

# Should "Low Motivation" be re-evaluated in light of new understandings of Bioenergetics in Neurodevelopmental and Psychiatric Disorders?

## Bioenergetics and "Low Motivation" in Psychiatry: Why the Concept Likely Needs Revision

Growing work on mitochondrial function and brain energy metabolism links classic "low motivation" symptoms in psychiatric and neurodevelopmental disorders to measurable bioenergetic disruption rather than pure psychological weakness or apathy.

### Biological Links Between Energy Metabolism and Motivational Symptoms

- In major depression, **fatigue, concentration problems and lack of motivation** are explicitly associated with **impaired mitochondrial ATP production**, altered mitochondrial network density, and symptom severity that correlates negatively with mitochondrial functioning (Karabatsiakos & Schönfeldt-Lecuona, 2020; Jiang et al., 2024; Rezin et al., 2009; Caruso et al., 2019).
- Reviews describe depression and other mood disorders as states of **energetic imbalance** in which impaired mitochondrial function compromises brain plasticity, mood, and behavior (Jiang et al., 2024; Morella et al., 2022; Caruso et al., 2019).
- Animal models of autism and depression show **reduced spontaneous activity and diminished motivation for voluntary exercise** tightly coupled to altered oxygen consumption, respiratory exchange ratio, and energy expenditure, indicating that motivational deficits and metabolic dysregulation co-emerge as core features (Kolář et al., 2021; Hwang et al., 2025).
- Mitochondrial dysfunction and oxidative stress are repeatedly reported across depression, bipolar disorder, schizophrenia, and autism, suggesting shared **brain energy metabolism deficits** underlying psychiatric symptoms (Tanaka et al., 2022; Ni et al., 2022; Kim et al., 2019; Büttiker et al., 2023; Rezin et al., 2009; A et al., 2021; Valenti & Vacca, 2023; Nunes et al., 2025).

### Motivational Features with Bioenergetic Correlates

Clinical / behavioral feature	Related bioenergetic findings	Citations
Fatigue, "lack of motivation" in MDD	Reduced ATP, altered mitochondrial networks	(Karabatsiakos & Schönfeldt-Lecuona, 2020; Jiang et al., 2024; Rezin et al., 2009; Caruso et al., 2019)
Reduced activity / exercise engagement	Abnormal O <sub>2</sub> use, energy expenditure in ASD/MDD models	(Kolář et al., 2021; Hwang et al., 2025)
Mood instability, cognitive dysfunction	Vulnerable, energy-dependent interneurons; oxidative stress	(Yang et al., 2025; Ni et al., 2022; Büttiker et al., 2023)

FIGURE 1 Motivational symptoms mapped to energy deficits

## Implications for How “Low Motivation” Is Conceptualized

- Several reviews argue psychiatric disorders are **systemic bioenergetic conditions**, not just neurotransmitter or purely psychological disorders (Karabatsiakos & Schönfeldt-Lecuona, 2020; Tanaka et al., 2022; Ni et al., 2022; Kim et al., 2019; Büttiker et al., 2023; Rezin et al., 2009; A et al., 2021; Valenti & Vacca, 2023; Nunes et al., 2025; Wallace, 2017).
- A viewpoint proposes that as systemic mitochondrial energy declines, the brain—using ~20% of body mitochondrial energy—crosses a **bioenergetic threshold**, producing symptoms like hyperactivity or depression even when biochemical defects are hard to detect individually (Wallace, 2017).
- In primary mitochondrial disease, there are **elevated rates of bipolar, depressive, and anxiety disorders**, supporting a causal contribution of mitochondrial abnormalities to affective symptoms (Yang et al., 2025; Wallace, 2017).

## Clinical and Research Consequences

- Treating “low motivation” solely as a volitional or cognitive deficit risks **moralizing an energy-based limitation** and overlooking metabolic targets.
- Multiple reviews highlight mitochondrial-targeted strategies (e.g., CoQ10, antioxidants, lifestyle and nutritional interventions, mitoprotective psychotropics) as promising for mood and cognitive symptoms (Karabatsiakos & Schönfeldt-Lecuona, 2020; Kim et al., 2019; Morella et al., 2022; Rezin et al., 2009; A et al., 2021; Valenti & Vacca, 2023; Nunes et al., 2025; Yang et al., 2025).
- There is active interest in **bioenergetic biomarkers** from blood or imaging to refine diagnosis, subtyping, and treatment personalization in psychiatric disorders (Karabatsiakos & Schönfeldt-Lecuona, 2020; Kim et al., 2019; Büttiker et al., 2023; A et al., 2021; Valenti & Vacca, 2023; Nunes et al., 2025).

## Conclusion

Across depression, bipolar disorder, schizophrenia, and neurodevelopmental conditions, motivational symptoms frequently co-occur with demonstrable mitochondrial and energy-metabolism abnormalities. This convergence supports re-evaluating “low motivation” in psychiatry as, at least partly, an expression of impaired bioenergetics, with direct implications for assessment, explanation to patients, and development of metabolism-focused treatments.

