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Chest distortion sleep state
CO_2

Effect of Sleep State on Chest Distortion and on the Ventilatory Response to CO_2 in Neonates

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Summary

The authors studied 10 preterm infants (birth weight, 1840 ± 270 g; gestational age, 31 ± 3 wk) and 10 term infants (birth weight, 3700 ± 320 g; gestational age, 40 ± 1 wk) to evaluate the effect of sleep state on chest distortion and on the ventilatory response to CO_2. Sleep state was defined on the basis of body movements, eye movements, and electroencephalogram. Chest distortion was assessed using micromagnetometers applied to the rib cage and abdomen. After a control period breathing 21% O_2 in each sleep state, infants were given 3% CO_2 to breathe. Respiratory minute volume and frequency, tidal volume, alveolar PCO_2 and PO_2, CO_2 response curves, and chest distortion were measured. It was found that: 1) respiratory minute volume increased and $PaCO_2$ decreased during REM as compared to non-REM sleep in preterm and term infants ($P < 0.05$); 2) chest distortion was not affected by sleep state, but was more frequent in preterm than in term infants ($P < 0.02$); 3) the ventilatory response to CO_2 was not affected by sleep state ($P > 0.4$); and 4) CO_2 did not affect chest distortion ($P > 0.1$). These findings indicate: 1) contrary to previous observations, chest distortion is independent of sleep state; and 2) the ventilatory response to CO_2 was not affected by sleep state. The authors suggest that the higher prevalence of chest distortion in preterm infants is related to their highly compliant chest wall rather than to differences in sleep state.

Speculation

Teleologically, almost anything increases with gestational age. Chest stability, non-REM sleep, ventilatory response to CO_2, and prevalence of regular breathing, all increase with maturation. The authors would like to speculate, therefore, that the differences in chest distortion are immaturity rather than sleep state dependent. The authors believe that distortion is present not only because the rib cage muscles are weak or chest wall reflexes inefficient, but also because the bone structure of the rib cage is highly cartilagenous and cannot afford stability.

It has long been known that the respirator pattern is more regular during non-REM than during REM sleep. Only recently, however, the physiologic differences between these two sleep states have been more thoroughly investigated (2, 4, 5, 7, 8, 14, 16, 19, 20). In this regard, two provocative observations were made. First, it was suggested that the clinical "see-saw" breathing of preterm and, less frequently, term infants, with indrawing of the rib cage and outward displacement of the abdomen, is characteristic of REM sleep (17). This paradoxical movement of rib cage and abdomen has also been named "chest distortion," because the rib cage moves inwards instead of outwards during inspiration. Second, the ventilatory response to CO_2 was decreased during REM as compared to non-REM sleep in adult dogs (19). The issue became controversial, however, when one study in newborn primates showed similar (13) and another in newborn infants showed a decreased (6) response to CO_2 during REM sleep. Because chest distortion seems to be associated with increased work of breathing (11), it was hypothesized that REM sleep might decrease the ventilatory response to CO_2, if chest distortion is indeed present during REM sleep only. This study was designed, therefore, to define the effect of sleep state on chest distortion and on the ventilatory response to CO_2.

SUBJECTS AND METHODS

SUBJECTS

Ten healthy preterm infants were studied (birth weight, 1840 ± 270 g; gestation age, 31 ± 3 wk) and 10 term infants (birth weight, 3700 ± 320 g; gestational age, 40 ± 1 wk). Postnatal ages were 21 ± 15 and 3 ± 2 days, respectively. In preterm infants, there were 8 females and 2 males; in term infants, 2 females and 7 males.

METHODS

The system to measure ventilation has been described previously (22, 23, 25). Briefly the infant breathed through nostril adaptors of a nosepiece and added (expiration) or subtracted (inspiration) flow from a constant background flow. The flow signal was integrated to give volume.

We monitored breath-to-breath PO_2 and PCO_2 using a catheter (PE-20) connected to a vacuum pump (Welch Scientific Co., Duo Seal, Model 1400). The 95% rise time of the CO_2 analyzer (Beckman LB-2) was 0.14 sec and that of the O_2 analyzer (Beckman OM-11) was 0.18 sec. To obtain appropriate O_2 concentration (in this study 21% O_2), O_2 and N_2 were mixed in a low flow blender (Bird Corp., Model 9992901). This mixture was then fed into a second blender where 3% CO_2 could be added (25).

