

Behavioral effects of increased CO₂ load in divers

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Henning RA, Sauter SL, Lanphier EH, Reddan WG. Behavioral effects of increased CO₂ load in divers. *Undersea Biomed Res* 1990; 17(2):109-120.—The behavioral effects of elevated PACO₂ were examined to clarify risks due to CO₂ retention in diving. In two separate laboratory studies, experienced divers breathed 6% CO₂ mixtures under normobaric conditions. Normoxic study: Subjects ($n = 8$) first breathed air (control); then 6% CO₂, 21% O₂, balance N₂ (exposure); and then air again (postexposure). Hyperoxic study: Subjects ($n = 10$) first breathed 100% O₂; then 6% CO₂ in O₂; and then O₂ again. Subjects performed a test battery in each condition. In the control and postexposure conditions, tests consisted of simple and choice reaction time, postural sway, tremor, and hand steadiness. In the exposure conditions, only the simple and choice reaction time tests were performed. No significant performance decrements during CO₂ exposure were found in either study. However, regression analyses indicated that changes in postural sway, tremor, and decision-making time after normoxic CO₂ exposure were proportional to decrements in individual end-tidal PCO₂ levels following CO₂ exposure. We conclude that divers may be at risk for performance impairment immediately after a period of CO₂ retention.

CO ₂ exposure	reaction time
CO ₂ retention	normoxic
diving	hyperoxic
body sway	normobaric
tremor	end-tidal PCO ₂

The object of this study was to explore the behavioral effects of CO₂ retention while using underwater breathing apparatus. CO₂ retention is common among divers (1-4) and usually occurs when pulmonary ventilation is not increased sufficiently during work at depth. End-tidal (E-T) PCO₂ values as much as 30 mmHg above the normal value of 40 mmHg have been encountered in experimental dives (5).

Carbon dioxide retention has been implicated as the major contributing factor in diving accidents (6) that involved loss of consciousness. CO₂ retention may also increase the risk of O₂ toxicity (7), N₂ narcosis (8), and decompression sickness (9). It is known that an inspired CO₂ concentration of 10% can lead to unconsciousness (10, 11) and untoward effects seem to be negligible for short-term exposures in the 0-5% range (12, 13). However, there has been little investigation of the behavioral effects of CO₂ exposure in the 5-10% range. Sayers et al. (14) used normoxic expo-

tures between 4.5 and 7.5% CO₂ and found decrements in logical and mathematical problem-solving ability whenever E-T PCO₂ levels exceeded approximately 51 mmHg. The 51-mmHg threshold was usually reached during exposure to 5.5% CO₂. Their results indicated that performance impairment may depend on the individual's arterial PCO₂ level rather than on the concentration of CO₂ in the inspired gas.

In the present research, experienced divers with a tendency to retain CO₂ were administered gas mixtures containing 6% CO₂ under normobaric conditions to induce high arterial CO₂ concentrations. The effects of CO₂ exposure on postural sway, simple and choice reaction time, tremor, and hand steadiness were evaluated. Two separate within-subjects studies were conducted. In the normoxic study, subjects breathed gas mixtures of normoxic 6% CO₂ (exposure) and air (preexposure control and postexposure). In the hyperoxic study, hyperoxic CO₂ mixtures were used in an attempt to duplicate PO₂ values at depth; gas mixtures were hyperoxic 6% CO₂ (exposure) and oxygen (preexposure control and postexposure).

METHODS

Methods were nearly identical for the normoxic and hyperoxic studies. The normoxic study is described below. Unless otherwise indicated, the hyperoxic protocol was identical.

Subjects

Eight certified sport scuba divers (6 males), aged 18–33 yr, were paid volunteer participants. (Hyperoxic study: 10 divers, 8 males.) Most of the subjects were selected based on a demonstrated tendency to retain CO₂ during tethered fin-swimming in the laboratory or because they reported symptoms associated with CO₂ retention, such as unusually low air-use rates or frequent headaches from diving. Subjects were informed of possible discomfort and potential risks and signed a consent form approved by the Committee for the Protection of Human Subjects, University of Wisconsin-Madison Center for Health Sciences.

