

How is Homeostasis related to Bioenergetics in Neurodevelopmental and Psychiatric Disorders?

Homeostasis, Bioenergetics, and Brain Disorders

In neurodevelopmental and psychiatric disorders, “homeostasis” (keeping internal conditions stable) and “bioenergetics” (how cells produce and use energy) are tightly intertwined. Many papers now frame these illnesses as disorders of disrupted energy and cellular homeostasis, rather than only neurotransmitter imbalance.

Cellular Homeostasis Depends on Bioenergetics

- Mitochondria regulate **energy metabolism, redox status, calcium balance and apoptosis**, all core elements of cellular homeostasis (Kim et al., 2019; Valenti & Vacca, 2023; Streck et al., 2014; Collier et al., 2023).
- Brain mitochondria are described as **crucial mediators of allostasis** (adaptive stability under stress), integrating autonomic, metabolic and immune signals to maintain cellular homeostasis; chronic stress can push them into “mitochondrial allostatic load,” with oxidative stress, inflammation and cell death (Morella et al., 2022).
- In neurodevelopmental disorders, disrupted **mitochondrial dynamics and mitophagy** lead to defective mitochondrial homeostasis, oxidative stress and impaired neuronal function (Yang et al., 2025; Valenti & Vacca, 2023; A et al., 2021).

Brain Energy Homeostasis and Neurodevelopment

- In childhood disorders, diseases from **primary defects of brain energy homeostasis** show how precise energy balance is essential for normal neurodevelopment (A et al., 2021).
- Neurodevelopmental syndromes such as Down, Rett and Fragile X share **lower brain ATP, higher lactate, and respiratory-chain defects**, indicating a shift from efficient oxidative phosphorylation to glycolysis and chronic redox imbalance (Valenti & Vacca, 2023; A et al., 2021).
- Reviews emphasize **mitochondrial homeostasis as a unifying therapeutic axis** in neurodevelopmental pathophysiology (Yang et al., 2025; Valenti & Vacca, 2023; A et al., 2021).

Examples of Homeostatic Axes Linked to Bioenergetics

Homeostatic domain	Bioenergetic link in disorders	Citations
Energy & redox balance	↓ ETC activity, ATP; ↑ oxidative stress in many NDD/PDs	(Kolář et al., 2021; Morella et al., 2022; Kim et al., 2019; Yang et al., 2025; Nunes et al., 2025; Valenti & Vacca, 2023; A et al., 2021; Büttiker et al., 2023; Jiang et al., 2024; Streck et al., 2014)
Mitochondrial quality control	Impaired dynamics/mitophagy → accumulation of damaged mitochondria	(Yang et al., 2025; Nunes et al., 2025; Valenti & Vacca, 2023; Collier et al., 2023)

Homeostatic domain	Bioenergetic link in disorders	Citations
Systemic stress/allostasis	Mitochondrial “allostatic load” under chronic stress	(Morella et al., 2022; Kim et al., 2019; Nunes et al., 2025; Büttiker et al., 2023)

FIGURE 1 Key homeostatic systems tied to energy

Psychiatric Disorders as Bioenergetic–Homeostatic Syndromes

- Major depression, bipolar disorder and schizophrenia are increasingly described as **systemic syndromes** with impaired oxidative phosphorylation, altered mitochondrial dynamics, and redox imbalance, affecting brain energy homeostasis (Kolář et al., 2021; Kim et al., 2019; Nunes et al., 2025; Trigo et al., 2022; Büttiker et al., 2023; Jiang et al., 2024; Streck et al., 2014).
- Schizophrenia has been reframed as a disorder of **impaired dynamic metabolic flexibility**: loss of the ability to maintain metabolic homeostasis of fuels, ions, and neurotransmitters under near-capacity brain energy budgets (Büttiker et al., 2023).
- Pathways such as the **AMPK–mTOR axis** explicitly couple cellular energy status to restoration of metabolic homeostasis and neuroplasticity; their dysregulation is linked to multiple psychiatric conditions (G et al., 2025).

Conclusion

Across neurodevelopmental and psychiatric disorders, homeostasis and bioenergetics are inseparable: mitochondrial energy production, quality control, and redox balance maintain cellular and network stability. When these energy-dependent homeostatic systems fail, the result is altered brain development, stress responses, and behavior that characterize many mental and neurodevelopmental conditions.

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