Peripheral chemoreceptor contribution to ventilatory control during steady-state exercise

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ABSTRACT

We tested the hypothesis that the carotid body chemoreceptors (CB) contribute to ventilatory control during steady-state exercise. Six men completed two randomized bouts of cycling exercise at 65% VO_2max for up to 2 hours during an IV infusion of dopamine (D; 2 µg/kg/min) to acutely inactivate the CB, or a saline infusion (S). Expired gases were analyzed at baseline, resting-infusion, and during exercise (25%, 50%, 75% and 100% of total exercise time). A hypoxic ventilatory response (HVR) test was performed after exercise during the infusion condition. Subjects were classified as responders (RS; n=3) if their HVR was lower during D vs. S (1.03 ± 0.6 vs. 2.14 ± 0.4 L/min/%S_aO_2). In the non-responders group (NR), partial pressure of end-tidal CO_2 had a greater delta from baseline at 75% (2.9 ± 2.1 vs. 1.1 ± 1.9 mmHg) and 100% (0.9 ± 3.4 vs. -0.3 ± 3.3 mmHg) during D than S, and the increase in oxygen uptake at 100% was greater during D vs. S (34.7 ± 2.6 vs. 33.0 ± 2.6 mL/min/kg). In NR, there were no differences in the changes from baseline for ventilation (VE), VE/VCO_2, respiratory rate, tidal volume, and respiratory exchange ratio between conditions. In RS, there were no differences between D and S in any variables. When the data was pooled, HVR accounted for 37% of the variance in VE at 100%. Despite evidence that CB chemosensitivity was blunted, the CB appear to play a minor role in controlling ventilation during steady-state exercise.
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INTRODUCTION

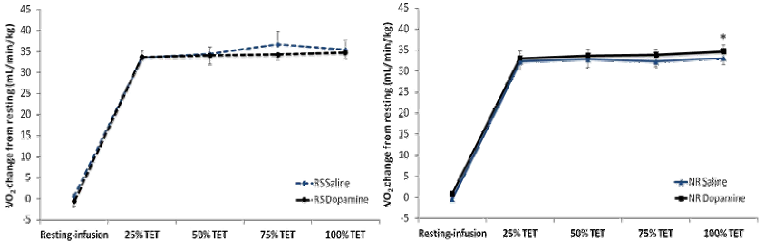
- Data obtained from denervated animal preparations suggest a potential role for the carotid body chemoreceptors (CB) in mediating a portion of the hyperventilatory response to heavy exercise (1).
- In humans, the CB appear to play a role in fine tuning ventilation during exercise (2).
- Low dose infusions (2-5 µg/kg/min) of IV dopamine have been shown to blunt CB chemosensitivity, similar to hyperoxia. In this context, using an IV infusion of low dose dopamine can be used as a tool to inhibit CB activity during exercise without directly influencing arterial oxygen content, that would otherwise be observed if hyperoxia were used.
- The aim of this study was to examine the contribution of the CB to ventilatory control during steady-state exercise in healthy exercise trained humans.

