



Effect of oral contraceptive pill phase on carotid body chemosensitivity

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BACKGROUND

- Patients with sleep apnea experience periods of low oxygen (hypoxia) during sleep.
- The carotid body chemoreflex promotes an increase in breathing in response to low oxygen (hypoxic ventilatory response).
- Sleep apnea is more prevalent in young men than young women.
- An impact of female sex hormones on chemoreceptor sensitivity to low oxygen has been postulated to explain sex differences in the prevalence of sleep apnea.
- However, the effect of sex hormones on the hypoxic ventilatory response remains unclear.

AIM

We sought to examine the impact of changes in exogenous estradiol and progesterone on carotid body chemosensitivity to hypoxia.

HYPOTHESES

We hypothesized the hypoxic ventilatory response would be greater during the active pill (AP) phase of oral contraceptive use when compared to the placebo pill (PP) phase.

METHODS

- **Participants:** 10 healthy women (24 ± 1 yrs, 21 ± 1 kg/m²). Women were studied twice, once during the placebo pill phase (PP) of oral hormonal contraceptive use and once during the active pill phase (AP).

- **Instrumentation:** Participants were instrumented with a mask connected to a non-rebreathing value for measures of tidal volume (pneumotach), a respiratory belt (breathing rate), and finger pulse oximeter (oxygen saturation, S_pO_2).



Figure 1: Experimental set-up. Participants wore a mask connected to a non-rebreathing valve and were instrumented for measures of heart rate, blood pressure.

METHODS

- **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 is reported as the slope of the relationship between arterial oxygen saturation (SpO_2 , %) and ventilation (L/min).