Experimental design

Subjects served as their own controls in a repeated-measures design. The sequence of conditions in the normoxic study was: a) control (air); b) exposure (6% CO₂); and c) postexposure (air). The sequence in the hyperoxic study was: a) control (O₂); b) exposure (6% CO₂ in O₂); and c) postexposure (O₂).

Carbon dioxide delivery and monitoring

Breathing gases were delivered to the subjects by a single-hose, scuba demand regulator (Dacor Corporation, Northfield, IL). Before experiments the demand regulator was cleaned for oxygen service and adjusted for minimum resistance. The weight of the scuba regulator and supply hose was supported by an overhead elastic strap to prevent subject discomfort. Gas mixtures were supplied to the demand regulator at a pressure of approximately 10 ATA from cylinders equipped with

individual first-stage regulators. A remote rotary select valve permitted rapid switching between gas mixtures without the subjects' knowledge. In the normoxic study, gases were a) compressed air and b) a premixed CO₂ mixture (6% CO₂, 21% O₂, balance N₂). In the hyperoxic study, the gases were a) 100% O₂ and b) 6% CO₂ in O₂.

End-tidal FCO₂ was monitored continuously with a Godart capnograph, and recorded. Expired gas was sampled through 1.2 m of 0.8-mm (i.d.) tubing at a constant flow of 450 ml · min⁻¹ from a port installed in the mouthpiece. Calibration of the capnograph was checked before and after each experiment. E-T FCO₂ values were measured with the subject at rest. E-T PCO₂ values at the start and end of each condition were averaged together to estimate the arterial PCO₂ level for that condition.

Performance battery

A battery of behavioral tests was administered during each condition. As described below, the full battery consisted of the following measures: postural sway, tremor, hand steadiness, simple and choice reaction time, and memory-demand choice reaction time. Because increased ventilation during CO₂ breathing caused movement artifacts, which confounded postural sway, tremor, and hand steadiness, only the reaction time tests were administered during CO₂ breathing.

Postural sway

The subject was instructed to stand as steadily as possible on a force platform designed to measure postural sway. Analog signals corresponding to anterior-posterior and lateral sway were low-pass filtered (-3 dB at 35 Hz) and then sampled at 256 Hz over 1-min trials using a laboratory minicomputer (PDP 11/34a, Digital Equipment Corporation). Sway was sampled for 1 min with eyes open, and for 1 min with eyes closed. A single-channel radius-of-sway record was derived by geometrically combining coincident anterior-posterior and lateral sway samples and then calculating the instantaneous distance from the subject's center of sway.

The radius-of-sway record was spectral analyzed to provide sway measurements in three frequency ranges: 0–15 Hz (full); 0–1 Hz (low); and 1–15 Hz (high). In addition, a mean frequency of sway was calculated as the frequency value that divided the 0–15 Hz radius-of-sway spectrum into two equal power bands (50% of the power above and 50% of the power below this frequency value). Also, a Romberg quotient (eyes-closed sway power divided by eyes-open sway power) was calculated using radius-of-sway power over the (full) 0–15 Hz range.

Tremor

Using the index finger of the dominant hand, subjects exerted 5 g of downward force on a metal wand which transduced slight variations in vertical finger position (5–25 Hz tremor). Subjects monitored an analog meter that displayed average downward force to maintain a constant displacement of the metal wand. The tremor signal was low-pass filtered (-3 dB at 35 Hz) and then sampled at 256 Hz over two 1-min trials in each experimental condition. In the first (supported) trial, the arm and hand were supported to isolate movement about the metacarpophalangeal joint. In the second (unsupported) trial, the arm and hand were unsupported. Tremor scores for

each individual were obtained by calculating the spectral power in three frequency ranges: 5–28 Hz (full); 5–15 Hz (low); and 15–28 Hz (high).

