

Central nervous system reactions during heliox and trimix dives to 31 ATA

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Vaernes R, Bennett PB, Hammerborg D, Ellertsen B, Peterson RE, Tønjum S. Central nervous system reactions during heliox and trimix dives to 31 ATA. Undersea Biomed Res 1982; 9(1): 1-14.—Two groups of divers were compressed to 300 msw (984 fsw) with heliox ($n=3$) and trimix ($n=3$). Neuropsychological/neurological testing was performed repeatedly during the compression and on reaching 250 (820 fsw) and 300 msw. On the second day the trimix group was tested before and after a gas change to heliox. For the heliox group there was a marked increase in tremor and EEG slow waves, and reduction of alpha band and in hand-grip strength. For the trimix group visuomotor coordination was impaired. In the cognitive performance tests the heliox group was most impaired at 250 msw, whereas the trimix group was most impaired at 300 msw. Before the gas change to heliox the trimix group showed impaired performance in some tests. After the gas change, performance returned to pre-dive levels, except for perceptual speed. There was an increase in tremor immediately after the gas change. Conclusion: There was a marked HPNS effect during compression on heliox. This effect was not observed in the trimix group, but this group was mildly intoxicated on reaching saturation depth. The tests indicated slight narcotic effects also after 26 h, but this disappeared after the change to heliox.

trimix
heliox

HPNS
tremor

cognitive performance test

Compression with helium and oxygen to depths greater than 150 msw (492 fsw; 16 ATA) produce signs and symptoms of the high pressure nervous syndrome (HPNS) (1). The syndrome includes tremor in the hands and arms, increased slow-wave activity (2-7 Hz) and depression of alpha waves (8-13 Hz) in the electroencephalogram (EEG), dizziness, nausea, and vomiting. At depths greater than 300 msw (984 fsw; 31 ATA) lapses of consciousness may occur (2). The symptoms of HPNS become more severe with increasing depth and during fast rates of compression.

Previous studies, especially in animals, have shown that the HPNS can be counteracted by addition of a mild narcotic agent, such as an increased partial pressure of nitrogen (3-5). Bennett et al. (6) examined the effects of exposure to 220 msw (722 fsw; 23 ATA) and 300 msw when breathing a helium-nitrogen-oxygen mixture (trimix). The percentage of nitrogen in the

trimix was 25% at 220 msw and 18% at 300 msw. Although the addition of nitrogen to heliox was effective in counteracting the HPNS symptoms, the partial pressure of nitrogen caused symptoms of nitrogen narcosis. Subsequent work in 1975 (7) tested a mathematical model predicting that 10% nitrogen would effectively counteract HPNS symptoms. The prediction was found to be quite reliable according to the definition of HPNS given by Bennett (7).

More recently Bennett et al. (8, 9) examined the effects of exposure to 460 msw (1509 fsw) using 5% nitrogen in Atlantis I and 10% in Atlantis II. Whereas the first dive with 5% nitrogen caused symptoms of HPNS as predicted, the dive with 10% nitrogen and the same compression rate caused no nausea, dizziness, or other symptoms of HPNS. Performance tests indicated impairment of motor and cognitive skills, however, which partly can be explained as an effect of nitrogen narcosis and partly as an effect of HPNS.

In the present study we wanted to investigate the possible effects of trimix on the central nervous system (CNS), using 10% nitrogen as compared to heliox during compression to 300 msw. A change of gas from trimix to heliox made it possible to study the elimination of nitrogen narcosis and the possible occurrence of HPNS symptoms in a design comparable to the one reported by Bennett et al. (6).

METHODS

Subjects and experimental design

Subjects. Six males participated as subjects. The mean age was 31 years (SD = 4.5). Three subjects were commercial divers; the others were a physiologist, an engineer, and a student, all involved in hyperbaric research.

Experimental design. The subjects were subdivided into two groups, both of which were compressed to 300 msw (31 ATA). One group ($n=3$) breathed heliox during the compression (heliox group), and the other group ($n=3$) breathed trimix with 10% nitrogen (trimix group). The compression profile (see Table 1) was to be identical for both groups, provided that no severe symptoms occurred. However, the holding period at 250 msw had to be extended from

TABLE 1
INITIAL COMPRESSION SCHEDULE

Depth, msw	Rate of Travel, msw/min	Travel Time, min:s	Stop Time, min:s	Total Time, min:s
0-125	6.0	20:50	—	20:50
125	—	—	1:10	22:00
125-188	3.0	21:00	—	43:00
188	—	—	1:00	44:00
188-250	1.5	41:20	—	85:20
250	—	—	180:00	266:00
250-275	6.0	4:10	—	270:10
275	—	—	0:50	271:00
275-288	3.0	4:20	—	275:20
288	—	—	0:40	276:00
288-300	1.5	8:00	—	284:00

3 h to 8 h 41 min for the heliox group. The entire trimix compression and other aspects of the heliox compression went according to schedule. The trimix group had a change of gas from a trimix atmosphere to a heliox atmosphere after 26 h at 31 ATA.