Chest distortion was measured using magnetometers applied to the rib cage and abdomen (17). The exciter coils were placed in the midline at the level of the fourth intercostal space and just above the umbilicus, with the receiving coils placed directly opposite on the posterior surface. The signal voltage was linear for the distance ranges being studied. Sleep state was monitored according to standardized methods (21). EEG was monitored with electrodes placed in the C_4-A_1 position (21). The EOG was recorded from the upper outer canthus of the left eye and the lower outer canthus of the right eye and referred to the left ear lobe. Non-REM and REM sleep were characterized according to previous recommendation (10). Respiratory pattern was not used as one of the criterion. The rationale for this is that it makes no sense to ask what the respiratory behavior is during the two types of sleep state if such behavior is used to define sleep state. Accordingly, non-REM sleep was defined by occasional slow body movements, no eye movements, and "tracé alternant" on EEG. REM sleep was defined by the presence of jerky movements of the body, eye movements detected visually and on record (EOG) and irregular lower voltage on EEG.

PROCEDURE

Infants were studied on the Ohio Neonatal Intensive Care Unit in a neutral thermal environment (skin abdominal temperature was 36.5 ± 0.003°C). After appropriate placement of the EEG, EKG, and EOG electrodes and magnetometers, infants were allowed to breathe 21% O_2 for 3–5 min in each sleep state. They were then given 3% CO_2 to breathe for 5 min. During administration of CO_2, PaO_2 was kept within ± 5 mm Hg of control O_2 breathing. A representative tracing is shown in Figure 1.

ANALYSIS

Respiratory minute volume and frequency, tidal volume, alveolar PCO_2 and PO_2, and chest distortion during the two sleep states, before and after administration of CO_2, were determined. Measurements were made between 3 and 5 min while the infant was breathing 21% O_2 or 21% O_2 + 3% CO_2, in a particular sleep state. Maximal response to CO_2 was always obtained by 3 min, corroborating our previous observations (23, 24). The CO_2 response curve was calculated from minute ventilation and $PaCO_2$ while the infant was breathing 21% O_2 and while breathing 21% O_2 + 3% CO_2.

The paired *t*-test was used to characterize the significance of the difference between non-REM vs. REM sleep in the same infants. The χ^2 analysis was used to assess the significance of the differences in the prevalence of chest distortion in preterm vs. term infants.

RESULTS

Our findings are shown in Tables 1 and 2. Respiratory minute volume increased and $PaCO_2$ decreased when preterm and term infants switched from non-REM to REM sleep ($P < 0.05$). This means that alveolar ventilation increased during REM sleep. The changes in ventilation were predominantly due to changes in respiratory frequency with little change in tidal volume.

Sleep state did not affect the prevalence of chest distortion ($P > 0.1$), but gestational age did ($P < 0.02$). Preterm infants distorted more frequently than term infants. In preterm infants, chest distortion was observed in 7 of 10 and in 9 of 10 infants during non-REM and REM sleep, respectively ($P > 0.1$). In term infants, 2 of 10 and 4 of 10 showed chest distortion during non-REM and REM sleep, respectively ($P > 0.1$). This prevalence of distortion did not change with CO_2 administration ($P > 0.1$, Fig. 2). Also, the administration of CO_2, within the limits outlined in this study, did not affect sleep state.

The slope of the ventilatory response to CO_2 was not different during non-REM and REM sleep, both in preterm and term infants ($P > 0.4$, Figs. 3 and 4). The intercept, however, was shifted to the left during REM sleep ($P < 0.005$). In preterm infants, slopes were 0.050 ± 0.009 and 0.039 ± 0.007 liter/min/kg/mm Hg $PaCO_2$, the corresponding intercepts being 40 ± 2 and 35 ± 1 mm Hg $PaCO_2$, during the non-REM and REM sleep, respectively. In term infants, slopes were 0.045 ± 0.011 and 0.038 ± 0.007 liter/min/kg/mm Hg $PaCO_2$, the corresponding intercepts being 39 ± 1 and 37 ± 1 mm Hg $PaCO_2$ during the non-REM and REM sleep, respectively.