Hand steadiness

Using the unsupported nondominant hand, subjects held a metal stylus so that it protruded through a small hole drilled in a metal plate (Lafayette Instruments, LaFayette, IN). Trial lengths were 15 sec for each of four holes of progressively smaller diameter. A steadiness score for each hole was obtained by multiplying the total number of stylus contacts with the template by the total time of stylus contacts.

Simple reaction time

Light-emitting diodes (LEDs) were illuminated for 200 msec at random intervals, and the subject responded with a finger-actuated, spring-loaded toggle switch. Each test consisted of 20 stimuli. Mean reaction time was calculated after excluding late responses (i.e., response times >2 SD above the mean).

Choice reaction time

Four LEDs were arranged in a diamond pattern. Each stimulus consisted of one of four pairwise combination LEDs. Subjects were provided with a spring-loaded toggle switch for each hand and were taught a decision rule requiring activation of the left or right switch for each stimulus. Two of the four possible stimuli were assigned to each switch. Left-hand switch assignments were a) top and left LEDs, and b) bottom and right LEDs. Right-hand switch assignments were a) top and right LEDs and b) bottom and left LEDs. Each test consisted of 32 stimuli. Interstimulus intervals were random. Mean choice reaction time was calculated based on correct responses after excluding late responses (i.e., response times >2 SD above the mean). In addition, the portion of the total response time attributed to the additional challenge of stimulus decoding, decisionmaking, and response selection (hereafter referred to simply as “decision time”) was estimated by subtracting the mean simple reaction time from the mean choice reaction time.

Memory-demand choice reaction time: hyperoxic study

A variation of the choice reaction time test was developed to assess short-term memory performance. Information from the previous stimulus (whether top or bottom LED had been illuminated) had to be recalled before the appropriate (left hand or right hand) response to the current stimulus could be made. Top LED: response rule identical to choice reaction time task. Bottom LED: reverse the response, i.e., activate the left switch if the “usual” response was to activate the right switch, and vice versa. Each test consisted of 32 stimuli. The portion of the total response time attributed to memorizing whether the top or bottom LED had been illuminated in the previous stimuli and applying the new response rule (hereafter referred to simply as “memory time”) was estimated by subtracting the mean choice reaction time from the mean memory-demand choice reaction time.

Procedure

Subjects were familiarized with the experimental protocol and trained to perform the choice reaction time tests at a 5% or less error rate on a day before the experiment. Warm-up trials on the reaction time tests were performed on the day of the experiment. The gases breathed and the performance tests administered in each condition are shown in Table 1.

Control condition

Postural sway, tremor, and hand steadiness were measured without use of the breathing apparatus. The subject then sat before the reaction time display and breathed air (hyperoxic study: O₂) from the scuba regulator while wearing a noseclip. After E-T PCO₂ had stabilized (5–7 min), the subject performed the reaction time test battery.

Exposure condition

The gas supply was switched to the normoxic 6% CO₂ mixture (hyperoxic study: hyperoxic 6% CO₂ mixture) and 5–7 min were allowed for E-T PCO₂ to stabilize. The reaction time tests were then repeated.

Postexposure condition

The control gas was readministered and 5–7 min were allowed for E-T PCO₂ to stabilize. The reaction time tests were then repeated. The breathing apparatus was then removed so that the postural sway, tremor, and hand steadiness tests could be performed.

In an exit interview, subjects were asked to report if they had experienced symptoms such as headache, dizziness, or lightheadedness during the experiment.

TABLE 1
GASES BREATHED AND PERFORMANCE TESTS ADMINISTERED IN EACH CONDITION

Control, Air (normoxic) Oxygen (hyperoxic)	Exposure, Normoxic CO ₂ or Hyperoxic CO ₂	Postexposure, Air (normoxic) Oxygen (hyperoxic)
Simple reaction time	simple reaction time	simple reaction time
Choice reaction time	choice reaction time	choice reaction time
Memory-demand reaction time ^a	memory-demand reaction time ^a	memory-demand reaction time ^a
Postural sway		postural sway
Hand steadiness		hand steadiness
Tremor		tremor

^aHyperoxic study only.

