These data highlight the role of immune-brain crosstalk in shaping the ASD phenotype and suggest an avenue for intervention beyond traditional neurotransmitter models.

4.5. The Endocannabinoid System in ASD

Emerging evidence implicates the endocannabinoid system (ECS) in the regulation of social behavior, emotional homeostasis, and cognition. Children with ASD have been shown to exhibit reduced circulating levels of anandamide (AEA), correlating with symptom severity [65,66]. In animal models, enhancing AEA signaling improves social interaction and play, whereas blockade of cannabinoid type-1 (CB1) receptors exacerbates social deficits [67,68]. These findings point to ECS dysregulation as a mechanistic contributor to core ASD symptoms and support its consideration as a therapeutic target.

4.6. Nutraceutical Rationale and Therapeutic Potential

Cannabidiol (CBD), a non-intoxicating botanic cannabinoid, has demonstrated benefits in reducing anxiety, aggression, and hyperactivity in preliminary clinical studies of ASD [69,70]. By modulating both endocannabinoid tone and immune signaling, CBD, and related botanic cannabinoids such as cannabigerol (CBG) and cannabichromene (CBC), offer multimodal therapeutic potential. The proposed “entourage effect,” reflecting synergy between cannabinoids, terpenes, and other phytochemicals, may further broaden efficacy while reducing adverse events relative to single-molecule approaches. Early clinical findings, though limited in scale, suggest improvements in social responsiveness and quality of life, warranting larger controlled trials [71,72].

4.7. Clinical Implications and Future Directions

Framing ASD as a condition of neuroimmune and endocannabinoid imbalance opens new therapeutic avenues beyond symptom management. Nutraceutical interventions targeting the ECS hold promise to address social and cognitive deficits that remain untouched by current pharmacotherapies. Future priorities include biomarker-guided clinical trials to stratify ASD subgroups, optimize cannabinoid-based formulations, and measure endocannabinoid tone as both a

diagnostic and treatment-monitoring tool. Such efforts could shift ASD care toward a more precise, biologically anchored model of intervention.

5. Depressive Disorders: Molecular Mood States

5.1. Clinical Overview and Epidemiology

Depressive disorders, encompassing major depressive disorder (MDD) and related subtypes, represent one of the leading causes of disability worldwide, with lifetime prevalence estimates approaching 20% in some populations [73]. Core symptoms include persistent sadness, anhedonia, psychomotor changes, and cognitive impairment. Despite their psychological presentation, depressive syndromes are increasingly recognized as systemic conditions involving neurochemical imbalance, altered immune signaling, and impaired neuroplasticity [74,75]. This biologically grounded perspective positions depression not merely as a disorder of mood but as a dysregulation of cellular and molecular homeostasis.

5.2. Current Treatment Limitations

Conventional antidepressants, including selective serotonin reuptake inhibitors (SSRIs), serotonin–norepinephrine reuptake inhibitors (SNRIs), and tricyclics, target monoamine transmission indirectly and require weeks to achieve partial effect [76]. Even then, up to one-third of patients remain treatment-resistant [77]. Psychotherapies such as cognitive-behavioral therapy (CBT) or interpersonal therapy provide benefit but are limited by relapse and inconsistent access. These shortcomings reflect the reductionist focus on serotonin alone, neglecting the broader molecular milieu that regulates affect, motivation, and resilience.

5.3. Neural Circuitry and Network Dysregulation

Neuroimaging meta-analyses implicate disrupted functional connectivity between the prefrontal cortex, anterior cingulate, hippocampus, and amygdala—regions integral to emotional regulation and reward processing [78,79]. Hypoactivity of the prefrontal cortex and hyperactivity of limbic circuits drive negative bias and emotional rigidity, while reduced hippocampal neurogenesis contributes to impaired memory and stress reactivity. Structural and functional changes within these networks mirror alterations observed in chronic stress, suggesting shared pathophysiology between major depression and stress-related disorders.

5.4. Molecular and Immune Signatures

Molecularly, depressive disorders are associated with dysregulation of monoaminergic signaling, diminished brain-derived neurotrophic factor (BDNF), and increased oxidative stress [80]. Psychoneuroimmunology reveals a consistent pro-inflammatory phenotype, with elevated interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor- α (TNF- α) levels correlating with symptom severity and treatment resistance [81]. Microglial activation and impaired mitochondrial function further compromise neuronal energy metabolism, linking immune activation directly to mood disturbance.

