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Peer Review

Review of: "The Bio-Psycho-Social Holobiont Model of Health: Integrating the Biopsychosocial Paradigm, Microbiota Science, and Psychoneuroendocrinoimmunology"

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This manuscript addresses an important and timely question for contemporary health sciences: how the human microbiota and the holobiontic perspective should be explicitly incorporated into clinical psychology and biopsychosocial approaches to health and disease. The topic is highly relevant, particularly given the growing evidence that microbial communities participate in physiological regulation, immune and endocrine signaling, neurobiological processes, and behavioral and affective dynamics. I agree with the author's general premise that health and disease cannot be adequately understood if the role of the microbiota and its interactions with biological, psychological, social, and environmental dimensions are excluded. Although this perspective has received considerable attention in neuroscience, microbiota research, and the microbiota-gut-brain axis literature, it still appears to be insufficiently integrated into several areas of clinical psychology and across different theoretical and therapeutic orientations.

In this regard, the manuscript raises an important conceptual problem. Its main strength lies in its attempt to articulate the biopsychosocial model, the holobiontic perspective, microbiota research, and psychoneuroendocrinoimmunology within a single integrative framework. It is also positive that the author does not present the model as a closed or definitive formulation, but rather as a proposal that requires further conceptual refinement, empirical validation, and indicators capable of operationalizing holobiont coherence.

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However, I consider that the manuscript requires a more exhaustive and critical literature review. The general intuition is pertinent, but the proposal would be strengthened by engaging more explicitly with the literature on systems medicine, ecological models of health, psychobiotics, physiological network approaches, antifragility in living systems, and current debates on the concept of the holobiont. In particular, it would be useful to incorporate ecological and relational perspectives that do not understand the organism solely as a host-microbiota unit, but rather as a living system situated within biological, microbial, social, cultural, and environmental couplings.

I support the manuscript's general view that the microbiota should be integrated into the biopsychosocial understanding of health and disease. Nevertheless, if the proposal is presented as a new extension of the classical biopsychosocial model, it requires further conceptual and operational development. Central notions such as "coherence", "informational convergence", "teleonomy", and "bio-psycho-social holobiont" are relevant to the architecture of the manuscript, but they remain insufficiently defined to sustain a clearly differentiated theoretical contribution. In their current form, some of these notions may be interpreted more as terminological reformulations than as conceptual categories with explanatory value of their own. It is not clear how these constructs could be measured, how they would guide clinical assessment, or what specific hypotheses they would allow researchers or clinicians to formulate beyond those already possible within existing integrative models.

A similar observation applies to the proposal to refer to a "microbiota-gut-brain-mind axis". I find it appropriate that the author emphasizes both descending and ascending mechanisms, namely the influence of psychological processes on intestinal physiology and microbial dynamics, as well as the influence of the microbiota and the gut on neurobiological, affective, and behavioral processes. However, the conceptual need to add the term "mind" to the axis is not sufficiently clear. In its current formulation, this proposal appears to function more as a terminological reorganization than as a substantive epistemological or mechanistic shift. The manuscript should clarify whether this expression is intended to introduce a new explanatory framework, a conceptual refinement, or simply a more complete terminology.

Overall, I consider the manuscript relevant and potentially valuable as a theoretical contribution. Its main contribution is to integrate and make visible a dimension that clinical psychology and the biopsychosocial perspective should no longer treat as peripheral: the role of microbial communities associated with the human organism in health and disease processes. Its main limitation is that, in its current form, the proposal remains more conceptual and terminological than operational. I would

recommend major revision before publication, with particular attention to a broader literature review, a more precise definition of the central concepts, a clearer formulation of the model's novelty, and a more concrete explanation of how it could be applied or tested in clinical and research contexts.

Declarations

Potential competing interests: No potential competing interests to declare.