

Peer Review

Review of: "The Pause That Protects? A New Framework for Autistic Regression and Strategies for Recovery"

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General Assessment

This is a thought-provoking and conceptually original commentary that reframes autistic regression not as a pathological loss but as an adaptive *neurodevelopmental pause*—a bioenergetic recalibration period allowing the brain to protect fragile circuits during early maturation. The author's integrative approach—linking synaptic overabundance, mitochondrial function, and energy dynamics—represents a highly original contribution that may stimulate further interdisciplinary dialogue among neuroscientists, clinicians, and developmental psychologists.

However, while the commentary is compelling, it remains largely speculative and narrative. Strengthening the methodological framing, clarifying clinical implications, and tempering certain generalizations would enhance both its scientific robustness and interpretive safety for readers.

Strengths

1. Conceptual Innovation

- The hypothesis that regression reflects an adaptive neuroenergetic “pause” rather than a neurological breakdown is novel and intellectually stimulating.
- The link between synaptic overproduction, mitochondrial capacity, and developmental timing is articulated with scientific coherence.

2. Multifactorial Framework

- The paper integrates mitochondrial, vascular, myelination, and immune processes within a unified explanatory model—offering a rich, systems-level perspective on regression.

3. Updated and Appropriate References

- The author cites recent and relevant studies (e.g., Frye et al., 2024; Tian et al., 2024; Giliberti et al., 2025), showing a strong awareness of current neurobiological literature.

4. Balanced Approach to Vaccination and Fever

- The discussion on fever, seizures, and vaccination is balanced and avoids common misinterpretations; it correctly emphasizes that immune activation, not vaccines per se, may precipitate regression in vulnerable children.

5. Readable and Engaging Style

- The writing combines scientific reasoning with accessibility and empathy, making it suitable for an interdisciplinary readership that includes clinicians and parents.

Weaknesses

1. Lack of Empirical Support

- The framework is entirely theoretical, with no direct empirical data or proposed method for validation. The argument would benefit from referencing potential biomarkers or longitudinal studies that could test the hypothesis.

2. Overgeneralization of Regression Prevalence

- The statement that “the majority of children with ASD experience regression” may overstate current evidence. Prospective studies indicate rates of 10–30%, depending on definitions and instruments used.

3. Potential Clinical Misinterpretation

- The claim that “overstimulating the system could deepen regression” risks being misunderstood as discouraging early intervention. The author should clarify that *timing and pacing* of therapy, not its existence, are the key concerns.

4. Limited Structural Rigor

- The commentary lacks clear subsections (e.g., *Limitations*, *Future Directions*, *Clinical Implications*). Its narrative form makes it more philosophical than analytical.

5. Ambiguous Terminology

- Phrases such as “energy-limited systems,” “electrical instability,” and “lost circuitry” need operational definitions or supporting references to avoid interpretive ambiguity.

Major Comments

1. Add a “Limitations and Future Directions” Section

- Explicitly acknowledge that this is a theoretical framework.
- Suggest measurable research pathways: e.g., longitudinal neuroimaging of metabolic function, mitochondrial biomarkers, high-density EEG during regression, or sleep studies assessing energy recovery patterns.

2. Rephrase Potentially Misleading Statements

- Revise:

“Overstimulating the system could interfere with the brain’s maturation...”

to a more neutral version such as:

“Excessive stimulation at inappropriate developmental stages might transiently disrupt neuroenergetic reorganization.”

3. Clarify Epidemiological Data

- Include accurate data on regression prevalence (citing Ozonoff & Iosif, 2019) and specify that milder, transient regressions differ from severe language/social skill loss.

4. Include a Table or Figure

- A table summarizing the six biological contributors (mitochondrial insufficiency, synaptic density, vascular factors, myelination, electrical instability, lost circuitry) and related recovery strategies would improve clarity and visual structure.

5. Add a More Concrete Conclusion

- The final paragraph is powerful but abstract. End with a forward-looking statement, e.g., a call for *biologically informed early-intervention models* or *neuroenergetic monitoring during developmental pauses*.

Minor Comments

- Some references (e.g., [21]–[23]) could be grouped and shortened for readability.
- Consider italicizing scientific terms (e.g., *synaptic pruning*, *bioenergetic adaptation*) for emphasis.
- The section “One cause, two kinds of silence” could be shortened slightly to maintain an academic tone while preserving its illustrative power.
- The citation style should be standardized (some entries list full URLs unnecessarily).

Declarations

Potential competing interests: No potential competing interests to declare.