5.5. The Endocannabinoid System in Depression

The endocannabinoid system (ECS) plays a critical role in regulating emotional homeostasis, reward sensitivity, and stress recovery. Reduced circulating levels of anandamide (AEA) and 2-arachidonoylglycerol (2-AG) have been documented in individuals with MDD, paralleling findings in PTSD and ASD [82]. Animal models demonstrate that CB₁ receptor activation exerts antidepressant-like effects, while genetic or pharmacological blockade induces depressive phenotypes [83]. Restoration of endocannabinoid tone enhances neurogenesis, modulates monoamine release, and dampens stress-induced HPA-axis hyperactivity, identifying the ECS as a mechanistic bridge between emotional and biological homeostasis.

5.6. Nutraceutical Rationale and Therapeutic Potential

Phytocannabinoids such as cannabidiol (CBD) have demonstrated antidepressant-like and anxiolytic effects across preclinical and emerging clinical studies [84,85]. Acting through indirect CB₁/CB₂ modulation, serotonin 5-HT_{1A} receptor activation, and attenuation of pro-inflammatory cytokines, CBD offers a multimodal approach distinct from monoamine-based antidepressants. Cannabigerol (CBG) and cannabichromene (CBC) further enhance serotonergic and dopaminergic tone while exhibiting neuroprotective and anti-inflammatory properties. The proposed “entourage effect,” encompassing synergistic interactions among cannabinoids and terpenes, may enhance efficacy and safety through balanced receptor engagement and reduced tolerance development [86].

5.7. Clinical Implications and Future Directions

Viewing depression as a biomolecular disorder reframes treatment from symptom suppression to molecular restoration. Future priorities include quantifying circulating endocannabinoids, cytokines, and BDNF as biomarkers of treatment response, and evaluating nutraceutical formulations targeting the ECS alongside conventional antidepressants. Integrating biomarker-guided nutraceutical therapy within standard psychiatric practice could not only personalize treatment but also address the substantial population of patients resistant to monoamine-based approaches. Ultimately, restoring endocannabinoid and neuroimmune balance represents a path toward sustained remission and the reconnection of mood to molecular equilibrium.

6. Conclusion

Across the conditions examined: PTSD, ADHD, ASD, and depressive disorders, a unifying pattern emerges. Disturbances in molecular signaling, immune regulation, and neural circuitry converge to produce what has long been interpreted as purely psychological phenomena. These findings affirm that behavior, mood, and cognition are biological expressions, not abstractions, of molecular states. The artificial division of “mental” and “physical” disorders dissolves under the weight of convergent evidence from neuroscience, psychoneuroimmunology, and endocannabinology.

The endocannabinoid system stands out as a central regulator within this framework—modulating neurotransmission, immune tone, and emotional homeostasis. Dysregulation within this system contributes not only to affective instability and cognitive dysfunction but also to the persistence of trauma-related and developmental pathologies. Quantifying endogenous cannabinoids such as anandamide (AEA) and 2-arachidonoylglycerol (2-AG) provides a measurable biomarker of neurobiological health, bridging the gap between psychiatry and laboratory medicine.

From a therapeutic standpoint, the convergence of molecular biology and psychology necessitates a paradigm shift. Nutraceutical interventions targeting the ECS—through phytocannabinoids, terpenes, and natural FAAH inhibitors, represent a safer, multimodal alternative to single-target pharmaceuticals. By restoring molecular balance rather than merely suppressing symptoms, these approaches embody a biologically anchored psychology capable of precision-guided intervention.

In sum, understanding psychological disorders through the lens of biological expression redefines mental health as a branch of life sciences. As measurement technologies advance and integrative research expands, biomolecular psychology offers not only explanatory power but a roadmap toward truly personalized diagnostics and therapeutics—where healing begins at the molecular level and manifests as the restoration of mind.

Compliance with ethical standards

Acknowledgments

The author thanks TruLab DX for analytical collaboration and the AMCANN Research Board for their continued scientific support.

Disclosure of conflict of interest

The author declares no conflict of interest.

