

ABSURD HEALTH INSTITUTE

The Biological Origins of Mental Illness

Oxalates, Neuroimmunity, Endocrine Dysfunction,
Metabolic Mimics & Treatment Resistance

MEDICAL CONCEPT PAPERS · VOLUME FIVE · 2026

43 independent essays • 18 papers on oxalate physiology and psychiatric hypotheses

These are open-access medical concept essays, not reports of original trials, validated diagnostic tests, individualized medical advice, or exhaustive systematic reviews. Hypotheses and evidence limits are stated in each article. Do not postpone emergency medical or psychiatric care to pursue a proposed dietary mechanism.

Contents

The Oxalate-Brain Hypothesis

01. The Oxalate-Brain Hypothesis: Can a Dietary Metabolite Become a Psychiatric Stressor?
02. Oxalate Is Not Merely a Dietary Substance
03. The Spinach Paradox: When a Healthy Diet Becomes a High-Oxalate Exposure
04. The Calcium Paradox: Why Less Dietary Calcium Can Mean More Oxalate Absorption
05. Bile, Fat Malabsorption and the Enteric Oxalate Trap
06. The Microbiome and the Fate of Oxalate
07. The Kidney-Brain Oxalate Axis
08. Crystal-Driven Inflammation: Calcium Oxalate and the NLRP3 Inflammasome
09. Oxalate, Oxidative Stress and Mitochondrial Injury
10. Oxalosis of the Nervous System: What Human Pathology Actually Shows
11. The Ethylene Glycol Experiment: What Extreme Poisoning Reveals—and What It Does Not
12. Mineral Balance and Neural Excitability: Could Oxalate Contribute Indirectly?
13. Vitamin B6, Glyoxylate Metabolism and the Limits of Nutritional Compensation
14. Vitamin C and Endogenous Oxalate: When Supplementation Changes Metabolic Exposure
15. Oxalates and Autism: Investigating a Controversial Metabolic Association
16. Could Oxalate Burden Contribute to Anxiety, Brain Fog or Cognitive Dysfunction?
17. The Postpartum Oxalate Vulnerability Hypothesis: A Multi-Hit Model of Psychiatric Deterioration
18. How to Disprove the Oxalate-Psychiatry Hypothesis

Neuroimmune Psychiatry

19. When the Immune System Produces Psychiatric Symptoms
20. Autoimmune Encephalitis: When Psychosis Is a Neurological Emergency
21. Cytokines, Kynurenine and the Chemistry of Sickness Behavior
22. Mast Cells, Histamine and the Neuroimmune Interface
23. Infection-Associated Psychiatric Syndromes
24. Inflammatory Depression or Depression with Inflammation?

Endocrine Origins of Psychiatric Symptoms

- 25. When Thyroid Disease Looks Like Anxiety, Depression or Psychosis
- 26. The Postpartum Endocrine Transition and Psychiatric Vulnerability
- 27. Cortisol and the Brain: From Adaptive Stress to Pathological Regulation
- 28. Sex Hormones, Neurosteroids and Mood Regulation
- 29. Parathyroid Disease, Calcium Regulation and Neuropsychiatric Symptoms

Metabolic and Neurological Psychiatric Mimics

- 30. Acute Intermittent Porphyrria: When Abdominal Pain and Psychosis Share a Metabolic Cause
- 31. Wilson Disease: Copper Metabolism and the Psychiatric Brain
- 32. Hyperammonemia and the Metabolic Encephalopathy That Resembles Psychiatric Illness
- 33. B12, Thiamine and the Nutritional Neurology of Psychiatric Symptoms
- 34. The Diluted Mind Revisited: Psychiatric Symptoms of Water and Sodium Imbalance
- 35. When Epilepsy Presents as Behavioral or Psychiatric Change
- 36. Delirium Is Not Primary Psychosis

Treatment Resistance Reconsidered

- 37. When Treatment-Resistant Depression Is Not Simply Depression
- 38. Psychiatric Pharmacogenomics: Metabolism, Exposure and Variable Response
- 39. Iatrogenic Psychiatry: When Treatment Produces New Symptoms
- 40. Could Biological State Determine Treatment Response?
- 41. When Symptom Improvement Is Not Functional Recovery

Synthesis and Integrated Medical Psychiatry

- 42. The Biological Differential Diagnosis of Mental Illness
- 43. The Psychiatric Symptom as a Biological Signal: Toward an Integrated Medicine of Mind and Body

The Oxalate-Brain Hypothesis: Can a Dietary Metabolite Become a Psychiatric Stressor?

ABSURD HEALTH INSTITUTE · 2026-10-16 · Frontier hypothesis with established renal mechanisms

Abstract

Oxalate is an endogenous and dietary organic anion whose clinical relevance has traditionally been considered within nephrolithiasis and oxalate nephropathy. Severe systemic oxalosis can involve extra-renal tissues. The possibility that oxalate-associated disturbances contribute to neuropsychiatric symptoms deserves careful analysis, but the evidentiary distance between renal crystallopathy and common psychiatric disorders is considerable. We propose an **oxalate-associated neuropsychiatric vulnerability hypothesis (OANVH)**: in narrowly defined susceptible hosts, substantial oxalate burden might contribute indirectly to cognitive, affective, or behavioral disturbance through renal impairment, disordered mineral physiology, systemic inflammation, or severe multisystem deposition. We do not claim that everyday dietary oxalate causes psychosis or autism.

A metabolite is not a diagnosis

The first conceptual error would be to speak of “oxalate toxicity” as though every concentration, exposure, and tissue distribution meant the same thing. Oxalic acid is the final product of several metabolic routes. Dietary oxalate can be absorbed in the intestine, whereas hepatic glyoxylate metabolism supplies another source. The kidneys excrete much of the circulating burden. Urinary oxalate, plasma oxalate, calcium oxalate supersaturation, actual crystal deposition, kidney filtration and cerebral function are different measurements with different meanings. A person with modestly increased urinary oxalate and normal kidney function cannot be equated with a person with primary hyperoxaluria, renal failure, and systemic oxalosis.

A hierarchy of possible mechanisms

The most defensible indirect chain begins with a susceptible host: fat malabsorption, particular genetic disorders, unusually concentrated dietary exposure, or diminished renal clearance. Excess freely absorbable oxalate can increase urinary supersaturation; crystallization can injure renal tissue, sometimes with inflammatory amplification. If kidney function deteriorates, metabolic disturbances and retained solutes can produce encephalopathy, impaired attention, and behavioral changes. In that scenario, oxalate may be an initiating renal stressor, but it is not necessarily the immediate neuroactive molecule. A second, rarer mechanism concerns systemic oxalosis in advanced disease, where tissue deposition has been documented beyond the kidneys. A third mechanism—direct low-level oxalate neurotoxicity in individuals without renal impairment—remains insufficiently demonstrated in humans.

The psychiatric leap

Psychosis, severe depression, mania and delirium are clinically and biologically heterogeneous. Their occurrence after ingestion of an oxalate-rich meal would not establish a cause. Anxiety may follow pain, poor sleep, a frightening kidney-stone episode, or the physiological stress of severe illness. Fatigue and concentration problems may accompany chronic kidney disease, restrictive dieting, iron deficiency, insomnia or medications. Each of these explanations may be more probable than direct cerebral oxalate injury. An unusual exposure history is useful only when it changes the probability of a defined medical pathway.

What the hypothesis predicts

If OANVH has clinical content, psychiatric or cognitive findings should cluster preferentially in objectively characterized hyperoxaluric patients with appropriate biological intermediates rather than in everyone consuming spinach or almonds. Findings should relate to renal status, measurable oxalate handling, metabolic disturbance or credible tissue injury; effects should differ between primary hyperoxaluria, enteric hyperoxaluria and ordinary dietary exposure. A carefully documented negative result in otherwise healthy high-oxalate consumers would weaken the broad dietary hypothesis without refuting severe systemic oxalosis.

Critical interpretation: direct toxicity versus downstream illness

A useful causal diagram should not hide the asymmetry in the evidence. The arrows from fat malabsorption to hyperoxaluria, from severe hyperoxaluria to renal damage, and from major renal dysfunction to encephalopathy each have clinical support. The proposed arrow from ordinary oxalate exposure to a specific psychiatric syndrome lacks comparable evidence. The distinction prevents three unrelated findings—high dietary intake, urine crystallization and a psychiatric diagnosis—from being treated as a single demonstrated chain.

An explanatory model should therefore rank mechanisms by a priori likelihood and by the availability of intervening evidence. In a person with acute hallucinations and no kidney history, normal renal function and no other systemic signs, a primary psychiatric or neurological condition is generally more plausible than oxalate nephropathy. In a patient with childhood kidney stones, progressive renal failure and unusual multisystem deposits, the oxalate hypothesis moves upward because it has a real

biological setting. That shifting likelihood is what makes the model clinically useful rather than ideological.

The theory also predicts different outcomes depending on the phenotype. If reduction in oxalate production protects kidneys but leaves an established psychiatric disorder unchanged, the kidney contribution may have been real while the psychiatric theory was wrong. Such divergence should not be labeled treatment resistance; it is discriminating causal information.

Conclusion

The innovation is not to rename mental illness “oxalate poisoning.” It is to ask whether the known clinical spectrum of oxalate-associated disease contains a small, distinguishable neuropsychiatric component that is currently misattributed or poorly described. The current evidence supports renal and rare systemic pathology much more strongly than common psychiatric causation. Precision about that asymmetry is the foundation of useful frontier science.

Selected readings

- Witting et al., Pathophysiology and Treatment of Enteric Hyperoxaluria (2021)
- Mulay et al., Calcium oxalate crystals induce renal inflammation by NLRP3-mediated IL-1 β secretion (2013)
- Konstantynowicz et al., A potential pathogenic role of oxalate in autism (2012)

Oxalate Is Not Merely a Dietary Substance

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established metabolism; neuropsychiatric extrapolation unproven

Abstract

Oxalate is commonly discussed as a property of particular foods. That framing is incomplete. Human oxalate burden results from gastrointestinal absorption, endogenous glyoxylate metabolism, renal elimination, and changing distribution across biological compartments. The balance explains why a restricted diet cannot correct every hyperoxaluric state and why diet histories without renal and metabolic context can mislead. This paper reconstructs the causal architecture before any neurological claim is considered.

Two origins, several consequences

Many edible plants contain soluble or insoluble oxalate, but only a portion of the ingested material becomes systemically available. Food preparation, simultaneous dietary calcium, intestinal transit, gut disease and fat malabsorption can influence absorption. Independently, glyoxylate formed through intermediary metabolism can be diverted toward oxalate. In primary hyperoxaluria type 1, pathogenic AGXT variants impair peroxisomal alanine:glyoxylate aminotransferase function, increasing oxalate production; other primary hyperoxaluria types involve different enzymes. A patient may therefore have substantial oxalate overproduction despite meticulous avoidance of spinach.

The meaning of a high measurement

Twenty-four-hour urinary oxalate reflects excretion, not simply dietary intake. Plasma oxalate becomes particularly relevant when clearance is reduced. Supersaturation depends on urinary volume and a wider chemistry of calcium, citrate, pH and competing solutes. Crystal formation and injury depend on more than one value. A single non-standardized spot urine result can invite overinterpretation, while a low urine excretion rate in severe renal impairment does not prove that total oxalate burden is low. Even well-designed oxalate assays require attention to collection conditions and laboratory methodology.

A lesson from genetic disease

Primary hyperoxaluria makes a strong causal point: the body can generate a damaging exposure internally. Genotype can alter the probability of pyridoxine responsiveness, and newer therapies aimed at hepatic oxalate production demonstrate that substrate generation can be a legitimate therapeutic target. But evidence from rare enzyme deficiencies cannot be transposed onto healthy people without measuring a comparable biochemical disturbance. The severity, chronicity and concentration range matter as much as the name of the metabolite.

Implications for neuropsychiatric inquiry

Before connecting oxalate to cognition or mood, an investigation must decide which exposure is being asserted: food intake, absorbed oxalate, systemic oxalate, crystalline deposition or downstream renal dysfunction. These variables need not move together. A claim that reducing dietary oxalate improves psychiatric symptoms is additionally confounded by concurrent changes in calories, minerals, fiber, food additives, caffeine, sleep and expectations. The appropriate comparison is not a high-oxalate menu versus an entirely different diet; it is a defined change in oxalate burden against otherwise measured influences.

Conclusion

Oxalate must be treated as a system of production, absorption, excretion and tissue interaction. The distinction is essential both to recognizing real oxalate disease and to preventing speculative psychiatric claims from outrunning exposure science.

Selected readings

- [GeneReviews, Primary Hyperoxaluria Type 1](#)
- [Witting et al., Enteric Hyperoxaluria](#)

The Spinach Paradox: When a Healthy Diet Becomes a High-Oxalate Exposure

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established oxalate nephropathy risk in specific exposures; psychiatric causation unproven

Abstract

Foods ordinarily recommended for cardiovascular health may carry substantial oxalate loads, especially when concentrated into smoothies, juices, powders or repetitive meal patterns. Yet “high in oxalate” is not equivalent to “dangerous for everyone.” This paper examines the combination of dose, bioavailability and host susceptibility that converts an ordinary food component into a clinically consequential exposure, and asks what—if anything—can responsibly be inferred about mental symptoms.

Why concentration changes risk

A serving of cooked vegetables differs from a large raw blend consumed every day. The total plant mass, the presence of calcium at the same meal, soluble oxalate fraction, preparation technique, and other dietary constituents modify exposure. Spinach is often cited as a high-oxalate food; concentrated preparations can substantially exceed usual portion-based consumption. There are clinical reports of oxalate nephropathy associated with extreme dietary patterns, but case reports do not define the risk to someone eating ordinary mixed meals with preserved kidney function.

The vulnerable person

A patient after malabsorptive bariatric surgery, with inflammatory bowel disease, pancreatic insufficiency or chronic diarrhea may absorb more oxalate than expected because unabsorbed fatty acids bind intestinal calcium. Patients with prior calcium oxalate stones, decreased kidney function or primary hyperoxaluria represent other distinct phenotypes. Vitamin C megadosing may add endogenous production. The same glass of spinach juice is therefore not physiologically identical for all drinkers. That observation supports individualized risk assessment, not blanket prohibitions on vegetables.

Why psychiatric inference is harder

Suppose an individual reports insomnia, anxiety or agitation after adopting a high-spinach diet. The association could be related to energy restriction, caffeine in accompanying drinks, sleep changes, gastrointestinal symptoms, hypoglycemia, medication changes, anxiety about health or an unrelated psychiatric process. If there is severe renal dysfunction, the relationship becomes more clinically plausible through an indirect metabolic pathway. Without a biochemical bridge, the specific assertion that spinach-derived oxalate reached the brain and disturbed neurotransmission remains conjecture.

A better study of a suspicious exposure

Useful reports would document the actual food quantities, meal calcium, kidney history, 24-hour urinary oxalate where indicated, serum kidney markers, medications, symptoms and their timeline. Repeated measurements, appropriate comparisons and the exclusion of alternative metabolic injuries would make a case more informative than an anecdote. Deliberate high-dose challenges in vulnerable patients are unjustified; the practical question is how to understand naturally occurring exposures and documented cases safely.

Conclusion

The spinach paradox is a lesson in context-dependent toxicology. A food can be broadly nutritious and still pose a genuine hazard under unusual exposure or susceptibility. The evidence justifies attention to renal risk; it does not establish that spinach causes psychosis.

