Chemogenetic activation of the carotid body chemoreflex plays a fundamental role in response to acute hypobaric-hypoxia and maximal physical exertion in rats

Poster

Fisiología Respiratoria

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Background: The cardiorespiratory responses to physical exercise are expected to meet the organism's metabolic demands. The carotid body (CB), specifically glomus cells, is one of the most critical homeostatic mediators, and it has been proposed that they are necessary to mediate maximum metabolic activity during exercise (peak O_2 uptake, VO_2peak). However, it has not been demonstrated whether the CB is sufficient to promote an increase in maximum metabolic activity during exercise.
Objective: To study the activation of the CB chemoreflex, through a chemogenetic approach, on VO_2peak during exertion in rats.
Methods: 4 adult male Wistar Kyoto rats (approved by CEIC University of Antofagasta) were bilaterally co-injected with an adeno-associated virus (AVV) at the carotid bifurcation to chemogenetically activate the CB (AVV-TH-Cre-SV40 and AVV-hSyn-DREADD(Gq)-mCherry); later on, clozapine-N-oxide (CNO) (1 mg/kg i.p.) was administered to activate the DREADD(Gq) receptor and activate the glomus cells. Three weeks post-infection, and before and after CNO administration, whole-body

plethysmography was used to assess the hypobaric-hypoxic ventilatory response (HHVR) (5,500 m of simulated altitude, PO2 ~ 60 mmHg). Additionally, exercise performance was assessed to evaluate VO_2 at rest and VO_2 peak. The data were analized with a two-way ANOVA, following Holm-Sidak post hoc.
Results: Acute chemogenetic activation of CB chemoreceptors elicited an augmentation of peripheral chemoreflex, assessed through HHVR. Notably, our data revealed that a single dose of CNO maintained the response of VO2peak in these animals. Interestingly, even when a maintained VO2peak was observed, the maximum aerobic speed significantly increased ($p = 0.0469$).

Conclusions: Our findings reveals that CB chemoreflex activation is sufficient to promote an increase in HHVR during an HH stimuli. Nonetheless, the maintaining of VO2peak at exertion accompanied by an improvement in maximal running capacity suggests a mismatch between oxygen consumption and the work performed.

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