Title: SLEEP DEPRIVATION ATTENUATES HYPERCAPNIC VENTILATORY RESPONSE IN MAN

Authors: Ochiai R., Motoyama E.K., Winter P.M., Walczak S.A.

Affiliation: Departments of Anesthesiology/Critical Care Medicine and Pediatrics, University of Pittsburgh and Children's Hospital of Pittsburgh, Pittsburgh, PA 15213

INTRODUCTION: Sleep deprivation is often associated with psychological and medical disorders. In particular, critically ill patients in the intensive care unit (ICU) are often chronically sleep deprived. Our previous study (1) clearly demonstrated that one night of sleep deprivation dramatically depressed the ventilatory response to hypoxia in healthy male volunteers and that such respiratory depression is likely due to reduced central inspiratory drive. We evaluated the effect of sleep deprivation on the hypercapnic ventilatory response in the same volunteers and compared these data with our data on the hypoxic response (1).

METHODS AND SUBJECTS: With the approval of the IRB and written consent, we studied seven male volunteers, aged 28 to 32 yr, without known cardiovascular or sleep disorders. Each subject was studied twice, once after normal sleep (control) and once after one night of total sleep deprivation. The subjects were studied in the morning without breakfast or any caffeine-containing beverage in the preceding 12 h. The pulmonary function test (PFT), including forced vital capacity (FVC), maximum voluntary ventilation (MVV), and maximum inspiratory and expiratory pressure against mouth occlusion (PIP and PEP), was performed first to rule out respiratory muscle fatigue. The hypercapnic ventilatory response was studied using the rebreathing technique of Read (2). The rebreathing bag was filled with 7% CO_2 and balanced O_2. The initial volume of gas mixture was one liter above the subject's vital capacity. The subject rebreathed through a mouthpiece while lying on a reclining chair. The measurement continued as end-tidal CO_2 ($P_{ET}CO_2$) increased gradually by CO_2 rebreathing until it reached 60 mmHg in 7 to 10 min. The signals of the air flow at the mouth, end-tidal O_2 and CO_2 concentration, oxygen saturation by means of pulse oximetry, and inductive plethysmography were processed by an A/D converter and a computer system. Mouth occlusion pressure 100 ms after the onset of inspiratory effort (P0.1) was measured intermittently throughout the study. From the data we calculated inspiratory minute ventilation ($\dot{V}_I$), tidal volume (V_T), respiratory frequency (f), mean inspiratory flow (V_T/T_I), inspiratory duty cycle (T_I/T_{TOT}), and mouth occlusion pressure ($P_{0.1}$) as well as $P_{ET}CO_2$ and O_2. The linear regression of each respiratory parameter was calculated using the least squares method in relation to the unit change in $P_{ET}CO_2$ (mmHg). Statistical analysis was performed by t-test; $p < 0.05$ was considered significant.

RESULTS: $\dot{V}_I$ increased significantly in response to hypercapnia in both control and sleep-deprived states (758 ± 47 and 697 ± 52 ml/kg/min at $P_{ET}CO_2$ = 60 mmHg, respectively), but there was no significant difference between the 2 conditions. V_T, f, V_T/T_I, and $P_{0.1}$ also increased in response to hypercapnia, but were not significantly different between the 2 conditions. T_I/T_{TOT} did not change significantly. When the slope of each ventilatory parameter was calculated against $P_{ET}CO_2$, the slope of $\dot{V}_I$ after sleep deprivation was significantly reduced (-24%, $p < 0.05$, Table 1). Although the reduction was less than that for hypoxic ventilatory response, a similar reduction occurred in the slope of V_T/T_I and $P_{0.1}$ (-24 and -18%, respectively, $p < 0.05$). The PFT, including FVC, MVV, PIP, and PEP, showed no significant difference between the 2 conditions.

DISCUSSION: As the response to hypoxia, the ventilatory response to hypercapnia was significantly decreased after sleep deprivation in terms of the slope against $P_{ET}CO_2$. The degree of decrease (-24%), however, was much less than that for the hypoxic response (-48%) (1). The slopes of V_T/T_I and $P_{0.1}$, which represent central inspiratory drive (3), showed a similar degree of reduction (-24 and -18%, respectively, after sleep deprivation, $p < 0.05$). The fact that these two respiratory parameters correlated well with $\dot{V}_I$ suggests that the reduction in ventilatory response is due to a reduction in central drive. Further studies are needed to elucidate the possible contribution of carotid bodies to the observed blunting of hypoxic and hypercapnic response. Furthermore, since the pulmonary function tests showed no significant change, such respiratory depression is not due to respiratory muscle fatigue. The observed attenuation of CO_2 response may be of clinical importance since patients being weaned from mechanical ventilation in the ICU are often sleep-deprived, and thus their ability to breathe adequately is further compromised.

Table 1. Hypercapnic Ventilatory Response (n=7)

	CONTROL	SLEEP-DEPRIVED
$\dot{V}_I$ (ml/kg/min/mmHg)	48.81 ± 6.67	37.27 ± 3.51*
V_T (ml/kg/mmHg)	1.25 ± 0.90	0.90 ± 0.14
f (/min/mmHg)	0.95 ± 0.25	0.73 ± 0.17*
V_T/T_I (ml/kg/s/mmHg)	1.66 ± 0.20	1.26 ± 0.27*
$P_{0.1}$ (cmH2O/mmHg)	0.62 ± 0.18	0.51 ± 0.14

*$p < 0.05$ compared with control.

REFERENCES:
1. Ochiai R, Motoyama EK, Schertz CW, et al: Sleep deprivation attenuates hypoxic ventilatory response. Anesthesiology 65: A491, 1986
2. Read DJ: A clinical method for assessing the ventilatory response to carbon dioxide. Australas Ann Med 16(1): 20-32, 1967
3. Milic-Emili J, Grunstein MM: Drive and timing components of ventilation. Chest 70(Suppl):131-133, 1976.