Selected readings

- Witting et al., Enteric Hyperoxaluria
- Fijen and Weijmer, Acute oxalate nephropathy due to high vitamin C doses and pancreatic insufficiency (2019)

The Calcium Paradox: Why Less Dietary Calcium Can Mean More Oxalate Absorption

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established intestinal chemistry; hypothesized psychiatric implications

Abstract

Oxalate biology illustrates a counterintuitive nutritional principle: consuming less of a mineral may increase absorption of a potentially harmful dietary anion. Calcium binds soluble oxalate in the intestinal lumen; when adequate calcium is available alongside meals, insoluble calcium oxalate can leave in stool rather than cross into circulation. This relationship complicates low-calcium dietary approaches to stone prevention and underscores why serum calcium, dietary calcium and oxalate-binding calcium must not be conflated.

Where the binding actually occurs

The intestine is the relevant chemical reactor. Calcium present in the meal can lower the freely available oxalate fraction. By contrast, taking calcium at a different time is not necessarily equivalent, and excess supplementation has its own considerations. Calcium consumed through ordinary food matrices may have different gastrointestinal timing from isolated supplements. In fat malabsorption, calcium may preferentially bind free fatty acids, reducing its availability to precipitate oxalate. Increased soluble oxalate can then reach the colon, where absorption may be enhanced.

Why blood calcium is a different variable

Serum ionized calcium is tightly regulated through parathyroid hormone, vitamin D, renal handling and bone exchange. Most patients with elevated urinary oxalate do not thereby develop hypocalcemia. Severe poisoning, renal failure or other disorders may disturb calcium physiology, but it is biologically inaccurate to suggest that eating an oxalate-containing vegetable routinely steals enough calcium from blood to impair neurotransmission. The distinction separates plausible gut chemistry from unsupported systemic conclusions.

The neuropsychiatric question

Clinically significant calcium abnormalities can cause confusion, depressed mood, lethargy or, in severe cases, psychiatric or neurological disturbance. That fact provides a route by which some metabolic illnesses can affect behavior. To attribute a particular episode to oxalate, however, one would need evidence that oxalate exposure altered systemic calcium regulation rather than merely binding calcium in the intestine. A normal serum calcium measurement cannot establish or exclude abnormal urinary oxalate, and abnormal urinary oxalate alone cannot establish a neuroactive calcium disturbance.

How to avoid the wrong prescription

Patients prone to calcium oxalate stones are sometimes tempted to eliminate calcium. That can be counterproductive, particularly when it reduces dietary calcium intake without addressing high oxalate or enteric absorption. Individual dietary decisions depend on kidney function, stone chemistry, gastrointestinal status and clinician evaluation. The insight is not “more calcium cures oxalate poisoning,” but “the location and timing of a biochemical interaction determine its effect.”

Conclusion

Calcium illustrates the organizing theme of this volume: physiology is relational. Intestinal binding, systemic homeostasis and neural excitability are linked only through specific intermediates. Removing those intermediates produces an attractive narrative but a poor medical explanation.

Selected readings

- Witting et al., Enteric Hyperoxaluria
- Clinical review of psychiatric sequelae of primary hyperparathyroidism

Bile, Fat Malabsorption and the Enteric Oxalate Trap

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established enteric hyperoxaluria mechanism; psychiatric bridge uncertain

Abstract

Among oxalate-related mechanisms, the relationship between fat malabsorption and increased oxalate absorption is particularly relevant to systems medicine. It connects pancreatic function, intestinal disease, bile physiology, calcium binding and kidney injury in a demonstrable causal chain. It does not follow that mild nonspecific “bile sluggishness” causes psychiatric illness. This paper develops the established mechanism and specifies what would be necessary to extend it toward neuropsychiatry.

Why fat changes oxalate chemistry

Normally, digestive bile acids emulsify lipids and facilitate their absorption in concert with pancreatic enzymes and intestinal transport. When fat remains in the intestinal lumen, unabsorbed fatty acids bind calcium; less calcium is then available to form insoluble calcium oxalate. Soluble oxalate can cross the intestinal wall, particularly in the colon. Bile salts and fatty acids can also alter mucosal permeability under some conditions. The resulting elevated urinary oxalate is called enteric hyperoxaluria. It has been described in disorders involving inflammatory bowel disease, bowel resection, pancreatic insufficiency and malabsorptive bariatric surgery.

The specificity that makes the theory useful

A person can have genuine fat malabsorption with steatorrhea, weight loss, nutrient deficiency or demonstrable pancreatic and bowel disease. By contrast, “poor bile flow” is often invoked without a defined test or phenotype. Cholecystectomy alters bile delivery but does not automatically imply clinically significant fat malabsorption or hyperoxaluria. Functional symptoms may be important, yet the mechanism should be linked to observable absorption abnormalities rather than assumed from digestive discomfort.

Three consequences, not one

First, excessive urinary oxalate increases risk of calcium oxalate stone formation. Second, in more severe or prolonged cases, calcium oxalate may damage renal tissue and contribute to chronic kidney disease. Third, serious kidney dysfunction can influence mental status through uremic and metabolic pathways. Each transition requires evidence. A patient with a gallbladder complaint and anxiety has not traversed this chain merely because both symptoms exist. The most plausible causal route is mediated by clinically significant intestinal and renal illness, not by an unidentified direct action of dietary oxalate on the amygdala.

A clinical framework

When a psychiatric presentation coexists with chronic diarrhea, weight loss, abdominal surgery, kidney stones or unusual dietary practices, targeted attention to malabsorption and renal disease may be reasonable. Appropriate evaluation is individualized and may include history, renal chemistry, urine testing and investigation of an established gastrointestinal disease. Psychiatric emergencies remain emergencies even if an intestinal theory is being considered; physiological investigation should supplement, never postpone, necessary mental-health and neurological care.

The biliary distinction

Bile enters this model through lipid digestion and intestinal contents, not as an unspecified universal detoxification fluid. Impaired pancreatic enzyme output, mucosal disease, short bowel anatomy and altered bile-acid availability can all disrupt absorption, but each has its own diagnostic criteria. It is physiologically imprecise to infer enteric hyperoxaluria from an ultrasound finding, a history of cholecystectomy or a patient's impression that fatty meals are poorly tolerated. Even established bile-acid diarrhea is not automatically proof of elevated systemic oxalate burden.

The more interesting theoretical extension concerns **co-occurring transport failures**. If an individual has significant malabsorption and impaired kidney function, increased oxalate absorption could coincide with reduced elimination. These mechanisms could reinforce renal risk. Whether this produces a measurable neuropsychiatric effect depends on subsequent systemic derangements. The model becomes testable by requiring each proposed transition to be observed rather than inferred from symptoms alone.

Conclusion

This is a robust example of a legitimate multi-organ pathway. It connects diet, digestion and kidney injury. Its possible psychiatric consequences are most defensibly sought downstream of documented metabolic or renal disturbance. The specificity of that chain is what gives the theory clinical value.

Selected readings

- Witting et al., Pathophysiology and Treatment of Enteric Hyperoxaluria (2021)
- Fijen and Weijmer, Oxalate nephropathy with pancreatic insufficiency

The Microbiome and the Fate of Oxalate

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established microbial metabolism; clinical efficacy mixed

Abstract

The intestinal microbiome contains species capable of degrading oxalate, potentially changing how much reaches systemic circulation. This makes oxalate an informative example of host-microbial co-metabolism. It also exposes a major error in microbiome medicine: a bacterium's ability to perform a useful chemical reaction does not guarantee that administering it improves disease outcomes. The distinction is essential before making neurological claims.

Microbial metabolism and ecological dependence

Oxalobacter formigenes uses oxalate as a metabolic substrate. Other genera may participate in oxalate breakdown, with effects influenced by colonization stability, antibiotic exposure, dietary substrate, competition and community structure. Presence of a species does not mean its pathway is expressed at a clinically relevant rate. The intestinal oxalate available for degradation also depends on food matrix, luminal calcium, intestinal transit and fat absorption. Therefore the same species may have different effects in different hosts.

What interventions have actually shown

A randomized trial in primary hyperoxaluria did not demonstrate a significant reduction in its primary urinary oxalate endpoint following oral *O. formigenes* over eight weeks. A later phase-three trial likewise did not meet its main plasma oxalate endpoint at the conventional significance threshold. More recently, a small controlled investigation in healthy adults reported reduced urinary oxalate after induced colonization, with variable persistence and modest average effect on urine output. These results are neither proof of futility nor evidence for an established probiotic therapy; they show why the microbial effect requires direct measurement in the specific clinical phenotype.

Does this connect to psychiatric disease?

The broader gut-brain literature demonstrates many routes by which microbial communities may influence host physiology. Nevertheless, a microbiome association in depression or autism cannot be assigned to oxalate handling without an intervening demonstration that oxalate itself changes and that this change relates causally to symptoms. Antibiotic exposure, diet restriction, bowel dysfunction and inflammation could produce both altered microbiota and psychiatric symptoms without oxalate playing a decisive role.

A useful research question

Rather than claiming that adding an oxalate-eating organism will relieve anxiety, a coherent inquiry would examine whether subjects with documented enteric hyperoxaluria and impaired microbial degradation exhibit a distinct metabolic phenotype. It would also distinguish urinary oxalate improvement from kidney outcomes and psychiatric outcomes. If the intervention changes neither oxalate metrics nor symptoms, that finding would weaken the proposed pathway; if it changes oxalate but not mood, the result would narrow it.

Conclusion

Microbial oxalate metabolism is real and potentially useful. Its translation into reliable treatment remains an open clinical question. The microbiome adds a plausible modifier to oxalate burden, not a shortcut to explaining mental illness.

Selected readings

- [Phase I/II randomized *O. formigenes* trial](#)
- [ePHex phase-three trial](#)
- [Inducing *O. formigenes* colonization in healthy adults](#)

The Kidney-Brain Oxalate Axis

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established kidney-brain communication; oxalate-specific psychiatric causation unproven

Abstract

The kidney and brain are coupled through fluid balance, electrolytes, circulating metabolites, blood pressure, endocrine signaling and inflammation. Oxalate-related kidney injury therefore offers a plausible indirect route to neurological disturbance. The essential question is whether oxalate is acting as a direct neurotoxin, an upstream driver of renal damage, or merely a correlated metabolic measurement. Those explanations must not be collapsed into one.

From crystalluria to systemic consequences

Hyperoxaluria increases the potential for calcium oxalate supersaturation. Renal tubular crystal deposition can promote epithelial damage, inflammatory signaling and, in severe instances, decline in filtration. Uremic encephalopathy, however, is multifactorial: retained organic solutes, altered neurotransmission, electrolyte and acid-base abnormalities, endothelial dysfunction and medication accumulation may all contribute. An affected patient can show impaired attention, sleep-wake disruption, agitation, disorientation, myoclonus or seizures. These are neurological manifestations of systemic dysfunction, not proof of a primary psychiatric disorder.

The causal sequence matters

An ideal causal account has at least five separately testable links: an exposure or metabolic defect; increased circulating or excreted oxalate; renal crystallization or tissue injury; changes in filtration or systemic metabolism; and altered cerebral function. Each step has alternative routes. A person may have CKD for reasons unrelated to oxalate; a person with hyperoxaluria may have entirely normal renal function; and a person with depression may have neither. The hypothesis becomes weak when a clinician substitutes a questionnaire about oxalate foods for evidence of these intermediate events.

A distinction between encephalopathy and mood disorder

Encephalopathy commonly involves attention, level of awareness, fluctuation and global cognitive function. Major depressive disorder or bipolar disorder can present without these phenomena. Symptoms overlap, and serious metabolic illness can contribute to mood problems, but the diagnoses are not interchangeable. A psychiatric presentation with fluctuating consciousness, new neurological signs or severe biochemical abnormality requires urgent medical evaluation; a normal renal panel with persistent affective symptoms points away from a simple kidney-mediated oxalate mechanism.

What would strengthen the model?

Longitudinal records showing rising oxalate burden before renal deterioration, followed by objective cognitive changes, would be more informative than cross-sectional diet associations. Recovery of mental status as renal physiology normalizes may support a metabolic contribution but would still not isolate oxalate from other retained solutes. The stronger and narrower claim is that **oxalate can contribute to renal disease that, if severe enough, can cause brain dysfunction**. The weaker and wider claim—that ordinary oxalate intake causes common psychiatric conditions—needs separate evidence.

Causal attribution under competing renal syndromes

The syndrome of kidney-associated cognitive dysfunction cannot be reduced to one retained metabolite. Renal failure affects drug clearance and the handling of many organic solutes, sodium, acid-base balance and calcium-phosphate physiology. Hypertension, vascular disease and poor sleep may independently alter cognition. Oxalate-related nephropathy might be one initiating kidney disorder among many, while encephalopathy reflects multiple consequences of reduced filtration.

An appropriate comparison would examine cognitive trajectories among patients with similar degrees of renal disease but different reasons for the disease. If psychiatric effects were distinctly greater in those with objectively elevated oxalate at comparable filtration and other covariates, an oxalate-specific contribution would become more plausible. If outcomes track renal severity rather than oxalate burden, the more conservative model wins. The question is worth asking precisely because both results would be informative.

Conclusion

The kidney-brain axis is a legitimate bridge from oxalate physiology to neurological disease. Its scientific value lies in clarifying which disturbances are documented, where the causal chain becomes inferential and when primary psychiatric disease remains the better explanation.

Selected readings

- Witting et al., Enteric Hyperoxaluria
- Mulay et al., Calcium oxalate nephropathy and NLRP3

Crystal-Driven Inflammation: Calcium Oxalate and the NLRP3 Inflammasome

ABSURD HEALTH INSTITUTE · 2026-10-16 · Direct animal and cellular evidence for renal mechanism

Abstract

The ability of crystals to recruit innate immune activity gives oxalate disease a mechanistic dimension beyond passive obstruction. Calcium oxalate deposits can injure renal epithelium and activate an NLRP3-associated inflammatory cascade in experimental systems. Yet the presence of a kidney mechanism does not establish a neurological mechanism. This paper examines exactly what the experiments show and where the inference must stop.

Crystals as biologically active particles

Calcium oxalate crystals are physical structures with surfaces capable of interacting with epithelial and immune cells. Their effects depend on location, quantity, size and local clearance. In a landmark experimental study, Mulay and colleagues showed that calcium oxalate-induced renal injury in mice involved IL-1 β -related innate inflammatory responses; deficiency of several components of the NLRP3/ASC/caspase-1 pathway reduced renal inflammatory injury despite crystal deposition. In this system, inflammation was not merely a passive reaction observed after injury. It amplified tissue pathology.

Why this matters to a systems model

Inflammasome activation reveals how a physical deposit can become a persistent biological signal. Cellular stress, injury-derived ATP and immune recruitment may form reinforcing loops. The renal microenvironment determines whether a crystal is tolerated, expelled or associated with chronic injury. Similar pattern-recognition machinery participates in diverse inflammatory diseases, but common molecular machinery does not imply that every disease has the same cause. NLRP3 activity in renal phagocytes is not interchangeable with NLRP3 activity in brain microglia.

The missing evidence in psychiatry

A tempting argument is: oxalate crystals activate inflammation; inflammation can affect the brain; therefore oxalates cause depression or psychosis. Each premise concerns a different level of evidence. To establish this route in humans, researchers would need evidence of relevant systemic or central nervous system inflammatory mediators after real-world oxalate exposure, evidence linking those mediators to a psychiatric outcome, and adequate control of kidney disease and other sources of inflammation. Direct crystals in the brain would represent a different, exceptional biological state from renal crystalluria.

A counterargument

Many crystal-induced pathways occur in conditions with no discernible psychiatric syndrome. Conversely, elevated inflammatory biomarkers in depression may arise from infection, obesity, sleep loss, smoking, medication or comorbidity. If the proposed oxalate-psychiatry link is real, it should explain why particular patients—not all patients with kidney stones—show the relevant symptoms. Susceptibility and dose are indispensable to the theory.

