Qeios

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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This commentary proposes two models of aging: "fragmented aging," in which different organs progressively fail and require medical interventions, and "coherent aging," in which the organism maintains its functional integration until a short terminal decline. The Holmes' carriage metaphor is interesting and easy to understand. However, the manuscript appears to be too speculative, and several important statements are not sufficiently supported.

Major comments

1. The concept of "systemic coherence" is central, but it is not clearly defined. The authors should explain how coherence can be measured. Possible indicators could include physiological resilience, recovery after stress, allostatic load, frailty, inter-organ communication, or differences between organ-specific biological ages.

2. The distinction between fragmented and coherent aging is presented as a strict dichotomy. It may be more realistic to consider them as two ends of a continuum. Moreover, some organs can age faster than others without necessarily causing a loss of global function.

3. The comparison between wealthy and traditional populations is not sufficiently supported. Traditional populations may have a shorter morbidity period because of underdiagnosis, lower access to healthcare, or selective mortality. The authors should provide epidemiological evidence or present this idea more cautiously as a hypothesis.

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4. The comparison between wealthy and rural populations could also be further developed as a possible hypothesis. Wealthier populations have greater access to medical resources that can repair specific dysfunctions and extend lifespan. However, some aspects of technological and urban development may contribute to the loss of systemic coherence. These may include higher psychological stress, lower physical activity, consumption of more processed food, irregular daily and eating routines, exposure to urban pollution, reduced participation in domestic or manual activities, and weaker family or community relationships. In contrast, some rural populations may preserve lifestyles that are closer to the conditions under which human physiology evolved, including regular and simpler routines, daily physical activity, less processed diets, and stronger social interactions. However, this interpretation is speculative and should not be generalized to all wealthy or rural populations. The authors may present it as a testable hypothesis and may support it with appropriate epidemiological evidence.

5. The Blue Zones book is not sufficient as scientific support. Primary demographic and epidemiological studies should be included.

6. Repair and preservation are not necessarily opposite strategies. Many medical treatments can prevent further damage and preserve systemic function. Similarly, senolytics, regenerative medicine, or other anti-aging interventions may potentially improve, rather than disrupt, organismal coordination.

7. The manuscript should better discuss previous concepts such as physiological resilience, allostasis, frailty, homeostasis, network physiology, and compression of morbidity. The authors should clarify what “systemic coherence” adds to these existing frameworks.

8. The text is repetitive. The same contrast between local repair and global preservation is repeated several times. The manuscript could be shortened considerably, especially the sections about billionaires and the “war against death.”

Minor comments

1. A space is missing in the title: “Whole?Holmes’”.

2. The original source of the metaphor should be correctly cited.

3. “Terminal morbidity” should be clearly defined.

4. The extensive use of numbered lists “(i), (ii), (iii)” sometimes makes the text difficult to read.

5. Statements concerning the possible risks of epigenetic reprogramming, excessive regeneration, and other longevity interventions would require references.

6. The accuracy and formatting of the references should be checked.

7. A simple conceptual figure comparing the two proposed aging trajectories would improve the manuscript.

Declarations

Potential competing interests: No potential competing interests to declare.