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Effects of CO_2 and N_2 partial pressures on cognitive and psychomotor performance

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Fothergill DM, Hedges D, Morrison JB. Effects of CO_2 and N_2 partial pressures on cognitive and psychomotor performance. Undersea Biomed Res 1991; 18(1):1–19.—This study examined N_2 and CO_2 components of narcosis by comparing the effects of three levels of $P_{ET_{CO_2}}$ [low = 29 mmHg (SD = 4 mmHg), medium = 47 mmHg (SD = 1 mmHg), high = 57 mmHg (SD = 2 mmHg)] at 1 and 6 atm abs in 12 male volunteers. Cognitive and psychomotor performances were examined using a variety of tasks, including a modified Stroop test, an arithmetic test, number comparison, a figure copying test, and the Purdue pegboard test. Performance on all tasks demonstrated significant ($P < 0.05$) decrements at 6 atm abs. High CO_2 tensions significantly impaired cognitive and psychomotor performance at 1 atm abs and caused further decrements at 6 atm abs ($P < 0.05$). However, no significant N_2-CO_2 interaction ($P > 0.05$) or global threshold for the onset of CO_2 narcosis was indicated by the test scores. The pattern of intratest results were different for N_2 and CO_2. At high $P_{ET_{CO_2}}$, performance deficits were due to a slowing of performance rather than a disruption of the accuracy of processing. Nitrogen narcosis, conversely, produced significant impairment through both decreases in the speed and accuracy of processing on the majority of performance tests. It was concluded that within the $P_{ET_{CO_2}}$ ranges studied: a) $P_{ET_{CO_2}}$ and P_{IN_2} are additive in their effects on impaired cognitive and psyhomotor performance at depth; b) high $P_{ET_{CO_2}}$ and $P_{I_{N_2}}$ induce distinctly different strategic responses on the speed accuracy trade-off function of the performance tests; c) decrements in cognitive and psychomotor performance under high $P_{ET_{CO_2}}$ do not conform to the predicted narcotic potency of CO_2 according to the lipid solubility theory of narcosis.

carbon dioxide, hypercapnia, narcosis, performance, diving

The influence of high partial pressures of carbon dioxide (P_{CO_2}) on diving performance and safety was identified some time ago. In 1939, Behnke and Willmon (1) observed mental disturbances in divers working at 8.3 atm abs (240 fsw) during the salvage of the U.S.S. *Squalus*. These authors reported that the symptoms were of unusually high intensity and concluded that, at this depth, the accumulation of CO_2 in the divers' helmets may have augmented the narcotic action of nitrogen.

Case and Haldane (2) confirmed this observation during an experiment in which subjects were exposed to an inspired P_{CO_2} of 30–45 mmHg at 10 atm abs in a hyperbaric chamber. Initially, individual symptoms of confusion, distress, impending syncope, euphoria, and elation were experienced by their subjects when breathing air at 8.5 and 10 atm abs. These symptoms became more severe when CO_2 was added to the air at 10 atm abs, resulting in a significant decrement in manual dexterity and an increase of 46% in the mean percentage of mistakes on an arithmetic task.

More recently, underwater gas sampling techniques have provided evidence of CO_2 accumulation in working divers (3, 4), and end-tidal CO_2 partial pressures ($P_{ET_{CO_2}}$) above 70 mmHg have been recorded in experimental dives (5–7).

At these CO_2 tensions the resulting narcosis may seriously jeopardize the divers' safety. Case and Haldane (2) noted that the majority of their subjects lost consciousness within 5 min when the inspired P_{CO_2} was raised to 68 mmHg at 10 atm abs. Loss of consciousness may, however, be precipitated at lower atmospheric pressures by exercise-induced hypercapnia (6). Divers who exhibit a natural CO_2 retention during exercise at depth have been shown to be particularly at risk from the combined effects of hypercapnia and compressed air narcosis (8).

Although it is well recognized that high P_{CO_2} levels enhance the severity of narcosis, the underlying relationship between CO_2 intoxication and N_2 narcosis in terms of additive or synergistic effects is still unclear. Confusion in this area has been compounded by lack of consistency in the terminology used in the literature. In view of this, the terms additivity, synergy, and potentiation in this paper conform to the definitions suggested by Fowler et al. (9).

To date, several authors have quantitatively assessed the effects of hypercapnia on cognitive and psychomotor function in the hyperbaric environment (10–12). However, conclusions emanating from these studies have been based on a relatively small number of subjects completing a limited number of performance tests. From the evidence available, the CO_2 component of compressed air narcosis seems to be negligible at alveolar CO_2 pressures below 40 mmHg. Above this "threshold," N_2 narcosis and CO_2 intoxication have been shown to have additive effects on cognitive and motor efficiency (10, 12) but synergistic effects on standing steadiness (11).

Because of the limited amount of quantitative data presently available in this area, further research is needed to provide a clearer understanding of the narcotic effects of CO_2. The objective of the current study was therefore to determine the role of CO_2 in compressed air narcosis by investigating behavioral responses under three levels of $P_{ET_{CO_2}}$ (induced by a rebreathing circuit) at surface pressure (1 atm abs) and at 6 atm abs. The relationship between the narcotic effects of N_2 and CO_2 was assessed using a variety of cognitive and psychomotor factors thought to be important for efficient performance in the hyperbaric environment.

MATERIALS AND METHODS

Subjects

Twelve healthy male volunteers (mean age = 25.6 ± 0.6 yr, mean body weight = 76.4 ± 0.7 kg) from the university population participated in this study. To obtain medical clearance for diving, in accordance with the Workers Compensation Board

of British Columbia, all subjects were required to complete a medical questionnaire and be examined by a physician. Candidates with current or a history of significant cardiorespiratory disease or other physical disorder which would contraindicate hyperbaric exposure were excluded from the study. All subjects received information packages and each signed an informed consent release.

Nine of the 12 subjects had previously experienced compressed air exposure in the hyperbaric chamber before volunteering for the present study. The remaining 3 subjects were provided with an extensive orientation of the hyperbaric chamber facilities, culminating in a test dive to 2 atm abs. Five of the subjects had previously been involved in studies using similar tests of cognitive and psychomotor function. All subjects were given sufficient practice on the tasks in the test battery to reach a learning plateau of performance before commencing the experimental trials.

Apparatus

All experiments were conducted in a dry hypo-hyperbaric chamber at the Environmental Physiological Unit of Simon Fraser University. This facility permitted simulation of the pressure effects of diving to be conducted within the relative safety of a controlled laboratory setting, thereby reducing some of the potential risks associated with hyperbaric exposure in open water.

