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Peer Review Report

Manuscript Title: *Delirium: Multiple Aetiologies Converging on Common Anatomopathological Pathways – Insights from Recent Discoveries and Artificial Intelligence Models*

Reviewer: [Anonymous Peer Reviewer]

Date: 26 June 2025

1. Overall Recommendation

Accept with Minor Revisions

The manuscript is a robust, interdisciplinary systematic review that bridges neuropsychiatric pathophysiology and applied artificial intelligence (AI), offering both conceptual innovation and practical relevance. Its scholarly rigour, depth of synthesis, and relevance for clinical translation make it a strong candidate for publication in a high-impact journal focused on neurology, psychiatry, or digital medicine.

2. Strengths

a. Scientific Merit and Novelty

- The article offers a **novel synthesis**: positioning delirium as a "final common pathway syndrome" with converging inflammatory and neuroglial mechanisms is both convincing and transformative.
- Excellent integration of **AI in medicine**—linking mechanistic understanding with real-world implementation in clinical settings (e.g., Mount Sinai case study).

b. Structure and Clarity

- Excellently organised: From background through to discussion and conclusion, the paper reads fluidly.
- **Figures and Tables**: Meta-analytical tables and model performance data are clear and well-integrated into the narrative.
- APA references are **complete and up to date**, including landmark studies and very recent data (2023–2024).

c. Methodology

- Follows **PRISMA 2020 guidelines**.
 - Inclusion/exclusion criteria, search strategy, and risk of bias tools (e.g., PROBAST, AMSTAR-2) are properly described.
 - Longitudinal and meta-analytic synthesis of inflammatory biomarkers is exemplary.
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3. Suggestions for Minor Revisions

a. Add PRISMA Flow Diagram

- Though mentioned, the flow diagram is not embedded. Include the **actual PRISMA figure** to comply with transparency standards.

b. Minor Clarifications

- On p. 9 (Pathophysiological Convergence), clarify if **network connectivity** findings refer to fMRI or EEG-based analyses, or both.
- In the *Limitations* section, briefly discuss **gender representation** in delirium biomarker studies (since older male/female responses may differ in inflammatory cascades).

c. Stylistic Adjustments

- Consider tightening expressions like “remarkable consistency” which appear frequently—variation in tone may enhance academic tone.
 - Consider **condensing a few paragraphs** in the Discussion (~p. 12–14) where arguments slightly overlap.
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4. Ethical and Practical Considerations

- No ethical concerns are evident; the review uses published data only.
 - The Mount Sinai AI case is exemplary; however, a note on **AI equity and bias risks** (e.g., demographic generalisability of training data) could add depth.
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5. Impact and Suitability for Publication

This manuscript would suit journals such as:

- *Nature Reviews Neurology*

- *The Lancet Digital Health*
- *npj Digital Medicine*
- *Journal of the American Geriatrics Society*

Its interdisciplinary scope (neurobiology, geriatrics, AI implementation) makes it highly citable and relevant across specialties.

6. Summary Verdict

- **Originality:** ★★★★★
- **Scientific Rigor:** ★★★★★
- **Writing Quality:** ★★★★★☆
- **Relevance:** ★★★★★