

The Biological Differential Diagnosis of Mental Illness

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Abstract

Psychiatric symptoms arise within brains embedded in bodies and environments. Some presentations reflect primary psychiatric syndromes; others arise directly from neurological, endocrine, metabolic, inflammatory or toxic disease; many combine several mechanisms. This paper proposes an organized differential-diagnosis framework intended to improve causal reasoning without inviting indiscriminate testing or assuming hidden biological disease in every patient.

Begin with the syndrome, not the favorite mechanism

The first task is to identify what is actually happening: depressed mood, psychosis, mania, delirium, cognitive decline, dissociation, anxiety or a combination. Time course is as informative as symptom content. Abrupt change over hours or days, impaired attention, altered consciousness, focal neurological signs, seizures or severe systemic illness can alter clinical urgency. Long-standing affective symptoms with preserved cognition and stable physical health carry a different prior probability of encephalopathy or rare metabolic disease.

Organize plausible causal families

The principal medical categories include thyroid and parathyroid disorders; electrolyte and osmotic disturbances; hepatic and renal encephalopathy; nutritional deficiencies; medication and substance effects; epilepsy and structural neurological disease; autoimmune encephalitis; selected infections; and rare inherited metabolic conditions such as acute porphyria or Wilson disease. Pregnancy and postpartum transitions warrant additional consideration of reproductive hormones, sleep, bipolar vulnerability and rare neurological causes. None of these categories can be diagnosed from psychiatric symptoms alone.

Testing must answer a question

A laboratory finding becomes meaningful through its relationship to the clinical presentation. Serum sodium helps when acute confusion suggests osmotic disturbance; renal chemistry is relevant in systemic illness; thyroid studies may clarify a compatible endocrine picture. Indiscriminate panels can generate incidental findings and unnecessary interventions. A normal common screening test also does not exclude every rare disease; suspicion must depend on the specific phenotype rather than a checklist of all possible disorders.

Where oxalate belongs

In a patient with recurrent kidney stones, enteric malabsorption, kidney failure or known hyperoxaluria, oxalate physiology can be relevant. For isolated anxiety or psychosis without renal disease, evidence does not support routine oxalate attribution. The proposed OANVH should therefore occupy a narrowly qualified investigative position, not a mandatory diagnostic branch. Its proper place in clinical reasoning is lower than better-established and more plausible alternative causes until discriminating evidence emerges.

Coexistence and urgent care

A patient can have bipolar disorder and thyroid disease, schizophrenia and epilepsy, depression and a nutrient deficiency, or severe psychiatric illness alongside entirely normal routine laboratories. Treating one does not erase the other. Suspected delirium, encephalitis, seizures, rapidly evolving psychosis or postpartum psychosis requires timely qualified medical and psychiatric care. The aim of integration is to shorten dangerous diagnostic delay, not to obstruct established treatment with endless speculative testing.

A clinical reasoning sequence rather than a universal panel

The first branch of a responsible framework concerns acute safety and neurological instability. Severe confusion, impaired attention, seizure activity, rapidly progressive neurological findings, suicidal or violent risk and postpartum psychosis require prompt assessment. The second branch concerns the most likely and treatable common conditions, guided by history and examination: medication effects, intoxication, withdrawal, sleep deprivation, endocrine disease, infection or metabolic derangement. Only then should unusual inherited or autoimmune processes be considered according to their specific warning signs.

This sequence is not meant to suppress curiosity about rare mechanisms. It is a safeguard against opportunity cost. Every unhelpful test consumes time, introduces incidental findings and may divert attention from a more probable treatable condition. Conversely, a rare illness with a coherent constellation of signs deserves investigation even if routine screening is unrevealing. The task is to change probabilities with evidence, not to generate an endless catalogue of hidden causes.

Conclusion

The biological differential of mental illness is a disciplined way to decide when and how a psychiatric presentation merits medical explanation. Its strength lies in prioritization: first recognize dangerous patterns; then identify testable causes; finally keep uncertainty visible where no complete mechanism is known.

Selected readings

- [Pollak et al., Autoimmune psychosis consensus](#)
- [Wilson disease psychiatric manifestations](#)
- [Hypothyroidism presenting as psychosis](#)
- [Acute intermittent porphyria psychiatric manifestations](#)