A semiclosed respiratory circuit was designed to raise and maintain the subjects' PET_{CO_2} at the desired level for the duration of the experiment (Fig. 1). The respiratory

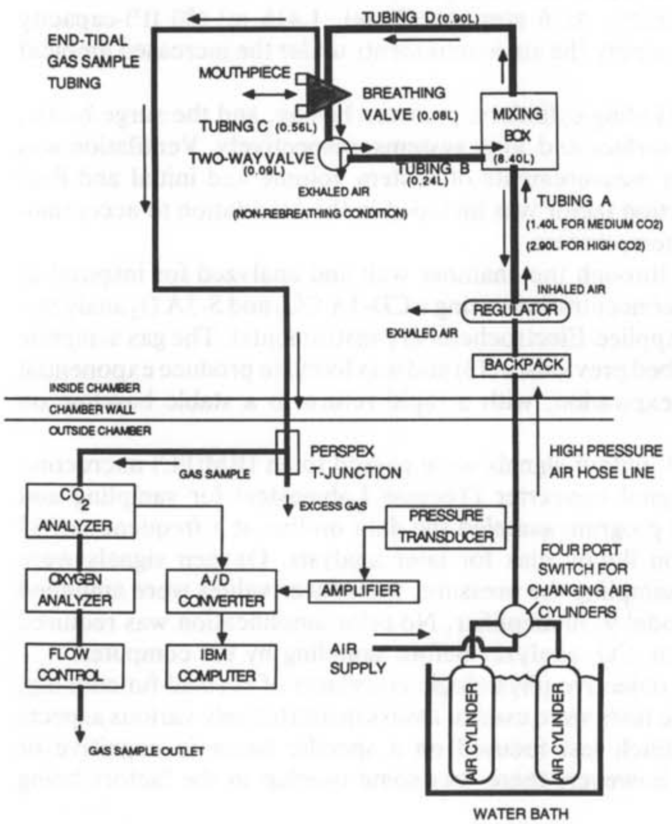

Fig. 1. Schematic diagram of the apparatus and instrumentation used during the experiments. Figures in brackets represent volumes in liters.

circuit consisted of lengths of 0.04-m diameter respiratory tubing, an 8.4-liter mixing box containing several baffles to mix inspired and expired gases, a two-way valve, a mouthpiece and breathing valve, and a Conshelf 30 (U.S. Divers) open circuit demand regulator connected to a high-pressure air supply. The subject inspired from the gas mixing box, whose contents were replenished through a length of respiratory tubing connected to the regulator. Expired gases were either vented to the chamber via a two-way valve in the exhalation line (for the low $P_{ET_{CO_2}}$ condition) or directed to the mixing box for rebreathing (for the medium and high $P_{ET_{CO_2}}$ conditions) with excess gas being vented from the mixing box via a relief valve.

The level of hypercapnia produced by this apparatus was modified by the introduction of appropriate lengths of 0.04-m diameter tubing in the subject's breathing circuit (i.e., extending or shortening the length of *tubing A* shown in Fig. 1). Pilot studies indicated that for the majority of subjects, the volume of tubing A required to induce $P_{ET_{CO_2}}$ values in the range of 45–50 and 55–60 mmHg was 1.4 and 2.9 liters, respectively.

Air supply to the subjects was provided from two calibrated gas cylinders located outside the chamber. At the end of each minute, subjects were switched from one cylinder to the next, with the cylinder pressures being recorded at the start and end of each minute [Celesco Transducer Production Inc., model PLD, ± 34.53 MPa (± 5000 psi)]. The cylinder not in use was refilled to a pressure of 13.8 MPa (2000 psi) from the reserve cylinder bank. Between the air cylinders and the subject was a small surge bottle to prevent transient pressure drops at the regulator while changing cylinders. For surface trials, 0.566 m^3 (20 ft^3)-capacity cylinders were used to enhance pressure measurement accuracy. At 6 atm abs (50 m), 1.416 m^3 (50 ft^3)-capacity cylinders were necessary to supply the air requirements under the increased ambient pressure.

Total system volumes, including cylinders, pressure hosing, and the surge bottle, were 3.68 and 7.85 liters for surface and 50-m systems, respectively. Ventilation was computed each minute from measurements of system volume and initial and final cylinder pressures. A correction factor was included in the calculation to accommodate for change in cylinder temperature.

Gas samples were drawn through the chamber wall and analyzed for inspired as well as end-tidal CO_2 and O_2 concentrations using a CD-3A CO_2 and S-3A O_2 analyzer, respectively (both Ametek Applied Electrochemistry instruments). The gas sampling arrangement has been described previously (13) and was found to produce exponential CO_2 growth curves during expiration, with a rapid return to a stable baseline on inspiration.

Cylinder pressure and CO_2 output signals were passed to an IBM(PC) microcomputer via an analogue-to-digital converter (Tecmar Labmaster) for sampling and storage. A custom-designed program sampled the data on-line at a frequency of 33 Hz and stored the values on floppy disk for later analysis. Oxygen signals were recorded manually. Before sampling the pressure, transducer values were amplified using a Daytronic LVDT model 9130 amplifier. No prior amplification was required for the analogue output of the CO_2 analyzer before sampling by the computer.

In the absence of reliable objective physiologic correlates of cortical functioning, paper-and-pencil psychologic tests were used to assess quantitatively various aspects of cognitive performance. Each test focused on a specific factor in cognitive or psychomotor performance; however, there was some overlap in the factors being

tested among the different tasks in the test battery. The individual tasks included in the test battery are described below:

Math test

The math test described by Hesser et al. (12) was used. The scores recorded were the number of problems attempted, the number correct, and the total number of errors for the 2-min time period allowed for this test.

Copying test

Each item consisted of a four-line geometric configuration and a square matrix of dots. The task was to copy the figure onto the dots. It is believed that this task requires flexibility of closure in the act of superimposing the particular configuration on a strong visual field (14). The subject was instructed to work as rapidly as possible without sacrificing accuracy. The score recorded was the number of correctly copied patterns, or portions of patterns, in a time period of 2 min. In addition, the number or portion of patterns attempted, as well as the errors, were recorded.

Number comparison test

In this test subjects inspected pairs of multidigit numbers and indicated whether the numbers in each pair were the same or different. The performance was scored on the number marked correctly, the number marked incorrectly, and the total number attempted in a time period of 45 s. This test primarily measures perceptual speed. It may be the centroid of several subfactors (including form discrimination) which can be separated but are more usefully treated as a single phenomenon for research purposes (14).

Letter cancellation test (modified Stroop test)

This test consisted of the words red or blue typed on a page, followed by 10 letters. The color name was underlined in either red or blue ink randomly. If the color word was underlined in the same colored ink then succeeding vowels were cancelled, otherwise consonants in the following 10 letters were cancelled. Overall performance on the test was calculated according to the number attempted, the number correct, and the number of errors within a time period of 1 min. This test has been regarded as a measure of stress sensitivity in decision making (15).

Purdue pegboard test

For this test subjects used both hands simultaneously. They assembled a series of pins, collars, and washers in the order of (for one assembly) a pin, a washer, a collar, and a washer. The score recorded was the number of individual parts assembled in 1 min. This test primarily measures fine manual dexterity (16).

Procedure

Ethical and medical approval was sought and informed consent obtained specifying the purpose and nature of the experiment and possible adverse effects.