Data analysis

Separate analyses were conducted to test if reaction time was affected during CO₂ exposure (exposure effects), and if either steadiness and/or reaction time were affected in the postexposure condition (postexposure effects).

Exposure effects

Paired comparisons of reaction time in the control and exposure conditions were used to test for performance decrements during exposure without regard to individual differences in E-T PCO₂. In addition, regression analyses were used to evaluate the effects of exposure-induced changes in individual E-T PCO₂ levels on reaction time performance during the exposure condition.

Postexposure effects

Paired comparisons between the control and postexposure conditions were used to test for performance decrements in steadiness and reaction time in the postexposure condition without regard to individual differences in E-T PCO₂. Additionally, regression analyses were used to evaluate the changes in reaction time and steadiness (control condition to postexposure condition) due to changes in E-T PCO₂ (control or exposure conditions to postexposure condition).

RESULTS

End-tidal CO₂ levels

Individual E-T PCO₂ values in each condition are shown in Table 2 (normoxic) and Table 3 (hyperoxic). Breathing 6% CO₂ resulted in large increases in E-T PCO₂ for all subjects, with average increases of 10.7 mmHg (normoxic) and 9.5 mmHg (hyper-

TABLE 2
END-TIDAL PCO₂ VALUES FOR EACH SUBJECT IN EACH CONDITION, NORMOXIC STUDY

Subject	Control, Air	Exposure, Normoxic CO ₂	Postexposure, Air
1	40.9	50.9	38.8
2	37.7	48.3	33.6
3	35.5	48.3	35.5
4	39.3	48.0	36.9
5	40.3	48.1	39.3
6	38.0	51.4	34.2
7	39.1	52.5	34.9
8	42.8	51.5	39.3

TABLE 3
END-TIDAL PCO₂ VALUES FOR EACH SUBJECT IN EACH CONDITION, HYPEROXIC STUDY

Subject	Control, Oxygen	Exposure, Hyperoxic CO ₂	Postexposure, Oxygen
1	42.2	49.9	39.8
2	37.6	48.6	37.6
3	31.7	44.2	30.2
4	37.9	46.8	25.0
5	36.9	48.3	36.4
6	43.5	50.2	40.1
7	42.7	49.8	38.5
8	28.8	45.5	31.1
9	42.5	50.3	31.0
10	41.8	47.4	39.3

oxic). Mean E-T PCO₂ during normoxic exposure (49.9 mmHg) was higher ($P < 0.05$) than during hyperoxic exposure (48.1 mmHg). The highest E-T PCO₂ value during exposure was 52.5 mmHg (normoxic study). Mean postexposure values of E-T PCO₂ were lower than control values: -2.6 mmHg, $P < 0.001$ (normoxic); -3.7 mmHg, $P < 0.05$ (hyperoxic). The largest decrease in E-T PCO₂ (control condition to postexposure condition) in the normoxic study was -4.2 mmHg; hyperoxic study, -12.9 mmHg.

Performance effects

No significant decrements in performance were detected by the paired comparison tests in either the normoxic or hyperoxic study. In the normoxic study however, regression analyses revealed significant relationships between changes in individual E-T PCO₂ levels and postexposure performance.

In the normoxic study, changes in low-frequency (0–1 Hz), eyes-open sway between the control and postexposure conditions were predicted by the decreases in E-T PCO₂ between these same conditions (Fig. 1). The regression relationship ($R^2 = 0.869$, $P < 0.01$) was as follows:

$$(\text{Percentage change in sway}) = -37.9 - 21.2 \times (\text{Change in E-T PCO}_2)$$

While sway did not increase in all individuals, the subject with the greatest decrease in E-T PCO₂ exhibited the largest (58%) increase in sway (0–1 Hz).

