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TO THE EDITOR: We thank Broxterman and colleagues for their comments regarding our recent work on the effects of prior upper body exercise on subsequent cycling exercise tolerance and associated changes in neuromuscular function and perceptual responses (3).

Previous studies suggested that prior upper body exercise reduces subsequent knee 24 extensor and cycling exercise tolerance by accelerating the development of quadriceps muscle 25 fatigue. The stated aim of our study was to test the hypothesis that prior upper body exercise 26 reduces subsequent cycling exercise tolerance and that this is associated with less peripheral 27 locomotor muscle fatigue incurred but a greater/accelerated perceptual response. Using prior 28 arm-cranking exercise followed by leg cycling exercise performed to the limit of tolerance 29 30 ensured that our study was appropriately designed to address this research question and our data confirmed our hypothesis. Thus, it is important to clarify that (contrary to the critique of 31 32 Broxterman and colleagues) our aim was not to evaluate the validity of the critical threshold of 33 peripheral fatigue concept. Furthermore, we do not conclude that our data "disprove" this 34 concept.

35 A key finding of our study was that individuals experience less peripheral locomotor muscle fatigue after cycling exercise to the limit of tolerance preceded by upper body exercise. 36 37 Our study therefore extends the observations of single-leg knee extension exercise studies (1) by demonstrating that peripheral fatigue *per se* is not a variable that is *independently* regulated 38 during whole-body exercise. Rather, our findings indicate an important limiting role for the 39 ensemble group III/IV muscle afferent feedback in mediating exercise tolerance, since it can 40 be assumed that prior upper body exercise results in an elevated ensemble group III/IV muscle 41 42 afferent feedback at the start of subsequent cycling exercise (2). Our data suggest that the limit of exercise tolerance is largely determined by the attainment of a critical sensory tolerance limit 43 that is primarily mediated by the ensemble group III/IV muscle afferent feedback and which 44 45 coincides with, but is not exclusively mediated by or reflective of, a certain degree of peripheral

46 locomotor muscle fatigue. This notion is supported by three observations from our study: (1) ratings of leg discomfort during cycling were higher despite quadriceps muscle activation being 47 unaffected by prior upper body exercise; (2) ratings of leg discomfort during cycling were 48 49 higher despite less quadriceps muscle fatigue incurred when cycling was preceded by upper body exercise; and (3) the reduced cycling exercise tolerance after prior upper body exercise 50 51 was correlated with accelerated increases in ratings of leg discomfort and dyspnea. These findings are important because they indicate that potentially limiting perceptions of leg 52 discomfort during cycling exercise may be potentiated by group III/IV afferent projections 53 54 originating at remote sites.

To conclude, our data shed light on the determinants of whole-body exercise tolerance and the mechanisms by which prior upper body exercise reduces subsequent cycling exercise tolerance. The notion that individuals cannot surpass a task-specific maximum level of peripheral fatigue was not the focus of our study and, therefore, remains an exciting avenue for future investigation.

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61 **Disclosures:** The authors report no conflicts of interest.

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and revised manuscript; M.A.J., G.R.S., N.C.W., and R.H approved final version of
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