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## References

- A, O., U, M., Lf, B., & A., G. (2021). Energy metabolism in childhood neurodevelopmental disorders. *EBioMedicine*, 69. <https://doi.org/10.1016/j.ebiom.2021.103474>
- Büttiker, P., Weissenberger, S., Esch, T., Anders, M., Raboch, J., Ptáček, R., Kream, R., & Stefano, G. (2023). Dysfunctional mitochondrial processes contribute to energy perturbations in the brain and neuropsychiatric symptoms. *Frontiers in Pharmacology*, 13. <https://doi.org/10.3389/fphar.2022.1095923>
- Caruso, G., Benatti, C., Blom, J., Caraci, F., & Tascetta, F. (2019). The Many Faces of Mitochondrial Dysfunction in Depression: From Pathology to Treatment. *Frontiers in Pharmacology*, 10. <https://doi.org/10.3389/fphar.2019.00995>

- Hwang, D., Kim, K., & Kim, T. (2025). Diminished Motivation for Voluntary Exercise and Metabolic Dysfunction in Psychiatric Disorders: A Behavioral Perspective on Autism Spectrum Disorder and Depression. *International Neuropsychology Journal*, 29, S3 - S12. <https://doi.org/10.5213/inj.2550134.067>
- Jiang, M., Wang, L., & Sheng, H. (2024). Mitochondria in depression: The dysfunction of mitochondrial energy metabolism and quality control systems. *CNS Neuroscience & Therapeutics*, 30. <https://doi.org/10.1111/cns.14576>
- Karabatsiakos, A., & Schönfeldt-Lecuona, C. (2020). Depression, mitochondrial bioenergetics, and electroconvulsive therapy: a new approach towards personalized medicine in psychiatric treatment - a short review and current perspective. *Translational Psychiatry*, 10. <https://doi.org/10.1038/s41398-020-00901-7>
- Kim, Y., Vadodaria, K., Lenkei, Z., Kato, T., Gage, F., Marchetto, M., & Santos, R. (2019). Mitochondria, Metabolism, and Redox Mechanisms in Psychiatric Disorders. *Antioxidants & Redox Signaling*, 31, 275 - 317. <https://doi.org/10.1089/ars.2018.7606>
- Kolář, D., Kleteckova, L., Brožka, H., & Valeš, K. (2021). Mini-review: Brain energy metabolism and its role in animal models of depression, bipolar disorder, schizophrenia and autism. *Neuroscience Letters*, 760. <https://doi.org/10.1016/j.neulet.2021.136003>
- Morella, I., Brambilla, R., & Morè, L. (2022). Emerging roles of brain metabolism in cognitive impairment and neuropsychiatric disorders.. *Neuroscience and biobehavioral reviews*, 104892. <https://doi.org/10.1016/j.neubiorev.2022.104892>
- Ni, P., , Y., & Chung, S. (2022). Mitochondrial dysfunction in psychiatric disorders.. *Schizophrenia research*. <https://doi.org/10.1016/j.schres.2022.08.027>
- Nunes, P., Benjamin, S., De Sousa Brito, R., De Aguiar, M., Neves, L., & De Bruin, V. (2025). Mitochondria, Oxidative Stress, and Psychiatric Disorders: An Integrative Perspective on Brain Bioenergetics. *Clinical Bioenergetics*. <https://doi.org/10.3390/clinbioenerg1010006>
- Rezin, G., Amboni, G., Zugno, A., Quevedo, J., & Streck, E. (2009). Mitochondrial Dysfunction and Psychiatric Disorders. *Neurochemical Research*, 34, 1021-1029. <https://doi.org/10.1007/s11064-008-9865-8>
- Tanaka, M., Szabó, Á., Spekker, E., Polyák, H., Tóth, F., & Vécsei, L. (2022). Mitochondrial Impairment: A Common Motif in Neuropsychiatric Presentation? The Link to the Tryptophan–Kynurenine Metabolic System. *Cells*, 11. <https://doi.org/10.3390/cells11162607>
- Valenti, D., & Vacca, R. (2023). Brain Mitochondrial Bioenergetics in Genetic Neurodevelopmental Disorders: Focus on Down, Rett and Fragile X Syndromes. *International Journal of Molecular Sciences*, 24. <https://doi.org/10.3390/ijms241512488>
- Wallace, D. (2017). A Mitochondrial Etiology of Neuropsychiatric Disorders.. *JAMA psychiatry*, 74 9, 863-864. <https://doi.org/10.1001/jamapsychiatry.2017.0397>
- Yang, Z., Luo, Y., Yang, Z., Liu, Z., Li, M., Wu, X., Chen, L., & Xin, W. (2025). Mitochondrial dynamics dysfunction and neurodevelopmental disorders: From pathological mechanisms to clinical translation. *Neural Regeneration Research*, 21, 1926 - 1946. <https://doi.org/10.4103/nrr.nrr-d-24-01422>