Why are Psychotropic Medication and Cognitive Behavioral Therapy insufficient to address Multi-System Neuro-Developmental and Psychiatric Disorders involving Neuro-Immune, Mitochondrial, Metabolic and Neuro-Endocrine Dysregulations?

Psychotropic drugs and **CBT are insufficient** when disorders reflect **whole-body dysregulation**, not symptoms alone.

Psychotropic medication and cognitive behavioral therapy are often insufficient because these disorders involve **interacting immune, mitochondrial, metabolic, and neuroendocrine abnormalities** that extend beyond the symptom targets of standard psychiatric care. Across the literature, the main gaps are biological scope, incomplete symptom coverage, and treatment-emergent metabolic burden (Ciubuc-Batcu et al., 2023; Gaspary et al., 2025; Karabatsiakis & Schönfeldt-Lecuona, 2020).

Multi-System Treatment Limits

Evidence Strength	Claim
Strong	Many psychiatric disorders are now described as **systemic disorders**, with reciprocal interactions among immune, endocrine, metabolic, and neural systems rather than isolated neurotransmitter imbalance (Ortega et al., 2024; Rawani et al., 2024; Gaspary et al., 2025).
Strong	**Monotherapies** aimed at single nodes, such as symptoms or neurotransmission alone, tend to have limited value in networked disorders like depression and psychosis (Ciubuc-Batcu et al., 2023; Rawani et al., 2024; Almulla & Maes, 2025).
Strong	Standard psychotropics can add **metabolic burden**, including weight gain, insulin resistance, dysglycemia, dyslipidemia, and hypertension, which can worsen the same systemic dysfunction linked to psychiatric illness (Dhieb & Bastaki, 2026; Carmellini et al., 2025; Chokkakula et al., 2026).

FIGURE 1 Evidence strength for major reasons standard care falls short

Biological Scope

These disorders appear to arise from a **brain-body network**, not from one pathway. Immune dysfunction can drive neuroinflammation while also altering endocrine, metabolic, gut, and other organ systems, and those same systems can feed back to worsen immune dysfunction (Ortega et al., 2024; Almulla & Maes, 2025; Ciubuc-Batcu et al., 2023).

Mitochondria sit near the center of this network because they regulate energy production, oxidative stress, calcium handling, apoptosis, and neuronal plasticity. When mitochondrial function is impaired, the effects can reach cognition, mood, psychosis, stress adaptation, and peripheral organs, so a therapy aimed mainly at thoughts or synaptic signaling will often leave major disease drivers unaddressed (Pal et al., 2026; Ciubuc-Batcu et al., 2023; Tanaka et al., 2022).

What Standard Care Misses

- Antipsychotics help **positive symptoms** in schizophrenia but poorly address negative and cognitive symptoms (Ni & Chung, 2020).
- Drug treatments in neurodevelopmental disorders have shown **limited effects**, reflecting heterogeneity and unclear pathogenesis (Yang et al., 2025).
- Monoamine-based pharmacotherapies frequently produce **inadequate outcomes** and substantial treatment resistance in depression, bipolar disorder, and schizophrenia (Almulla & Maes, 2025).

Why Broader Care Is Studied

Research increasingly shifts toward adjunctive or multimodal strategies because diet, exercise, anti-inflammatory agents, mitochondrial targets, and metabolic therapies can act on pathways that standard care only partly influences. Exercise is consistently antidepressant and enhances mitochondrial biogenesis, while immune-targeted augmentation, nutraceuticals, and metabolic agents such as GLP-1 receptor agonists are being studied to address inflammation, insulin resistance, neuroplasticity, and energy balance together (Ciubuc-Batcu et al., 2023; Almulla & Maes, 2025; Carmellini et al., 2025).

CBT and psychotropics can still help symptoms, but they are often insufficient for **multi-system neurodevelopmental and psychiatric disorders** because the underlying dysfunction spans immune, mitochondrial, metabolic, and neuroendocrine systems that standard treatments do not comprehensively correct.

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