Once selected, each subject participated in a block practice session (five practice trials) in the chamber at surface (1 atm abs) on the test battery described above. It was expected that this practice session would familiarize subjects with the protocol and provide a plateau of learning performance on the individual tests. In addition, throughout the study each subject was required to complete a practice test battery immediately before commencing each experimental condition.

After the practice trials, the subjects were split randomly into 2 groups of 6. Group 1 completed control trials at 1 atm abs, breathing normal air. Group 2 were compressed to 6 atm abs [at a compression rate of 18.3 msw · min^{-1} (60 fsw · min^{-1})] where they breathed hyperbaric air. In each group, every subject experienced three levels of end-tidal carbon dioxide ($P_{ET_{CO_2}}$), induced and regulated via the rebreathing circuit. After group 1 completed the 1 atm abs trials, they underwent the 6 atm abs condition, and vice versa for group 2. To minimize unwanted sequence effects between trials, administration of the three $P_{ET_{CO_2}}$ levels were counterbalanced across subjects according to a fully randomized and balanced design. Successive trials on the same subject were conducted no earlier than 24 h after the previous experiment.

The CO_2 concentrations breathed at each pressure level were regulated so that $P_{ET_{CO_2}}$ values fell within the ranges of 25–35 mmHg (mean = 29 mmHg, SD = 4 mmHg), 45–50 mmHg (mean = 47 mmHg, SD = 1 mmHg), and 55–60 mmHg (mean = 57 mmHg, SD = 2 mmHg). Using the above $P_{ET_{CO_2}}$ ranges, the upper time limit for breathing hypercapnic air was no more than 20 min during any one chamber run. Immediately before each experiment the gas analyzers were calibrated using primary standard gas containing known concentrations of CO_2 and O_2.

Once the required depth was reached, the subject rebreathed from the respiratory circuit for a minimum of 7 min. For most subjects this rebreathing time period was sufficient to reach the target $P_{ET_{CO_2}}$ range. Following this initial rebreathing period and upon reaching the desired $P_{ET_{CO_2}}$ level the first test of cognitive function was administered. The order in which the tests were presented was the same for each subject at each trial and followed the same order as described above.

Throughout each experimental trial $P_{ET_{CO_2}}$ levels were continuously monitored and the air supply cylinder switched every minute. If at any time during the experiment the subject's $P_{ET_{CO_2}}$ rose above the desired range, it was lowered by opening a two-way valve on the exhalation side of the rebreathing apparatus. This allowed exhaled concentrations of CO_2 to be vented to the chamber atmosphere, thus lowering the $P_{I_{CO_2}}$ in the respiratory circuit until the $P_{ET_{CO_2}}$ returned to the target range.

During the surface trials 100% O_2 was supplied to the mixing box at a flow rate of 0.5 liters · min^{-1}. This was done to prevent the inspired oxygen ($P_{I_{O_2}}$) dropping below normal levels during rebreathing. Inspired P_{O_2} was therefore maintained between 0.21 and 0.30 atm abs (mean = 0.25 atm abs), during experimental trials at surface. At 6 atm abs the increase in $P_{I_{O_2}}$ caused by the ambient pressure increase was considered sufficient to prevent hypoxic stress during rebreathing ($P_{I_{O_2}}$ at 6 atm abs = 1.26 atm abs). The $P_{I_{N_2}}$ difference between surface and 6 atm abs was 4 ± 0.05 atm abs under all experimental conditions.

Decompression for all dives was conducted according to the Canadian Forces Air Diving Tables and Procedures (DCIEM), February 1986 revision). Most dives were completed within a bottom time of 20 min, resulting in a total decompression time of 1 h.

Analysis

A comparison of cognitive and psychomotor performance differences between the three levels of $P_{ET_{CO_2}}$ at 1 and 6 atm abs and between the two levels of $P_{I_{N_2}}$ over the full range of hypercapnic conditions was conducted using two-way analysis of variance ANOVA with repeated measures. Following significant F statistics, post hoc multiple comparisons (using Tukey's honestly significant difference test) were used to isolate sources of significant difference (17). Where there was an insignificant interaction between N_2 and CO_2 the pooled data were used during subsequent post hoc analysis. A priori significance was set at the 0.05 level for all statistical tests.

RESULTS

Common symptoms of mild CO_2 toxicity, including frontal headache and slight dizziness, were reported following rebreathing experiments under the medium and high hypercapnic conditions. Subjectively, these symptoms were reported to be most severe following the highest hypercapnic level.

Respiratory responses to hypercapnia at 1 and 6 atm abs

Mean values and standard errors for respiratory responses to the three levels of $P_{ET_{CO_2}}$ at 1 and 6 atm abs are shown in Table 1. $P_{ET_{CO_2}}$ values in the non-rebreathing condition were very similar at surface and 6 atm abs. There was little difference (approximately 1 mmHg) in the mean $P_{ET_{CO_2}}$ values at surface and pressure for the medium level of hypercapnia. The mean value of $P_{ET_{CO_2}}$ under the high level of hypercapnia at 6 atm abs, however, was approximately 3.5 mmHg greater than for the corresponding level of hypercapnia at surface.

Inspired CO_2 tensions demonstrated markedly different results at surface compared to depth (Fig. 2). In the non-rebreathing conditions there was little difference (approximately 1 mmHg) in $P_{I_{CO_2}}$ at surface and depth. Under the rebreathing conditions, however, a greater level of $P_{I_{CO_2}}$ was required to raise the $P_{ET_{CO_2}}$ to the required ranges at 1 atm abs than during the 6 atm abs trials. As indicated in Fig. 2, a greater positive slope for the $P_{I_{CO_2}}$ curve at 1 atm abs compared to the curve at 6 atm abs was found, suggesting that the relationship between $P_{I_{CO_2}}$ and $P_{ET_{CO_2}}$ changed with depth.

As the levels of hypercapnia increased, inspired minute ventilation ($\dot{V}_I$) rose proportionately at surface and depth ($F = 92.43$; df = 2, 22; $P < 0.05$); however, the increase in $\dot{V}_I$ was significantly greater at 1 atm abs than at 6 atm abs ($F = 16.51$; df = 2, 22; $P < 0.05$). At 6 atm abs an overall significant hypoventilation was observed, compared to the normal ventilatory responses to CO_2 at surface pressures ($F = 9.84$; df = 1, 11; $P < 0.05$). Although respiratory rates increased with increases in $P_{ET_{CO_2}}$, they were lower at 6 atm abs throughout the entire range of hypercapnic

TABLE 1

GROUP MEAN VALUES AND STANDARD ERRORS FOR RESPIRATORY RESPONSES TO THREE LEVELS OF PET_{CO_2} AT 1 AND 6 ATM ABS IN A HYPERBARIC (DRY) PRESSURE CHAMBER, $n = 12$