A battery of neurological, neuropsychological, and cognitive performance tests was used for evaluation of signs and symptoms of HPNS and nitrogen narcosis.

Tests administered during compression

The following five tests were administered repeatedly throughout the compression (see Table 2). Each test block lasted about 6 min without intermissions. The subjects then repeated the tests 15 times during the compression period.

Electroencephalography (EEG). A Beckman 511 Dynograph was used for recording the EEG and the depth in meters. Two channels were used for the EEG and the third channel recorded depth in meters as a DC signal from a pressure transducer in the chamber (Teledyne Taber model 2801, Teledyne Gurley, Troy, NY). Experimental events and noise in the EEG signal were manually marked on channel 4. High-pass EEG signals were filtered with a time constant of 1.5 Hz, and low-pass signals were filtered at 30 Hz.

The EEG electrodes were located at C3–F3 and C4–F4 according to the 10–20 system, and bipolar EEG recordings from both hemispheres were thus obtained (C3–F3 and C4–F4). The EEG was sampled for 6 min every 14 min for each subject during compression. The subjects had their eyes closed during sampling. The EEG signals were stored with an analogue tape recorder (Tandberg, series 100 Tandberg, Norway) for later off-line Fast Fourier Transform (FFT) computer analysis.

Static Steadiness Test. For recording postural tremor of the hands the Static Steadiness Test from the Kløve/Matthews motor steadiness battery was used (4605C, Lafayette Instrument Co., Lafayette, IN). The subject was required to insert a stylus into holes of varying

TABLE 2
PROCEDURE FOR ADMINISTRATION OF TESTS DURING COMPRESSION TO 300 MSW

Period	Diver 1	Diver 2	Diver 3
First 6-min period	EEG monitoring	Tremor, tapping, strength, visuomotor response	Registering the results for Diver 2
Second 6-min period	Registering the results for Diver 3	EEG monitoring	Tremor, tapping, strength, visuomotor response
Third 6-min period*	Tremor, tapping, strength, visuomotor response	Registering the results for Diver 1	EEG monitoring

*The cycle was repeated throughout the compression with about 1 min between periods.

diameters (range from 8 to 2 mm) for 15 s. The subject was not allowed to brace or rest his arm. The test equipment was connected to a data accumulation unit outside the chamber. Total time of contact and number of contacts were recorded for each trial.

Finger oscillation test. The Finger Tapping Test from the Halstead-Reitan test battery was used. Each subject was given 5 trials, each lasting for 10 s, and was required to use the index finger on his dominant hand throughout all trials.

Dynamometer test. Strength of hand grip in kg was measured with a dynamometer (78010, Lafayette Instrument Co., Lafayette, IN).

Trails test. Visuomotor speed and coordination were tested with the Trail Making Test (10). This is a paper-and-pencil test wherein the subject is asked to draw a line between circles containing letters and numbers. The instruction is to alternate between increasing numbers and the letters of the alphabet.

Tests administered at 250 ms and 300 ms

A cognitive performance test battery and a questionnaire were administered during the intermission at 250 ms and at 300 ms.

Arithmetic. The subjects were presented with sheets of mathematical statements (additions) for 1 min. Half of the statements were wrong and half correct, and they were in random order. The subjects were required to mark as many as possible as F (false) or C (correct).

Reasoning. The subjects were presented with sheets of verbal assertions for 1 min (11); example: "A precedes B-BA." Half of the assertions were correct, half were false, presented in random order. The subjects were required to rate the statements true or false.

Digit span. Thirty 8-digit numbers were presented at a regular pace during 5 s, followed by a 5-s pause during which the subjects were required to write down the numbers that had been read.

Long-term memory. The subjects were given 30 s to memorize a list of 10 pairs of words (e.g., where: bay, depth: 50m). The first word of each pair was presented 15 min later and memory for the paired word was tested.

Perceptual speed. Forty pairs of numbers were presented on a sheet. The subjects were given 1 min to compare the numbers and mark pairs having different numbers.

Status questionnaire. A checklist questionnaire regarding signs and symptoms of HPNS and narcosis was presented. The subjects were allowed to add comments not specified on the questionnaire.

Test procedure

The test procedure was the same for both groups. Pre-dive testing that included all tests was done repeatedly during the 2 weeks before the dive started. This was done in order to have a

minimum of three pre-dive test samples, to familiarize the subjects with the test procedures to be used in the pressure chamber, and to reduce learning effects.

During compression the subjects were rotated physically between the different test setups (Table 2). This rotation was repeated throughout the compression with about 1 min between periods of testing. For the trimix group, all tests described were repeated on the second day except for the EEG, which was not possible at that time. Tests were administered immediately after the change to heliox. A second testing was done 3 h later.