References

- [1] Descartes R. *Meditations on First Philosophy*. Cambridge: Cambridge University Press; 1641.
- [2] Freud S. *The Interpretation of Dreams*. New York: Basic Books; 1900.
- [3] Watson JB. *Psychology as the Behaviorist Views It*. Psychol Rev. 1913;20(2):158–77. doi:10.1037/h0074428
- [4] Dawson DA. Theoretical frameworks toward a nutraceutical approach to treating PTSD. World J Biol Pharm Res. 2023;5(1):1-14. doi:10.53346/wjbpr.2023.5.1.0056
- [5] Di Marzo V, Piscitelli F. The Endocannabinoid System and its Modulation by Phytocannabinoids. Neurotherapeutics. 2015;12(4):692-698. doi:10.1007/s13311-015-0374-6
- [6] Nestler EJ, Hyman SE. Animal models of neuropsychiatric disorders. Nat Neurosci. 2010;13(10):1161-1169.

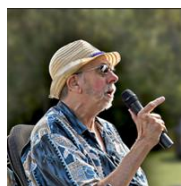
- [7] Pertwee RG. Cannabinoid pharmacology: the first 66 years. *Br J Pharmacol.* 2006;147 Suppl 1(Suppl 1):S163-S171. doi:10.1038/sj.bjp.0706406
- [8] Dawson DA, Persad CP. Targeting the endocannabinoid system in the treatment of addiction disorders. *GSC Biol Pharm Sci.* 2022;19(2):64-74. doi:10.30574/gscbps.2022.19.2.0175
- [9] Aran A, Eylon M, Harel M, Poliansky L, Nemirovsky A, Tepper S, et al. Lower circulating endocannabinoid levels in children with autism spectrum disorder. *Mol Autism.* 2019;10:2. doi:10.1186/s13229-019-0256-6
- [10] Bright U, Akirav I. Modulation of endocannabinoid system components in depression: Pre-clinical and clinical evidence. *Int J Mol Sci.* 2022;23(10):5526. doi:10.3390/ijms23105526
- [11] North CS, Surís AM, Smith RP, King RV. The evolution of PTSD criteria across editions of DSM. *Annals of clinical psychiatry.* 2016 Aug;28(3):197-208.
- [12] Ehlers A, Hackmann A, Michael T. Intrusive reexperiencing in post-traumatic stress disorder: Phenomenology, theory, and therapy. *Memory.* 2004 Jul 1;12(4):403-15.
- [13] Bisson JI, Cosgrove S, Lewis C, Roberts NP. Post-traumatic stress disorder. *Bmj.* 2015 Nov 26;351.
- [14] Steel Z, Chey T, Silove D, Marnane C, Bryant RA, Van Ommeren M. Association of torture and other potentially traumatic events with mental health outcomes among populations exposed to mass conflict and displacement: a systematic review and meta-analysis. *Jama.* 2009 Aug 5;302(5):537-49.
- [15] Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the National Comorbidity Survey. In *Fear and Anxiety* 2013 Oct 8 (pp. 22-34). Routledge.
- [16] Schou TM, Joca S, Wegener G, Bay-Richter C. Psychiatric and neuropsychiatric sequelae of COVID-19—A systematic review. *Brain, behavior, and immunity.* 2021 Oct 1;97:328-48.