Similar effects were observed for tremor (Fig. 2). The changes in tremor (5–28 Hz) between the control and postexposure conditions were predicted by decreases in E-T PCO₂ between these same conditions. The regression relationship ($R^2 = 0.667$, $P < 0.5$) was as follows:

$$(\text{Percentage change in tremor}) = -68.9 - 17.7 \times (\text{Change in E-T PCO}_2)$$

The subject with the greatest decrease in E-T PCO₂ exhibited the largest (21%)

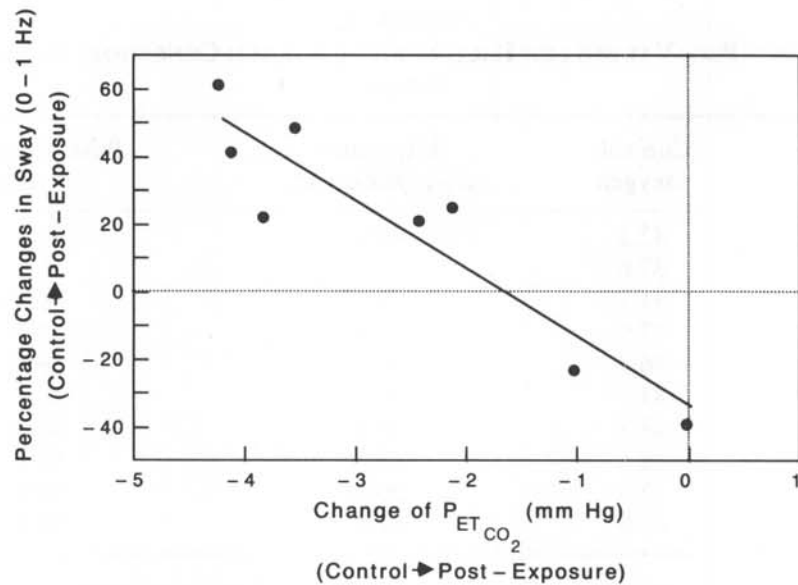


Fig. 1. Percentage changes in low frequency (0-1 Hz), eyes-open, postural sway in relation to changes in E-T PCO_2 (from control to postexposure conditions).

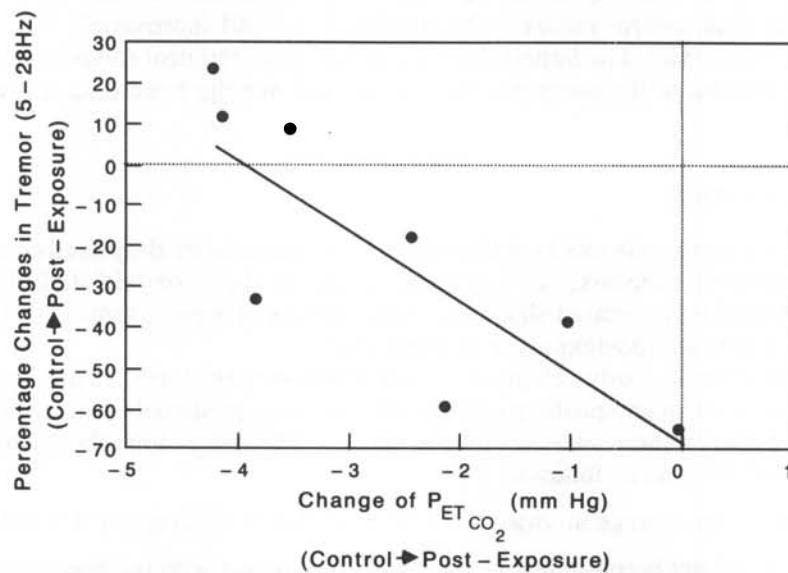


Fig. 2. Percentage changes in tremor (supported arm, 5-28 Hz) in relation to changes in E-T PCO_2 (from control to postexposure conditions).

increase in tremor. As with sway, individuals with only a small decrease in E-T PCO_2 between the control and postexposure conditions exhibited decreased tremor in the postexposure condition.