RESULTS

Compression period

Electroencephalography (EEG). The FFT analysis revealed a marked increase of power for slow waves (2–7 Hz) and a reduction of the alpha band (8–13 Hz) during compression to 300 msw for the heliox group (see Fig. 1). There was, however, considerable variance between subjects. Hemispheric differences were also found in the EEG (Fig. 1). The results are expressed as percentage of change from pre-dive EEG for each subject.

For the trimix group there was no comparable increase of slow waves (2–7 Hz) or reduction in the alpha band (8–13 Hz) (see Fig. 2). Some variance between subjects and slight hemispheric asymmetries were found. The changes noted during the dive seem to have persisted through the immediate post-dive period (Figs. 1 and 2).

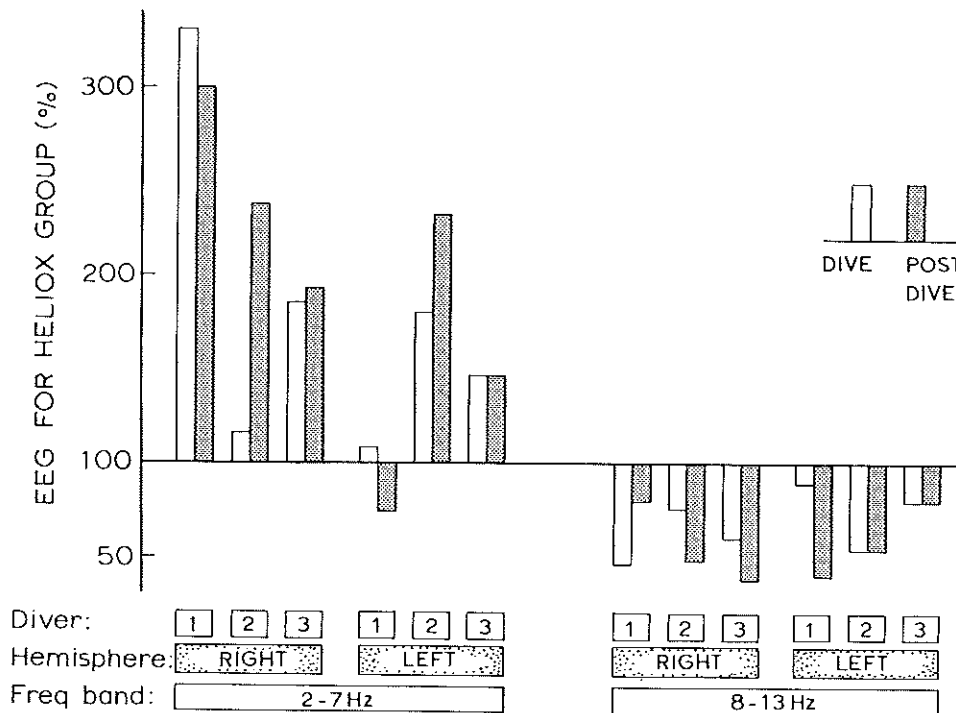


Fig. 1. Heliox group. Percentage of change from pre-dive level for slow waves (2–7 Hz, left) and alpha band (8–13 Hz, right) during compression to 300 msw.

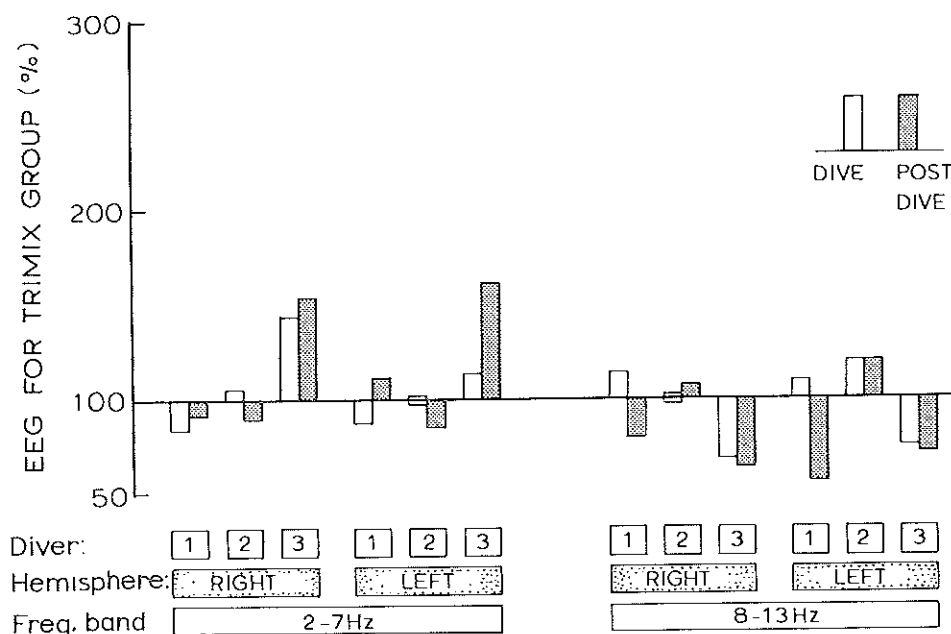


Fig. 2. Trimix group. Percentage of change from predive level for slow waves (2-7 Hz, *left*) and alpha band (8-13 Hz, *right*) during compression to 300 msw.