DISCUSSION

It was found that, 1) sleep state did not affect chest distortion or the ventilatory response to CO_2, and 2) administration of CO_2 did not change sleep state or the prevalence of chest distortion. Because chest distortion was more frequent in preterm than in

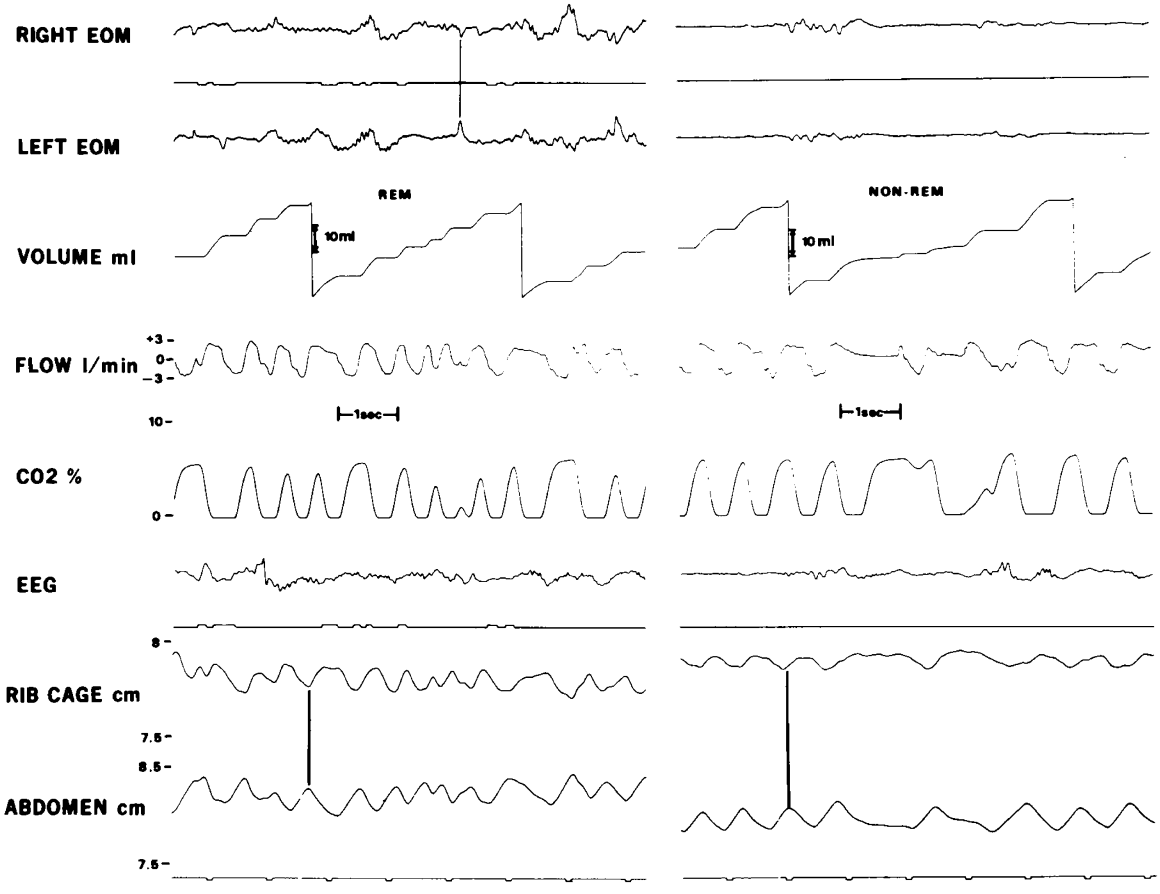

Fig. 1. Representative tracing in one preterm infant (No. 4, birth wt, 1460 g; gestational age, 28 wk) during REM and non-REM sleep. Note that chest distortion, *i.e.*, paradoxical movements of rib cage and abdomen, is present during both sleep states.