METHODS

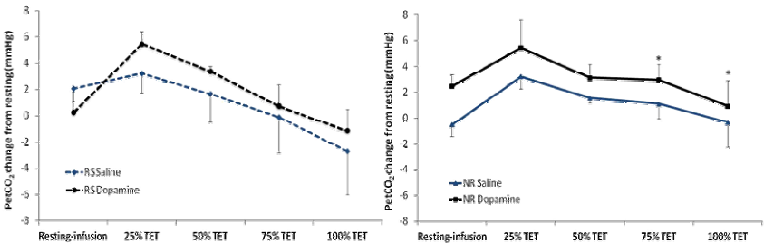
- Six trained, healthy males (32 ± 9 yrs; BMI: 23.0 ± 1.1 kg/m^2; VO_2max: 58.2 ± 2.6 ml/kg/min) completed two randomized bouts of cycling exercise at 65% VO_2max for up to 2 hours.
- One session was performed with an IV infusion of dopamine (D; 2 µg/kg/min) to blunt CB chemosensitivity and the other with an IV infusion of saline (S).
- Subjects consumed a macronutrient-controlled (50% carbohydrate, 20% protein, 30% fat) diet for 3 days prior to each study day.
- Expired gases were analyzed at baseline, resting-infusion, and during exercise (25%, 50%, 75% and 100% of total exercise time; TET). Blood was drawn for blood gases analysis at each timepoint.
- A hypoxic ventilatory response (HVR) test was performed during the infusion conditions 15 minutes following exercise. Three minutes at: room air, 16% O_2, and 10% O_2.
- Subjects were classified as responders (RS) if their HVR was lower during D vs. S and as non-responders (NR) if their HVR during D was equal to or greater than S.
- Statistical comparisons were made using a two way repeated-measures ANOVA. P values of ≤0.05 were considered statistically significant. Data are expressed as means ± SEM.

RESULTS

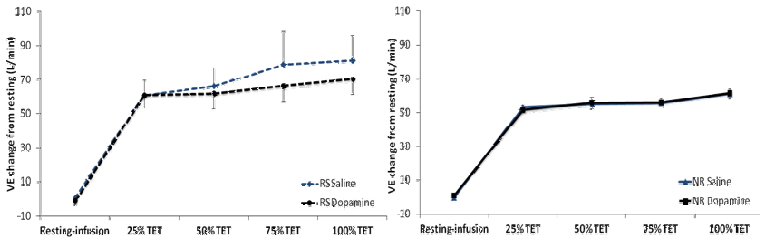
Three subjects were classified as RS as D reduced their HRV from 2.14 ± 0.40 L/min/%S_aO_2 to 1.03 ± 0.57 L/min/%S_aO_2. The other three subjects were classified as NR as their HVR during D was greater than S (1.17 ± 0.45 vs. 0.71 ± 0.38 L/min/%S_aO_2, respectively).



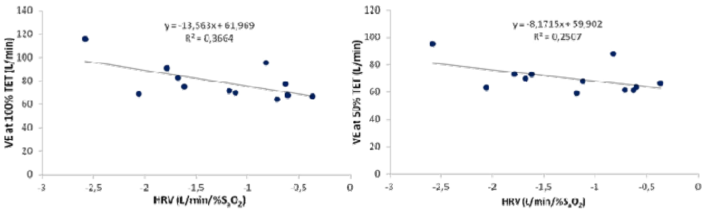
The increase in oxygen uptake (VO_2) at 100% TET was greater during D vs. S (p=0.005) in NR, while there was no difference in RS.



In NR, the partial pressure of end-tidal CO_2 ($PetCO_2$) had a greater change from baseline at 75% (p=0.05) and 100% TET (p=0.05) during D than S. There were no differences between conditions for the changes from baseline in $PetCO_2$ in RS.



There were no differences in the changes from baseline for ventilation (VE) between conditions. In RS, the ventilatory response was greater during D vs. S although not statistically distinguishable between conditions.



When the data was pooled, HVR accounted for 37% of the variance in VE at 100% TET and 25% at 50% TET.