	1 atm abs			6 atm abs		
	Level of End-Tidal P_{CO_2}					
	Low	Medium	High	Low	Medium	High
PET_{CO_2}, mmHg						
Mean	29.00	46.83	55.13	29.09	47.92	58.62
SEM	1.42	0.42	0.54	1.05	0.33	0.31
PI_{CO_2}, mmHg						
Mean	2.00	38.61	49.67	3.03	20.06	28.97
SEM	0.42	0.73	0.97	0.22	1.75	3.40
Respiratory rate, breaths · min^{-1}						
Mean	16.54	22.93	24.96	13.03	18.53	21.33
SEM	1.21	1.51	1.80	1.13	1.21	1.13
$\dot{V}I$, liters · min^{-1} BTPS						
Mean	8.90	36.71	61.37	12.16	30.56	39.27
SEM	1.09	3.89	6.22	1.29	1.84	1.29
VT, liters, BTPS						
Mean	0.58	1.60	2.46	1.00	1.68	1.93
SEM	0.07	0.11	0.15	0.08	0.09	0.13

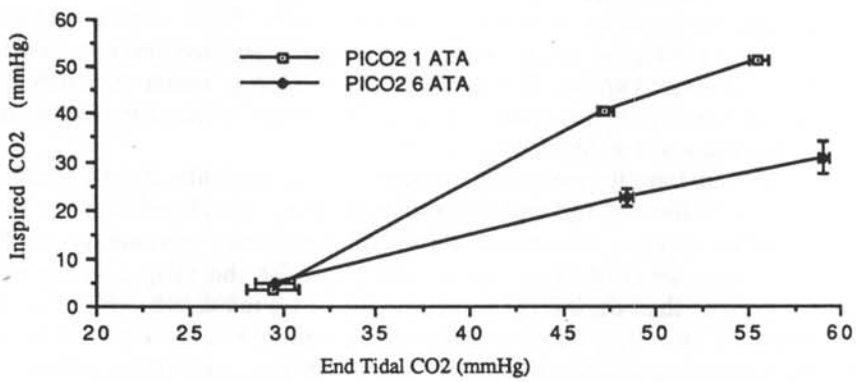

Fig. 2. Inspired CO_2 vs. end-tidal CO_2 at 1 and 6 atm abs. Values are means ($n = 12$); *bars* = SEM.

conditions. Correspondingly, for a given ventilation, the mean tidal volume was greater at depth compared to surface.

Cognitive and psychomotor responses at 1 and 6 atm abs

Most performance tests demonstrated acceptable test-retest correlation coefficients, indicating reasonable reliability. Apart from the copying test, which gave an

r^2 value of 0.56, the estimated test-retest accuracy of the performance tests (r^2) fell between 0.7 and 0.8.

The influence of PI_{N_2} and PET_{CO_2} changes on the performance scores in the various tasks in the test battery are illustrated in Fig. 3–7. These figures show mean test scores (attempted, correct, and error scores) for each cognitive test at the two pressure levels (1 and 6 atm abs) over the entire range of PET_{CO_2} conditions. Performance on the Purdue pegboard test is presented according to the number of parts assembled per minute.

Performance scores for each task were compared with their respective control values at 1 atm abs under the non-rebreathing condition (i.e., the low PET_{CO_2} level). The resulting mean percentage change in performance scores for the different PET_{CO_2} tensions at each pressure level are illustrated in Table 2.

None of the performance scores on any of the tests in the test battery demonstrated a significant interaction between PI_{N_2} and PET_{CO_2} ($P > 0.05$). Consequently, for the purpose of post hoc analysis, performance scores under the three end-tidal CO_2 conditions were collapsed over the two levels of PI_{N_2}.

Nitrogen effect

The difference in PI_{N_2} tension between the two pressure levels was maintained at 4 atm abs throughout the experiments. At this elevated level of PI_{N_2} all the cognitive

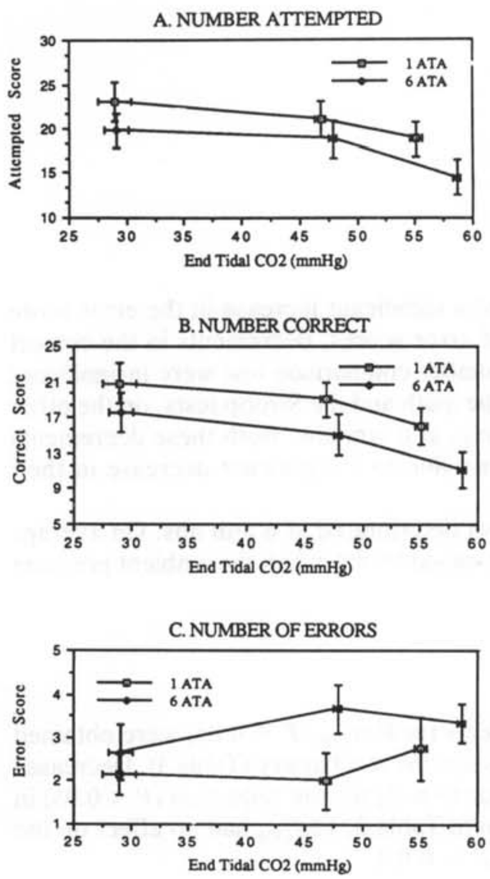

Fig. 3. Separate and combined effects of changes in PI_{N_2} and PET_{CO_2} on performance scores in the math test. *A*, number of problems attempted; *B*, number of problems correct; *C*, number of incorrectly solved problems. *Bars* = SEM (n = 12).

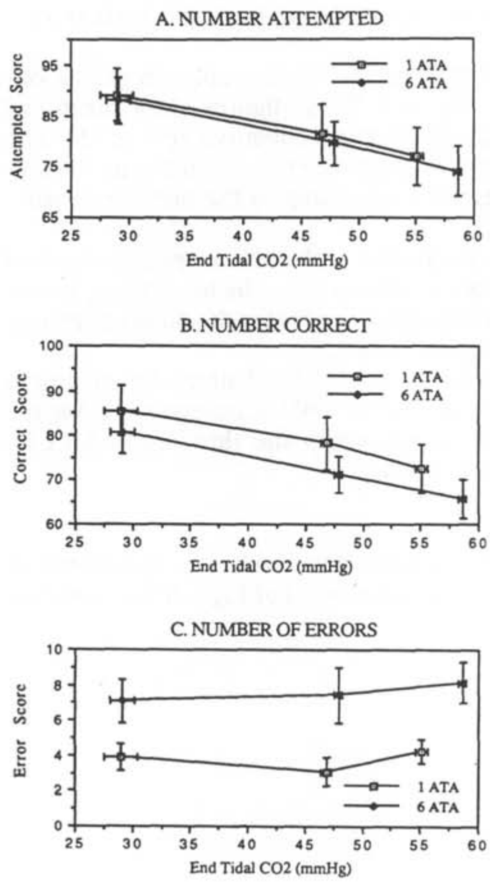

Fig. 4. Separate and combined effects of changes in PI_{N_2} and PET_{CO_2} on performance scores in the copying test. *A*, number/portion of patterns attempted; *B*, number/portion of patterns correct; *C*, number of errors. *Bars* = SEM (n = 12).

tests except for the math test demonstrated a significant increase in the error score ($P < 0.05$) (Table 3). Despite the increased error scores, decrements in the correct responses on the figure copying test and number comparison test were insignificant ($P > 0.05$) at 6 atm abs. Correct scores on the math and the Stroop tests, on the other hand, decreased by 22 and 11%, respectively, at 6 atm abs. Both these decrements were significant ($P < 0.05$) and were mainly due to a significant decrease in their respective attempted scores.