Table 1. *Physiological measurements in preterm infants during non-REM and REM sleep*

				Non-REM												REM											
Infants	Gestational age (wk)	Birth wt (g)	Age (days)	$\dot{V}_E$ (liter/min/kg)		Frequency (breaths/min)		V_T (ml/kg)		$PaCO_2$ (mm Hg)		Chest distortion		Slope liter/(min kg·mm Hg)	Intercept mm Hg[1]	$\dot{V}_E$ (liter/min/kg)		Frequency (breaths/min)		V_T (ml/kg)		$PaCO_2$ (mm Hg)[2]		Chest distortion		Slope liter/(min kg·mm Hg)	Intercept mm Hg[1]
				Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2			Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2			
1	29	1610	18	0.298	0.523	30	34	9.9	15.4	44	46	–	–	0.113	44	0.355	0.487	31	43	11.5	11.3	39	44	–	–	0.026	37
2	32	1930	15	0.272	0.496	43	50	6.3	9.9	35	40	+	+	0.045	36	0.348	0.732	65	83	5.4	8.8	31	36	+	+	0.077	30
3	28	2110	59	0.311	0.514	56	92	5.6	5.6	46	50	+	+	0.051	46	0.364	0.450	72	61	5.1	7.4	44	46	+	+	0.043	43
4	28	1460	36	0.320	0.527	49	60	6.5	8.8	44	48	+	+	0.052	44	0.455	0.680	85	69	5.4	9.9	41	45	+	+	0.056	38
5	35	1630	13	0.337	0.513	58	49	5.8	10.5	38	42	+	–	0.044	37	0.364	0.670	49	64	7.4	10.5	36	41	+	–	0.061	35
6	30	1940	19	0.285	0.442	35	53	8.1	8.3	39	41	+	+	0.079	39	0.370	0.547	48	62	7.7	8.8	35	40	+	+	0.035	33
7	33	2130	13	0.376	0.495	70	65	5.4	7.6	34	38	–	–	0.030	32	0.417	0.582	72	78	5.8	7.5	33	37	+	+	0.041	30
8	33	1810	11	0.304	0.401	42	43	7.2	9.3	33	36	+	+	0.032	33	0.371	0.406	50	52	7.4	7.8	33	36	+	+	0.012	27
9	31	1560	8	0.222	0.313	33	44	6.7	7.1	41	55	+	+	0.007	53	0.229	0.285	38	43	6.0	6.6	41	46	+	+	0.011	48
10	35	2250	21	0.358	0.451	71	58	5.0	7.8	36	38	–	–	0.047	35	0.321	0.447	39	49	8.2	9.1	34	39	+	+	0.025	33
Mean	31	1843	21	0.308	0.468	49	55	6.7	9.0	39	43			0.050	40	0.359[2]	0.529	55	60	7.0	8.8	37[2]	41			0.039	35[2]
± SE	1	86	5	0.014	0.022	5	5	0.5	0.8	1	2			0.009	2	0.019	0.044	6	4	0.6	0.5	1	1			0.007	1

[1] 0.3 liter/kg/min.

[2] $P < 0.05$ in relation to non-REM sleep.

Table 2. *Physiological measurements in term infants during non-REM and REM sleep*

				Non-REM												REM											
Infants	Gestational age (wk)	Birth wt (g)	Age (days)	$\dot{V}_E$ (liter/min/kg)		Frequency (breaths/min)		V_T (ml/kg)		$PaCO_2$ (mm Hg)		Chest distortion		Slope liter/(min kg·mm Hg)	Intercept (mm Hg)[1]	$\dot{V}_E$ (liter/min/kg)		Frequency (breaths/min)		V_T (ml/kg)		$PaCO_2$ (mm Hg)		Chest distortion		Slope liter/(min kg·mm Hg)	Intercept (mm Hg)[1]
		Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2	Control	CO_2
1	40	3230	1	0.201	0.295	33	35	6.1	8.4	34	36	–	–	0.047	35	0.247	0.297	41	33	6.0	9.0	33	36	–	–	0.017	36
2	40	3320	2	0.150	0.197	38	40	3.9	4.9	34	36	–	–	0.024	40	0.225	0.375	51	47	4.4	8.0	32	36	–	–	0.038	34
3	40	5020	4	0.138	0.257	45	47	3.1	5.5	41	43	+	+	0.060	44	0.198	0.341	46	54	4.3	6.3	40	43	+	+	0.048	42
4	40	3530	7	0.265	0.382	52	42	5.1	9.1	39	43	–	–	0.029	40	0.346	0.459	66	59	5.2	7.8	38	41	+	+	0.035	37
5	40	3490	3	0.250	0.355	53	45	4.7	7.9	36	41	–	–	0.021	39	0.260	0.376	49	51	5.3	7.4	36	41	–	+	0.023	37
6	42	3880	2	0.199	0.231	34	33	5.9	7.0	37	39	–	–	0.016	43	0.194	0.270	34	38	5.7	7.1	37	38	–	–	0.076	38
7	40	3910	3	0.235	0.489	37	51	6.4	9.6	34	36	–	–	0.127	35	0.353	0.507	63	63	5.6	8.0	31	34	–	–	0.051	30
8	42	3890	5	0.158	0.244	31	28	5.1	8.7	38	40	–	–	0.043	41	0.180	0.237	38	34	4.7	7.0	36	39	+	+	0.019	42
9	39	3670	3	0.223	0.356	48	47	4.6	7.6	35	37	+	+	0.067	36	0.294	0.358	74	64	4.0	5.6	36	37	+	+	0.064	36
10	38	3660	1	0.220	0.247	57	46	3.9	5.4	33	35	–	–	0.014	39	0.289	0.329	61	46	4.7	7.2	33	37	–	–	0.010	34
Mean	40	3760	3	0.204	0.305	43	41	4.9	7.4	36	39			0.045	39	0.259[2]	0.355	52[2]	49	5.0	7.3	35[2]	38			0.038	37[2]
± SE	0.4	158	1	0.014	0.028	3	2	0.3	0.5	1	1			0.011	1	0.019	0.026	4	4	0.2	0.3	1	1			0.007	1