Static Steadiness Test. For the heliox group a marked increase in tremor that lasted throughout the compression period was found. For the trimix group a slight increase in this tremor was found during the first phase of compression. On reaching saturation level (31 ATA) tremor returned to predive levels (Fig. 3). There was a significant difference between the two groups for this variable [$t(13) = 3.56, P < 0.01$]. A drop of 5°C in chamber temperature at 250 msw for the trimix group caused increased tremor due to hypothermia. These data were not included in the data analysis.

Finger oscillation test. There was no significant change in finger-tapping speed during compression for any group.

Dynamometer test. For the heliox group there was no reduction in hand-grip strength in the dominant hand during compression (Fig. 4). This was not found for the trimix group, and the difference was statistically significant [$t(14) = 5.09, P < 0.01$].

For the nondominant hand there was no significant difference between the groups during compression.

Trails test. For the heliox group there was no impairment of visuomotor coordination or speed during compression (Fig. 5). For the trimix group there was a marked slowing of performance (Fig. 5), yielding significant differences between the two groups [$t(14) = 7.20, P < 0.01$].

Comparison of 250- and 300-msw stages

Cognitive performance tests. For the heliox group there was no impairment of arithmetic performance at 250 msw. In the reasoning test the performance was reduced by 22%, with

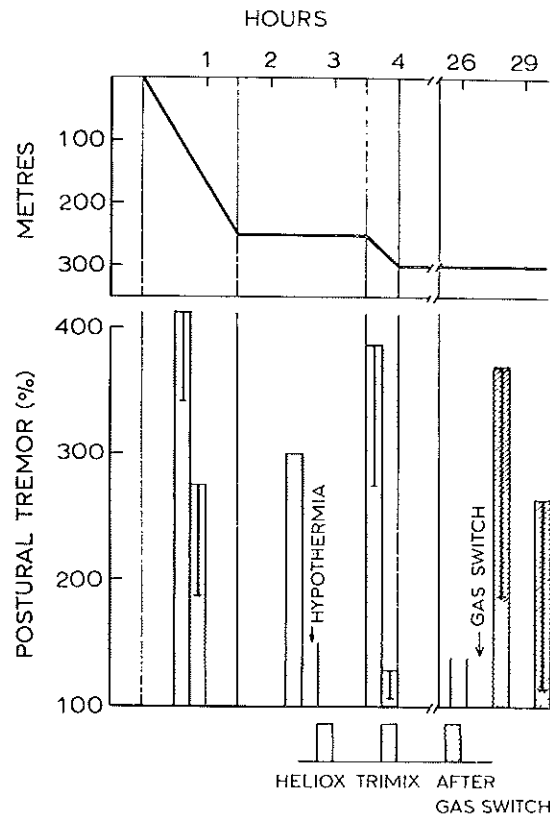


Fig. 3. Percentage of increase from prediv level for postural tremor during compression for heliox and trimix, and before and after change of gas for trimix group only.

considerable individual variation, however. For the digit span, there was a slight (9%) decrease in performance. The long-term memory test indicated a marked drop in performance at 250 msw (45%). The perceptual speed test showed a 17% reduction of performance (Fig. 6).

For the trimix group there was no reduction in arithmetic performance. With the reasoning test the reduction was 9% (Fig. 6), and for the digit span test a 31% reduction of performance was found, with considerable individual variation. The long-term memory test indicated a marked drop in performance (35%), while the perceptual speed test showed no reduction.

The cognitive performance tests at 300 msw indicated a marked change in performance in both groups compared to their performance at 250 msw. For the heliox group performance in the arithmetic test still was at prediv level. In the reasoning test the performance returned to prediv levels, while the digit span showed a further reduction (18%). The long-term memory test performance was slightly better than at 250 msw (40% reduction as compared to 45% reduction), whereas the perceptual speed scores returned to prediv levels of performance (Fig. 6). For the trimix group performance in the arithmetic test still was at prediv level. The reasoning test performance showed a further reduction (22% reduction as compared to 9% reduction). The same tendency was observed for the digit span test and for the long-term memory test (40% and 80% reduction, respectively). Perceptual speed was slightly decreased (10%).

