RESPONSE TO COMMENT ON PATAKY ET AL.

Divergent Skeletal Muscle Metabolomic Signatures of Different Exercise Training Modes Independently Predict Cardiometabolic Risk Factors. Diabetes 2024;73:23–37

Mark W. Pataky and K. Sreekumaran Nair

https://doi.org/10.2337/dbi24-0017

We appreciate Dr. Astrada's interest (1) in our recent article (2). Although he raised concern around using BMI as a screening parameter for our study, BMI was not the only defining parameter for screening criteria in our study. Fasting glucose >110 mg/dL was also a critical exclusion criterion for the study, as it limits variation in metabolic characteristics in our study cohort. These and other criteria for participation in the study were reported in the original article (3) from which the samples in our current study (2) were obtained. Furthermore, after participants were screened and included in the study, DEXA scans provide information on body composition, which we reported in the online supplementary material. Within a given age-group, we found no differences in body composition (body fat percentage) between treatment groups at baseline. As for the participants' daily activities, we did not collect occupation information, but an exclusion criterion for the study was participation in regular exercise (>20 min more than twice per week), which was reported in the original manuscript (3). Thus, none of the participants were regular exercisers, further limiting baseline metabolic variability.

As we mentioned in our article, "Plasma [branched-chain amino acids] are consistently shown to be unresponsive after exercise training (4–6), likely because the plasma amino metabolites represent the net balance of exchanges between muscle and liver (7)." We reported no effect of high-intensity interval training (HIIT) on plasma branched-chain amino acids (2). As part of a basic metabolic panel conducted as a part of screening, AST levels were measured and no participants had abnormal liver function, indicating that the results were not due to abnormal liver function. Furthermore, exclusion criteria included alcohol abuse, cardiovascular disease, metabolic diseases (type 2 diabetes, fasting blood glucose >110 mg/dL, and untreated hypo- or hyperthyroidism), and renal disease, ruling out these pathological conditions as confounding variables.

The exercise training was performed under supervision. Of the participants who completed the exercise training, all participants completed the reported number of sessions allocated for their randomized training group (4 sessions of resistance training per week for 12 weeks, for a total of 48 sessions, or 5 sessions of high-intensity interval training or resistance training per week for 12 weeks, for a total of 60 sessions). If a session was missed for any reason, then an additional session was completed at the end of the 12-week period to accomplish the total number of sessions. Thus, participant adherence was excellent and was consistent among all training groups and likely did not contribute to variability in the results. Unfortunately, sleep/rest information was not collected from these studies. We did not collect dietary information during the study, but all participants were instructed to maintain their normal diet throughout the duration of the study.

Funding. No funding was received for this work.
Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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Division of Endocrinology and Metabolism, Mayo Clinic, Rochester, MN
Corresponding author: K. Sreekumaran Nair, nair@mayo.edu

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