From crystal sensing to whole-organ dysfunction

In crystalline kidney injury the NLRP3 pathway is not an abstract inflammatory label. An extracellular deposit first interacts with a particular cellular environment; tubular injury and released danger signals alter the behavior of resident and recruited immune cells. Subsequent cytokine signaling amplifies local tissue injury, and the injured organ may then change systemic physiology. Each step creates an opportunity for intervention but also a possible mismatch between mechanism and clinical outcome.

A favorable response to an inflammasome inhibitor in an animal kidney model does not prove a safe or effective treatment for humans with nephrolithiasis, let alone for psychiatric disorders. Mechanistic experiments are powerful because they isolate components; clinical decisions require evaluating what those components actually contribute at organism level. The Institute should consider NLRP3 a biological anchor for renal injury and an unproven candidate mediator in psychiatric extrapolation.

Conclusion

Crystal-driven innate immunity is established enough to sustain a substantive conceptual paper. Its connection to ordinary psychiatric disease remains an open hypothesis. A mature analysis preserves the strength of the renal evidence rather than exaggerating it into a universal neuroimmune explanation.

Selected readings

- [Mulay et al., J Clin Invest \(2013\)](#)
- [Witting et al., Enteric Hyperoxaluria](#)

Oxalate, Oxidative Stress and Mitochondrial Injury

ABSURD HEALTH INSTITUTE · 2026-10-16 · Experimental cell/tissue mechanisms; clinical generalization limited

Abstract

Oxalate-related cell injury has been investigated through reactive oxygen species production, mitochondrial changes and inflammatory signaling, especially in renal tubular models. This invites a larger question: could local metabolic stress propagate into whole-body or neuropsychiatric consequences? The answer cannot be inferred from a cell culture exposed to an arbitrary concentration. Biological compartment, dose, route and tissue identity govern translation.

Chemistry becomes injury in context

Oxalate can participate in calcium oxalate crystal formation. In renal tissue, crystals interact with epithelial surfaces, provoke oxidative injury under experimental conditions and recruit inflammatory pathways. Mitochondria respond to oxidant exposure and calcium perturbation; their function can be affected by injury-induced changes in membrane potential, redox balance and cell survival signaling. But oxidative stress is a shared intermediate in countless diseases, not a distinctive signature proving one specific cause.

The difference between soluble oxalate and crystals

A paper about circulating oxalate must say whether effects are attributed to the soluble anion or to crystals formed under supersaturated conditions. The two are not interchangeable. Most experimental reports of strong tissue injury concern crystal contact or exposures not readily comparable to normal plasma concentrations. A model suggesting direct neurotoxicity at ordinary circulating concentrations requires evidence that biologically relevant exposure reaches nervous tissue in sufficient amounts and that effects persist after controlling for renal dysfunction.

Mitochondrial psychiatry is broader than oxalate

Energy metabolism and mitochondrial signaling are relevant to cognition, mood and cellular stress responses. That does not make every putative mitochondrial stressor a cause of mental illness. The brain consumes substantial energy, yet different psychiatric syndromes involve complex circuitry, neurodevelopmental history, genetics, environment and experience. A valid oxalate model would need to predict a distinctive tissue exposure or biomarker signature rather than invoking the universal phrase “mitochondrial dysfunction.”

Falsification and clinical meaning

If individuals with objectively high oxalate excretion and preserved renal function lack reproducible mitochondrial or cognitive abnormalities, the case for a common direct pathway weakens. If abnormalities occur only with severe renal insufficiency, kidney-related metabolic stress is the more cautious interpretation. The value of the theory lies in specifying intermediates—crystal deposition, tubular damage, inflammation, disturbed systemic metabolism—not in treating oxidative stress as causal proof.

Conclusion

Oxalate-associated renal oxidative injury is a plausible and partially documented cellular phenomenon. Extending it to psychiatric disease requires tissue-specific exposure evidence and human outcomes, neither of which can be supplied by biochemical analogy alone.

Selected readings

- [Mulay et al., Renal inflammation and calcium oxalate](#)
- [GeneReviews, Primary Hyperoxaluria Type 1](#)

Oxalosis of the Nervous System: What Human Pathology Actually Shows

ABSURD HEALTH INSTITUTE · 2026-10-16 · Rare clinical and pathological observations

Abstract

Systemic oxalosis is a serious complication of sustained oxalate overproduction or impaired clearance, especially in advanced primary hyperoxaluria. Calcium oxalate may deposit in tissues outside the kidneys. Rare pathological observations of nervous-system involvement deserve attention because they show the anatomical possibility of oxalate-associated neural injury. The rarity and severity of the underlying disease, however, make these observations poor evidence for ordinary dietary psychiatric toxicity.

Systemic oxalosis is not merely kidney stones

Primary hyperoxaluria can create a chronic metabolic excess, while declining renal function reduces oxalate excretion. As circulating levels rise, calcium oxalate deposition may extend into bone, vessels, myocardium, retina and other tissues. The pattern differs fundamentally from an otherwise healthy individual with a remote history of one calcium oxalate stone. Where nervous-system lesions are described, they generally occur in the setting of severe, advanced illness and multisystem involvement.

What pathological observation can and cannot establish

A crystal seen histologically in a brain or meningeal vessel establishes tissue deposition in that specimen. It does not by itself establish that a patient's prior anxiety, delusion or depressive episode was caused by that deposit. Pathology also needs to account for uremia, vascular disease, blood-pressure fluctuations, seizure activity, dialysis-related physiology, medications and other effects of terminal illness. The location of deposits matters: vascular deposition causing ischemic injury would produce a different syndrome from hypothetical neuronal exposure to soluble oxalate.

Lessons for psychiatric differential diagnosis

Rare metabolic disorders sometimes enter medical care through unusual neurological, cognitive or behavioral changes. The presence of kidney stones beginning in childhood, progressive renal disease, family history, multisystem calcification or other highly atypical findings should change the threshold for considering an inherited metabolic disorder. Isolated depression in a person without renal disease is a poor screening signal for systemic oxalosis. Seeking diagnostic specificity protects against both missed rare conditions and overdiagnosis.

A cautious extension of the theory

Severe systemic oxalosis supplies a form of natural experiment demonstrating that oxalate may leave its usual renal context when elimination fails. But dose and disease stage cannot be discarded. The most productive question is what neurological syndromes have been demonstrably associated with deposition and whether those syndromes have a plausible anatomical correlate. That is narrower—and scientifically stronger—than treating reports of crystals as evidence that everyday vegetable intake is neurotoxic.

Why a rare pathology is informative but not generalizable

Case-based neuropathology often arises from the severest end of a disease spectrum. Advanced renal failure, prolonged accumulation and multisystem complications are not random features: they are the conditions that permit unusual tissue deposition to be observed. If one samples only terminal cases, one cannot infer how often brain deposition occurs among patients with mild hyperoxaluria or whether subtle psychiatric symptoms precede it.

Anatomical specificity is equally important. A crystal in a meningeal or cerebral blood vessel may matter through vascular injury, whereas a lesion in neural tissue could potentially affect local signaling through other mechanisms. To connect pathology to symptoms one must establish timing, distribution, alternative causes and coherence between the damaged region and the syndrome. Naming “brain oxalate” without those details replaces anatomy with rhetoric.

Conclusion

The neurological pathology of advanced oxalosis expands the recognized reach of oxalate disease. It does not warrant naming a common oxalate-induced psychiatric syndrome. The boundary between severe systemic disease and ordinary exposure must remain visible throughout the investigation.

Selected readings

- GeneReviews, Primary Hyperoxaluria Type 1 (systemic oxalosis and phenotype)
- Witting et al., Pathophysiology of hyperoxaluria

The Ethylene Glycol Experiment: What Extreme Poisoning Reveals—and What It Does Not

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established toxicology; analogy to diet inappropriate

Abstract

Ethylene glycol poisoning is sometimes invoked as proof that oxalate causes neurological injury. The analogy is instructive only if its chemical complexity is respected. Ethylene glycol undergoes metabolism to several acidic products, including glycolate and ultimately oxalate. Severe intoxication can produce metabolic acidosis, altered consciousness, seizures, calcium oxalate crystallization and kidney failure. These effects do not isolate oxalate as the principal cause of all neurological signs, and they cannot be extrapolated to normal dietary intake.

The chain of metabolites

The toxic effects of ethylene glycol are shaped by alcohol dehydrogenase and subsequent metabolic reactions. Glycolic acid is an important contributor to the high-anion-gap acidosis characteristic of serious poisoning, while oxalate can combine with calcium to generate crystals, particularly in renal tubules. Hypocalcemia may occur, but its severity varies. Treatment strategies directed at interrupting metabolism highlight that the parent compound, intermediate metabolites and downstream tissue injury make different contributions. A patient with encephalopathy after ingestion of an industrial toxicant has experienced an exposure unlike eating spinach.

Neurological syndromes have several causes

Severe acidemia, hypoxia, seizures, hypotension, renal failure and direct metabolic toxicity can all disturb consciousness. If a poisoned person is confused, the symptom is not automatically a readout of oxalate acting on synapses. Neurological impairment may precede measurable renal deposition, while delayed complications can involve distinct anatomical pathways. Treating one metabolite as the universal explanatory agent misses the causal complexity of toxicology.

An upper-bound experiment, not a dietary model

Extreme poisoning can reveal what biological systems do when overwhelmed, but it does not establish the response to a much smaller chronic dietary exposure. Concentration-dependent toxic effects, saturation kinetics, organ distribution and competing metabolites all differ. The fallacy is to reason that because a compound appears in both scenarios, the mechanisms and outcomes must be comparable. Serious toxicology demands quantitative exposure assessment.

What the analogy does contribute

The case illustrates the importance of calcium, acid-base regulation, renal filtration and compartment-specific injury. It also demonstrates that symptoms classified as psychiatric or behavioral can be generated by acute metabolic catastrophe. That general lesson supports broad medical differential diagnosis. It does not establish a psychiatric hazard from ordinary oxalate-rich meals in otherwise healthy people.

Conclusion

Ethylene glycol poisoning is a useful teaching case about mechanistic attribution. Its complexity argues for more discriminating oxalate research, not for equating diet with poisoning.

Selected readings

- Mulay et al., Calcium oxalate and nephrotoxicity
- GeneReviews, Primary Hyperoxaluria Type 1

Mineral Balance and Neural Excitability: Could Oxalate Contribute Indirectly?

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established calcium neurophysiology; oxalate-mediated psychiatric effects unproven

Abstract

Calcium and magnesium participate in neuronal excitability, synaptic transmission and cellular signaling. This makes mineral physiology an attractive bridge between dietary oxalate and mental symptoms. Yet most popular arguments omit the crucial difference between binding calcium in food, changing urinary stone risk and changing ionized calcium in blood. We assess the plausible indirect mechanisms and the frequent inferential error that follows.

A calcium story with three compartments

Calcium in the intestinal lumen can bind oxalate and reduce absorption. Calcium in urine can combine with oxalate to form kidney stones. Ionized calcium in plasma is regulated by parathyroid hormone, vitamin D and the kidneys, and influences neuromuscular excitability. These processes interact through physiology but are not interchangeable. The body does not allow meal-by-meal fluctuations in intestinal free calcium to translate freely into corresponding changes in brain extracellular calcium.

What mineral disorders actually do

Marked hypocalcemia can cause paresthesias, tetany, seizures and neuropsychiatric changes. Hypercalcemia, especially in severe parathyroid or malignant disease, may produce fatigue, impaired concentration, mood changes or delirium. Significant magnesium abnormalities likewise affect neuromuscular and cardiac function. These examples establish that mental symptoms can have mineral causes. They do not establish that dietary oxalate regularly provokes these abnormalities. Severe ethylene glycol intoxication and advanced kidney failure are special clinical settings, not representative exposures.

The role of kidney function

Renal disease can disturb calcium, phosphorus, vitamin D and acid-base homeostasis. That offers a credible indirect path from severe oxalate-related nephropathy to altered neurological function. But the risk depends on the actual extent of renal impairment and mineral derangement, not on a theoretical dietary ratio alone. Symptoms without abnormal systemic physiology require competing explanations rather than an assumed hidden calcium depletion.

A useful boundary

The compelling hypothesis is that oxalate can change mineral handling in defined intestinal and renal contexts, which may influence systemic physiology if disease becomes sufficiently severe. The unsupported hypothesis is that normal oxalate intake continuously removes calcium from the brain and thereby causes anxiety or psychosis. Any persuasive account would require appropriately timed ionized calcium measurements, kidney assessment, exposure context and a neurologically coherent clinical presentation.

Conclusion

Mineral physiology links the intestine, kidney and nervous system through established mechanisms. Scientific rigor consists in identifying the circumstances in which the link becomes clinically active, not equating the presence of oxalate in food with a disturbed brain.

Selected readings

- [Witting et al., Enteric Hyperoxaluria](#)
- [Primary Hyperparathyroidism and Psychiatric Sequelae](#)

Vitamin B6, Glyoxylate Metabolism and the Limits of Nutritional Compensation

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established inherited-disease biochemistry; broader treatment claims unsupported

Abstract

Pyridoxal phosphate, the active cofactor derived from vitamin B6, participates in many enzymatic reactions including the alanine:glyoxylate aminotransferase pathway relevant to primary hyperoxaluria type 1. In selected patients with pathogenic AGXT variants, pharmacological pyridoxine can reduce oxalate production. This is a valuable example of genotype-dependent metabolic treatment. It does not show that nonspecific psychiatric symptoms reflect B6-deficient oxalate metabolism or that escalating vitamin doses is universally safe.

The pathway and its specificity

AGT normally converts glyoxylate toward glycine. When enzyme function is deficient or protein targeting is abnormal, glyoxylate can be diverted toward oxalate production. Some variant proteins respond to pyridoxine because the cofactor supports residual enzymatic activity or stabilizes the enzyme. The response is not uniform; genotype and biochemical measurement matter. Inherited enzyme disease provides a clear mechanism against which vague claims about “detoxification support” should be tested.

Why supplementation cannot substitute for diagnosis

High-dose pyridoxine has recognized adverse-effect potential, notably sensory neuropathy from excessive chronic exposure. A patient with tingling, imbalance or cognitive complaints may become worse if an unproven metabolic hypothesis prompts indiscriminate supplementation. Furthermore, endogenous oxalate production is not governed by B6 alone; substrate availability, other enzymatic pathways, kidney clearance and dietary absorption contribute. Correcting one presumed cofactor deficiency does not necessarily normalize an entire pathway.

The psychiatric boundary

Vitamin B6 is relevant to neurotransmitter synthesis more broadly, but that fact does not connect every depression or anxiety syndrome to hyperoxaluria. A theory could posit that oxalate overproduction and neural vulnerability coexist in a rare metabolic phenotype, yet it would need simultaneous demonstration of pathway dysfunction, neurologically relevant consequences and symptom associations. A reported improvement after B6 administration alone cannot distinguish correction of oxalate metabolism from other nutritional or psychological effects.

Conceptual implication

This case demonstrates a stronger alternative to generalized supplement theories: identify the molecular lesion, measure the relevant pathway and observe whether a targeted intervention changes its output. It also shows that systems medicine and molecular medicine are not enemies. The best explanations often connect a specific biochemical defect with downstream context and adaptation.

Conclusion

Pyridoxine responsiveness in selected primary hyperoxaluria phenotypes is an established clinical phenomenon. The conjecture that broad psychiatric illness reflects a similar B6-oxalate deficiency remains unsupported. Metabolic precision should sharpen—not relax—the standard of evidence.

Selected readings

- [GeneReviews, Primary Hyperoxaluria Type 1](#)
- [Treatment of primary hyperoxaluria type 1](#)

Vitamin C and Endogenous Oxalate: When Supplementation Changes Metabolic Exposure

ABSURD HEALTH INSTITUTE · 2026-10-16 · Documented biochemical conversion and case-associated nephropathy

Abstract

Ascorbic acid can be metabolized to oxalate. Under many circumstances this contribution is clinically modest, but unusually high intake, kidney impairment or malabsorptive disease can change the risk calculation. Reports of oxalate nephropathy associated with high-dose vitamin C illustrate how an ostensibly beneficial intervention may add metabolic burden in a susceptible host. Claims that this causes psychiatric disease remain speculative.