Performance on the Purdue pegboard also deteriorated at 6 atm abs. On average the number of parts assembled in 1 min decreased by 9% when the ambient pressure was raised from 1 to 6 atm abs.

Carbon dioxide effect

After analysis of variance, significant effects for PET_{CO_2} ($P < 0.05$) were obtained for the correct scores on all the cognitive tests in the test battery (Table 3). Decreases in the correct scores were predominantly due to a significant reduction ($P < 0.05$) in the attempted scores in all cases. As shown in Table 3, PET_{CO_2} had no effect on the error scores on any of the cognitive tests ($P > 0.05$).

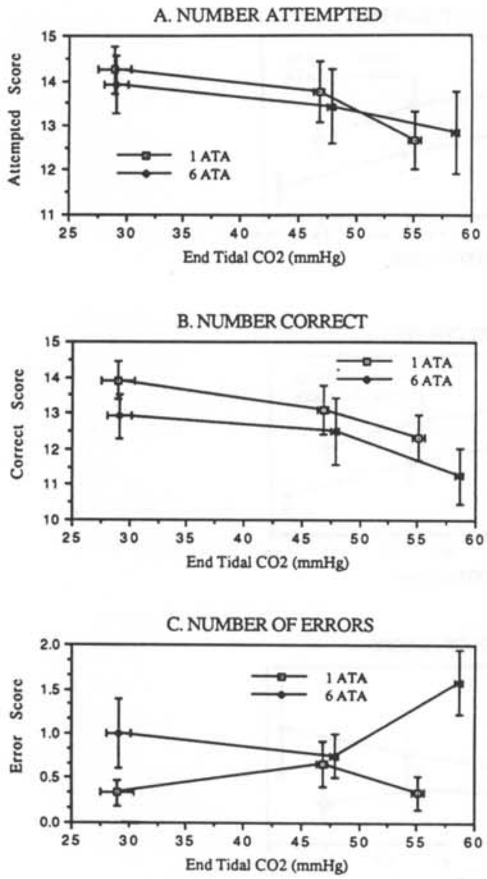

Fig. 5. Separate and combined effects of changes in PI_{N_2} and PET_{CO_2} on performance scores in the number comparison test. *A*, number attempted; *B*, number correct; *C*, number of errors. *Bars* = SEM (n = 12).

Performance on the Purdue pegboard gradually deteriorated when the PET_{CO_2} was raised at a constant ambient pressure (Fig. 7). Statistically significant decrements on performance ($P < 0.05$), however, only occurred when the PET_{CO_2} was raised above 48 mmHg.

Post hoc analysis revealed performance on all cognitive tests deteriorated significantly ($P < 0.05$) under the high level of PET_{CO_2} at both surface and 6 atm abs pressures. Performance on the figure copying test and the Stroop test also demonstrated significant decrements under the medium level of hypercapnia ($P < 0.05$). The Purdue pegboard test and the math test were the only tasks to demonstrate a significant deterioration in performance ($P < 0.05$) between medium and high PET_{CO_2} levels.

DISCUSSION

Respiratory responses to hypercapnia at depth

Ventilatory responses to hypercapnia at depth were similar to those observed in previous studies (18–22). Characteristically, a reduced breathing frequency and lower

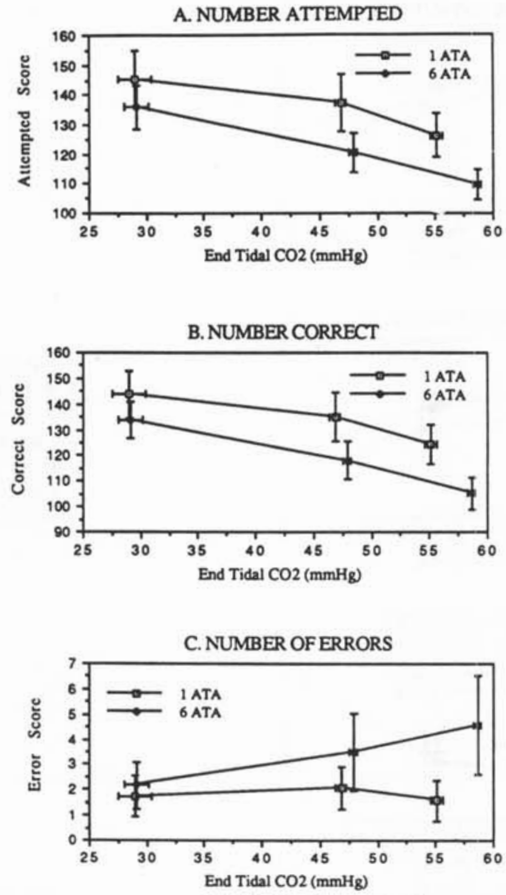

Fig. 6. Separate and combined effects of changes in PI_{N_2} and PET_{CO_2} on performance scores in the modified Stroop test. *A*, number of letters attempted; *B*, number of letters correctly crossed out; *C*, number of letters incorrectly crossed out. *Bars* = SEM (n = 12).

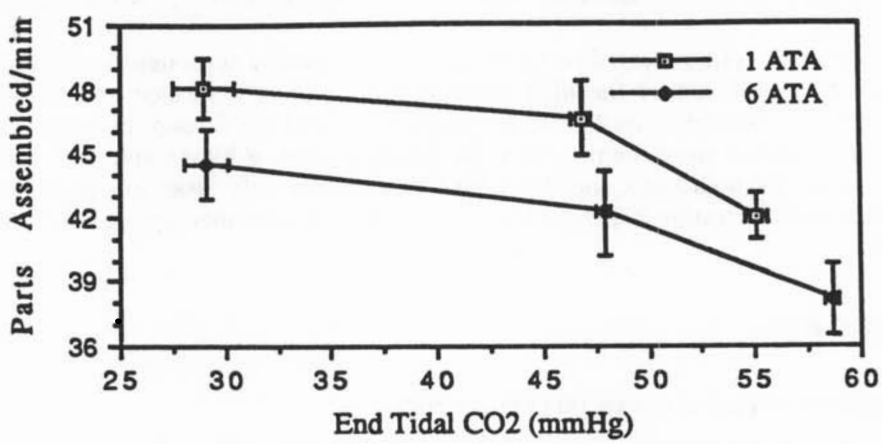

Fig. 7. Separate and combined effects of changes in PI_{N_2} and PET_{CO_2} on performance on the Purdue pegboard. *Bars* = SEM (n = 12).