- [17] Bajoulvand R, Hashemi S, Askari E, Mohammadi R, Behzadifar M, Imani-Nasab MH. Post-pandemic stress of COVID-19 among high-risk groups: A systematic review and meta-analysis. *Journal of affective disorders.* 2022 Dec 15;319:638-45.
- [18] Pitman, R. K., Rasmusson, A. M., Koenen, K. C., Shin, L. M., Orr, S. P., Gilbertson, M. W., Milad, M. R., & Liberzon, I. (2012). Biological studies of post-traumatic stress disorder. *Nature Reviews Neuroscience*, 13(11), 769.
- [19] Hori H, Kim Y. Inflammation and post-traumatic stress disorder. *Psychiatry and clinical neurosciences.* 2019 Apr;73(4):143-53.
- [20] María-Ríos CE, Morrow JD. Mechanisms of shared vulnerability to post-traumatic stress disorder and substance use disorders. *Frontiers in behavioral neuroscience.* 2020 Jan 31;14:6.
- [21] Detweiler MB, Pagadala B, Candelario J, Boyle JS, Detweiler JG, Lutgens BW. Treatment of post-traumatic stress disorder nightmares at a veterans affairs medical center. *Journal of clinical medicine.* 2016 Dec 16;5(12):117.
- [22] Dunlop BW, Kaye JL, Youngner C, Rothbaum B. Assessing treatment-resistant posttraumatic stress disorder: The Emory treatment resistance interview for PTSD (E-TRIP). *Behavioral Sciences.* 2014 Dec 8;4(4):511-27.
- [23] Hoskins, M., Pearce, J., Bethell, A., Dankova, L., Barbui, C., Tol, W. A., van Ommeren, M., de Jong, J., Seedat, S., Chen, H., & Bisson, J. I. (2015). Pharmacotherapy for post-traumatic stress disorder: Systematic review and meta-analysis. *The British Journal of Psychiatry*, 206(2), 93-100.
- [24] Watkins LE, Sprang KR, Rothbaum BO. Treating PTSD: A review of evidence-based psychotherapy interventions. *Frontiers in behavioral neuroscience.* 2018 Nov 2;12:258.
- [25] Hayes JP, Hayes SM, Mikedis AM. Quantitative meta-analysis of neural activity in posttraumatic stress disorder. *Biology of mood & anxiety disorders.* 2012 May 18;2(1):9.
- [26] Pitman RK, Rasmusson AM, Koenen KC, Shin LM, Orr SP, Gilbertson MW, Milad MR, Liberzon I. Biological studies of post-traumatic stress disorder. *nature Reviews neuroscience.* 2012 Nov;13(11):769-87.
- [27] Dahl J, Ormstad H, Aass HC, Sandvik L, Malt UF, Andreassen OA. Recovery from major depressive disorder episode after non-pharmacological treatment is associated with normalized cytokine levels. *Acta Psychiatrica Scandinavica.* 2016 Jul;134(1):40-7.
- [28] Pace TW, Heim CM. A short review on the psychoneuroimmunology of posttraumatic stress disorder: from risk factors to medical comorbidities. *Brain, behavior, and immunity.* 2011 Jan 1;25(1):6-13.
- [29] Ong AD, Benson L, Zautra AJ, Ram N. Emodiversity and biomarkers of inflammation. *Emotion.* 2018 Feb;18(1):3.