The dose problem

Vitamin C is essential for human physiology; it is not inherently a toxin. Its breakdown can nevertheless contribute to oxalate formation, particularly at high exposures. The amount converted and excreted varies with dose, route, kidney function and other host factors. Clinical case reports, including one involving high vitamin C exposure combined with pancreatic insufficiency, document the possibility of clinically important renal oxalate deposition. A case report demonstrates possibility in a specific setting, not prevalence across ordinary supplement users.

Two simultaneous causes

When an individual has both excess precursor availability and increased intestinal oxalate absorption, there may be contributions from more than one route. In pancreatic insufficiency, fat malabsorption alters intestinal binding, while vitamin C can add endogenous oxalate. Renal clearance then determines how long metabolites persist. The relevant object of treatment is the pathway actually causing injury, not the abstract category “vitamin toxicity.” Other causes of acute kidney injury must also be considered.

A neuropsychiatric hypothesis

If substantial oxalate nephropathy led to metabolic encephalopathy, vitamin C might be implicated as one upstream exposure. But a patient taking vitamin C who reports low mood cannot be presumed to have oxalate-mediated neural injury. Direct evidence of kidney impairment or another credible biochemical intermediary would be essential. In studies claiming psychiatric benefits from restricting vitamin C, changes in illness, diet, other supplements and expectation would be serious confounders.

Practical intellectual lesson

This is a useful antidote to the idea that nutrients have purely beneficial effects independent of dose and host state. It equally rejects the opposite claim that any dose of a substance with a toxic metabolic product is unsafe. A rigorous model makes its exposure scale explicit and defines vulnerability rather than converting rare events into blanket dietary warnings.

Conclusion

Oxalate formation from ascorbate is a real metabolic route with documented relevance in some renal injury cases. There is no convincing basis for asserting that routine vitamin C intake causes psychosis, depression or autism through oxalate.

Selected readings

- Fijen and Weijmer, Acute oxalate nephropathy due to high vitamin C doses and pancreatic insufficiency
- Treatment of primary hyperoxaluria type 1

Oxalates and Autism: Investigating a Controversial Metabolic Association

ABSURD HEALTH INSTITUTE · 2026-10-16 · Small observational association; causal claim unestablished

Abstract

A small study reported elevated plasma and urinary oxalate in children diagnosed with autism spectrum disorder relative to matched controls. The finding merits direct methodological examination because it touches a plausible but poorly characterized link between dietary metabolism, kidney physiology and neurodevelopmental conditions. An association in cross-sectional measurements, however, neither establishes causation nor supports dietary treatment as an autism intervention. This paper specifies what the evidence does and does not mean.

The published observation

Konstantynowicz and colleagues studied 36 children and adolescents with autism and 60 non-autistic comparison participants. They reported higher plasma oxalate and urinary oxalate concentrations among the autism group. This was a real reported observation, but it came from a small cross-sectional sample. Neither oxalate exposure before the emergence of autism nor a causal developmental trajectory was demonstrated. The paper did not establish that reducing oxalate changes core autism characteristics or that oxalate enters the brain in sufficient concentrations to alter neurodevelopment.

Reverse causality is a serious possibility

Dietary selectivity, gastrointestinal conditions, hydration differences, supplements, medications and differing activity or body composition may influence urinary metabolites in autistic children. Some factors may emerge as consequences or correlates of neurodevelopmental differences rather than precede them. Renal function and assay methods are also relevant. A metabolic measurement taken after diagnosis cannot reveal whether it contributed to development or followed the behavioral and dietary phenotype.

A susceptible-host hypothesis

A narrower hypothesis could be that a subset of autistic individuals experiences clinically meaningful hyperoxaluria or stone risk because of diet, malabsorption, genetic metabolic disease or other factors. That would be worthy of appropriate medical attention independently of whether it explains autism. A second claim—that oxalate itself affects some associated behaviors such as sleep or irritability—would need rigorously controlled longitudinal evidence and objective exposure assessment. A third claim—that oxalate causes autism—is much more demanding and is not supported by existing observations.

Why clinical endpoints matter

Improved constipation, less abdominal pain or fewer kidney-related symptoms could improve quality of life and observed behavior without changing autism's neurodevelopmental basis. That is still an important outcome, but it should be described accurately. Diet elimination could also produce nutritional deficiency, family burden or unnecessary restriction. The ethical goal is to identify treatable comorbid illness without presenting children as metabolically defective simply because of a diagnosis.

What a serious causal study would need to distinguish

A future study should begin by prespecifying the target: autism diagnosis, associated gastrointestinal disease, sleep disruption, irritability or kidney-stone risk. These outcomes are not equivalent. Diagnosis-related differences in diet could explain altered urinary oxalate without any causal role in neurodevelopment. Such reverse causation cannot be overcome by matching age and sex alone.

The strongest design would use longitudinal exposure data collected before or around developmental milestones, replicated biochemical assays, dietary intake, kidney measures and appropriate control for family and medical variables. Ethical observational work could investigate a subgroup with independently established hyperoxaluria and ask whether treating the renal condition improves kidney outcomes and quality of life. A reported change in behavior after dietary adjustment would require separation from placebo effects, symptom fluctuation and improved gastrointestinal comfort. This is not an objection to inquiry; it specifies the evidence the claim would need to earn.

Conclusion

Oxalate-autism research contains a legitimate preliminary association but not a demonstrated causal mechanism. The scientifically defensible next question concerns identifiable metabolic subgroups and comorbid renal or gastrointestinal disease, not a universal low-oxalate treatment for autism.

Selected readings

- Konstantynowicz et al., A potential pathogenic role of oxalate in autism
- Witting et al., Enteric Hyperoxaluria

Could Oxalate Burden Contribute to Anxiety, Brain Fog or Cognitive Dysfunction?

ABSURD HEALTH INSTITUTE · 2026-10-16 · Plausible indirect pathways; direct evidence inadequate

Abstract

Anxiety, impaired concentration and “brain fog” are common, nonspecific complaints. Oxalate burden has been proposed as one possible physiological contributor, particularly when symptoms coexist with gastrointestinal disease, kidney injury or restrictive dietary practices. This paper asks how such a theory could be investigated without mistaking temporal association for causation or medical uncertainty for evidence of a hidden toxin.

A symptom is not a mechanistic endpoint

Brain fog may encompass slowed processing, impaired sustained attention, fatigue, sleepiness or subjective detachment. Anxiety includes psychological, cognitive, autonomic and behavioral components. Neither symptom supplies a unique biochemical signature. A patient can have these symptoms because of inadequate sleep, anemia, endocrine disturbance, medication effects, anxiety disorder, depression, chronic pain or renal illness. An oxalate theory must specify which functional deficit it predicts and why.

The strongest indirect scenarios

Documented kidney disease can impair cognitive function; painful kidney stones can cause insomnia and intense anxiety; fat malabsorption can produce nutritional problems; restrictive diets can lower energy intake and disturb sleep. In such situations oxalate may participate as a renal exposure or dietary marker, but the immediate mechanisms may be pain, inflammation, metabolic encephalopathy or nutritional insufficiency. Relief following removal of the provoking exposure would be clinically relevant, yet multiple causal pathways remain possible.

What would make the hypothesis convincing?

The strongest evidence would pair a defined oxalate phenotype with standardized cognitive measures, an appropriate biochemical intermediary and a temporal relationship that survives adjustment for sleep, anxiety, diet and kidney function. A self-selected online series of people reporting improvement after low-oxalate diets is vulnerable to expectation and concurrent lifestyle changes. Objective renal biomarkers without a corresponding symptom pattern would weaken an oxalate-specific interpretation.

Beware the elimination spiral

A person convinced that ordinary foods are harming the brain can progressively restrict diet, impair nutrition and become hypervigilant to normal sensations. Such a cycle may worsen anxiety independently of any oxalate mechanism. This does not mean dietary symptoms are imaginary. It means an accurate clinical account must include both biological exposure and the consequences of living under a theory of danger. Supportive evaluation should preserve nutritional adequacy and established treatment for psychiatric symptoms.

Conclusion

Oxalate burden could contribute indirectly to cognitive or affective symptoms in the setting of meaningful systemic illness. Direct causation of common brain fog or anxiety by usual dietary oxalate remains unproven. A useful paper must tell readers exactly where the evidence ends.

Selected readings

- [Witting et al., Hyperoxaluria pathophysiology](#)
- [Konstantynowicz et al., Oxalate measurements in ASD](#)

The Postpartum Oxalate Vulnerability Hypothesis: A Multi-Hit Model of Psychiatric Deterioration

ABSURD HEALTH INSTITUTE · 2026-10-16 · Explicitly speculative oxalate contribution; established postpartum psychiatric emergency

Abstract

Severe postpartum psychiatric illness is a medical and psychiatric emergency whose origins involve interacting vulnerabilities, with strong evidence for roles of bipolar-spectrum liability, sleep loss and the reproductive transition. We propose a narrow exploratory question: could clinically meaningful hyperoxaluria or oxalate-related renal stress occasionally amplify postpartum neuropsychiatric instability in a susceptible patient? This possibility has not been demonstrated and must not be used to explain any particular criminal case or to diminish the importance of urgent psychiatric treatment.

Why postpartum physiology is unusually dynamic

After childbirth, reproductive hormones change rapidly. Sleep may become severely fragmented, and breastfeeding, nutritional intake, fluid balance, anemia, infection, thyroid dysfunction and medication exposure may alter physiology. In a vulnerable individual, mood episodes can emerge abruptly. Postpartum psychosis commonly requires immediate specialist assessment and, frequently, inpatient treatment. It is clinically mistaken to replace these established risk considerations with a single dietary theory.

The proposed oxalate-specific contribution

A testable subset might involve a postpartum patient with unusually concentrated oxalate intake, fat malabsorption, a history of calcium oxalate stones, renal impairment or an inherited metabolic predisposition. If this produced measurable hyperoxaluria and clinically significant renal or mineral disturbance, it could plausibly add stress to an already vulnerable system. This is a multi-hit argument in the true sense: none of the factors must be sufficient alone, and the same symptoms may arise entirely without oxalate. Crucially, ordinary postpartum intake of spinach, nuts or vegetables has not been shown to provoke psychosis.

Differential diagnosis cannot be postponed

Postpartum psychosis may overlap with mania, severe depression with psychotic features, delirium, thyroid disease, intoxication or withdrawal and, rarely, autoimmune encephalitis. Bergink and colleagues found a small subset of women with postpartum psychosis had neuronal autoantibodies, including two anti-NMDA receptor-positive cases in a cohort of 96. The finding does not mean autoimmune encephalitis is usual; it means concerning neurological features should not be dismissed. Any presentation with impaired reality testing, inability to sleep, disorganization, suicidal thoughts or risk to children requires urgent care irrespective of nutritional hypotheses.

What would count against this model?

If renal function and oxalate handling are normal, a clinically significant kidney-mediated pathway becomes less plausible. If symptoms clearly precede dietary changes, exposure-driven causal inference weakens. If the clinical presentation meets a robust bipolar or psychosis trajectory without metabolic intermediates, there may be no reason to invoke oxalate. No inference about an individual patient's motives, culpability or diagnosis should be drawn from these theoretical mechanisms.

Postpartum causality cannot be inferred from dramatic outcomes

A severe psychiatric event may prompt investigators to search retrospectively for an unusual food, supplement or biochemical marker. This approach risks selecting one vivid exposure after the outcome is known while neglecting much more strongly established risk factors. Dietary causation would require a chronology showing that the relevant exposure preceded objective physiological change and that this change preceded the psychiatric deterioration. Even then, co-occurring sleep loss, endocrine change, medication effects and underlying psychiatric vulnerability could explain the sequence.

The responsible application of a multi-hit model is therefore probabilistic. The more ordinary and nonspecific a dietary exposure, the more compelling the intermediate evidence must be. A patient with documented hyperoxaluria, acute kidney injury and delirium would present one kind of question; a patient with an isolated postpartum manic episode and a spinach smoothie would present another. Neither nutrition history nor speculation can substitute for urgent assessment when reality testing and safety are impaired.

Conclusion

The value of this paper is to define a possible but unverified metabolic cofactor within a larger and much better-established postpartum psychiatric framework. The hypothesis is worth stating only if its uncertainty and the need for emergency psychiatric care remain unmistakable.

Selected readings

- Bergink et al., Autoimmune Encephalitis in Postpartum Psychosis
- Bhat et al., Postpartum Psychosis: A Preventable Psychiatric Emergency
- ACOG, Screening and Diagnosis of Perinatal Mental Health Conditions

How to Disprove the Oxalate-Psychiatry Hypothesis

ABSURD HEALTH INSTITUTE · 2026-10-16 · Methodological paper; no positive effect assumed

Abstract

A frontier hypothesis deserves publication when it creates discriminating predictions, not merely a convincing story. The oxalate-psychiatry hypothesis spans several non-equivalent claims: renal complications causing encephalopathy, rare cerebral oxalosis, and direct psychiatric effects from ordinary food intake. We propose a falsification framework that makes the last and most controversial claim vulnerable to negative evidence.

Separate the causal graphs

Model A is the established renal route: increased oxalate burden leads to renal deposition and injury, which in severe cases contributes to systemic metabolic disturbance and altered cerebral function. Model B is a rare systemic-deposition route. Model C proposes a direct or partly independent neural effect at concentrations encountered in common diets. These models predict different exposure thresholds, biomarker patterns and clinical presentations. A study finding no direct effect cannot refute Model A, while observing kidney injury does not validate Model C.

Design around competing causes

A good observational analysis would characterize habitual diet, 24-hour oxalate excretion where relevant, renal filtration, stone history, malabsorption, calcium intake, vitamin C use, medications, sleep, psychiatric history and objective outcomes. Samples should distinguish inherited hyperoxaluria, enteric hyperoxaluria and healthy controls. Because diet and mental health can influence one another, longitudinal measurements are preferable to single snapshots. Autistic participants require assessment of dietary selectivity and gastrointestinal comorbidity rather than assumptions about developmental causation.

Strong disconfirming observations

Repeatedly normal oxalate biomarkers during psychiatric episodes would undermine the hypothesis of a circulating burden in those episodes. Lack of any association after adjusting for renal impairment, nutritional status and medication exposure would weaken broad claims. An intervention that reduces urinary oxalate without changing psychiatric outcomes would specifically undermine an oxalate-mediated symptom pathway, though not the intervention's value for stones. A clinically important psychiatric effect only in end-stage kidney disease would favor indirect systemic illness rather than a common dietary syndrome.

Ethics and communication

Provocative research should not expose susceptible people to deliberate nephrotoxic oxalate challenges or deny psychiatric treatment while searching for a dietary cause. Publication must explicitly reject using oxalate theories to infer guilt, innocence or moral responsibility in specific tragedies. The Institute should present estimated plausibility in proportion to data, avoid unverified numerical predictions and correct its preferred theory if evidence fails.

Publication standard and falsifiability ledger

Every strong claim should have a paired rival explanation. “High urinary oxalate correlates with anxiety” competes with changes in hydration, diet, kidney function, sleep, pain and selection bias. “A reduction diet improved behavior” competes with caloric normalization, medication adjustments, attention effects, regression to the mean and symptom fluctuation. “Oxalate causes autism” competes with reverse causality through dietary selectivity and other downstream physiological differences.

The hypothesis should be stratified into tiers. **Tier one:** established intestinal, metabolic and renal oxalate mechanisms. **Tier two:** neurological consequences of advanced systemic disease or kidney-mediated encephalopathy. **Tier three:** direct or independent psychiatric effects at everyday dietary exposure. A result supporting one tier cannot be quietly counted as evidence for the others. Publishing this ledger beside the theory makes the Institute's stance auditable: uncertainty is a feature of the work, not a defect to conceal.