TABLE 2

MEAN PERCENTAGE CHANGE IN PERFORMANCE SCORES AS COMPARED TO CONTROL VALUES (LOW PET_{CO_2} AT 1 ATM ABS) DURING EXPOSURE TO THREE LEVELS OF PET_{CO_2} AT 1 AND 6 ATM ABS

	1 atm abs		6 atm abs		
	Mean End-Tidal P_{CO_2} level, mmHg				
	Medium 46.8	High 55.1	Low 29.1	Medium 47.9	High 58.6
Math test					
Attempted	−8.7	−18.3	−13.9	−18.3	−37.4
Errors	−25.9	+3.7	+22.7	+37.0	+22.2
Correct	−8.7	−23.1	−15.4	−27.4	−46.6
Copying test					
Attempted	−8.7	−13.7	−1.1	−10.9	−16.9
Errors	−20.5	+10.3	+82.0	+89.7	+110.3
Correct	−8.4	−15.0	−5.5	−16.7	−23.0
NComp test					
Attempted	−3.5	−11.1	−2.8	−6.3	−10.5
Errors	+133.0	0.0	+233.0	+166.7	+433.3
Correct	−5.8	−11.5	−7.2	−10.1	−18.7
Stroop test					
Attempted	−5.8	−13.3	−6.6	−17.4	−24.6
Errors	+16.7	−11.1	+22.2	+94.4	+155.6
Correct	−6.1	−13.4	−7.0	−17.8	−26.8
Purdue pegboard					
Parts assembled per/min	−3.1	−12.7	−7.5	−12.3	−20.6

$\dot{V}_I$ was noted in the responses to CO_2 rebreathing at 6 atm abs compared to normal ventilatory responses to elevated P_{CO_2} at 1 atm abs. The reduced ventilatory response to hypercapnia under hyperbaric states has been attributed to the increased gas density and breathing resistance rather than to any depressant action of high P_{N_2} on the respiratory center (18, 21, 23, 24).

The reason for the slight hypocapnia during the non-rebreathing conditions at surface and depth is uncertain. Unfamiliarity with breathing through a mouthpiece with the nasal passage occluded, as well as the change in awareness of respiration (as a result of the audible sound of the demand regulator), may have altered the subjects' natural breathing patterns. Evidence showing that breathing through a mouthpiece with the nostrils occluded changes the breathing pattern of humans has been demonstrated by Hirsch and Bishop (25), Askanazi et al. (26), and Sackner et al. (27).

TABLE 3

ANALYSIS OF VARIANCE SUMMARY STATISTICS FOR THE MAIN EFFECTS OF PI_{N_2} AND PET_{CO_2} ON THE PERFORMANCE SCORES, $n = 12$

	N_2 Analysis, df 1, 11			CO_2 Analysis, df 2, 22		
	MSE	*F*	*P*	MSE	*F*	*P*
Math test						
Attempted	6.6	29.2	0.0004[a]	5.5	26.1	0.0000[a]
Errors	4.8	3.2	0.1005	3.1	0.8	0.4741
Correct	11.0	26.6	0.0005[a]	9.7	20.3	0.0000[a]
Copying test						
Attempted	220.7	0.3	0.5900	78.5	13.5	0.0003[a]
Errors	14.4	18.2	0.0016[a]	6.8	0.9	0.4340
Correct	273.5	2.6	0.1360	82.1	14.3	0.0002[a]
NComp test						
Attempted	6.3	0.1	0.7733	2.5	4.4	0.0243[a]
Errors	0.8	10.2	0.0086[a]	0.5	1.3	0.2935
Correct	4.7	3.0	0.1063	3.2	5.0	0.0160[a]
Stroop test						
Attempted	223.9	16.3	0.0022[a]	219.9	14.1	0.0002[a]
Errors	6.2	7.6	0.0181[a]	14.5	0.6	0.5826
Correct	237.0	17.9	0.0017[a]	270.3	12.7	0.0004[a]
Purdue pegboard						
Parts assembled per/min	17.9	15.7	0.0025[a]	14.2	17.1	0.0001[a]

[a] $P < 0.05$; MSE = Mean square of the error term.

Breathing responses under control conditions at 1 and 6 atm abs were, however, different. Comparing the data in Table 1 with resting respiratory responses quoted by McArdle et al. (28), it was found that at 1 atm abs, tidal volume was normal and breathing frequency was slightly elevated. At 6 atm abs the reverse was true; breathing frequency was at normal resting levels while tidal volume was slightly elevated.

Cognitive and psychomotor responses to raised PN_2 and PCO_2

The influence of raised PI_{N_2} on performance has been discussed at length by many authors (9, 29, 30). The following discussion will therefore center around the lesser known effects of CO_2 narcosis and its interaction, or lack of interaction, with N_2 narcosis.

When the effects of raised PCO_2 and PN_2 were analyzed separately for the correct scores, it was found that on average, an increase of 3.4 mmHg in PET_{CO_2} would have the equivalent narcotic effect as the addition of 1 atm abs of air. Based on these figures, CO_2 was calculated to be about 175 times more narcotic than N_2. This figure

is slightly higher than the calculation of narcotic potency of CO_2 reported by Morrison et al. (8) based on the data of Severinghaus (31) and Brauer and Way (32). Hesser et al. (12), however, reported a narcotic potency of CO_2 "several hundred times" greater than that of N_2. One reason for this discrepancy may be the 1 atm abs difference in the $P_{I_{O_2}}$ between surface and 6 atm abs conditions in the current study.

If performance decrements on the tasks at 6 atm abs were affected by a narcotic influence of O_2 as well as N_2, the actual narcotic potency of CO_2 relative to N_2 will be slightly greater than that quoted above. Although high tensions of oxygen have been reported to elicit narcotic effects (23), the narcotic potency of oxygen is much less than that of CO_2 (12). In addition, no observable O_2-CO_2 or O_2-N_2 interaction has been found from cognitive performance tests at depth (12). Any performance decrements due to the raised $P_{I_{O_2}}$ will therefore be purely additive on the performance decrements caused by CO_2 and N_2. Since partial pressures of O_2 and N_2 increase in parallel when breathing air mixtures at depth, decrements due to elevated P_{CO_2} tensions should be related to those decrements caused by the combined effects of N_2 and O_2 if realistic life working conditions of a diver are to be considered. Under these latter conditions, the present results indicated that high CO_2 pressures were additive in their effects on impaired cognitive and psychomotor performance at depth.

Evidence for additivity of CO_2 on performance decrements is clearly shown in Figs. 3–7. From these figures it is seen that most performance curves at 1 and 6 atm abs were approximately parallel to each other over the measured range of $P_{ET_{CO_2}}$. This suggests that changes in CO_2 tension had little effect on the degree of narcosis produced by the high N_2 pressure itself. These observations further support the conclusions of Hesser et al. (10) "that variations in alveolar CO_2 tension have no significant influence on the magnitude of the nitrogen component in compressed air narcosis."