[1] 0.3 liter/kg/min.

[2] $P < 0.05$ in relation to non-REM sleep.

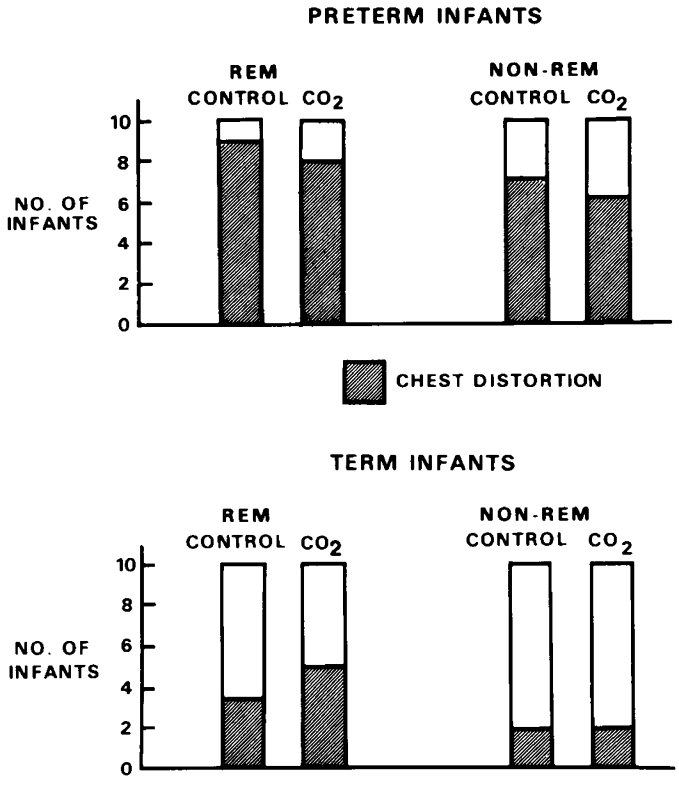

Fig. 2. Effect of CO_2 on chest distortion during REM and non-REM sleep in preterm and term infants. The *shaded area* represents the number of infants with chest distortion. There is no difference in the prevalence of chest distortion before and during administration of CO_2 in both sleep states. Note, however, that the prevalence of chest distortion is significantly higher in preterm than in term infants.

term infants, it was speculated that this was due to the highly compliant chest wall of these small infants rather than to sleep state.

These findings are contrary to previous observations that chest distortion is characteristic of REM sleep (17). They are more in agreement with data showing respiration in or out of phase in REM sleep (9). In some babies, sleep was tediously monitored as the infant switched from one state to the other on numerous occasions and a change could not be detected in the prevalence or magnitude of chest distortion. It is difficult, therefore, to reconcile these observations with those obtained previously (17). The clinical evidence that small babies breathe in a see-saw manner, and that this is not so frequent in term infants, lends support to the view that chest distortion is an attribute of the highly cartilagenous rib cage of preterm infants. Indeed, what is the diaphragm holding to in these infants, if not to a very pliable bone structure? Observations that static pulmonary compliance practically equals total static chest compliance is another evidence that rib cage serves the preterm little in terms of mechanical stability of the chest (1, 3). It is not surprising, therefore, that paradoxical movements of rib cage and abdomen are very common in preterm infants. The authors believe the immature structure of the rib cage as well as incompetence of chest wall musculature and reflexes are responsible for this.