Finally, changes in mean "decision time" between the control and postexposure conditions were weakly predicted by the decreases in E-T PCO_2 between the exposure

and postexposure conditions (Fig. 3). The regression relationship ($R^2 = 0.513$, $P < 0.05$) was as follows:

$$(\text{Percentage change in decision time}) = -51.6 - 3.95 \times (\text{Change in E-T PCO}_2)$$

The subject with the greatest decrease in E-T PCO₂ exhibited the largest (35%) increase in decision time. (This data point influenced substantially the reported regression relationship. It was from the same subject who exhibited the largest increase in both tremor and sway in the postexposure condition.) Subjects with only a small decrease in E-T PCO₂ exhibited slight reductions in decision time.

Subject-reported symptoms

Several subjects reported discomfort during the exposure or postexposure conditions or both. In the normoxic study, headache was reported by 3 of 8 subjects, and 5 reported lightheadedness. In the hyperoxic study, 6 of 10 subjects reported headache, and 3 reported lightheadedness.

DISCUSSION

Performance effects during CO₂ breathing

The lack of performance impairment during 6% CO₂ exposure was surprising because we had deliberately enlisted divers suspected to be at risk for CO₂ retention. It is possible that an arterial PCO₂ threshold for behavioral impairment is reached at exposures between 6% CO₂, where effects seem to be negligible, and 10% CO₂, where

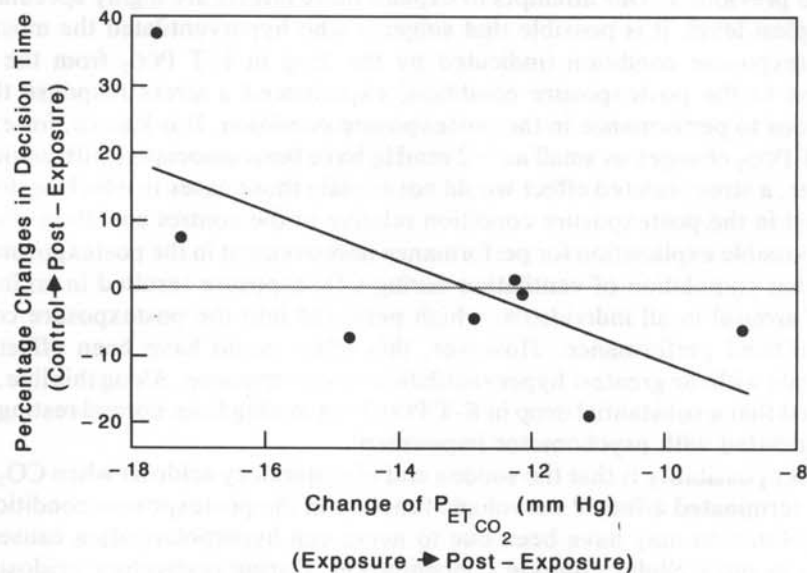


Fig. 3. Percentage changes in decision time (from control to postexposure conditions) in relation to changes in E-T PCO₂ (from exposure to postexposure conditions).

loss of consciousness can occur (10). For example, Sayers et al. (14) administered up to 7.5% CO₂ and found decrements in logical and mathematical problem-solving ability when E-T PCO₂ levels exceeded approximately 51 mmHg. Only 1 subject in our study exceeded this threshold (reaching 52.5 mmHg in the normoxic study). We did not feel comfortable using exposure levels above 6% CO₂ in the present study due to the subjective distress that was experienced by some subjects at this level.