Conclusion

The oxalate–psychiatry hypothesis gains scientific value by agreeing in advance to circumstances under which it would be narrowed or abandoned. The present strongest propositions concern kidney disease and rare systemic oxalosis; common psychiatric causation remains an unanswered question, not a discovered fact.

Selected readings

- Witting et al., Enteric Hyperoxaluria
- Konstantynowicz et al., Oxalate and autism association
- Mulay et al., Oxalate and NLRP3

When the Immune System Produces Psychiatric Symptoms

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established neuroimmune mechanisms; etiologic relevance varies by disorder

Abstract

The immune system and central nervous system are continuously communicating. Cytokines, vascular and meningeal interfaces, glial cells and peripheral immune signals influence motivation, sleep, pain, cognition and behavior. In exceptional cases, specific immune processes cause profound psychiatric symptoms; in more common conditions, inflammation may be a modifier, consequence or correlate rather than the primary disease mechanism. This paper proposes a disciplined neuroimmune framework that distinguishes those possibilities.

Four separate causal relationships

Immune activity can **cause** a neural syndrome, as in selected autoimmune encephalitides. It can **modify** an established psychiatric illness through sleep, fatigue, pain or sickness behavior. Psychiatric stress and behaviors can **change** immune measurements, creating reverse causation. Finally, a third factor—obesity, infection, social adversity, medication or substance use—can independently affect both immune biomarkers and mood. These four paths can produce similar cross-sectional correlations. The phrase “brain inflammation” should not be used without specifying a compartment, pathway and measurement.

Known routes of communication

Peripheral inflammatory mediators can signal through vascular and neural interfaces. Activated microglia and astrocytes participate in central immune responses, while interferon and cytokine exposure can alter monoamine and kynurenine metabolism. In selected clinical circumstances, antibodies bind specific neuronal proteins and disrupt synaptic function. The latter mechanism is causally more specific than an elevated nonspecific C-reactive protein result, which may arise from many tissues and does not diagnose neuroinflammation.

The problem of treatment inference

The fact that some antidepressant nonresponders have elevated inflammatory biomarkers does not mean suppressing immunity is broadly therapeutic. A randomized infliximab trial in treatment-resistant depression did not show an overall antidepressant benefit, although exploratory baseline inflammatory differences generated important questions. Such results argue against a universal inflammatory-depression model and for careful phenotype definition. Antimicrobial, immunomodulatory or corticosteroid treatment is not justified by a speculative immune explanation without an established clinical indication.

Clinical implications

Rapid-onset behavioral change with seizure, dyskinesia, catatonia, autonomic instability, fluctuating consciousness or major neurological findings deserves attention to inflammatory and other medical disease. Stable chronic depression without these features has a different prior probability. Immune explanations should neither erase a person's psychological history nor force patients to accept psychiatric symptoms as “only in their head.” The brain is biological; causes nonetheless remain heterogeneous.

Conclusion

Neuroimmune psychiatry is most useful when it replaces vague inflammatory rhetoric with identifiable mechanisms, meaningful differentials and measured uncertainty. The immune system can sometimes create a psychiatric syndrome, often shape one, and frequently merely coexist with it.

Selected readings

- Dalmau et al., Anti-NMDA receptor encephalitis
- Pollak et al., International consensus on autoimmune psychosis
- Raison et al., Infliximab trial for treatment-resistant depression

Autoimmune Encephalitis: When Psychosis Is a Neurological Emergency

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established neurological disease with frequent psychiatric presentation

Abstract

Autoimmune encephalitis demonstrates why the presenting symptom and the underlying pathology cannot always be equated. Some patients initially appear to have primary psychosis, anxiety or mood disturbance but develop seizures, movement disorders, impaired consciousness or autonomic instability. Recognition matters because the diagnosis, investigations and treatments differ from those of primary psychiatric illness. The existence of this condition does not justify assuming autoimmunity in every first-episode psychosis.

From antibodies to circuitry

In anti-NMDA receptor encephalitis, pathogenic immunoglobulins interact with neuronal NMDA receptors and disrupt receptor-mediated synaptic function. Early features may include behavioral disorganization, hallucinations, insomnia or agitation; evolving neurological manifestations may include seizures, dyskinesias, catatonia, autonomic disturbance and decreased consciousness. Other antibody-mediated encephalitides have different clinical signatures, demographics and associated conditions. Autoimmune encephalitis is therefore not one disease with one blood test.

Why routine psychiatric categories can mislead

Diagnostic classification helps describe symptoms, but a first episode unfolding over days with profound sleep disruption and rapid neurological change deserves a broader approach. EEG, CSF studies, MRI, antibody testing and assessment for alternative causes may be appropriate according to the clinical picture. MRI can be unrevealing in some encephalitis cases, and serum antibody results alone may be misleading; interpretation belongs in a neurological and clinical context. The goal is neither indiscriminate panels nor reflex attribution to psychiatric illness.

The postpartum example

In a study involving 96 women with postpartum psychosis, Bergink and colleagues found two patients with anti-NMDA receptor antibodies, alongside other neuronal antibody findings. This identifies a rare but important differential; it does not establish that all postpartum psychosis is autoimmune. The ordinary clinical emergency of postpartum psychosis remains urgent regardless of antibody status. Likewise, patients with primary bipolar disorder may become very unwell without having encephalitis.

Treatment and safety

Immune-directed treatment for confirmed or strongly suspected encephalitis is a specialty decision, often involving intensive neurological assessment. Psychiatric symptom management, seizure control and supportive care may also be necessary. High-potency dopamine blockade may create particular challenges in some encephalitic syndromes, but drug selection must be individualized. The appropriate lesson is coordinated care, not substitution of a single unproven immune intervention for established emergency treatment.

Diagnostic error in both directions

The spectacular clinical stories of autoimmune encephalitis can distort base-rate reasoning. Because a small fraction of psychosis may reflect immune disease, it does not follow that every person with first-episode psychosis needs a broad commercial antibody panel. Conversely, because most psychiatric episodes are not encephalitis, rapid neurological deterioration must not be dismissed as ordinary psychotic behavior. The correct threshold for testing depends on red flags, examination, timing and specialized interpretation.

This problem is particularly important with serum-only testing. Some antibody results may be false positive or clinically nonspecific; some conditions require cerebrospinal fluid or other contextual evidence. A negative imaging study cannot reliably exclude all forms of encephalitis. The best care occurs when psychiatry and neurology treat the patient as one person, share the evolving timeline and revise the differential as new findings appear.

Conclusion

Autoimmune encephalitis is a powerful proof that a psychiatric presentation can conceal a neurological process. The duty is to recognize the pattern that merits investigation while resisting the equally dangerous temptation to call every unexplained psychiatric symptom autoimmune.

Selected readings

- Dalmau et al., Anti-NMDA receptor encephalitis case series
- Pollak et al., Autoimmune psychosis consensus
- Bergink et al., Postpartum psychosis autoantibodies

Cytokines, Kynurenine and the Chemistry of Sickness Behavior

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established immune-neural signaling; transdiagnostic models incomplete

Abstract

During infection or inflammation, people often withdraw socially, sleep differently, lose appetite, slow their movement and find less pleasure in daily life. These experiences resemble components of depression without being equivalent to major depressive disorder. Immune signaling through cytokine networks, tryptophan metabolism and central neural pathways offers one explanation for the overlap. The clinical challenge is determining when the pathway is primary, secondary or incidental.

Sickness behavior is adaptive until it becomes costly

Transient sickness behavior can conserve energy and alter priorities during infection. Peripheral cytokine signaling affects the central nervous system through vascular, humoral and neural routes. Changes in sleep architecture, appetite, fatigue and motivation may arise without a primary psychiatric lesion. However, prolonged immune activation, repeated stress or chronic systemic illness could contribute to a persistent affective burden. Calling all such presentations “inflammatory depression” prematurely erases important differences in the underlying causes.

Tryptophan is not one pathway

Immune activation can regulate indoleamine 2,3-dioxygenase and the kynurenine pathway, diverting tryptophan metabolism through compounds with complex immunological and neural effects. Some kynurenine metabolites interact with excitatory neurotransmission or oxidative pathways, while others may have different actions. A peripheral kynurenine measurement cannot be assumed to reveal synaptic concentrations or receptor effects. Diet, hepatic metabolism, kidney function and inflammatory status all complicate interpretation.

What interventions teach us

Clinical experiments using inflammatory modulation have not produced a general cure for depression. A randomized infliximab trial found no overall efficacy in treatment-resistant depression, with exploratory suggestions that inflammatory status might matter for subgroup response. That pattern supports phenotype-specific questions and cautions against treating elevated CRP as a stand-alone prescription for immune suppression. It also illustrates how a mechanism can be biologically sound without yielding a broadly effective drug strategy.

A discriminating model

A more useful classification would separate acute sickness behavior, depression with medical inflammatory comorbidity, hypothesized immune-modified depressive phenotypes and clear central inflammatory neurological disease. These categories differ in duration, symptom architecture, biomarkers and treatment implications. None justifies assuming that psychiatric suffering is always a sign of a hidden pathogen, nor that emotional experience has no biological consequences.

Conclusion

Cytokine–kynurenine signaling creates a meaningful bridge between systemic illness and mental symptoms. Its predictive value depends on careful phenotyping and direct biological measurement rather than broad claims that depression is simply inflammation.

Selected readings

- Raison et al., Randomized infliximab trial
- Dalmau et al., neuroimmune disease and psychiatric symptoms

Mast Cells, Histamine and the Neuroimmune Interface

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established histamine signaling; psychiatric causal subtypes unverified

Abstract

Histamine is both an inflammatory mediator and an important neuromodulator involved in arousal and wakefulness. Mast cells participate in allergy and tissue immune signaling, and severe mediator release can produce cardiovascular or gastrointestinal symptoms accompanied by distress. These facts invite hypotheses connecting mast-cell activity to anxiety, sleep disorders and cognitive complaints. They do not establish a generalized “mast-cell psychiatric syndrome,” nor do they justify diagnosing one from nonspecific symptoms alone.

Two histamine systems

Peripheral histamine release during allergic responses differs from centrally synthesized histamine in the brain's wake-promoting networks. H1-antihistamines can produce drowsiness because some agents cross the blood-brain barrier, demonstrating that histaminergic neurotransmission matters. But this pharmacological observation is not evidence that peripheral histamine excess causes psychosis. The blood-brain barrier, drug distribution, receptor selectivity and feedback regulation make the compartments distinct.

When mast-cell disease is relevant

Mast-cell disorders have defined diagnostic criteria and can involve episodic flushing, urticaria, gastrointestinal symptoms, hypotension or anaphylaxis-like reactions. Anxiety during such episodes may be a normal response to threatening bodily sensations or part of autonomic stress. It is also possible for chronic illness and poor sleep to amplify affective symptoms. Clinicians should not confuse this reasonable multifactorial account with a demonstrated unique brain-inflammation phenotype.

The temptation of biomarker certainty

Histamine concentrations vary with sampling conditions and disease state, while tryptase and other investigations have condition-specific limitations. Isolated symptom checklists cannot establish mediator-driven pathology. Common manifestations—fatigue, fogginess, palpitations, anxiety and food intolerance—have many differential diagnoses. An explanatory model gains value by predicting reproducible mediator relationships, not by absorbing every unexplained symptom.

Clinical consequence

A patient with severe allergic or cardiovascular symptoms requires appropriate medical evaluation. Psychiatric treatment should not be withheld merely because an allergic mechanism is hypothesized. Conversely, repeated anxiety-like episodes temporally coupled with objective allergic features should not be dismissed without considering appropriate immunological causes. The clinical task is discriminating overlapping phenomena, not choosing between “physical” and “mental” labels.

Conclusion

Mast-cell signaling and central histamine physiology intersect at the level of arousal, sickness and bodily threat. Their exact contribution to common psychiatric syndromes remains unsettled. The research question is a legitimate one only when diagnostic criteria and compartment-specific mechanisms are respected.

Selected readings

- [Histamine in the Regulation of Wakefulness](#)
- [AAAAI Mast Cell Activation Syndrome Work Group Report](#)

Infection-Associated Psychiatric Syndromes

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established for selected pathogens and syndromes; general occult-infection theories unsupported

Abstract

Infections can produce psychiatric presentations through central nervous system invasion, inflammation, systemic metabolic disturbance, seizures and post-infectious mechanisms. The relevant organisms, tissue distributions and manifestations differ greatly. This paper proposes an organism-specific framework that protects patients against both missed treatable infections and speculative explanations that attribute nonspecific symptoms to occult microbes without diagnostic support.

Multiple routes to similar symptoms

Central nervous system infections can cause altered behavior, confusion, delirium, hallucinations or seizures. Some parasites produce structural cerebral lesions; bacterial and viral encephalitis may alter consciousness and cognition; severe systemic infection can generate encephalopathy through inflammatory and metabolic pathways. A chronic infection may cause prolonged illness without directly invading neural tissue. These mechanisms must be identified separately because neither a psychiatric symptom nor an elevated inflammatory marker identifies a pathogen.

A hierarchy of evidence

The strongest infectious attribution combines compatible epidemiology, syndrome, organism-specific testing and, where possible, neuroanatomical or microbiological confirmation. A positive antibody may reflect past exposure, whereas active disease may require different evidence. Negative testing may be falsely reassuring in selected circumstances, but that does not permit indefinite diagnosis based on symptom resemblance alone. Pretest probability governs the meaning of every test result.

Consequences of indiscriminate diagnosis

Attributing long-standing anxiety, depression or autism to an unproven parasitic burden can lead to unnecessary antiparasitic therapy, toxicity and delayed appropriate care. The opposite error—failing to investigate fever, new seizures, focal signs, altered consciousness or immunosuppression—can be equally serious. A defensible psychiatric differential uses clinical red flags, geography, exposure and appropriate medical examination rather than reflexively searching for every known pathogen.

Why post-infectious does not mean persistent infection

Symptoms may continue after pathogen clearance through autonomic changes, residual organ damage, altered sleep, persistent inflammatory activity or psychological consequences of severe illness. This distinction matters because treating an ongoing adaptive state with repeated antimicrobials may not help and can cause harm. It is possible for infection to trigger a disease without the organism remaining present; equally, not all prolonged symptoms are post-infectious.

Conclusion

Infectious psychiatry requires more specificity, not less. Its strongest contribution is to connect documented microbial or immune mechanisms with recognizable clinical syndromes and to resist both dismissal and overattribution.

Selected readings

- [ASTMH/IDSA Guideline for Neurocysticercosis](#)
- [Dalmau et al., Anti-NMDA encephalitis](#)

Inflammatory Depression or Depression with Inflammation?

ABSURD HEALTH INSTITUTE · 2026-10-16 · Epidemiologic and treatment-response signals; causal phenotyping unsettled

Abstract

Many patients with major depression have measurable inflammatory abnormalities, but the observation is not a stand-alone causal diagnosis. Inflammation may precede symptoms, accompany medical comorbidity, follow adverse health behaviors or act as a moderator of treatment response. The distinction between inflammatory depression and depression with inflammation determines whether a biomarker can guide therapy or merely describe additional risk.

A common marker, many sources

C-reactive protein rises in numerous inflammatory and metabolic states. Obesity, infection, autoimmune disease, poor sleep, tobacco exposure and other factors can produce elevated CRP independent of psychiatric diagnosis. Depression itself may influence activity, diet, stress and sleep, which in turn affect inflammation. Cross-sectional findings are therefore insufficient to establish direction of effect. Even when an inflammatory association is statistically significant at population level, the individual patient may have a different causal pathway.

