

Peer Review

Review of: "The Future of Longevity Medicine: Repairing the Parts or Preserving the Whole? Holmes' Carriage as a Metaphor for Two Fundamentally Different Models of Aging"

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I believe the conceptual framework proposed in this work is thought-provoking and original. However, the central hypothesis would be considerably strengthened by discussing biological mechanisms that could plausibly maintain "systemic coherence" and by providing examples from the existing literature that support this concept.

The authors are encouraged to provide a more rigorous definition of "systemic coherence." It would be helpful to discuss whether this concept can be objectively measured and whether candidate biomarkers or physiological indices could be used to distinguish coherent aging from fragmented aging.

In my opinion, the relationship between the proposed framework and the established concept of compression of morbidity deserves further clarification. Please explain whether coherent aging should be considered a distinct biological paradigm or an extension of existing theories of healthy aging.

The comparison between technologically advanced societies and traditional populations is interesting but would benefit from additional supporting evidence. The authors should provide appropriate epidemiological or clinical studies supporting the proposed differences in aging trajectories.

The discussion would be strengthened by outlining potential experimental strategies that could be used to investigate the mechanisms responsible for preserving systemic coherence. Proper experimental approaches should be proposed to facilitate future validation of the conceptual model.

The possibility that certain anti-aging interventions may inadvertently disrupt systemic coherence is an intriguing hypothesis. Data from experimental studies or examples from the literature should be discussed to support this assertion and to better define the circumstances under which such effects might occur.

I think it would be valuable to distinguish more explicitly between hypotheses that are currently supported by experimental evidence and those that remain speculative. Such clarification would help readers better appreciate the conceptual scope of the proposed model.

The authors should discuss how systemic coherence relates to the current hallmarks of aging and other established biological frameworks. Please clarify whether systemic coherence is intended to represent a novel hallmark, an integrative property emerging from multiple hallmarks, or a higher-level organizational principle governing aging.

Declarations

Potential competing interests: No potential competing interests to declare.