Use of the hyperoxic 6% CO₂ mixture (hyperoxic study) was not effective as a means to increase PA_{CO₂} levels above those obtained during normoxic 6% CO₂ exposure. The lower mean E-T PCO₂ level during CO₂ exposure in the hyperoxic study may be explained by the slight hyperpnea sometimes associated with hyperoxic exposure (15). Although high PO₂ values are known to potentiate the adverse behavioral effects of CO₂ under hyperbaric conditions (9), the lack of performance impairment in the hyperoxic study argues against oxygen potentiating the effects of CO₂ under normobaric conditions.

Postexposure effects

An unexpected finding was that performance impairment occurred during the postexposure condition. Subjects with the largest postexposure decrements in E-T PCO₂ exhibited postexposure performance impairment. Changes in tremor, low frequency sway, and decision time (control condition to postexposure condition) were proportional to decreases in E-T PCO₂ (control or exposure conditions to postexposure condition). Although it is possible that a large number of regression tests increased the probability of spurious correlations in our study, it is unlikely that such an effect would exclusively favor the postexposure relationships in only the normoxic study.

To our knowledge, performance effects following CO₂ exposure have not been reported previously. Our attempts to explain these effects are highly speculative. At the simplest level, it is possible that subjects who hyperventilated the most during the postexposure condition (indicated by the drop in E-T PCO₂ from the control condition to the postexposure condition) experienced a stress response that was deleterious to performance in the postexposure condition. It is known, for example, that E-T PCO₂ changes as small as -2 mmHg have been associated with anxiety (16). However, a stress-related effect would not explain those cases in which performance improved in the postexposure condition relative to the control condition (Fig. 1-3).

One possible explanation for performance improvement in the postexposure condition is that stimulation of ventilation during CO₂ exposure resulted in an increased level of arousal in all individuals, which persisted into the postexposure condition and facilitated performance. However, this effect could have been offset among individuals with the greatest hyperventilation-stress response. Along this line, Gibson (17) noted that a substantial drop in E-T PCO₂ (-14 mmHg from normal resting values) was associated with psychomotor impairment.

Another possibility is that the sudden end of respiratory acidosis when CO₂ breathing was terminated affected neurologic function in the postexposure condition. Nervous dysfunction may have been due to nerve cell hyperpolarization caused by an increase in intracellular chloride concentration. During respiratory acidosis, brain extracellular bicarbonate concentration increases and reacts with intracellular buffers causing a chloride shift to the intracellular space (18). This chloride shift would also

occur during CO₂ breathing. When CO₂ breathing terminates, it is possible that the concentration of intracellular chloride remains high for a brief time relative to the extracellular space, and nerve function is impaired by the resulting ionic imbalance. Individual differences in ventilatory response following CO₂ exposure (19–21) could influence the magnitude of this effect. Endogenous PCO₂ levels are reported to change more slowly following hyperoxic exposure than after normoxic exposure (19), and may explain the lack of effect in the hyperoxic study.

CONCLUSIONS

The results of this study indicate that divers with a low ventilatory response to CO₂ may be at risk for disequilibria, impaired decisionmaking, and disturbances in motor control. The extent of behavioral impairment may be determined by changes in arterial PCO₂ immediately after a period of CO₂ retention. It is likely that the effects observed in this laboratory study would be compounded by the increased demands of the underwater environment.

This work was funded by the University of Wisconsin Sea Grant Institute under grants from the National Sea Grant College Program, National Oceanic and Atmospheric Administration, U.S. Department of Commerce, and from the State of Wisconsin. Federal grant NA84AA-D-00065, project R/NA-11.

This work was performed in full at the University of Wisconsin-Madison. The opinions, findings and conclusions expressed in this report are not necessarily those of the National Institute for Occupational Safety and Health, nor does mention of company names or products constitute endorsement by the National Institute for Occupational Safety and Health.