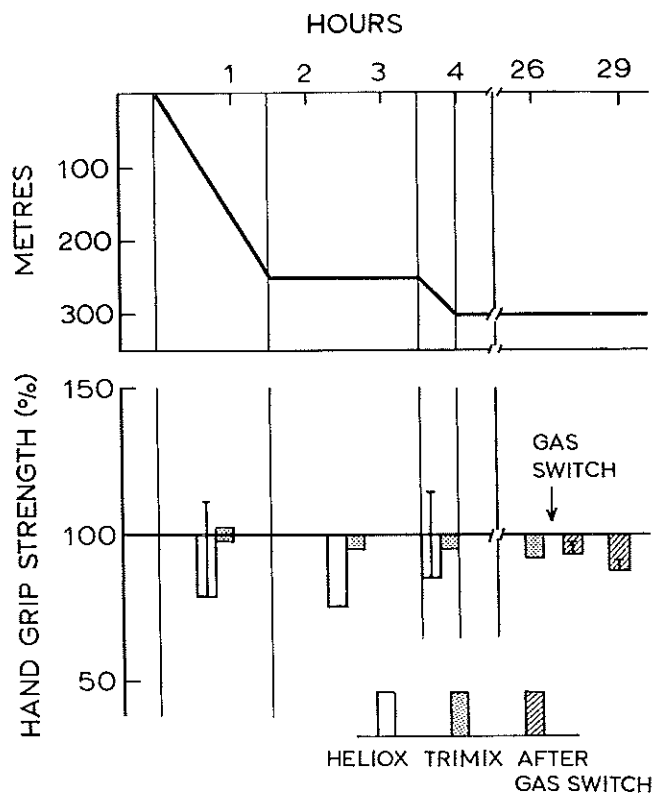


Fig. 4. Percentage of change from predive level for hand-grip strength (dominant hand) during compression for heliox and trimix groups, and before and after change of gas for trimix group only.

Status questionnaire. On arrival at 250 msw (26 ATA) two of the subjects in the heliox group reported nausea. They also reported dizziness, and one of them reported dry mouth and numbness (Table 3). On reaching 300 msw (31 ATA) about 9 h later one subject was still nauseated. The same subject also reported arthralgia. Two subjects reported dizziness.

One subject in the trimix group reported nausea, dizziness, euphoria, and ringing ears on reaching 250 msw. In addition he reported arthralgic pain in his shoulders. A second diver also reported arthralgia and pain in his shoulders at that depth. The symptoms were minor compared to those reported in the heliox group. While the heliox group had to stay at 250 msw for 8 h 41 min to recover from the symptoms, 2 h later the trimix group compressed to 300 msw according to the initial schedule. Arthralgia was still reported on reaching 300 msw on trimix. One subject had pain in shoulders and elbow, while the other reported pain in shoulders, elbow, and ankle. In addition, one of these subjects reported euphoria and ringing in the ears (Table 3).

Before and after gas change

Static steadiness. After the gas change there was a strong increase in tremor as compared with the results from the day before (Fig. 3). Three hours later the tremor had decreased, but the standard deviation indicated that the recovery time varied for the subjects. Immediately before the gas change there was an increase in tremor (Fig. 3) that was possibly due to physical

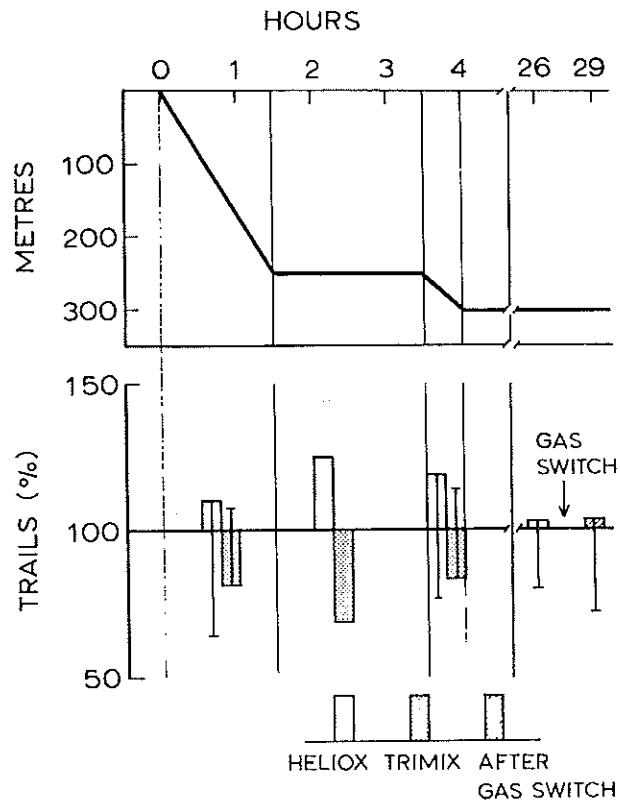


Fig. 5. Percentage of change from predive level for performance in trails test during compression for heliox and trimix groups, and before and after change of gas for trimix group only.