Treatment as a test of causal claims

If a specific inflammatory pathway sustains depression in a subset, modifying that pathway might improve symptoms in that subset. Yet broad anti-inflammatory treatment has not established itself as a general antidepressant strategy. The infliximab trial in treatment-resistant depression found no overall benefit, while generating exploratory hypotheses about baseline inflammatory status. The correct response is not to discard neuroimmune psychiatry or to declare it proven. It is to define prespecified populations and clinically meaningful outcomes more carefully.

A better phenotype

Potentially informative features include systemic inflammatory disease, metabolic syndrome, anhedonia, fatigue, sleep disruption and objective biomarkers in repeated measures. None is uniquely diagnostic. A good model would predict which measures change before mood improves and whether a pathway-specific intervention performs better than appropriate comparator care. The distinction between modifiable risk, causal driver and marker of severity is more important than the rhetorical appeal of the subtype label.

The patient-level consequence

An elevated inflammatory marker deserves contextual medical interpretation, not automatic immune suppression. A normal marker does not render depression less real. Conversely, depression in a patient with inflammatory bowel disease, rheumatoid arthritis or another significant medical disorder may reflect both psychological and biological burdens. Integrated care can address these simultaneously without assuming one explains everything.

Conclusion

The useful research question is not whether inflammation and depression ever coexist—they do—but whether specific immune states define reproducible, treatment-relevant subgroups. Until then, causal certainty is premature.

Selected readings

- Raison et al., Infliximab and treatment-resistant depression
- Pollak et al., Autoimmune psychosis evidence framework

When Thyroid Disease Looks Like Anxiety, Depression or Psychosis

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established endocrine-psychiatric association; causal attribution individualized

Abstract

Thyroid hormones influence metabolic rate, neural development, cognition, arousal and many bodily systems. Hypothyroidism and thyrotoxicosis can produce symptoms that overlap with mood and anxiety disorders, while severe cases occasionally cause psychosis or major changes in mental status. The diagnostic challenge is to recognize clinically meaningful thyroid disease without making minor laboratory variations the explanation for every psychiatric complaint.

Two different endocrine states

Hypothyroidism often presents with fatigue, slowed thought, depressed mood, constipation, cold intolerance and cognitive difficulty. Severe presentations can include psychosis, historically described as myxedema psychosis. Hyperthyroidism more often generates tremor, tachycardia, insomnia, irritability, heightened arousal and anxiety-like symptoms, although atypical affective changes occur. These patterns reflect systemic endocrine physiology and do not map neatly onto psychiatric diagnostic categories.

Why a symptom-based label may be incomplete

A patient initially treated for anxiety could have persistent palpitations and weight loss from thyrotoxicosis. Another with depressive symptoms and cognitive slowing could have clinically important hypothyroidism. Treatment of the endocrine disorder may improve psychiatric manifestations, but improvement is not necessarily immediate or complete. Some symptoms may predate thyroid disease or persist because an independent psychiatric illness also exists.

Interpretation is more than TSH alone

Thyroid-stimulating hormone, free thyroid hormone measurements, clinical context, acute illness and medication effects must be evaluated together. Borderline changes may be transient or clinically insignificant. Symptoms like fatigue or depression are common in euthyroid people; an isolated positive antibody does not automatically establish active thyroid failure. Over-treatment can itself cause anxiety, insomnia, tachycardia and cardiovascular risk. The intervention should follow a validated endocrinological diagnosis rather than a favored psychiatric narrative.

What this proves about diagnostic medicine

The thyroid provides an unusually clear example of systemic physiology producing psychiatric symptoms. It also illustrates why molecular and whole-person models need each other. A defined hormone deficit can be causal; sleep, age, cardiac status and history may determine the phenotype and recovery trajectory. A systematic differential diagnosis improves care without treating all depression as a missed thyroid disorder.

Conclusion

Endocrine psychiatry becomes effective when it respects the distinction between a reversible medical cause, a modifying comorbidity and an incidental laboratory finding. Thyroid disease is a serious differential, not a universal explanation.

Selected readings

- Heinrich and Grahm, Hypothyroidism presenting as psychosis
- Myxedema psychosis case and review

The Postpartum Endocrine Transition and Psychiatric Vulnerability

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established postpartum psychiatric syndrome; mechanisms multifactorial

Abstract

Childbirth initiates one of the most rapid physiological transitions in adult life. Reproductive hormones change, sleep is interrupted, feeding demands alter daily rhythms, and a genetically or clinically vulnerable person may experience severe affective or psychotic illness. The question is not whether postpartum psychiatry is “hormonal” instead of psychiatric, but how endocrine timing intersects with bipolar liability, sleep loss, immune changes and clinical history.

Endocrine transition as an exposure

Estrogen and progesterone levels fall sharply after delivery. Neurosteroid signaling, including GABA-A receptor modulation, may be altered. Thyroid disease can appear or change around the postpartum period, and stress-axis regulation adapts to birth, recovery and caregiving. Nevertheless, most people undergo these physiological transitions without psychosis. The transition is not a sufficient cause by itself; susceptibility and additional factors determine outcome.

Sleep and the threshold of illness

Profound sleep deprivation can destabilize mood, attention and reality testing, particularly in people vulnerable to bipolar-spectrum episodes. A person may be physically exhausted while unable to sleep, or may have escalating energy, agitation, grandiosity, unusual beliefs or severe depressive symptoms. The symptom pattern, not an assumed dietary mechanism, guides urgency. Postpartum psychosis requires immediate professional assessment and frequently inpatient care to protect both patient and child.

The medical differential remains necessary

Thyroiditis, infection, medication effects, electrolyte disturbance, substance exposure and rare neurological conditions can complicate presentation. In a cohort of women with postpartum psychosis, investigators identified a small number with neuronal autoantibodies, showing that alternative neurological processes can occasionally be relevant. Such exceptions do not overturn the major role of bipolar-spectrum risk in postpartum psychosis; they justify targeted attention to atypical features.

Beyond reductive explanation

A model that names only estrogen withdrawal misses clinical heterogeneity. A model that names only psychiatric history can miss endocrine or neurological illness. Good explanation incorporates timing, family and personal psychiatric history, sleep, objective medical findings and rapid changes in functioning. The presence of an oxalate-rich diet should not displace this differential; an oxalate mechanism would require separate objective evidence of hyperoxaluria and relevant organ effects.

Conclusion

The postpartum period exemplifies a state transition in which normal physiology can interact with pathological susceptibility. Recognition, safety, and prompt evidence-based treatment are paramount. Biological complexity is a reason to improve care, not to delay it.

Selected readings

- Bhat et al., Postpartum Psychosis: A Preventable Psychiatric Emergency
- Bergink et al., Autoimmune encephalitis in postpartum psychosis
- ACOG, Perinatal Mental Health Screening

Cortisol and the Brain: From Adaptive Stress to Pathological Regulation

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established Cushing-related psychiatric manifestations; ordinary stress extrapolation limited

Abstract

Glucocorticoids influence energy distribution, circadian timing, immune signaling, memory and threat responses. The psychiatric manifestations of Cushing syndrome offer a clinical example of excessive cortisol exposure affecting mood and cognition. Yet this does not establish that everyday anxiety represents adrenal disease or that routine cortisol measurements provide a universal psychiatric biomarker.

Endocrine exposure has magnitude and duration

Cortisol participates in adaptive responses to challenge, and its release changes across the day. Chronic pathologically elevated glucocorticoid exposure differs from transient stress responses. Patients with Cushing syndrome may experience depression, anxiety, irritability, cognitive changes and occasionally psychosis or mania. Exogenous glucocorticoid medications can also cause affective and behavioral side effects. Context and dose are essential to causal interpretation.

Why stress rhetoric becomes misleading

A patient under chronic psychosocial stress may have disrupted sleep, autonomic arousal and health behavior changes without having Cushing syndrome. The term “high cortisol” is commonly used as a shorthand for distress even when no endocrine disorder has been measured. Single random cortisol results are frequently hard to interpret because timing and physiological context matter. True endocrine evaluation uses condition-specific tests, not blanket wellness panels.

The brain's adaptation may persist

Psychiatric symptoms in Cushing syndrome may precede diagnosis and sometimes remain after biochemical remission. This illustrates a key systems principle: removing a hormonal excess does not instantly erase accumulated neural, metabolic or social consequences. Nevertheless, persistent symptoms do not prove irreversible brain injury in a particular person; clinical course and competing disorders require assessment. Treatment of the endocrine disease and attention to psychiatric needs may both be appropriate.

Clinical discrimination

Rapid behavioral change after starting high-dose corticosteroids, physical features of hypercortisolism, unusual metabolic derangements or severe muscle weakness should raise condition-specific suspicion. Ordinary depression alone usually does not warrant indiscriminate cortisol testing. Identifying genuine endocrine disease is valuable because its treatment differs materially from psychotherapy or antidepressant management alone.

Conclusion

Cortisol is a convincing example of a hormone capable of contributing to psychiatric illness under defined pathological exposures. The lesson is not that all mental illness is an adrenal imbalance, but that timing, magnitude and biological context change what the same molecule means.

Selected readings

- [Psychiatric Symptoms in Cushing's Syndrome: A Systematic Review](#)

Sex Hormones, Neurosteroids and Mood Regulation

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established neurosteroid signaling; phenotypic heterogeneity considerable

Abstract

Sex hormones influence brain circuits through genomic and rapid signaling effects, while neurosteroids derived from progesterone can modulate GABA-A receptors. Reproductive transitions therefore provide windows into the physiological regulation of mood and anxiety. Yet hormonal involvement does not imply simple deficiency or excess, and symptom timing may matter more than a single hormone concentration.

Circuits and changing sensitivity

Estrogen interacts with neurotransmitter systems, plasticity and sleep regulation. Progesterone-derived allopregnanolone can modulate GABAergic inhibition. During menstrual, peripartum and perimenopausal transitions, absolute hormone concentrations and neural sensitivity to change may both matter. A person may experience symptoms during a rapid shift without having concentrations outside population reference ranges. Stable hormone values may likewise coexist with severe psychiatric illness.

From mechanism to syndromes

Premenstrual dysphoric disorder, postpartum depression and perimenopausal affective complaints each demonstrate different patterns of temporal association. Neurosteroid-related therapies provide additional evidence that a hormone-related pathway can be therapeutically relevant in selected populations. But a treatment response does not establish that the entire disorder is a single-hormone deficiency, nor that the same agent will help all depressive syndromes.

The diagnostic problem

A clinician must distinguish reproductive-stage symptoms from bipolar disorder, thyroid disease, medication effects, sleep deprivation, substance use and primary psychiatric illness. Symptom tracking across time may be more informative than broad one-time hormone panels. Conversely, the presence of cyclical timing should not be used to dismiss severe symptoms as “merely hormonal.” Biological explanation and clinical seriousness are fully compatible.

Relevance to the broader systems model

Hormonal states may alter a patient's response to stress, sleep disruption and medications. This is a plausible interaction between timing, regulatory capacity and psychiatric vulnerability. It remains necessary to define which mechanisms are measurable and which remain analogies. No evidence presently establishes that oxalate exposure is an essential mediator of these sex-hormone effects.

Conclusion

Neurosteroid psychiatry demonstrates that the brain is sensitive to physiological transitions, not only static abnormalities. The challenge is to identify real temporal phenotypes without translating every complex psychiatric syndrome into one hormonal correction.

Selected readings

- Bhat et al., Postpartum Psychosis
- ACOG, Perinatal Mental Health Screening

Parathyroid Disease, Calcium Regulation and Neuropsychiatric Symptoms

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established medical association; mechanisms and effect sizes variable

Abstract

Parathyroid hormone governs calcium and phosphate homeostasis through its actions on kidney, bone and indirectly the intestine. Primary hyperparathyroidism can produce a spectrum of neuropsychiatric complaints ranging from fatigue and impaired concentration to mood disturbances and, rarely, psychosis. It provides a concrete example of mineral physiology influencing mental status, while illustrating the difficulty of attributing nonspecific symptoms to an endocrine abnormality.

The calcium signal

Altered calcium physiology affects neuromuscular function and neural excitability. Primary hyperparathyroidism often produces elevated calcium or a characteristic PTH-calcium relationship, but presentations and severity vary widely. Some patients have kidney stones, bone disease, gastrointestinal symptoms or changes in mood and cognition; others are asymptomatic. The coincidence of depression with mild biochemical hyperparathyroidism does not prove it is the cause of the depression.

Mechanisms beyond one ion

PTH itself, calcium changes, sleep disturbance, chronic discomfort, inflammatory signaling and coexisting illness may contribute to reported symptoms. Studies of psychiatric improvement after correction of parathyroid disease are difficult to interpret because outcomes and follow-up vary. Severe hypercalcemia can cause delirium, dehydration and major mental-status changes, which represent a different clinical category from long-standing depression with modest biochemical abnormalities.

Why this matters for the oxalate debate

The intestine can bind dietary oxalate with calcium without materially changing circulating calcium. Conversely, primary hyperparathyroidism may increase urine calcium and stone risk through systemic regulation. Calcium oxalate stone formation can therefore arise from high urinary calcium, high urinary oxalate, low urine volume or other factors. An individual with both kidney stones and psychiatric symptoms should not be assumed to have an oxalate-driven brain disorder when an independently testable parathyroid explanation may exist.

A clinically useful pathway

Appropriate evaluation of serum calcium, albumin or ionized calcium and PTH depends on context. Significant abnormalities call for endocrine interpretation; minor variants may not explain symptoms. The overarching goal is not indiscriminate laboratory hunting, but recognition of conditions where correction of a real endocrine process can alter health outcomes.

Conclusion

Parathyroid disease demonstrates the possibility of metabolic and endocrine psychiatric manifestations. It also provides a warning: a shared mineral—calcium—does not make two distinct disorders causally identical.

Selected readings

- [A Clinical Review of the Psychiatric Sequelae of Primary Hyperparathyroidism](#)

Acute Intermittent Porphyrria: When Abdominal Pain and Psychosis Share a Metabolic Cause

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established inherited metabolic disease; rare cause of psychiatric symptoms

Abstract

Acute intermittent porphyria is an inherited defect in heme synthesis that can manifest with abdominal pain, autonomic dysfunction, neuropathy and psychiatric symptoms. The syndrome illustrates how an apparently unrelated constellation of gut, neurological and behavioral complaints may share a coherent metabolic cause. It also demonstrates the importance of specificity: most people with abdominal pain and anxiety do not have porphyria, and some carriers never develop attacks.

The biochemical defect

Acute intermittent porphyria involves reduced activity of hydroxymethylbilane synthase, a heme-synthetic enzyme. During attacks, hepatic accumulation of aminolevulinic acid and porphobilinogen accompanies neurovisceral symptoms. Certain drugs, hormonal changes, alcohol exposure, illness and inadequate caloric intake can precipitate attacks in susceptible individuals. The relevant mechanism is not “toxin accumulation” in the abstract; it is a defined pathway with measurable precursors and an established inherited vulnerability.

A recognizable clinical constellation

Severe abdominal pain without a proportional structural explanation, tachycardia, hypertension, nausea, neuropathic symptoms, hyponatremia, seizures and behavioral change can occur together. Psychiatric presentations include anxiety, agitation, mood disturbance and occasionally psychosis. The presence of autonomic and neurologic findings alongside psychiatric symptoms may be an important clue. Conversely, the nonspecific nature of many complaints requires restraint in testing and interpretation.

A clinical case for avoiding diagnostic fragmentation

A patient might consult gastroenterology for pain, psychiatry for hallucinations and emergency medicine for weakness. If each specialty treats only its own symptom, the unifying metabolic syndrome can remain unidentified. Urinary porphobilinogen testing during suspected acute attacks helps establish the relevant disease process; a diagnosis cannot reliably be inferred from a family story or unexplained symptoms alone. Appropriate specialist management may be time-sensitive because severe attacks can be dangerous.

