Last Word on Counterpoint: Hypobaric hypoxia does not induce different physiological responses from normobaric hypoxia

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TO THE EDITOR: First, we would like to thank all the authors who contributed to make this a rigorous and thorough debate (see Ref. 2). As expected, we can note some very strong opinions and diverging points of view among the contributors even from the same institution or within members of the same family!!! We believe this diversity in the commentaries reflects the complexity of the question and the urge for further research. Trying to summarize the contributions, our point is outnumbered by Millet et al.’s (3) supporters by 8 commentaries vs. 5 (+1 remaining fairly neutral!). Shall we, therefore, conclude that we have it totally wrong? To address this question, we will bring back memories from a previous Point:Counterpoint between Prs. Wagner and Saltin and Calbet about the limiting factors of \( V_{O2\max} \) (5) published in the Journal of Applied Physiology during which Pr. Wagner rightfully pointed out that to answer a question we have to agree on the terms of the question. For instance, if we go back to the origin of this debate the question to be addressed was “is there a physiological difference between hypoxia induced by a change in inspired \( O_2 \) partial pressure \( (P_{T O_2}) \) vs. an alteration in the inspired \( O_2 \) fraction \( (F_{I O_2}) \)” Two commentaries are (rightfully) highlighting differences in air density between hypobaric hypoxia (HH) and normobaric hypoxia (NH) as explaining at least part of the discrepancies between the two paradigms; in so doing they are actually arguing for our stance as we mentioned confounding factors associated with HH in the first instance (4). Fueling our argument further, the only commentary, proposed by Conkin and Wessel (see Ref. 2), focusing on the heart of the debate, i.e., \( P_{T O_2} \) vs. \( F_{I O_2} \), is indeed arguing in our favor.

However, we acknowledge that to interpret a full body physiological response one has to look at the broad picture. Bearing this in mind, it therefore seems difficult to accurately compare HH and NH because they appear to be two different stimuli. A very clear illustration of this is the mitigating effect of hypocapnia induced by hyperventilation has on the hypoxia-induced increase in cerebral blood flow when compared with isocapnic hypoxia (1).

Overall, a more detailed reading of the available contributions to the present Point:Counterpoint actually brings the “underdog back into the game” with 6 commentaries pro-Millet et al. vs. 7 pro-Mounier and Brugniaux (plus the remaining neutral contribution). Even if a basic mathematical addition of the commentaries pros or cons Mounier and Brugniaux is somewhat simplistic, because the majority is not always right, we believe there is strong evidence allowing us to stand by our original point stating that (at least) in terms of \( O_2 \) sensing HH does not induce different physiological responses from NH. Nevertheless, as physiology is very integrative in nature, maybe future debates should move from the topical opposition between \( P_{T O_2} \) and \( F_{I O_2} \) to focus on a more integrative approach. Being able to address this latter point will, indeed, require further research.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS
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