- [30] Di Marzo V, Piscitelli F. The endocannabinoid system and its modulation by phytocannabinoids. *Neurotherapeutics*. 2015 Oct 1;12(4):692-8.
- [31] Pertwee, R. G. (2014). Elevating endocannabinoid levels: Pharmacological strategies and potential therapeutic applications. *The Proceedings of the Nutrition Society*, 73(1), 96-105.
- [32] Ney LJ, Matthews A, Hsu CM, Zuj DV, Nicholson E, Steward T, Nichols D, Graham B, Harrison B, Bruno R, Felmingham K. Cannabinoid polymorphisms interact with plasma endocannabinoid levels to predict fear extinction learning. *Depression and Anxiety*. 2021 Oct;38(10):1087-99.
- [33] Pavlov D. The contribution of CNS inflammation and Glycogen Synthase Kinase-3 (GSK-3)-cascades on adverse memory learning on mouse models of emotional stress.
- [34] Henshaw FR, Dewsbury LS, Lim CK, Steiner GZ. The effects of cannabinoids on pro-and anti-inflammatory cytokines: a systematic review of in vivo studies. *Cannabis and Cannabinoid Research*. 2021 Jun 1;6(3):177-95.
- [35] Russo EB. Clinical endocannabinoid deficiency (CECD). *Neuroendocrinology Letters*. 2008;29(2):192-200.
- [36] Orsolini L, Chiappini S, Volpe U, De Berardis D, Latini R, Papanti GD, Corkery JM. Use of medicinal cannabis and synthetic cannabinoids in post-traumatic stress disorder (PTSD): a systematic review. *Medicina*. 2019 Aug 23;55(9):525.
- [37] McNabb M, Mandile S, Ritter DJ, Brum A, Bacon R, MacCaffrie R, Stout D, White S, Rewegan AN, Tangney E. The 2019 Veterans Health and Medical Cannabis Study. *Cannabis Patient Care*. 2020 Nov 2;1(1):6-18.
- [38] Mayo LM, Rabinak CA, Hill MN, Heilig M. Targeting the endocannabinoid system in the treatment of posttraumatic stress disorder: A promising case of preclinical-clinical translation?. *Biological psychiatry*. 2022 Feb 1;91(3):262-72.
- [39] Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *British journal of pharmacology*. 2011 Aug;163(7):1344-64.
- [40] Mukherjee PK, Banerjee S, Kar A. Molecular combination networks in medicinal plants: understanding synergy by network pharmacology in Indian traditional medicine. *Phytochemistry reviews*. 2021 Aug;20(4):693-703.
- [41] Gnanavel S, Sharma P, Kaushal P, Hussain S. Attention deficit hyperactivity disorder and comorbidity: A review of literature. *World journal of clinical cases*. 2019 Sep 6;7(17):2420.
- [42] Ahn K, McKinney MK, Cravatt BF. Enzymatic pathways that regulate endocannabinoid signaling in the nervous system. *Chemical Reviews*. 2008; 108: 1687-1707.
- [43] Freitag C, Retz W. Family and Twin Studies in Attention-Deficit Hyperactivity Disorder. In: Retz W, Klein RG, editors. *Attention-Deficit Hyperactivity Disorder (ADHD) in Adults*. Basel: Karger; 2009. p. 38-57. doi:10.1159/000258448
- [44] Li Z, Chang SH, Zhang LY, Gao L, Wang J. Molecular genetic studies of ADHD and its candidate genes: a review. *Psychiatry research*. 2014 Sep 30;219(1):10-24.
- [45] Froehlich TE, Anixt JS, Loe IM, Chirdkiatgumchai V, Kuan L, Gilman RC. Update on environmental risk factors for attention-deficit/hyperactivity disorder. *Current psychiatry reports*. 2011 Oct;13(5):333-44.
- [46] Torres-Acosta N, O'Keefe JH, O'Keefe CL, Lavie CJ. Cardiovascular effects of ADHD therapies: JACC review topic of the week. *Journal of the American College of Cardiology*. 2020 Aug 18;76(7):858-66.
- [47] Yu CL, Kao YC, Thompson T, Stubbs B, Tseng PT, Hsu CW, Yang FC, Tu YK, Hsu TW, Liang CS. Response Trajectories and Temporal Trends of Viloxazine Treatment for Young People With ADHD: A Meta-Analysis. *JAMA Network Open*. 2024 Nov 4;7(11):e2445885-.
- [48] Volkow ND, Wang GJ, Newcorn JH, Kollins SH, Wigal TL, Telang F, et al. Motivation deficit in ADHD is associated with dysfunction of the dopamine reward pathway. *Mol Psychiatry*. 2011;16(11):1147-54. doi:10.1038/mp.2010.97
- [49] La Porta C, Bura SA, Llorente-Onaindia J, Pastor A, Navarrete F, García-Gutiérrez MS, et al. Role of the endocannabinoid system in the emotional brain. *Mol Psychiatry*. 2015;20(6):708-17. doi:10.1038/mp.2014.181
- [50] Millichap JG. Altered Anandamide Degradation in Attention Deficit Hyperactivity Disorder. *Pediatric Neurology Briefs*. 2009 Jun 1;23(6).