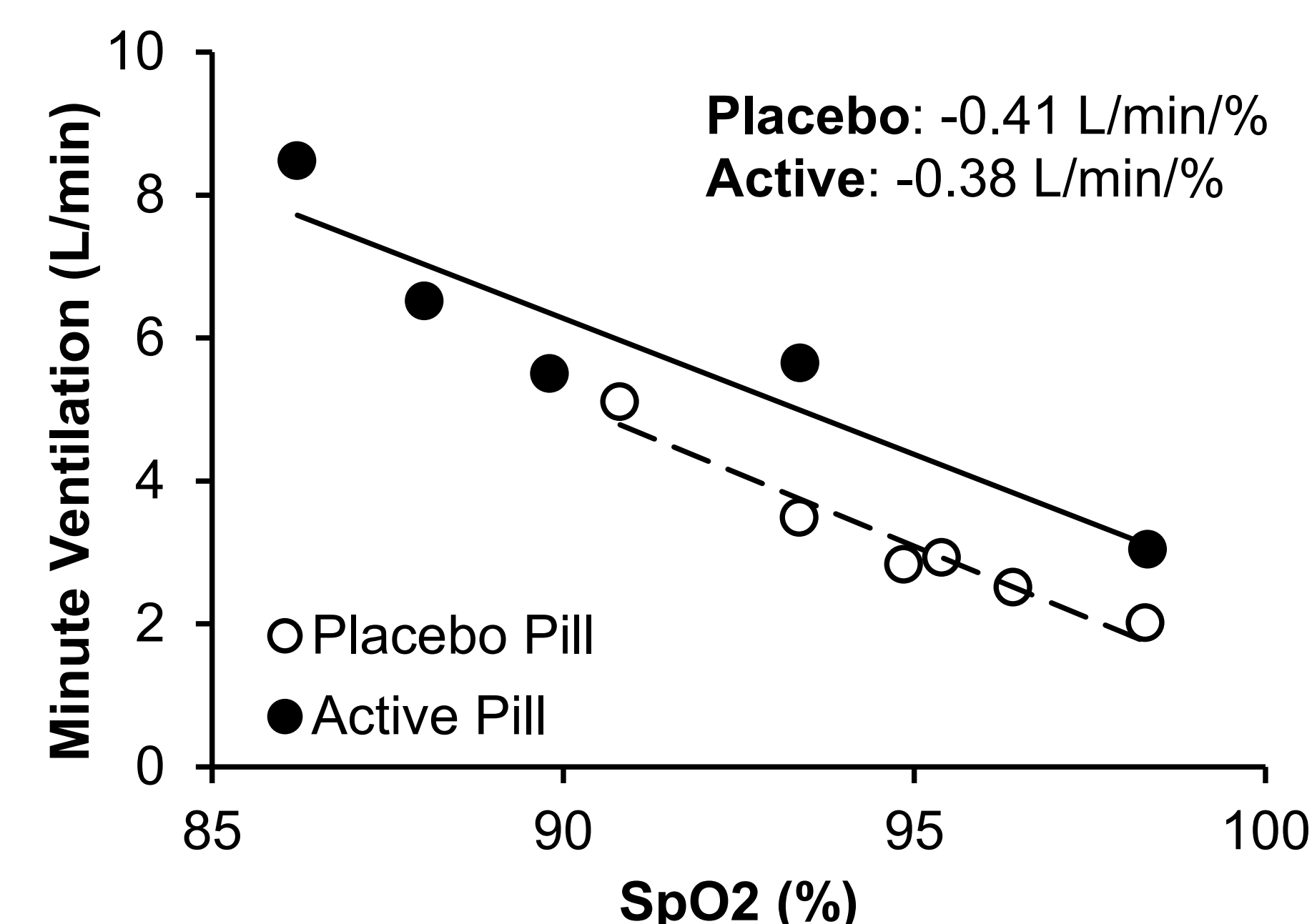


Figure 2: Hypoxic Ventilatory Response Analysis.

DEMOGRAPHICS

Variable (n=10)	Placebo Pill	Active Pill
Age (yrs)	24 \pm 1	
Height (cm)	164 \pm 2	
Weight (kg)	56 \pm 2	
Body Mass Index (kg/m ²)	21 \pm 1	
Study day (cycle day #)	5 \pm 1	17 \pm 1
Ethinylestradiol (pg/mL)	57 \pm 34	110 \pm 42
Estradiol (pg/mL)	37 \pm 5	18 \pm 2
Progesterone (ng/mL)	0.53 \pm 0.02	0.53 \pm 0.02
Testosterone (ng/dL)	36 \pm 6	28 \pm 4

Table 1: Participant demographics. Data are reported as Mean \pm SEM from women (n=10) during the placebo pill (PP) and active pill (AP) phase of oral contraceptive use. Ethinylestradiol (n=8), Estradiol (n=9), Progesterone (n=9), Testosterone (n=7).

Brand Name	EE (mg)	PG (mg)	Count
Sprintec	0.035	0.25 norgestimate	2
Enskyce	0.030	0.15 desogestrel	2
Estarylla/Femynor	0.025	0.25 norgestimate	3
Loryna/Gianvi	0.020	3.00 drospirenone	1
Mircette	0.020	0.15 desogestrel	1
Aviane/Falmina	0.020	0.10 levonorgestrel	1

Table 2: Oral hormonal contraceptives. Women were prescribed and actively taking a monophasic daily oral hormonal contraceptive pill (generations 2-4). Brands and pill formulations are reported. EE (ethinylestradiol), PG (synthetic progesterone).

