Role for the carotid body chemoreceptors in glucose homeostasis in healthy humans

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INTRODUCTION

- The carotid body (CB) chemoreceptors are important in sensing and responding to changes in arterial oxygen levels.
- CB chemosensitivity can be measured in humans using a breathing test known as a hypoxic ventilatory response (HVR).
- Recent data from pre-clinical rodent models suggests the CBs may play an important role in glucose homeostasis.

We sought to examine the contribution of the CB chemoreceptors to glucose regulation in humans.

HYPOTHESES

- We hypothesized attenuation of CB chemoreceptor activity (100% oxygen) would improve glucose tolerance in healthy humans.
- We further hypothesized the magnitude of the effect of CB desensitization on glucose tolerance would be related to the level of CB chemosensitivity (HVR).

METHODS

- **Participants:** 4 healthy adult men and women
- **Screen visit:** All participants completed a 2-hour screen visit which included a DEXA to assess body fat and a hypoxic ventilatory response test (HVR) to assess carotid body chemosensitivity to hypoxia.
- **Hypoxic Ventilatory Response Test (HVR):** Hypoxia was achieved using variable inspired breaths of low oxygen (5% oxygen) followed by normoxia (21% oxygen, room air) through the mask. This was repeated 4-5 times. The HVR was calculated as the slope of the relationship between arterial oxygen saturation (SpO2, %) and minute ventilation (L/min).

METHODS

- **Study visits:** All participants completed two 3-hour study visits randomized to normoxia (control) and hyperoxia (100% oxygen, CB desensitization). During the study visit, blood glucose and plasma insulin and C-peptide were measured every 15-min for 2-hours following consumption of a 75 g glucose drink. Data for insulin, glucose, and C-peptide are reported as area under the curve (AUC).

Figure 1: Study Visit Set-Up. Participants were instrumented with an intravenous catheter in the right arm for periodic blood sampling. Participants wore a mask connected to a non-rebreathing valve for administration of normoxic (21% oxygen, control) or hyperoxic (100% oxygen, experimental) gas. Blood pressure, heart rate, and oxygen saturation were periodically assessed.

DEMOGRAPHICS

	Control
Count (M/F)	1/3
Age (yrs)	53±6
Weight (kg)	70±5
Body Mass Index (kg/m^2)	24±1
Body Fat (%)	31±5
Glucose (mg/dL)	71±4
Insulin (uIU/L)	1.6±0.2
HbA1c (%)	5.0±0.2
HVR (L/min/%)	-0.26±0.04

Table 1: Participant characteristics. Data are presented as Mean±SEM. HVR = Hypoxic Ventilatory Response

RESULTS

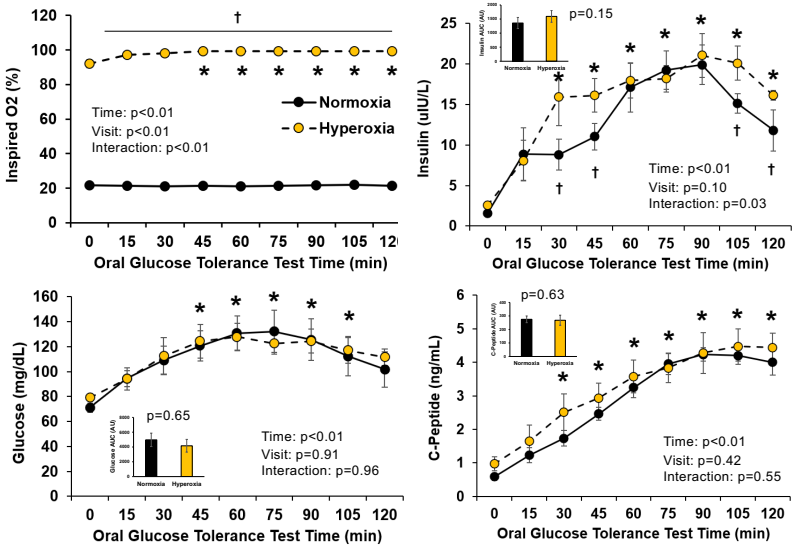

Figure 2: Effect of hyperoxia on glucose tolerance. Hyperoxia was achieved (inspired oxygen ~100%). Following consumption of the glucose drink, there was an increase in blood glucose and plasma insulin and C-peptide. *p<0.05 vs T0, †p<0.05 vs Normoxia.

CONCLUSIONS

- Following consumption of the glucose drink, there was an increase in blood glucose **(Fig 2C)** and C-peptide **(Fig 2D)** which did not differ between normoxic and hyperoxic conditions.
- The insulin responses following the glucose drink was greater during hyperoxia than normoxia at T30 and T45 **(Fig 2B)**. Higher insulin (but not C-peptide) may indicate a higher level of circulating versus secreted insulin.
- There was no relationship between the effect of hyperoxia on the main outcome variables and the HVR (a measure of peripheral chemosensitivity) in the healthy adults studied.

These data do not support a role for the carotid body chemoreceptors in glucose homeostasis in healthy humans. In the future, we seek to expand this work into adults with Type 2 Diabetes.

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