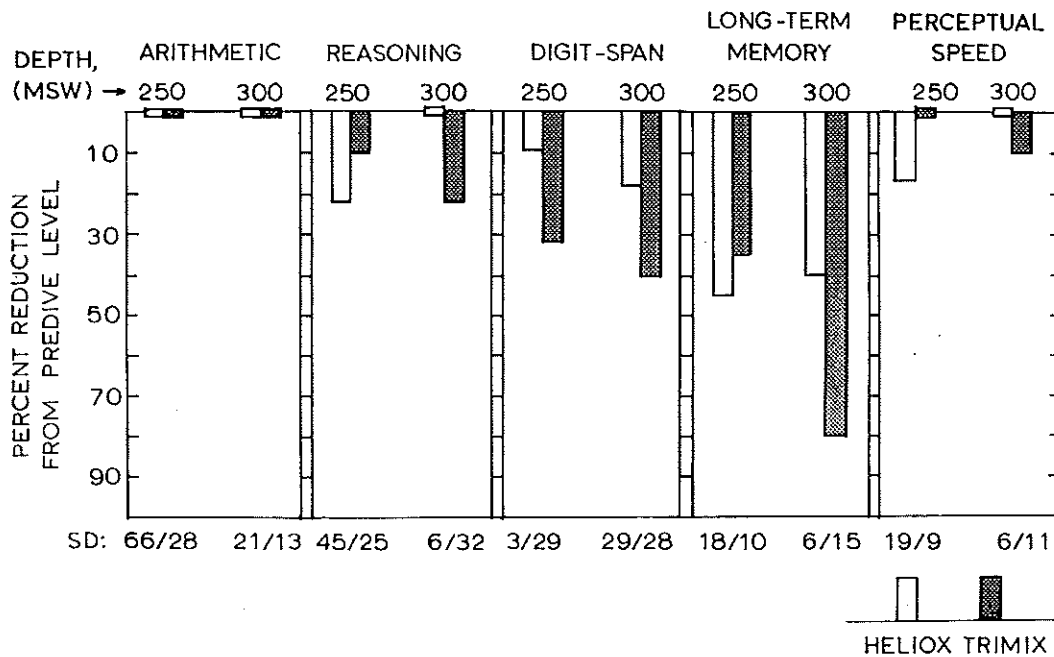


Fig. 6. Percentage of reduction from predive level of performance tests at 250 and 300 msw for heliox and trimix groups.

TABLE 3
SUBJECTIVE SYMPTOMS FOR DIVERS IN HELIOX AND TRIMIX GROUPS ON
REACHING 250 MSW AND 300 MSW

Group	Depth, msw	Diver No.	Symptoms	Localization of Pain	Breathing Difficulty
Heliox	250	1			No
Heliox	250	2	Nausea, dizziness		No
Heliox	250	3	Nausea, dizziness, numbness, dry mouth		No
Trimix	250	1			No
Trimix	250	2	Arthralgia	Shoulders	No
Trimix	250	3	Nausea, dizziness, euphoria, ringing ears	Shoulders	Some
Heliox	300	1			
Heliox	300	2	Nausea, dizziness, arthralgia	Knee	No
Heliox	300	3	Dizziness		No
Trimix	300	1			No
Trimix	300	2	Arthralgia	Shoulders, ankle, elbow	No
Trimix	300	3	Arthralgia, euphoria, ringing ears	Shoulders, elbow	No

activities in preparing for the gas change. Just as with the shivering due to hypothermia the previous day, the tremor in this case is not included here.

Finger oscillation. The subjects performed slightly better than 100% (compared with pre-dive level) immediately before and after the gas change and 3 h later.

Dynamometer. Before and immediately after the change of gas there was no change in hand-grip strength. Three hours later there was a slight, nonsignificant drop in hand-grip strength from 93% of pre-dive level to 87% (Fig. 4).

Trails. On the second day of saturation the trimix group performed slightly better than the 100% pre-dive level concerning visuomotor coordination and speed (Fig. 5). There was no change after the change of gas.

Cognitive performance tests. Immediately before and after the change to heliox the trimix group was tested with the performance test battery. For the arithmetic test, the result was at pre-dive levels before and after the gas change. For the reasoning test, there was still a 20% reduction on the second day before the gas change, but this performance returned to pre-dive level after the gas change (Fig. 7). The same was found for long-term memory: there was still a 45% reduction in performance, but the performance returned to pre-dive levels after the gas change. Performance on the digit span had returned to pre-dive levels on the second day, and there was no change after the gas change. With regard to perceptual speed, there was still a reduction of 17% the second day, and this reduction continued after the gas change to heliox (17% and 14%).