Responders		Resting-infusion	25% TET	50% TET	75% TET	100% TET
P_aO_2	D	3.3 ± 2.0	15.3 ± 2.8	14.7 ± 3.2	12.7 ± 2.3	11.0 ± 3.0
(mmHg)	S	5.3 ± 7.3	-18.0 ± 3.6	-13.0 ± 6.1	-1.3 ± 14.2	-5.3 ± 2.6
P_aCO_2	D	-0.3 ± 0.3	-2.3 ± 1.9	-3.2 ± 2.0	-4.3 ± 2.6	-6.0 ± 2.1
(mmHg)	S	1.7 ± 2.7	-1.3 ± 2.3	-3.3 ± 2.4	-5.7 ± 2.3	-8.0 ± 2.6
VE/VCO_2	D	-0.01 ± 1.9	-10.6 ± 2.5	-9.0 ± 2.3	-7.4 ± 3.0	-5.3 ± 3.1
	S	-0.4 ± 1.3	-7.6 ± 0.9	-6.1 ± 0.5	-4.1 ± 1.5	-1.4 ± 1.7
RR	D	-1.2 ± 3.2	19.1 ± 1.2	23.5 ± 2.8	24.7 ± 11.2	27.2 ± 1.6
(breaths/min)	S	4.1 ± 0.3	22.5 ± 2.0	25.6 ± 0.5	32.6 ± 0.5	32.3 ± 7.7
V_T	D	11.4 ± 37.4	1309.7 ± 227.9	1111.1 ± 210.2	1168.8 ± 235.1	1159.1 ± 222.1
(ml)	S	-135.6 ± 76.6	1148.9 ± 174.8	1141.4 ± 171.3	1129.2 ± 133.5	1213.5 ± 75.4
RER	D	-0.02 ± 0.04	0.17 ± 0.12	0.12 ± 0.11	0.12 ± 0.12	0.11 ± 0.12
	S	0.01 ± 0.04	0.12 ± 0.05	0.12 ± 0.06	0.13 ± 0.06	0.12 ± 0.06

Non-responders		Resting-infusion	25% TET	50% TET	75% TET	100% TET
P_aO_2	D	24.0 ± 8.5	13.0 ± 23.5	1.3 ± 4.8	-10.3 ± 9.1	0.7 ± 7.4
(mmHg)	S	-7.3 ± 3.3	-0.7 ± 14.4	17.0 ± 21.7	10.3 ± 22.2	-11.3 ± 2.2
P_aCO_2	D	0.3 ± 0.3	-1.3 ± 1.7	-2.7 ± 2.0	-2.0 ± 2.7	-3.7 ± 3.0
(mmHg)	S	0.0 ± 0.3	-2.7 ± 1.6	-4.0 ± 2.3	-3.3 ± 3.0	-4.3 ± 3.9
VE/VCO_2	D	-2.4 ± 1.5	-9.1 ± 2.1	-7.2 ± 2.0	-6.9 ± 2.2	-6.4 ± 2.9
	S	1.6 ± 0.4	-6.0 ± 1.1	-4.9 ± 1.3	-4.0 ± 2.0	-2.3 ± 2.6
RR	D	0.001 ± 0.7	17.7 ± 2.1	21.0 ± 2.6	19.8 ± 3.2	24.3 ± 5.6
(breaths/min)	S	0.5 ± 0.3	20.3 ± 3.6	21.0 ± 3.0	23.2 ± 5.5	27.7 ± 8.3
V_T	D	143.4 ± 112.1	1280.7 ± 218.8	1202.0 ± 234.3	1287.0 ± 293.5	1227.3 ± 353.2
(mL)	S	-25.2 ± 4.3	1139.8 ± 196.9	1137.6 ± 157.0	1086.6 ± 282.0	1032.4 ± 346.4
RER	D	0.002 ± 0.01	0.04 ± 0.01	0.03 ± 0.01	0.02 ± 0.01	0.03 ± 0.02
	S	0.01 ± 0.02	-0.01 ± 0.04	-0.04 ± 0.04	-0.04 ± 0.05	-0.03 ± 0.04

There were no differences between conditions for the changes from baseline for partial pressure of O_2 (P_aO_2) and CO_2 (P_aCO_2), VE/VCO_2, respiratory rate (RR), tidal volume (V_T), and respiratory exchange ratio (RER) in any group.

CONCLUSION

- Carotid body chemosensity appears to play a minor role in controlling ventilation during prolonged steady-state exercise.
- Although dopamine blunted the HVR during light exercise in the RS, it does not appear that this dose of dopamine affected CB-mediated ventilatory control during prolonged steady-state exercise.

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