- [51] Giuffrida A, Parsons LH, Kerr TM, Rodríguez de Fonseca F, Navarro M, Piomelli D. Dopamine activation of endogenous cannabinoid signaling in dorsal striatum. *Nat Neurosci*. 1999;2(4):358-63. doi:10.1038/7268
- [52] Kerbrat A, Ferré JC, Fillatre P, Ronzière T, Vannier S, Carsin-Nicol B, Lavoué S, Vérin M, Gauvrit JY, Le Tulzo Y, Edan G. Acute neurologic disorder from an inhibitor of fatty acid amide hydrolase. *New England Journal of Medicine*. 2016 Nov 3;375(18):1717-25.
- [53] Thors L, Burston JJ, Alter BJ, McKinney MK, Cravatt BF, Ross RA, Pertwee RG, Gereau 4th RW, Wiley JL, Fowler CJ. Biochanin A, a naturally occurring inhibitor of fatty acid amide hydrolase. *British Journal of Pharmacology*. 2010 Jun;160(3):549-60.
- [54] Patel AV, Shah BN. Transdermal drug delivery system: A review. *Pharma Science Monitor*. 2018; 9: 378-390.
- [55] Zeidan J, Fombonne E, Scora J, Ibrahim A, Durkin MS, Saxena S, Yusuf A, Shih A, Elsabbagh M. Global prevalence of autism: A systematic review update. *Autism research*. 2022 May;15(5):778-90.
- [56] Gitimoghaddam M, Chichkine N, McArthur L, Sangha SS, Symington V. Applied behavior analysis in children and youth with autism spectrum disorders: a scoping review. *Perspectives on behavior science*. 2022 Sep;45(3):521-57.
- [57] De Hert M, Dobbelaere M, Sheridan EM, Cohen D, Correll CU. Metabolic and endocrine adverse effects of second-generation antipsychotics in children and adolescents: a systematic review of randomized, placebo-controlled trials and guidelines for clinical practice. *Eur Psychiatry*. 2011;26(3):144-58. doi:10.1016/j.eurpsy.2010.09.011
- [58] Li L, He C, Jian T, Guo X, Xiao J, Li Y, Chen H, Kang X, Chen H, Duan X. Attenuated link between the medial prefrontal cortex and the amygdala in children with autism spectrum disorder: Evidence from effective connectivity within the "social brain". *Prog Neuropsychopharmacol Biol Psychiatry*. 2021;111:110147.
- [59] Sun S, Yu H, Yu R, Wang S. Functional connectivity between the amygdala and prefrontal cortex underlies processing of emotion ambiguity. *Transl Psychiatry*. 2023;13(1):334.
- [60] Rubenstein JL, Merzenich MM. Model of autism: increased ratio of excitation/inhibition in key neural systems. *Genes Brain Behav*. 2003;2(5):255-267.
- [61] Yeo XY, Lim YT, Chae WR, Park C, Park H, Jung S. Alterations of presynaptic proteins in autism spectrum disorder. *Frontiers in Molecular Neuroscience*. 2022 Nov 17;15:1062878.
- [62] Jiang CC, Lin LS, Long S, Ke XY, Fukunaga K, Lu YM, Han F. Signalling pathways in autism spectrum disorder: mechanisms and therapeutic implications. *Signal transduction and targeted therapy*. 2022 Jul 11;7(1):229.
- [63] Tartaglione AM, Cipriani S, Rossi G, Coppola G, D'Addario SL, Gangemi G, et al. Maternal immune activation induces autism-like changes in behavior, neuroinflammatory profile and gut microbiota in mouse offspring. *Transl Psychiatry*. 2022;12(1):384.
- [64] Majerczyk D, Ayad EG, Brewton KL, Saing P, Hart PC. Systemic maternal inflammation promotes ASD via IL-6 and IFN- γ . *Bioscience Reports*. 2022 Nov;42(11):BSR20220713.
- [65] Aran A, Eylon M, Harel M, Polianski L, Nemirovski A, Tepper S, Schnapp A, Cassuto H, Wattad N, Tam J. Lower circulating endocannabinoid levels in children with autism spectrum disorder. *Molecular autism*. 2019 Jan 30;10(1):2.
- [66] Karhson DS, Krasinska KM, Dallaire JA, Libove RA, Phillips JM, Chien AS, Garner JP, Hardan AY, Parker KJ. Plasma anandamide concentrations are lower in children with autism spectrum disorder. *Molecular autism*. 2018 Mar 12;9(1):18.
- [67] Wei D, Dinh D, Lee D, Li D, Anguren A, Moreno-Sanz G, Gall CM, Piomelli D. Enhancement of anandamide-mediated endocannabinoid signaling corrects autism-related social impairment. *Cannabis and cannabinoid research*. 2016 Feb 1;1(1):81-9.
- [68] Servadio M, Melancia F, Manduca A, Di Masi A, Schiavi S, Cartocci V, Pallottini V, Campolongo P, Ascenzi P, Trezza V. Targeting anandamide metabolism rescues core and associated autistic-like symptoms in rats prenatally exposed to valproic acid. *Translational Psychiatry*. 2016 Sep;6(9):e902.
- [69] Aran A, Harel M, Cassuto H, Polyansky L, Schnapp A, Wattad N, Shmueli D, Golan D, Castellanos FX. Cannabinoid treatment for autism: a proof-of-concept randomized trial. *Molecular autism*. 2021 Feb 3;12(1):6.

