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Title: The effects of inspiratory muscle training on the interleukin-6 response to intense volitional hyperpnoea

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Body: Vassilakopoulos et al. (Am. J. Physiol 1999; 277:R1013–R1019) demonstrated a breathing-induced interleukin-6 (IL-6) response. Whether inspiratory muscle training (IMT) can attenuate this response is unknown. Therefore, we tested the hypothesis that the IL-6 response to volitional hyperpnoea (VH) could be reduced with IMT and investigated whether this response was related to diaphragm fatigue (assessed by phrenic nerve stimulation) and/or changes in blood lactate concentration ($[\text{Lac}^-]_{\text{B}}$). Twelve male participants performed either 6 weeks of pressure-threshold IMT (n=6) or placebo (PLA) training (n=6). Prior to training, a maximal incremental cycling test (max) was performed. Before and after training, participants undertook two 1 h experimental trials on separate days: passive rest or VH. In VH, they voluntarily mimicked at rest the breathing and respiratory muscle recruitment pattern equal to 70-80% of the maximum minute ventilation achieved during max. IL-6 increased ($P < 0.01$) following the pre-training VH and was (mean \pm SD) 5.02 ± 0.63 and 4.87 ± 0.86 $\text{pg}\cdot\text{mL}^{-1}$ at 2 h post for IMT and PLA groups, respectively. $[\text{Lac}^-]_{\text{B}}$ remained ($P < 0.01$) elevated above baseline values for the duration of VH at 1.36 ± 0.24 and 1.29 ± 0.18 $\text{mmol}\cdot\text{L}^{-1}$. The IL-6 (-29%) and $[\text{Lac}^-]_{\text{B}}$ (-11%) responses were reduced ($P < 0.05$) for the IMT, but not for the PLA group. There were no increases in IL-6 or $[\text{Lac}^-]_{\text{B}}$ over time for either group during passive rest and no evidence of diaphragm fatigue during any trial. In conclusion, 6 weeks of IMT reduces the magnitude of the IL-6 response to VH with no evidence of diaphragm fatigue. The reduction in IL-6 may be related to the post-IMT reduction in $[\text{Lac}^-]_{\text{B}}$.