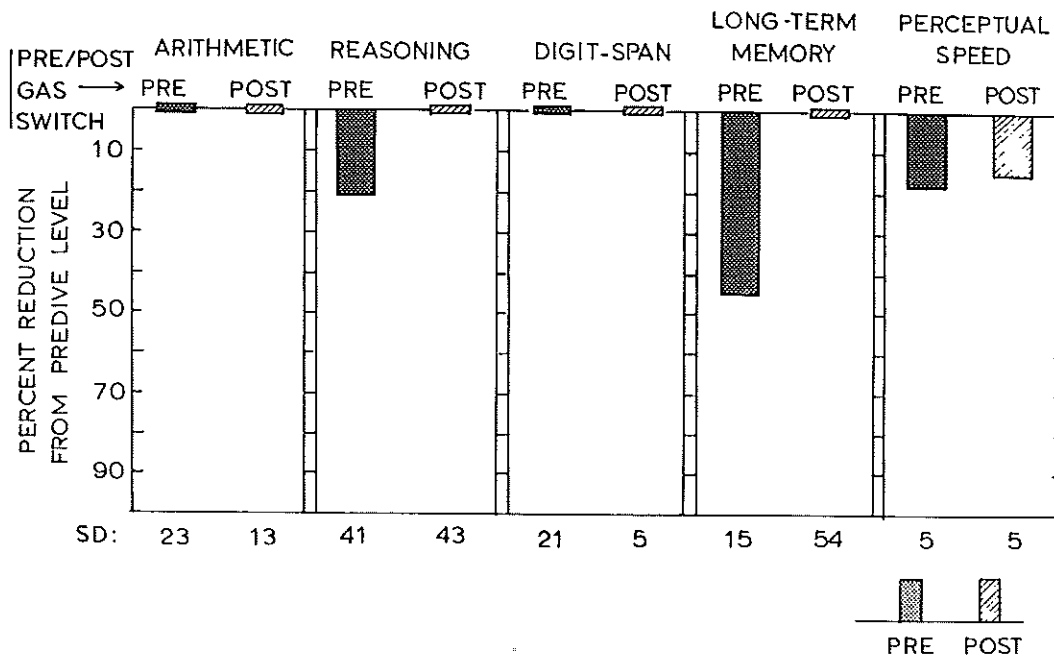


Fig. 7. Percentage of reduction from pre-dive level of performance before and after (*pre* and *post*) change of gas in trimix group only.

Status questionnaire. On the second day of saturation one subject in the trimix group reported pain in his shoulder, and a second subject reported pain in elbow and shoulder in addition to blurred vision, feeling cold, ringing ears, and a dry mouth. The first of these two subjects did not report any improvement after the gas change. The second of the two reported ringing ears and pain in ankle in addition to pain in shoulder and elbow. No symptoms were reported for the third subject (Table 4).

DISCUSSION

Compression to 300 msw in 95 min with heliox as the breathing gas caused severe symptoms of HPNS. At 250 msw, two of the subjects were nauseated and also reported dizziness and numbness and felt cold. Power spectrum analysis of the EEG showed a marked increase in slow waves (2–7 Hz) and inhibition of alpha-band (8–13 Hz) activity during the compression. In addition, there was a significant increase of postural tremor and reduction of hand-grip strength. The performance tests showed a marked disturbance of reasoning capacity and long-term memory at 250 msw. At 300 msw, 9 h later, the subjects still showed disturbances in the long-term memory function.

Compression to 300 msw in 95 min with a trimix breathing gas containing 10% nitrogen effectively prevented the major HPNS symptoms. Power spectrum analysis of the EEG showed no changes from base-line EEG recordings. Postural tremor and hand-grip strength also were unaffected. There was a significant decrease in visuomotor coordination and speed during the last phase of compression, and this was possibly due to a mild narcosis. There was a marked disturbance of reasoning and memory function at 250 msw, and a further deterioration of these cognitive functions at 300 msw, long-term memory being most strongly affected.

TABLE 4
SUBJECTIVE SYMPTOMS FOR DIVERS IN HELIOX AND TRIMIX GROUPS ON DAY 2 OF
SATURATION AT 300 MSW, AND FOR TRIMIX GROUP AFTER CHANGE OF GAS

Group	Event	Diver No.	Symptoms	Localization of Pain	Breathing Difficulties
Heliox	Day 2, 300 msw	1			No
Heliox	Day 2, 300 msw	2			No
Heliox	Day 2, 300 msw	3			No
Trimix	Day 2, 300 msw	1			
Trimix	Day 2, 300 msw	2	Arthralgia	Shoulder	No
Trimix	Day 2, 300 msw	3	Blurred vision, ringing ears, feeling cold	Shoulder, elbow	No
Trimix	After gas change	1			No
Trimix	After gas change	2	Arthralgia	Shoulder	No
Trimix	After gas change	3	Arthralgia, ringing ears	Shoulder, elbow, ankle	No

