

## What is the relationship between Energy and Psychosis?

### Energy Metabolism and Psychosis: What the Research Shows

Psychosis (including schizophrenia and related disorders) is increasingly viewed as involving “**broken**” **brain energy metabolism**, not just neurotransmitter imbalance. Energy problems appear in the brain, in the body, and even in people at genetic risk, and may be linked to symptoms, cognition, and treatment response.

#### Core Brain Bioenergetic Abnormalities

- Multiple MRS and postmortem studies show **reduced creatine kinase (CK) activity**, altered high-energy phosphates, lower NAD<sup>+</sup>/NADH ratio (redox imbalance), and a shift from oxidative phosphorylation to glycolysis in schizophrenia and other psychoses (Stein et al., 2023; Chouinard et al., 2025; Yuksel et al., 2021; Pruett & Meador-Woodruff, 2020; Fízíková et al., 2023; Dielemans et al., 2025; Chouinard et al., 2017; Henkel et al., 2022).
- Meta-analyses report **increased lactate and lower brain pH**, consistent with “Warburg-like” glycolytic metabolism (Pruett & Meador-Woodruff, 2020; Fízíková et al., 2023).
- Reviews frame schizophrenia as a disorder of **progressive bioenergetic failure and impaired metabolic flexibility** (Stein et al., 2023; Sarnyai & Ben-Shachar, 2024; Konradi & Öngür, 2017; Henkel et al., 2022; Büttiker et al., 2023).

#### Key Brain Energy Changes Across Illness Stages

| Stage / Group           | Main energy findings (brain)                                     | Citations   |
|-------------------------|--|---|
| First-episode psychosis | Reduced CK activity; PCr/ATP ratio reduced; early redox change   | (Stein et al., 2023; Yuksel et al., 2021; Dielemans et al., 2025; Chouinard et al., 2017)                                     |
| Chronic schizophrenia   | Further CK reduction; ↑ lactate, ↓ pH, stronger glycolytic shift | (Stein et al., 2023; Pruett & Meador-Woodruff, 2020; Sarnyai & Ben-Shachar, 2024; Fízíková et al., 2023; Henkel et al., 2022) |
| Unaffected siblings     | Lower PCr/ATP; subtle NAD changes (risk marker)                  | (Dielemans et al., 2025)  |

FIGURE 1 Brain energy abnormalities across psychosis stages

## Links to Symptoms, Cognition, and Connectivity

- **Cognition:** Greater cognitive impairment is associated with lower NAD<sup>+</sup>/NADH (more reductive stress) and lower CK activity, indicating worse energy dysregulation (Chouinard et al., 2025). Cognitive deficits and negative symptoms relate to ATP/PCr levels and pH changes (Pruett & Meador-Woodruff, 2020; Fízíková et al., 2023).
- **Functional connectivity:** Lower medial prefrontal CK flux is tied to disrupted large-scale network connectivity in schizophrenia and bipolar disorder, suggesting energy deficits may underlie abnormal communication between brain networks (Song et al., 2020).
- **Risk states:** Unaffected siblings show intermediate bioenergetic abnormalities, supporting energy metabolism as a **vulnerability pathway** (Dielemans et al., 2025).

## Systemic Metabolism, Fatigue, and Treatments

- Blood metabolomics in recent-onset psychosis show **altered lipid, redox, and energy metabolites** (e.g., reduced pyruvate, depleted antioxidants), pointing to systemic mitochondrial dysfunction and oxidative stress (Dielemans et al., 2025).
- Fatigue is very common in psychosis (≈55–59%), and may relate to illness, antipsychotics, sleep and negative symptoms, though mechanistic links to cellular energy are not yet clear (Poole-Wright et al., 2025).
- Emerging interventions target energy pathways: **ketogenic diets**, metabolic drugs, ECT-related metabolic reprogramming, and mitochondrial/oxidative phosphorylation genes and proteins are under active investigation (Zou et al., 2025; Sarnyai & Ben-Shachar, 2024; Zuccoli et al., 2017; Henkel et al., 2022; Palmer et al., 2019; Longhitano et al., 2024; Ding & Bao, 2026).

## Conclusion

Across many methods, psychosis—especially schizophrenia—is strongly linked to disturbed **brain and systemic energy metabolism**, involving mitochondria, redox balance, and glycolysis. These energy problems appear early, track with cognition and connectivity, and may partly explain fatigue and other disabling symptoms. Energy metabolism is now a major target for new diagnostic markers and treatments in psychotic disorders.

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