RESULTS

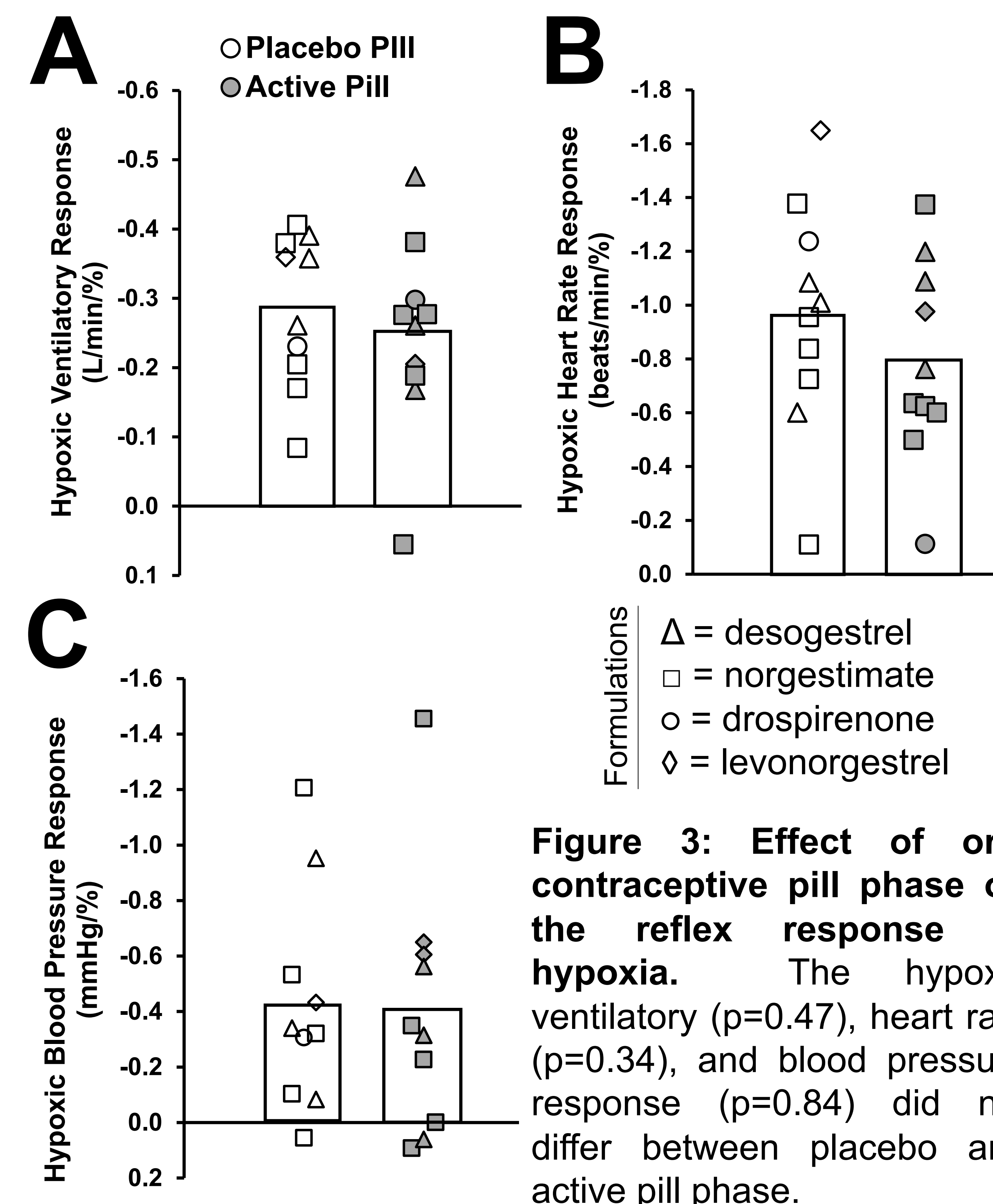


Figure 3: Effect of oral contraceptive pill phase on the reflex response to hypoxia. The hypoxic ventilatory ($p=0.47$), heart rate ($p=0.34$), and blood pressure response ($p=0.84$) did not differ between placebo and active pill phase.

CONCLUSIONS

- Contrary to our hypothesis, the hypoxic ventilatory response (a measure of carotid body chemosensitivity, **Figure 3A**) did not differ between the placebo pill and active pill phases of oral contraceptive use in the women studied.
- These data suggest there is no observable effect of changes in synthetic female sex hormones (ethinylestradiol, norgestimate) on the ventilatory response to hypoxia in healthy young women.
- Future studies examining the effects of different synthetic progesterone formulations and concentrations on carotid body chemosensitivity are warranted.

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