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REFERENCES

1. Kerem D, Melamed Y, Moran A. Alveolar PCO₂ during rest and exercise in divers and non-divers breathing O₂ at 1 ATA. *Undersea Biomed Res* 1980; 7:17–26.
2. Lally DA, Zechman FW, Tracy RA. Ventilatory responses to exercise in divers and non-divers. *Respir Physiol* 1974; 20:117–129.
3. Schaefer, KE. Respiratory pattern and respiratory response to CO₂. *J Appl Physiol* 1958; 13:1–14.
4. Florio JT, Morrison JB, Butt WS. Breathing pattern and ventilatory response to carbon dioxide in divers. *J Appl Physiol* 1979; 46:1076–1080.
5. Lanphier EH, Camporesi EM. Respiration and exercise. In: Bennett PB, Elliott DH, eds. *The physiology and medicine of diving*. London: Baillière Tindall; San Pedro, CA: Best Publishing Company, 1982:99–156.
6. Morrison JB, Florio JT, Butt WS. Observations after loss of consciousness under water. *Undersea Biomed Res* 1978; 5:179–187.
7. Lambertsen CJ. Effects of oxygen at high partial pressure. In: Fenn WO, Rahn H, eds. *Handbook of physiology*, vol II. Respiration. Washington, DC: The American Physiological Society, 1965:3, 1027–1046.
8. Hesser CM, Adolfson J, Fagraeus L. Role of CO₂ in compressed-air narcosis. *Aerosp Med* 1971; 42(2):163–168.
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. Dripps RD, Comroe JH Jr. The respiratory and circulatory response of normal man to inhalation of 7.6 and 10.4 percent CO₂ with a comparison of the maximal ventilation produced by severe muscular exercise, inhalation of CO₂ and maximal voluntary hyperventilation. *Am J Physiol* 1947; 149:43–51.

11. NOAA diving manual. Washington, DC: National Oceanic and Atmospheric Administration, 1979.
12. Sheehy JB, Kamon E, Kiser D. Effects of carbon dioxide inhalation on psychomotor and mental performance during exercise and recovery. *Hum Factors* 1982; 24(5):581-588.
13. National Institute for Occupational Safety and Health. Occupational exposure to carbon dioxide. NIOSH criteria document 76-194. Washington, DC: US Government Printing Office, 1976.
14. Sayers JA, Smith REA, Holland RL, Keatinge WR. Effects of carbon dioxide on mental performance. *J Appl Physiol* 1987; 63(1):25-30.
15. Cunningham DJC, Robbins PA, Wolff CB. Integration of respiratory responses to changes in alveolar partial pressures of CO₂ and O₂ and in arterial pH. In: Fishman AP, Cherniack NS, Widdicombe JG, Geiger SR, eds. *Handbook of physiology*, vol II. Control of breathing, part 2; section 3. The respiratory system. Bethesda, MD: American Physiological Society, 1986:3, 484.
16. Suess WM, Alexander AB, Smith DD, Sweeney HW, Marion RJ. The effects of psychological stress on respiration: A preliminary study of anxiety and hyperventilation. *Psychophysiology* 1980; 17(6):535-540.
17. Gibson TM. Effects of hypocapnia on psychomotor and intellectual performance. *Aviat Space Environ Med* 1978; 49(8):943-946.
18. Ahmad HR, Loeschcke HH. Transient and steady state responses of pulmonary ventilation to the medullary extracellular pH after approximately rectangular changes in alveolar PCO₂. *Pflugers Arch* 1982; 395:285-292.
19. Gelfand R, Lambertsen CJ. Dynamic respiratory response to abrupt change of inspired CO₂ at normal and high PO₂. *J Appl Physiol* 1973; 35:903-913.
20. Fuleihan FJD, Nakada T, Suero JT, et al. Transient responses to CO₂ breathing of human subjects awake and asleep. *J Appl Physiol* 1963; 18:289-294.
21. Benards JA, Dejours P, Lacaisse A. Ventilatory effects in man of breathing successively CO₂-free, CO₂-enriched and CO₂-free gas mixtures with low, normal or high oxygen concentration. *Respir Physiol* 1966; 1:390-397.