Although the narcotic potency of CO_2 has been expressed above relative to N_2, it should be noted that the narcotic effects of CO_2 are manifested differently from those induced by N_2 narcosis. The narcotic equivalency of these two gases should, therefore, not be taken to represent synonymous physiologic-psychologic causes and effects. Although all performance tests demonstrated significant decrements for the two main effects ($P_{I_{N_2}}$ and $P_{ET_{CO_2}}$), hypercapnia induced these decrements through decreases in the attempted scores rather than any changes in the error scores. Nitrogen narcosis, in contrast, produced significant impairment through changes in both the attempted and error scores on the majority of performance tests.

A similar pattern of results for CO_2 on cognitive performance has been observed recently by Sayers et al. (33) at surface pressures. These authors found that $P_{ET_{CO_2}}$ pressures above 51 mmHg significantly slowed performance on a reasoning task (AB logic problems) but had little effect on accuracy of reasoning. They also noted a significant rise in irritability and discomfort when subjects were exposed to inspired CO_2 concentrations >46 mmHg. Although no attempt was made to quantify the personal reports of subjects in the present study, it was interesting to note that most subjects became more irritable and found it harder to concentrate on the tasks when they were exposed to high levels of CO_2. Other notable symptoms observed during hypercapnic exposure were hyperactivity, irritability, and poor concentration, particularly under the highest level of CO_2. Several subjects also reported that the hyperventilation associated with high levels of CO_2 caused some discomfort and was particularly distracting while completing the test battery.

The speed and accuracy measures used to assess performance on the cognitive tests are closely related to the speed-accuracy trade-off function, which in turn is particularly sensitive to the strategy used by the subject. Consequently, the different pattern of results observed under hypercapnia compared to that observed under N_2 narcosis indicated that a different strategy was employed by the subjects under the two conditions. Whether these strategic changes were voluntary (induced possibly as a result of different subjective sensations under CO_2 and N_2 narcosis) or involuntary, manifested through structural or functional changes in the brain, cannot be answered by the current study.

The actual mechanism by which inert gases produce narcosis is not fully understood; however, good correlations between the lipid solubility of a number of inert gases and their narcotic potencies have been found (34). According to this theory, the lipid solubility of carbon dioxide is 13 times greater than that of nitrogen (35), and therefore CO_2 should be 13 times more potent a narcotic than N_2. The cognitive performance data, however, demonstrated CO_2 to be more than 10 times as narcotic than is predicted by the lipid solubility theory. This suggests that either the lipid solubility theory does not fully explain the underlying mechanism of narcosis, or that N_2 and CO_2 produce their narcotic effects through different mechanisms.

If nonconformity of the CO_2 data with the lipid solubility theory can be explained through a different mechanism of action for CO_2 narcosis, then this may be one explanation for the change in strategy observed on the performance tests under CO_2 and N_2 narcosis.

Unfortunately, the lipidlike anesthetic activity of CO_2 has not been tested because it seems to produce acidotic anesthesia at much lower P_{CO_2} levels (31). It is therefore likely that CO_2 narcosis effects are related to hydrogen ions or to the extracellular pH (36), which produce their effects at far lower P_{CO_2} levels than does molecular CO_2 in accordance with the lipid solubility theory.

Physiologically it is believed that the symptoms of CNS hyperactivity, as a result of high P_{CO_2}, are the paradoxical result of a depressant effect of CO_2 on the cerebral cortex, releasing subcortical centers from normally powerful inhibitory influences (37). This hyperactivity is manifested in extreme cases of CO_2 toxicity by convulsions. Lambertsen (38) has shown that $P_{I_{CO_2}}$ levels of 76 mmHg are sufficient to induce marked psychomotor excitation and myoclonic twitches within 3 min of administration of the CO_2. It is therefore not unreasonable to expect a certain degree of muscular tremor at lower concentrations of CO_2. The decrement in fine muscular coordination, shown by the Purdue pegboard results under the high $P_{ET_{CO_2}}$ level, could therefore be a result of increased muscular tremor induced by the hyperactive effect of CO_2.

Despite uncertainty over the mechanisms of action for CO_2 and N_2 narcosis, it was found that in most cases the comparative sensitivity of a particular task was the same for N_2 narcosis as it was for CO_2 narcosis. When the performance tests were arranged from least to most affected by N_2 narcosis (as determined from correct scores), the order remained almost the same for performance decrements induced by CO_2 narcosis.

Contrary to previous findings (12, 33), the current data show no evidence of a threshold of $P_{ET_{CO_2}}$, above which cognitive performance significantly deteriorates. Hesser et al. (12) reported that "the role of CO_2 as a causative factor [in impairment of mental function] is negligible as long as the alveolar (arterial) P_{CO_2} does not exceed 40 mmHg." Later work by Sayers et al. (33) showed a clearer but higher threshold of 51 mmHg for the effect of $P_{ET_{CO_2}}$ on a reasoning task.

Evidence against a threshold for CO_2 narcosis has been provided by the work of McAleavy et al. (39). These authors found the anesthetic potency of N_2O was altered by P_{CO_2}, so that less N_2O was required to induce loss of consciousness at high CO_2 tensions. The relationship between anesthetic potency of N_2O (the minimum alveolar concentration producing a nonresponsive anesthetic state) and PET_{CO_2} was found to be linear over the measured range (20–60 mmHg) of PET_{CO_2}. It is also possible that the concept of a threshold has in the past been confused with the magnitude of change necessary to obtain a statistically significant result. The present data provide further evidence against a threshold phenomenon, and suggest that a threshold, if present at all, is dependent on the sensitivity of the particular task or cognitive factor to hypercapnic stress. The sensibility of a particular cognitive factor to hypercapnic stress is probably related to different areas of the brain having different sensitivities to CO_2 (40).

The present findings affirm the importance of CO_2 as a major threat to diver safety in the hyperbaric environment. Carbon dioxide is an important factor in the ergonomic design of both open circuit breathing apparatus (i.e., dead space and helmet ventilation) and closed circuit rebreathing apparatus (i.e., CO_2 absorption) as well as in underwater habitats and hyperbaric chambers. Within the limitations of the current study (i.e., resting in a dry chamber at neutral temperature) it is suggested that PET_{CO_2} be kept below 47 mmHg to avoid the possibility of significant cognitive and psychomotor deficits at depth. Other factors, including cold, diving experience, level of exertion, and apprehension, may influence the severity of CO_2 narcosis. It is therefore necessary to compare the present research with the physiologic and psychologic responses of divers working in open water conditions to understand the real practical limitations of CO_2 narcosis on diver safety and performance.