How this differs from the oxalate hypothesis

Porphyria offers something oxalate psychiatry largely lacks: a defined metabolic lesion, characteristic biochemical accumulation, recognizable multisystem syndrome and therapeutic consequences. It should therefore serve as a calibration example. When constructing new metabolic psychiatric theories, the Institute should ask whether comparable bridges exist rather than assuming that biochemical plausibility is equivalent to clinical confirmation.

Conclusion

Acute intermittent porphyria demonstrates that psychiatric manifestations can be the visible portion of a systemic metabolic attack. Its rarity makes selective recognition more useful than indiscriminate screening.

Selected readings

- Psychiatric manifestations in three cases of acute intermittent porphyria
- Acute Porphyrias: A Case Report and Review

Wilson Disease: Copper Metabolism and the Psychiatric Brain

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established metabolic neurological disease

Abstract

Wilson disease demonstrates that a disorder of metal handling can generate psychiatric manifestations through defined molecular and organ-level mechanisms. ATP7B-related impairment of copper excretion leads to accumulation particularly in liver and brain. Mood disturbance, behavioral change, psychosis or cognitive decline may precede the recognition of a liver or movement disorder. The syndrome demonstrates the value of considering metabolic disease when mental and neurological signs converge.

From liver transport to brain disease

Copper is essential for enzymatic processes, but free or improperly distributed copper can participate in cellular injury. ATP7B dysfunction impairs normal biliary copper excretion and incorporation into physiological transport pathways. Accumulation and tissue injury can affect the liver and central nervous system, including basal ganglia circuits involved in movement and behavior. That combination may explain why patients present with mixtures of tremor, dystonia, dysarthria, cognitive change and psychiatric symptoms rather than a uniform syndrome.

The presentation problem

Some people first receive psychiatric assessment for depression, personality change, impulsivity or psychosis. Over time, neurological or hepatic signs make the diagnosis clearer. In atypical presentations, age of onset, movement abnormalities, liver chemistry, family history and slit-lamp or copper-related investigations can alter the differential. Neither a mood disorder nor a mildly unusual serum copper result alone diagnoses Wilson disease. The diagnostic pattern involves multiple lines of evidence.

A lesson in treatment response

Addressing copper burden may improve neurological and psychiatric manifestations, but the response can be uneven and some dysfunction may persist. Psychiatric medications may be useful while treatment of the underlying metabolic disease proceeds, with attention to liver and neurological risks. Treatment is not a simple matter of administering generic “detoxification” supplements. A genuine causal disorder requires the right intervention and monitoring.

Why this matters to the Institute

Wilson disease strengthens a broad thesis—systemic metabolism can cause mental symptoms—while undermining indiscriminate extension of that thesis to every substance with a plausible neural pathway. Here, the agent, transport defect, affected tissue and diagnostic tests are comparatively specific. Oxalate should be held to the same discipline before being proposed as a common psychiatric cause.

Conclusion

Wilson disease belongs prominently in a medical psychiatry research library because it makes a hidden cause discoverable in selected patients. Its lesson is not that ordinary psychiatric symptoms are usually copper poisoning, but that metabolic specificity can change the diagnosis and treatment plan.

Selected readings

- Psychiatric manifestations in Wilson disease
- Schilsky, Wilson disease: clinical manifestations, diagnosis and treatment

Hyperammonemia and the Metabolic Encephalopathy That Resembles Psychiatric Illness

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established metabolic encephalopathy

Abstract

Ammonia participates in nitrogen metabolism and is ordinarily converted into less toxic products through hepatic and other metabolic pathways. When ammonia accumulates, especially in hepatic failure or urea-cycle disorders, neurological impairment may become severe. Confusion, agitation, disorientation and behavioral change may initially resemble psychiatric disease. The central clinical distinction is that acute encephalopathy demands urgent physiological assessment, not merely a psychiatric label.

Ammonia and cerebral metabolism

Ammonia can affect astrocyte metabolism and glutamine handling, contributing to disturbances in brain osmotic regulation and neural signaling. The pathophysiology of hepatic encephalopathy is broader than ammonia alone: inflammation, infection, gastrointestinal bleeding, medications, electrolyte abnormalities and other precipitants may contribute. Some patients develop asterixis, slowed attention, altered sleep-wake patterns or progressive changes in consciousness. Isolated psychosis without global cognitive change has a different pretest probability.

When the liver is not the only source

Inherited urea-cycle disorders can present beyond infancy, sometimes triggered by catabolic stress, certain medications or high nitrogen loads. Valproate-associated hyperammonemia illustrates how drug exposure can disturb metabolic handling even in the absence of typical liver failure. Kidney function, nutritional status and infection also shape systemic risk. Ammonia sampling itself is vulnerable to preanalytical error; a result must be reconciled with the patient rather than treated as a diagnosis detached from clinical context.

A systems medicine test case

This syndrome connects metabolic production, enzymatic processing, liver capacity, intestinal sources, circulation and brain function. It therefore exemplifies the difference between a descriptive symptom and a causal physiological explanation. Correcting underlying precipitants can improve mental status, but persistent cognitive symptoms may require broader neurological and medical assessment. A low-grade subjective mood complaint is not automatically a sign of occult ammonia toxicity.

Implications for psychiatric care

New-onset confusion, marked fluctuation in awareness, neurological deterioration or serious systemic illness should change the urgency and scope of evaluation. While supportive psychiatric management may be necessary for agitation, treatment of the metabolic cause is central. No nutritional theory should delay established emergency interventions for suspected encephalopathy.

Conclusion

Hyperammonemia demonstrates that the brain can manifest failure of systemic waste handling through unmistakably neurobehavioral symptoms. It teaches a transferable principle: identify the metabolite, establish the pathway and measure the resulting dysfunction before attributing mental illness to a supposed clearance failure.

Selected readings

- [GeneReviews, Urea Cycle Disorders Overview](#)
- [Acute intermittent porphyria and metabolic neuropsychiatry](#)

B12, Thiamine and the Nutritional Neurology of Psychiatric Symptoms

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established deficiency-related neurological syndromes

Abstract

Vitamin B12 and thiamine deficiencies can produce cognitive, neurological and psychiatric manifestations. These disorders show that a nutritional deficiency can sometimes resemble or complicate primary psychiatric illness. They also demonstrate why nutritional medicine must remain diagnosis-specific: a broad catalogue of symptoms cannot establish a deficiency, and giving supplements without recognizing a serious neurological syndrome may be inadequate.

Two nutrients, distinct disease processes

Vitamin B12 is required for one-carbon metabolism and normal nervous-system function. Deficiency can cause macrocytic anemia, peripheral neuropathy, cognitive symptoms and neuropsychiatric presentations, sometimes without prominent anemia. Thiamine is essential to energy metabolism; severe deficiency can produce Wernicke encephalopathy, a potentially devastating disorder associated with confusion, ataxia and ocular motor abnormalities. These are not interchangeable “brain nutrition” problems, and each has a different clinical context and urgency.

Risk is about absorption as well as intake

Dietary restriction, pernicious anemia, intestinal disease and certain medications can contribute to B12 deficiency. Thiamine risk may arise with alcohol use disorder, malnutrition, prolonged vomiting, gastrointestinal surgery or serious systemic illness. A person may consume a nutrient yet fail to absorb or use it appropriately. This supports the Institute's recurring emphasis on transport and biological context, but it should not be stretched into the claim that every mood disorder is nutrient malabsorption.

Diagnostic nuance

Serum B12, complete blood counts, methylmalonic acid and related findings can be informative when interpreted appropriately; no single test is perfect. Wernicke encephalopathy is primarily a clinical emergency, and treatment should not be delayed in a highly suspicious presentation awaiting laboratory confirmation. Neurological examination and risk history often matter more than an indiscriminate micronutrient panel. Excessive doses of some supplements can also cause adverse effects, as illustrated by pyridoxine-related neuropathy.

Psychiatric outcomes

Correcting a true deficiency may improve mental status or cognitive function, yet neurological damage can persist after prolonged untreated disease. Patients can also have a genuine psychiatric disorder concurrent with nutrient deficiency. That dual possibility is more clinically useful than a false choice between psychology and biology.

Conclusion

Nutritional neuropsychiatry is strongest when it connects a defined deficiency to a compatible syndrome and an appropriate treatment. It provides a template for examining speculative dietary metabolites such as oxalate with greater rigor.

Selected readings

- [Neuropsychiatric manifestations in vitamin B12 deficiency](#)
- [Wernicke encephalopathy diagnostic challenges](#)

The Diluted Mind Revisited: Psychiatric Symptoms of Water and Sodium Imbalance

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established osmotic neurological risk

Abstract

Hyponatremia and other disturbances of water balance can manifest through headache, impaired attention, gait change, agitation, delirium and seizures. They are often interpreted through a single sodium number even though effective osmolality, rate of change, kidney water handling and cerebral adaptation determine risk. This paper applies the Institute's earlier Diluted Mind framework to the psychiatric differential diagnosis while emphasizing the dangers of both untreated hyponatremia and overly rapid correction.

The brain inside an osmotic system

A fall in effective plasma tonicity encourages water movement into brain cells. In acute hyponatremia, cerebral edema can develop before adaptation has time to protect tissue. Over longer periods, cells adjust osmolyte content to limit swelling. These adaptations alter the risk of correction; the chronically adapted brain can be injured if serum sodium rises too rapidly, producing osmotic demyelination. The clinical meaning of a sodium concentration is therefore contingent on timing and context.

Why behavior may be the presenting sign

A patient may become confused, irritable, slowed or inattentive before anyone recognizes a metabolic problem. Older adults with chronic hyponatremia may have impaired gait or falls. Severe cases can involve seizures or decreased consciousness. Psychotropic medications, SIADH, low-solute intake and excessive free-water consumption can contribute under different circumstances. An anxious patient who drinks large quantities of water while restricting food may have risk factors, but ordinary water consumption is not synonymous with hyponatremia.

More than one laboratory number

Serum sodium, measured serum osmolality, urine osmolality and urine sodium are interpreted with clinical volume status, kidney function, glucose and medication history. They help distinguish pathways; they do not, by themselves, supply a fixed treatment rate. Correction in symptomatic cases is a medical emergency governed by established protocols and careful monitoring. Patient-directed sodium or electrolyte experimentation is not an adequate substitute.

The psychiatric lesson

A person with new delirium or neurological signs may need urgent metabolic evaluation even when the earliest observable complaint is behavioral. Conversely, normal serum tonicity in a patient with chronic anxiety does not support a dilution hypothesis. The diagnostic strength of this model arises from testable biophysics rather than the metaphor of modern minds being “diluted.”

Conclusion

Water balance is a clear example of physiological state influencing mental function. The practical duty is to detect true osmotic disturbance and avoid iatrogenic injury, not to treat sodium supplementation as a psychiatric cure.

Selected readings

- Sterns et al., Treatment Guidelines for Hyponatremia: Stay the Course
- Absurd Health Institute, The Diluted Mind (conceptual source book)

When Epilepsy Presents as Behavioral or Psychiatric Change

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established neurological differential; presentation-dependent

Abstract

Seizures are not always dramatic convulsions. Focal seizures may involve altered awareness, behavioral arrest, automatisms, fear, unusual sensory experiences or transient confusion. Psychiatric changes can occur before, during or after seizure activity. Distinguishing these patterns from panic, dissociation, delirium and primary psychosis is a problem of timing, semiology and neurological evidence—not a simple choice between biological and psychological labels.

Time structure matters

An abrupt stereotyped episode lasting seconds or minutes differs from persistent hallucinations lasting days, though exceptions occur. Focal seizures involving temporal or related networks may produce sudden fear, déjà vu, unusual odors, visceral sensations or impaired awareness. Postictal states can include confusion, agitation or less commonly psychotic phenomena. Recurrent stereotyped events, nocturnal episodes, witnessed automatisms or new focal neurological findings make neurological evaluation more relevant.

EEG and its limitations

Electroencephalography can provide crucial evidence, but a normal routine study does not exclude epilepsy. The probability of detection depends on seizure frequency, event timing and recording duration. Brain imaging and neurological examination may be appropriate according to presentation. Conversely, an incidental EEG abnormality cannot automatically explain every psychiatric symptom, and psychogenic nonepileptic seizures require careful, non-stigmatizing differential assessment rather than dismissal.

Why medication interpretation matters

Antiseizure drugs can influence mood and cognition. Psychiatric medications can affect seizure threshold under some conditions. Drug changes, sleep loss, intoxication or withdrawal may alter the clinical picture. Treatment of an actual epileptic disorder and management of coexisting psychiatric illness can proceed together, but each requires its own diagnostic reasoning.

A bridge to inflammatory and metabolic disease

Autoimmune encephalitis, electrolyte disorders, toxic exposures and structural brain lesions may produce both seizures and psychiatric manifestations. The coexistence of two syndromes should prompt consideration of a unifying cause when the pattern warrants it, but it is also possible for them to be independent. This distinction safeguards against casually reclassifying all panic attacks as occult seizures.

Conclusion

Epilepsy offers a precise illustration of how a neural circuit event can appear behavioral. The most useful clues are temporal pattern, stereotypy, awareness, neurological signs and appropriate testing, not the mere strangeness of a reported experience.

Selected readings

- Dalmau et al., Anti-NMDA encephalitis and seizures
- Pollak et al., Neurological evaluation in atypical psychosis

Delirium Is Not Primary Psychosis

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established clinical diagnostic distinction

Abstract

Delirium is an acute disturbance of attention and awareness caused by diverse medical, toxic or physiological insults. It can produce frightening hallucinations, bizarre statements, emotional volatility and agitation. Misclassifying delirium as primary psychosis risks overlooking an immediately treatable cause; mislabeling a stable primary psychiatric disorder as delirium can also distort care. The defining question concerns the overall pattern of cognition and consciousness, not merely the content of unusual beliefs.

The distinguishing features

Delirium commonly develops over hours or days and fluctuates. Inattention, disorientation, sleep-wake disturbance and changes in arousal are central features. Hyperactive delirium may look like severe agitation or psychosis; hypoactive delirium may be mistaken for depression or apathy. A person with schizophrenia may also develop delirium, so preexisting psychiatric diagnosis does not immunize against new medical illness.

Why medical causation is heterogeneous

Infection, hypoxemia, medication toxicity, withdrawal, metabolic abnormalities, organ failure, surgery, severe pain and sleep deprivation can precipitate delirium. A single neurotransmitter explanation is inadequate; systemic illness interacts with neural networks, vulnerability and environmental stressors. The correct assessment does not automatically invoke rare causes before evaluating common and dangerous ones.

Oxalate in its proper place

Severe oxalate nephropathy could contribute to renal dysfunction, and severe renal dysfunction may be associated with encephalopathy. That is a conceivable indirect pathway. The presence of delirium, however, does not justify searching for dietary oxalate as a default cause, nor does elevated urinary oxalate prove that it caused the mental-state change. Kidney chemistry, fluid status, infection and medication exposures offer more immediate and generally more probable targets for evaluation.

Consequences of the distinction

Delirium can be a medical emergency requiring prompt identification and treatment of underlying contributors and careful supportive care. Sedating an agitated patient without investigating the underlying cause may conceal clinical deterioration. Yet behavioral safety can require simultaneous symptomatic management. The right response is integrated medicine, not the artificial opposition of psychiatry and general medical care.

Conclusion

Delirium illustrates why a psychiatric-looking symptom is not always a psychiatric syndrome. It also illustrates why the search for biological causes must be broad enough to consider ordinary disease before selecting a favored speculative explanation.