- [70] Hacohe M, Stolar OE, Berkovitch M, Elkana O, Kohn E, Hazan A, Heyman E, Sobol Y, Waissengreen D, Gal E, Dinstein I. Children and adolescents with ASD treated with CBD-rich cannabis exhibit significant improvements particularly in social symptoms: an open label study. *Transl Psychiatry*. 2022; 12 (1): 375 [Internet].
- [71] Silva, E. A. D., Junior, Medeiros, W. M. B., Santos, J. P. M. D., Sousa, J. M. M., Costa, F. B. D., Pontes, K. M., Borges, T. C., Espínola, C., Neto Segundo, Andrade E Silva, A. H., Nunes, E. L. G., Alves, N. T., Rosa, M. D. D., & Albuquerque, K. L. G. D. (2024). Evaluation of the efficacy and safety of cannabidiol-rich cannabis extract in children with autism spectrum disorder: randomized, double-blind, and placebo-controlled clinical trial. *Trends in psychiatry and psychotherapy*, 46, e20210396.
- [72] Mazza JA, Ferreira LS, Martins-Vieira AD, Beserra DD, Rodrigues VA, Malcher-Lopes R, Caixeta FV. Clinical and family implications of cannabidiol (CBD)-dominant full-spectrum phytocannabinoid extract in children and adolescents with moderate to severe non-syndromic autism spectrum disorder (ASD): an observational study on neurobehavioral management. *Pharmaceuticals*. 2024 Jun;17(6):686.
- [73] World Health Organization. Depression and Other Common Mental Disorders: Global Health Estimates. Geneva: WHO; 2017.
- [74] Nestler EJ, et al. The molecular neurobiology of depression. *Nature*. 2002;420:894–899.
- [75] Duman RS, et al. A neurotrophic model for stress-related mood disorders. *Biol Psychiatry*. 2016;80(9):681–689.
- [76] Cipriani A, et al. Comparative efficacy and acceptability of antidepressants. *Lancet*. 2018;391:1357–1366.
- [77] Rush AJ, et al. STAR*D study outcomes. *Am J Psychiatry*. 2006;163(11):1905–1917.
- [78] Sheline YI, et al. Depression and the brain: functional neuroimaging findings. *Am J Psychiatry*. 2019;176(1):21–31.
- [79] Kaiser RH, et al. Large-scale network dysfunction in major depressive disorder. *JAMA Psychiatry*. 2015;72(6):603–611.
- [80] Leonard BE, et al. Inflammation and depression: a causal relationship? *Neurosci Biobehav Rev*. 2018;90:307–316.
- [81] Miller AH, Raison CL. The role of inflammation in depression. *Nat Rev Immunol*. 2016;16:22–34.
- [82] Bright U, Akirav I. Modulation of endocannabinoid system components in depression: pre-clinical and clinical evidence. *Int J Mol Sci*. 2022;23(10):5526.
- [83] Bambico FR, Gobbi G. The role of endocannabinoids in the treatment of mood disorders. *Prog Neuropsychopharmacol Biol Psychiatry*. 2008;32(6):1356–1365.
- [84] Sales AJ, Joca SRL. Cannabidiol as a promising therapeutic candidate for depression. *Front Immunol*. 2020;11:1223.
- [85] Hundal H, Lister R, Evans N, Antal A, et al. Cannabidiol in depression: systematic review of clinical evidence. *J Psychopharmacol*. 2024;38(2):144–162.
- [86] Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid–terpenoid entourage effects. *Br J Pharmacol*. 2011;163(7):1344–1364.

Author short biography



Dr. David A. Dawson, PhD, Director of Research, Publication & Education at AMCANN, LLLP is a Biomolecular Psychologist specializing in endocannabinology and psychoneuroimmunology. His research explores how endocannabinoid signaling governs the molecular interplay between mental health and autoimmune disorders, advancing biomolecular approaches to diagnosis and treatment.