

Inter- and intra-day variability of the hypoxic ventilatory response during isocapnic hypoxia.

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1) Abstract

Aim:

To determine the within and between day variability of the HVR.

We used a breathing circuit to keep subjects isocapnic at eucapnic levels during hypoxic breathing (Fig. 1, (1)) and to evaluate the within and between day variability of the hypoxic ventilatory response (HVR) during repeated exposures to normoxia (21 % O₂, balance N₂) and hypoxia (8 % O₂, balance N₂).

Fifteen subjects were exposed to four intervals of hypoxia alternating with normoxic intervals each of 120 s (Fig. 2). Subjects were tested on a total of three days, either once (n = 6) or three times per day (n = 9). Isocapnia was maintained in all subjects. Measured HVR (-0.59 ± 0.42) did not differ within or between days, neither did its variability (CV = 27%) within and between days.

2) Introduction

Breathing hypoxic gas induces immediate hyperventilation, the magnitude of which is called the hypoxic ventilatory response (HVR). The HVR is most commonly used to measure carotid body levels of chemosensitivity to hypoxia.

Variability of the HVR within the same subjects between or within days is not well understood. Early studies suggested that the intra-individual variability within days ranged from 7.6 to 64 % (6), and repeated tests on different days on the same individual showed that HVR may differ significantly between days (2). Zhang and Robbins (2) estimated that between-day variability in HVR is approximately 26%. However, these authors could not estimate the within-day variability because the tests they performed on the same day used different protocols (2).

Still, single measurements of HVR have been used to evaluate physiological differences between and within populations in which conclusions have been made regarding the genetic differences of the populations (3,4).

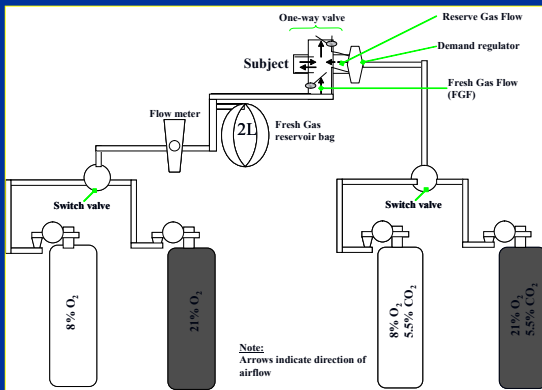


Figure 1. Schematic of the breathing circuit

3) Methods

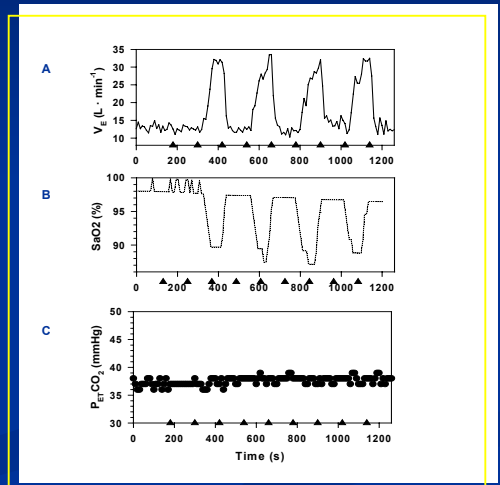
- 15 (7 male and 8 female) healthy volunteers (mean age =) were randomly divided into 2 groups (Gr1 and Gr2).
- HVR test: 4 intervals of 2-min exposure to eucapnic hypoxia (8% O₂, PAO₂ ~ 60 mmHg) alternating with 4 2-min normoxic intervals (see Fig 1 and 2, (1)).
- Data recorded:
 - 1) Minute ventilation volume (V_E, L·min⁻¹), tidal volume (V_T, L), breathing frequency (F_R, breaths·min⁻¹), using a metabolic system (Cortex).
 - 2) End-tidal CO₂ (P_{ET}CO₂, mmHg), using a capnograph (Orion)
 - 3) Arterial O₂ saturation levels (SaO₂, %), using a pulse oximeter (Nellcor).
- Gr1: 3 HVR tests on a single day, separated by 60 min, and repeated on 3 separate days (n = 9, five males and four females).
- Gr2: 3 identical HVR tests on each of 3 different days (n = 6, 2 males and 4 females).
- HVR, calculated as the $\Delta V_E \cdot \Delta SaO_2^{-1}$ (L · min⁻¹ · %⁻¹) using mean values from the last 30 s of each hypoxic period, and from the last 30 s from the normoxic period preceding that.

4) Results

- In a single test, V_E decreased with repeated hypoxic exposures (P < 0.05, repeated measures ANOVA) suggesting a mild degree of hypoxic ventilatory depression (HVD).
- There were no changes in HVR measured on the same day, or between days (P > 0.3, repeated measures ANOVA).
- The coefficient of variation (CV, SD divided by the mean) was 22-38% and 21-33% within and between days, respectively.
- The mean CV was 27%.

Figure 2.

A) Minute ventilation (V_E)
B) O₂ saturation (%) and
C) end-tidal CO₂ (P_{ET}CO₂)
for a complete HVR test
for a single subject.
This clearly indicates
hyperpnea (A) during
eucapnic (B) hypoxia (C).



5) Discussion & Conclusions

Our main findings were:

1. The V_E changed significantly with repeated short-term exposure to hypoxia over a 30-minute period, suggesting HVD.
2. The within and between day variability did not differ.
3. The variability in the HVR response amounted to approximately 27% between tests.
4. The high variability necessitates that **REPEATED TESTS** be performed for estimation of the HVR, to ensure variability falls within the known range.
5. The conclusions of existing population comparisons using single measurements (e.g. 3) may have to be re-evaluated.

6) References

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