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REFERENCES

1. Behnke AR, Willmon TL. U.S.S. *Squalus*. Medical aspects of the rescue and salvage operations, and the use of oxygen in deep-sea diving. US Nav Med Bull 1939; 37:629.
2. Case EM, Haldane JBS. Human physiology under high pressure. J Hyg 1941; 41:225–249.
3. Dwyer J. Measurement of O_2 consumption in scuba divers working in open water. Ergonomics 1977; 20:377–388.
4. MacDonald JW, Pilmanis A.A. Carbon dioxide retention with underwater work in the open ocean. In: Lanphier EH, ed. The unconscious diver: respiratory control and other factors. Bethesda, MD: Undersea Medical Society, 1982:88–90.
5. Lanphier EH. Carbon dioxide retention in working divers breathing N_2-O_2 mixtures at depth. Fed Proc 1956; 15:116.
6. Lanphier EH. Influences of increased ambient pressure upon alveolar ventilation. In: Lambertsen CJ, Greenbaum LJ, eds. Proceedings of the second symposium on underwater physiology. Washington, DC: National Academy of Sciences–National Research Council, 1963:124–133.
7. Morrison JB, Florio JT, Butt WS. Effects of CO_2 insensitivity and respiratory pattern on respiration in divers. Undersea Biomed Res 1981; 8:209–217.
8. Morrison JB, Florio JT, Butt WS. Observations after loss of consciousness under water. Undersea Biomed Res 1978; 5:179–187.

9. Fowler B, Ackles KN, Porlier G. Effects of inert gas narcosis on behavior—a critical review. Undersea Biomed Res 1985; 12:369–402.
10. Hesser CM, Adolfson J, Fagraeus L. Role of CO_2 in compressed air narcosis. Aerosp Med 1971; 42:163–168.
11. Adolfson J, Fagraeus L, Hesser CM. Deterioration of standing steadiness in the hyperbaric environment. Swed J Defence Med (Försvarsmedicin) 1973; 9:253–256.
12. Hesser CM, Fagraeus L, Adolfson J. Roles of nitrogen, oxygen, and carbon dioxide in compressed-air narcosis. Undersea Biomed Res 1978; 5:391–400.
13. Taylor N. Effect of breathing gas pressure on respiratory mechanics of immersed man. Burnaby, Canada: Simon Fraser University; 1987. Thesis.
14. Ekstrom RB, French JW, Harman HH, Darmen D. Manual for the kit of factor-referenced cognitive tests. Princeton, NJ: Educational Testing Service, 1976.
15. Stroop JR. Studies of interference in serial verbal reactions. J Exp Psychol 1935; 18:643–661.
16. Purdue Research Foundation. Examiner manual for the Purdue pegboard. Purdue, IL: Science Research Associates Inc, 1948.
17. Kleinbaum D, Kupper L, Muller K. Applied regression analysis and other multi-variable methods, 2nd ed. Boston: PWS-Kent Publishing, 1988.
18. Wood LDH, Bryan AC. Respiratory sensitivity to CO_2 at increased ambient pressure. Physiologist 1970, 13:348.
19. Wood LDH, Bryan AC. Mechanical limitations of exercise ventilation at increased ambient pressure. In: Lambertsen CJ, ed. Underwater physiology. Proceedings of the fourth symposium on underwater physiology. New York: Academic Press, 1971:307–316.
20. Doell D, Zutter M, Anthonison NR. Ventilatory responses to hypercapnia and hypoxia at 1 and 4 ATA. Respir Physiol 1973; 18:338–346.
21. Linnarsson D, Hesser CM. Dissociated ventilatory and central respiratory responses to CO_2 at raised N_2 pressure. J Appl Physiol 1978; 45:756–761.
22. Hickey DD, Norfleet WT, Påsche AJ, Lundgren CEG. Respiratory function in the upright, working diver at 6.8 ATA (190 fsw). Undersea Biomed Res 1978; 14:241–262.
23. Frankenhaeuser M, Graff-Lonnevig V, Hesser CM. Effects on psychomotor functions of different nitrogen-oxygen gas mixtures at increased ambient pressures. Acta Physiol Scand 1963; 59:400–409.
24. Fagraeus L, Hesser CM. Ventilatory response to CO_2 in hyperbaric environments. Acta Physiol Scand 1970; 80:19A–20A.
25. Hirsch JA, Bishop B. Human breathing patterns on mouthpiece or face mask during air, CO_2 or low O_2. J Appl Physiol 1982; 53:1281–1290.
26. Askanazi J, Silverberg PA, Foster RJ, Hyman, AI, Milic-Emili J, Kinney JM. Effects of respiratory apparatus on breathing pattern. J Appl Physiol 1980; 48:577–580.
27. Sackner JD, Boudy MJ, Davis B, Cohn MA, Sackner MA. Ventilation at rest and during exercise measured without physical connection to the airway. In: Stott FD, Raftery EG, Sleigh P, Gouldring L, eds. ISAM proceedings of the second international symposium on ambulatory monitoring. London: Academic Press, 1980:1–14.
28. McArdle, WD, Katch FI, Katch VL. Exercise physiology, energy, nutrition, and human performance, 2nd ed. Philadelphia: Lea & Faber, 1986.
29. Bennett PB. Inert gas narcosis. In: Bennett PB, Elliott DH, eds. The physiology of medicine and diving, 3rd ed. San Pedro, CA: Best Publishing, 1982.
30. Hamilton RW, Kizer KW, eds. Nitrogen narcosis. Proceedings of the twenty-ninth Undersea Medical Society workshop. Bethesda, MD: Undersea Medical Society, 1985.
31. Severinghaus JW. Carbon dioxide transport. In: Nahas G, Schaefer KE, eds. Carbon dioxide and metabolic regulations. New York: Springer, 1974:138–143.
32. Brauer RW, Way RO. Relative narcotic potencies of hydrogen, helium, nitrogen, and their mixtures. J Appl Physiol 1970; 29:23–31.
33. Sayers JA, Smith REA, Holland RL, Keatinge WR. Effects of carbon dioxide on mental performance. J Appl Physiol 1987; 63:25–30.
34. Bennett PB. The aetiology of compressed air intoxication and inert gas narcosis. International series of monographs in pure and applied biology; zoology division, vol 31. Oxford: Pergamon Press, 1966.
35. Dittmer DS, Grebe, eds. Handbook of respiration. Philadelphia: WB Saunders, 1958:9.

36. Eisele JH, Eger EI II, Muallem M. Narcotic properties of carbon dioxide in the dog. Anaesthesiology 1967; 28:856–865.
37. Woodbury DM, Karler R. The role of carbon dioxide in the nervous system. Anaesthesiology 1960; 21:686.
38. Lambertsen CJ. Therapeutic gases: oxygen, carbon dioxide and helium. In: DiPalma JR, ed. Drill's pharmacology in medicine, ed 4. New York: McGraw-Hill Book Co, 1971.
39. McAleavy JC, Way WL, Altstatt AH, Guadagni NP, Severinghaus JW. The effect of pCO_2 on the depth of anaesthesia. Anaesthesiology 1961; 22:260.
40. Schaefer KE. Following Severinghaus JW, discussion on carbon dioxide transport. In: Nahas G, Schaefer KE, eds. Carbon dioxide and metabolic regulations. New York: Springer-Verlag, 1974:138–143.