Criticisms might be raised that preterm infants breathe only in REM sleep and, therefore, changes during non-REM sleep would be difficult to define. The authors had no such experience. It was found that hours of patient and careful monitoring of these infants in the research laboratory clearly demonstrated that these infants are not in REM sleep only. They are frequently in non-REM sleep and not unusually in perfectly quiet sleep (15, 21). These observations agree with previous sleep state studies (10, 15). Even supposing that such babies were in REM sleep state only, it would still be necessary to justify why term infants, who show clear epochs of non-REM and REM sleep, do not present a change in prevalence of chest distortion during both sleep states.

These findings of similar ventilatory response to CO_2 during non-REM and REM sleep agree with observations made in newborn primates (12). They disagree, however, with observations in dogs (19) and in human neonates (6), which showed a decreased ventilatory response to CO_2 during REM sleep. The reason for the discrepancies is not clear. It might be that there is not much to compare between an adult dog and a preterm human neonate, but the findings of Bryan *et al.* (6) cannot certainly be explained. If analog models of the respiratory control system were taken as designed by physicists and bioengineers, a slightly oscillating respiratory system during REM sleep to respond more to CO_2 than a nonoscillatory system (12, 18) would be expected. It is difficult, therefore, to reconcile these differences at the present time and this subject needs further clarification.

In summary, these observations suggest that sleep state does not affect the prevalence of chest distortion or the ventilatory response to CO_2. Increased prevalence of chest distortion in preterm as opposed to term infants may be better explained on the basis of highly immature and cartilagenous structure of the rib cage, as well as incompetence of chest wall muscles and reflexes.

CONCLUSION

In 10 preterm and 10 term infants, the effect of sleep state on chest distortion and on the ventilatory response to CO_2 was assessed. It was found that chest distortion and ventilatory response to CO_2 were independent of sleep state. Chest distortion, however, was more frequent in preterm than in term infants. The authors suggest that the increased prevalence of chest distortion in preterm infants is related to their highly compliant chest wall rather than to differences in sleep state.

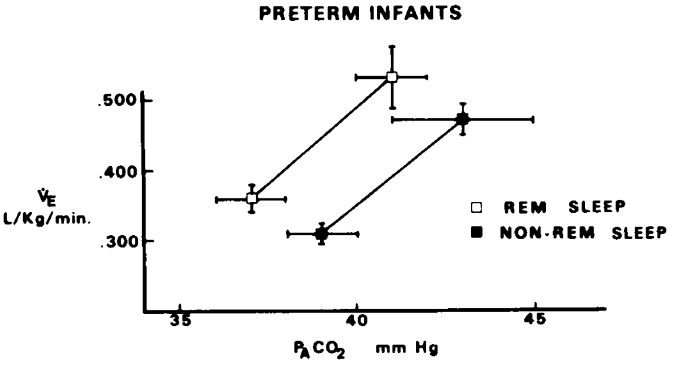

Fig. 3. Ventilatory response to CO_2 in preterm infants during REM and non-REM sleep. There is no difference in slopes, but the intercept was shifted to the left during REM sleep.

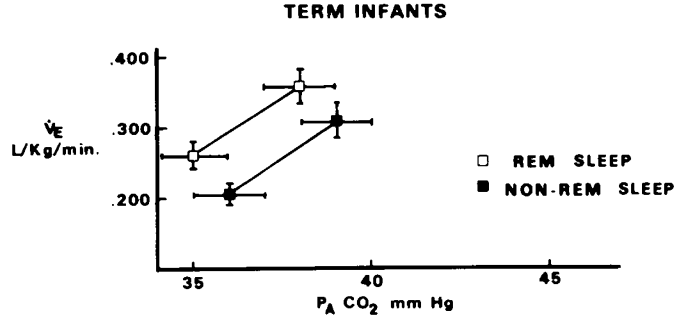

Fig. 4. Ventilatory response to CO_2 in term infants during REM and non-REM sleep. There is no difference in slopes, but the intercept was significantly shifted to the left during REM sleep.

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