LETTER

REPLY TO GRONWALD ET AL.:

Exercise intensity does indeed matter; maximal oxygen uptake is the gold-standard indicator

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There is no doubt that Gronwald et al.'s (1) message that exercise intensity does matter is true; however, we must respectfully disagree with their claim that the exercise intensity in our study (2) was not actually "very light."

Unlike most interventions in the field, with laboratory (pedaling) exercise testing, the workload is precisely determined based on individually measured cardiorespiratory fitness (CRF) to attain a target intensity. The gold-standard measure of CRF is maximal oxygen uptake ($\dot{V}_{O_2max}$), established by Åstrand et al. in the 1950s (3), not maximal heart rate (HR_{max}). As we emphasized in our article (2), we have established an acute-exercise model based on individual peak oxygen uptake ($\dot{V}_{O_2peak}$) and demonstrated the benefits of exercise on human cognitive function (4–6). In the current study (2), we estimate individual workload corresponding to a target exercise intensity (30% $\dot{V}_{O_2peak}$) according to individual $\dot{V}_{O_2}$-work-rate relationships during a graded exercise test to exhaustion (GXT). A pilot study with different participants (seven males, aged 25.0 ± 2.6 y, $\dot{V}_{O_2peak} = 43.2 \pm 6.7$ mL·kg^{-1}·min^{-1}) verified that the actual intensity for a workload estimated to be 30% $\dot{V}_{O_2peak}$ was 33.8 ± 3.2% $\dot{V}_{O_2peak}$, which is lower than the threshold (37% $\dot{V}_{O_2max}$) for "very light" exercise established by the American College of Sports Medicine.

We did not measure $\dot{V}_{O_2}$ in our subjects during exercise testing because wearing a sampling mask could affect cognition; however, we ensured exercise intensity by monitoring HR and Borg's rating of perceived exertion (RPE) scale (7). HR remained within the range for "very light" exercise (<57% HR_{max}; experiment 1: 50.3 ± 3.5% HR_{max}; experiment 2: 51.3 ± 4.4% HR_{max}). In the supporting information for ref. 2 we provided data for actual peak HR (HR_{peak}), but for our analysis we calculated %HR_{max} based on age-predicted HR_{max} (220-age) rather than HR_{peak} because 80% of participants did not reach ±10 beats per minute of age-predicted HR_{max} during the GXT. The lower-than-predicted HR_{peak} was likely due to our use of a recumbent ergometer, with which local muscular fatigue occurs before central circulation is maximally engaged (8). Furthermore, while RPE was very slightly higher than the threshold for "very light," this was likely due to the relatively lower validity of RPE for lower-intensity exercise (7). Thus, we reiterate that the exercise intensity of our experiments was correctly classified as "very light."

From a dose–response perspective, we have seen similar effects with moderate exercise (50% $\dot{V}_{O_2peak}$) (6) at around the lactate threshold, where hormonal and sympathetic nervous systems, associated with stress response, start to be activated. Acute stress has a negative impact on the hippocampus (9), and thus stress hormones released during higher-intensity exercise likely dampen any potential cognition enhancement. Our previous animal-model studies suggest that stress-free, mild exercise is preferable for enhancing hippocampal activation (10) and neural functions such as neurogenesis and memory (11). Our study (2) is an important step, as translational research, toward understanding exercise benefits to the hippocampus and their underlying neuronal substrates while specifying intensity based on reliable physiological parameters such as $\dot{V}_{O_2}$.

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