The postdive EEG results sampled 4 h after reaching surface differentiated the two groups in much the same way as the compression EEG results. These postdive profiles are in agreement with the Bevilacqua et al. study (12) and Rostain and Naquet (13). In the Rostain and Naquet study (13) there were post-exposure EEG changes for 1 to 2 days at normal atmosphere pressure in approximately 30% of the subjects studied, for 1 to 2 weeks in approximately 10%, and for as long as 3 weeks in a single subject. Their study also indicated that post-exposure EEG alterations appeared to be more persistent in those individuals who had more prominent changes during exposure. The same was found in the present study, but the initial change was connected to the heliox exposure.

On the second day of saturation the trimix group made a gas change to heliox only. One hour before this gas change the cognitive performance tests were administered. Results from the tests showed a markedly improved performance on reasoning and short-term memory tests in relation to the previous day. Long-term memory, however, still showed 45% impairment of performance, but this returned to predive levels after the gas change to heliox. The only disturbance of performance after the gas change was found with the steadiness test. Immediately after the gas change, there was a marked increase in tremor that was possibly due to HPNS. Three hours later there was still an increase in tremor, as compared to trimix levels. On the status questionnaire there was no euphoria reported in the trimix group on the second day of saturation. Before the gas change two subjects reported arthralgia, and this was unchanged after the change to heliox. One subject noted that his blurred vision had disappeared.

The results obtained in this study are different from those reported by Rostain et al. (14). We found that the trimix group tended to be least affected during compression, whereas the

opposite was reported by Rostain et al. (14). However, experimental conditions were different in the two studies: the depth was the same (300 msw), but the compression was slower and the percentage of nitrogen was lower in the study by Rostain et al. (14). In addition, the stay at bottom was short in the CORAZ experiments, and it has been shown that the HPNS, and especially the EEG changes, develop with a certain latency and do not appear immediately after compression (15, 16).

This study shows that 10% nitrogen is effective in preventing HPNS symptoms during compression to 300 msw, an effect which agrees with clinical observations by other authors (6, 17–20). The impaired cognitive functions at saturation depth, however, indicate the presence of effects of the nitrogen combined with compression and high pressure. After 26 h there was still a slight reduction on some tests. This indicated that the adaptation to or elimination of nitrogen narcosis lasted longer than the recovery from the HPNS symptoms.

The results confirm previous studies (14) that there is a complex central nervous reaction pattern to the hyperbaric condition. Nitrogen narcosis and HPNS reactions depend not only on gas mixture, compression rate, depth, and duration of the dive but also on the individual sensitivity to the different conditions. It is not sufficient to use only one type of variable (neurological or neuropsychological findings, cognitive performance tests, or subjective recital of symptoms) in evaluating the effects of deep dives. Even though no neurological signs or subjective symptoms of HPNS or nitrogen narcosis, or both, may occur, there may still be changes in performance on complicated cognitive tests, indicating that the diver may not be able to cope with tasks in the real diving situation.

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Vaernes R, Bennett PB, Hammerborg D, Ellertsen B, Peterson RE, Tønjum S. Réactions du système nerveux central au cours de plongées à 31 ATA à l'héliox et au trimix. *Undersea Biomed Res* 1982; 9(1):1–14. — Deux groupes de plongeurs ont été comprimés à 300 m (984 pieds), avec de l'héliox ($n = 3$) et du trimix ($n = 3$). Des tests neuropsychologiques/neurologiques étaient effectués de façon répétitive pendant la compression et en arrivant à 250 m (820 pieds) et 300 m. Le second jour, le groupe trimix a subi des tests avant et après un passage à l'héliox. Pour le groupe héliox, il y avait une nette augmentation du tremblement et des ondes lentes à l'EEG, et une réduction de la bande alpha et de la force de fermeture de la main. Pour le groupe trimix, la coordination visuomotrice était perturbée. Dans les tests de performance cognitive, le groupe héliox était le plus perturbé à 250 m alors que le groupe trimix était le plus perturbé à 300 m. Avant le passage à l'héliox, le groupe trimix présentait une altération des performances à certains tests. Après le changement de mélange, les performances revenaient aux niveaux d'avant la plongée sauf en ce qui concerne la vitesse de perception. Il y avait une augmentation du tremblement immédiatement après le changement de mélange. Conclusion: Il y avait un effet de SNHP, marqué pendant la compression à l'héliox. Cet effet n'était pas observé dans le groupe trimix, mais celui-ci était modérément intoxiqué à l'arrivée au niveau fond. Les tests indiquaient de légers effets narcotiques également après 26 h, mais ceux-ci ont disparu après le passage à l'héliox.

trimix
héliox

SNHP
tremblement

test de performance cognitive

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