Selected readings

- Dalmau et al., Neurological syndromes presenting with psychiatric features
- Bhat et al., Severe postpartum psychiatric differential

When Treatment-Resistant Depression Is Not Simply Depression

ABSURD HEALTH INSTITUTE · 2026-10-16 · Clinical differential and conceptual analysis

Abstract

Treatment-resistant depression is often operationally defined by insufficient response to multiple adequate antidepressant trials. That definition is useful but heterogeneous. Inadequate exposure, unrecognized bipolar disorder, substance use, sleep disorders, medical illness, psychosocial adversity and genuine drug nonresponse can produce the same label. The distinction matters because escalating a treatment that is mismatched to the underlying problem may add burden without improving function.

Resistance is a description, not a cause

A depression score that remains high after treatment establishes persistent symptoms; it does not specify why the treatment failed. Dose, duration, adherence, tolerability, drug interactions and access to appropriate psychotherapy may all matter. A trial interrupted by adverse effects is not equivalent to a fully adequate course that produces no improvement. Comorbid pain, insomnia, substance use or unresolved social stress may dominate clinical outcomes even if some depressive features respond.

Medical causes and modifying illness

Hypothyroidism, severe anemia, B12 deficiency, certain neurological disorders, inflammatory disease or medication effects may contribute to depression-like symptoms. True medical conditions should be investigated when history and examination support them, not assumed in every individual with persistent depression. Rare disorders such as Wilson disease, porphyria or autoimmune encephalitis become relevant through characteristic multisystem signs; broad testing without clinical clues can create incidental abnormalities and false confidence.

Psychological and social dimensions remain biological realities

Persistent trauma exposure, isolation, financial stress and sleep loss influence the patient's capacity to recover. Recognizing these factors does not reduce symptoms to weakness or imply that biochemical therapy is unnecessary. The point is that medication acts within an organism and a life, not in isolation. A patient receiving an appropriate drug while facing severe ongoing insomnia may remain unwell even if the drug's receptor effects are as expected.

A state-based interpretation with limits

The Institute's coherence model proposes examining energetic availability, regulatory flexibility and temporal organization as potential treatment moderators. That model has not been validated as a formal psychiatric stratification tool. It may nonetheless help organize questions about sleep, physiological illness and intervention burden. The alternative hypothesis is simply that the drug is not effective for that patient's disorder; any state-based theory must be able to admit this possibility.

Conclusion

Treatment resistance should trigger disciplined reassessment, not automatic distrust of psychiatric diagnosis or medication. An integrated differential protects against both missed medical illness and endless searches for a hidden toxin when a primary psychiatric disorder is the correct explanation.

Selected readings

- Raison et al., Inflammation and treatment-resistant depression
- CPIC antidepressant pharmacogenetics guideline
- Heinrich and Grahm, Thyroid disease presenting as psychiatric illness

Psychiatric Pharmacogenomics: Metabolism, Exposure and Variable Response

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established pharmacokinetic gene-drug associations; predictive scope limited

Abstract

Genetic variation in drug-metabolizing enzymes can change exposure to selected psychiatric medications. CYP2D6, CYP2C19 and CYP2B6 offer clinically actionable examples for certain antidepressants. Yet pharmacogenomics cannot reliably identify the one correct psychiatric drug for every patient, and commercial panels sometimes conflate well-supported pharmacokinetic findings with weaker claims about pharmacodynamic outcome prediction. This paper distinguishes the levels of evidence.

A concentration is not an effect

Drug response depends on dose, absorption, liver metabolism, kidney function, interactions, receptor sensitivity, illness type and adherence. A poor metabolizer may experience higher exposure to a medication cleared through a relevant pathway; a rapid metabolizer may experience lower exposure. Even then, the relationship between plasma concentration and clinical improvement is not uniform. Psychiatric symptoms arise from complex networks, and drug effects cannot be predicted from one enzyme genotype alone.

What the guideline evidence supports

The Clinical Pharmacogenetics Implementation Consortium has published recommendations addressing CYP2D6, CYP2C19 and CYP2B6 relationships with selected serotonin-reuptake inhibitors. Its 2023 guideline also examined SLC6A4 and HTR2A but did not find sufficient evidence to support their routine clinical use for antidepressant prescribing. This is an important contrast: some genomic information helps with exposure and tolerability while other appealing variants do not add useful clinical prediction.

Confounding from clinical state

Drug interactions can inhibit or induce relevant pathways, creating a functional phenotype different from genotype alone. Liver disease, age, inflammatory illness and concurrent drugs can affect metabolism. An apparent pharmacogenetic mismatch may actually reflect an interacting prescription or an unsuitable diagnosis. Conversely, a medication that is metabolized predictably may still fail because the underlying disorder does not respond to its therapeutic mechanism.

The future of personalized prescribing

The most rigorous model integrates validated genotype–drug information with symptoms, side effects, prior response, relevant laboratory information and patient goals. It does not sell a genetic result as a complete explanation of someone's depression. The clinical value of a test lies in whether it changes a prescribing decision and improves an outcome, not how many genes appear on a report.

Conclusion

Psychiatric pharmacogenomics is a genuine but bounded form of precision medicine. It illustrates why specific molecular insights and broad systems reasoning should complement rather than displace each other.

Selected readings

- Bousman et al., CPIC Guideline for Serotonin Reuptake Inhibitors (2023)

Iatrogenic Psychiatry: When Treatment Produces New Symptoms

ABSURD HEALTH INSTITUTE · 2026-10-16 · Established drug adverse-effect syndromes

Abstract

A patient may become more agitated, sleepless, emotionally blunted or cognitively slowed during treatment for a psychiatric disorder. Such changes can result from illness progression, environmental factors or the treatment itself. Distinguishing them requires a temporal medication history and careful examination. Akathisia, medication-induced activation, sedation, withdrawal phenomena and other adverse effects demonstrate that not every symptom arising during therapy represents the untreated disease.

The akathisia example

Akathisia involves an often intensely distressing internal restlessness with observable movement or difficulty remaining still. It is associated with antipsychotic medications and has also been reported with other psychotropic classes. A patient may describe panic, agitation or unbearable internal discomfort rather than use the term akathisia. Increasing medication under the assumption that agitation represents worsening psychosis could worsen an adverse drug effect in some situations. Standardized evaluation and recognition of timing are important.

Activation, sedation and withdrawal

Medication changes can alter sleep, autonomic state and cognitive performance. Activation after initiation or dose escalation requires distinction from mania, anxiety and ordinary treatment adjustment. Sedation can be mistaken for depressive slowing; emotional blunting for persistent anhedonia. Abrupt withdrawal of some medications can produce distressing physiological and psychiatric symptoms. The relationship between onset and prescription changes is informative but not sufficient by itself: worsening illness can happen at the same time.

A chronology-centered method

A useful medication timeline records agent, dose, start, titration, discontinuation, concurrent drugs and the first appearance of each symptom. The clinician asks whether symptoms were present before exposure, whether they are recognized adverse-effect patterns and whether an alternative medical explanation is plausible. A clinically supervised medication adjustment may clarify cause, but unsafe abrupt discontinuation or unmonitored changes are not appropriate experiments.

Why the idea matters for medical theory

The phrase “treatment resistance” can conceal an adverse-effect phenotype, while the phrase “drug toxicity” can conceal illness progression. Both are forms of premature causal closure. A serious systems model examines interventions as new biological exposures with intended and unintended effects, and accepts that the safest action may sometimes be simplification rather than intensification.

Conclusion

Iatrogenic neuropsychiatric symptoms are real and clinically significant. Accurate attribution requires temporal detail, recognized syndromes and medical judgment; it does not support dismissing psychiatric medications in general, many of which provide substantial benefit.

Selected readings

- Pringsheim et al., The Assessment and Treatment of Antipsychotic-Induced Akathisia
- Bousman et al., Antidepressant metabolism and tolerability

Could Biological State Determine Treatment Response?

ABSURD HEALTH INSTITUTE · 2026-10-16 · Conceptual synthesis; broad predictive model not validated

Abstract

The same psychiatric intervention may help one person and fail another despite broadly similar symptom scores. A state-based hypothesis proposes that sleep, inflammation, metabolic health, substance use, stress physiology, organ function and daily rhythms modify treatment response. This is a plausible systems question, but it must not be inflated into the claim that all nonresponse results from insufficient “coherence” or that a single composite score can guide treatment without validation.

The intervention enters a context

Drug distribution, receptor adaptation, learning, behavioral practice and stress responses occur within a patient whose physiology changes across time. Severe insomnia may worsen attention and emotional regulation, undermining psychotherapy participation. Inflammatory disease can increase fatigue and pain. Sedating medications may produce different burdens depending on occupational demands or respiratory illness. These effects can influence perceived improvement without meaning that the underlying treatment mechanism is wrong.

Why temporal sequencing sometimes matters

An acutely suicidal or psychotic patient may need rapid evidence-based treatment before attempts at broad lifestyle stabilization. Another patient with nonurgent chronic symptoms may benefit from addressing sleep apnea, substance use or endocrine dysfunction while continuing psychiatric care. State-sensitive treatment is therefore about determining urgency, contraindications and capacity, not insisting that every patient complete a nutritional program before receiving medication or psychotherapy.

Falsifiable possibilities

The model could predict that particular baseline measures—sleep variability, specific inflammatory profiles, medication exposure or functional reserve—moderate response to a defined therapy. This is a different claim from saying such variables cause the psychiatric syndrome. A valid state model would outperform simpler explanations, show reproducibility and improve actual decisions. If it does not, it should remain a descriptive clinical heuristic rather than a diagnostic scoring system.

The risk of ideological overreach

Systems language can become as reductionist as receptor language when used carelessly. Assigning every failed treatment to a hidden global state simply protects a favored theory from contradiction. A mature framework acknowledges that certain targeted drugs work exceptionally well, some patients require long-term maintenance and some therapies fail despite apparently favorable systemic conditions.

Conclusion

Biological state likely shapes aspects of psychiatric treatment response, but the size and clinical predictiveness of each influence vary. The next advance will come from identifying which state variables change specific treatment decisions, not from renaming treatment failure as incoherence.

Selected readings

- Bousman et al., CPIC antidepressant pharmacogenetics
- Raison et al., Inflammatory biomarkers and differential response

When Symptom Improvement Is Not Functional Recovery

ABSURD HEALTH INSTITUTE · 2026-10-16 · Clinical outcomes research; conceptual implications

Abstract

A lower depression or anxiety score may represent meaningful progress without indicating that a person has regained previous cognitive, occupational or relational functioning. The distinction between symptom remission and functional recovery is essential for chronic psychiatric disease and for evaluating proposed biological treatments. A therapy that improves one measurement but leaves persistent disability may still be valuable, but its effect should be described honestly.

What symptom scales measure

Psychiatric scales help quantify particular experiences—sadness, anxiety, sleep change, appetite, concentration and distress. They are not comprehensive measures of independent living, employment, social participation, physical endurance or sustained capacity. A person may report substantially less despair yet still be unable to work because of cognitive impairment or chronic pain. Another may return to employment despite residual symptoms. Both trajectories can be clinically meaningful.

Recovery is multidimensional

Relevant outcomes include daily functioning, cognitive performance, sleep, relationships, physical health, relapse frequency, self-directed goals and quality of life. These domains may improve at different rates, and measuring more does not automatically improve validity. Some outcomes are shaped by poverty, disability access, discrimination or social support rather than personal pathology. A functioning scale should not punish people because their environment is inaccessible.

Implications for biological hypotheses

Suppose a low-oxalate diet reduces urinary oxalate but does not change mood or function. That would be an intervention affecting a biochemical marker, not evidence of psychiatric recovery. Suppose treating hypothyroidism improves cognitive function while a depressive disorder persists. The endocrine treatment has achieved a valuable outcome without curing the psychiatric condition. Precise outcome language protects against exaggerated recovery claims on either side.

A trajectory instead of one endpoint

Repeated measures can reveal whether early symptom improvement leads to durable life changes or temporary relief. Functional restoration may require rehabilitation, environmental adjustments, ongoing therapy and medical management. One patient may recover rapidly; another may require prolonged support. The goal is not to enforce a single ideal of productivity but to assess capacities meaningful to the patient.

Conclusion

A credible medical research institute must distinguish biological change, symptom improvement and functional recovery. They are related but not identical. This distinction is especially important when publishing frontier concepts that may alter biomarkers long before their clinical value is known.

Selected readings

- Symptomatic and functional recovery in depression in later life

The Biological Differential Diagnosis of Mental Illness

ABSURD HEALTH INSTITUTE · 2026-10-16 · Clinical framework; not a validated diagnostic algorithm

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

The Psychiatric Symptom as a Biological Signal: Toward an Integrated Medicine of Mind and Body

ABSURD HEALTH INSTITUTE · 2026-10-16 · Conceptual synthesis; no universal cause claimed

Abstract

The distinction between psychiatric and medical disease reflects practical disciplinary history, not a separation within the patient. Thoughts, emotions, motivation, perception and behavior arise from neural circuits continuously influenced by endocrine, metabolic, immune and environmental conditions. Yet the existence of these interactions does not establish that every psychiatric symptom has a reversible peripheral cause. This concluding paper proposes a model of explanatory pluralism: use molecular causation where the evidence is specific, systems reasoning where interactions matter and direct psychiatric care where it is indicated.

From description to mechanism

Psychiatric diagnosis can be valuable even when its full mechanism is unknown. A diagnosis may summarize recurring symptom patterns, anticipated risks and treatments that help. It becomes incomplete when mistaken for a total causal account. A patient with hallucinations from autoimmune encephalitis, another with psychosis during severe hypothyroidism and a third with a primary psychotic disorder may share a descriptive symptom but not an underlying disease process. Precision begins by distinguishing phenotype from etiology.

A hierarchy of causal confidence

At one end are well-characterized syndromes such as electrolyte encephalopathy, Wilson disease, certain porphyrias and autoimmune encephalitis, where biochemical or pathological mechanisms can be specifically investigated. In the middle are complex associations such as inflammatory variation in depression, where causal effects may depend on phenotype and comorbidity. At the speculative end are proposals that ordinary dietary oxalate causes psychiatric disorders through unproven pathways. All three categories can motivate questions, but they cannot be written as though they share the same evidentiary status.

Why the oxalate question matters despite uncertainty

The oxalate series provides a test of intellectual discipline. It contains established intestinal chemistry, crystallization and renal injury; severe systemic oxalosis can involve extra-renal tissues; rare neurological consequences can occur through serious metabolic illness. These facts suggest a narrow inquiry into susceptible hosts. They do not prove that dietary oxalate is a common cause of psychosis, postpartum psychiatric illness, autism or depression. The Institute should treat that distinction as a virtue of frontier research rather than a concession to orthodoxy.

Treatment should follow the best causal account available

A patient with acute encephalopathy needs urgent medical care; a patient with confirmed endocrine disease needs appropriate treatment; a patient with severe bipolar disorder needs psychiatric care even if additional metabolic questions remain. Psychotherapy, pharmacology, sleep treatment, nutritional intervention and medical investigation are not philosophical rival camps. Their value depends on what they address in a particular patient's illness and how benefits and harms are measured over time.

What the Institute can contribute

An open-access research library can distinguish hypothesis, documented mechanism, contradictory evidence and practical implications more clearly than popular health commentary often does. The purpose of provocative papers is not to replace one dogma with another, but to show where current descriptions fail to explain and where new explanations could earn credibility. Each proposition should name the competing causal paths that might defeat it. An institute becomes trustworthy by preserving a record not only of promising hypotheses but of revisions and falsifications.

Conclusion

Mental illness is biological without being reducible to any one biological pathway. The path toward better explanation is neither wholesale rejection of psychiatric diagnoses nor uncritical acceptance of them as complete causes. It is disciplined integration: follow evidence where it is strong, investigate gaps where it is weak, and protect patients from the harms of both neglect and overclaiming.

Selected readings

- Pollak et al., Autoimmune psychosis consensus
- Bousman et al., CPIC pharmacogenetics
- Witting et al., Enteric Hyperoxaluria
- Mulay et al., NLRP3 renal injury