EEG and sleep disturbances during dives at 450 msw in helium-nitrogen-oxygen mixture

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Rostain, J. C., M. C. Gardette-Chauffour, and R. Naquet. EEG and sleep disturbances during dives at 450 msw in helium-nitrogen-oxygen mixture. *J. Appl. Physiol.* 83(2): 575–582, 1997.—To study the effects of nitrogen addition to the breathing mixture on sleep disturbances at pressure, two dives were performed in which helium-nitrogen-oxygen mixture was used up to 450 m sea water (msw). In total, sleep of 12 professional divers was analyzed (i.e., 184 night records). Sleep was disrupted by compression and by stay at 450 msw: we observed an increase in awake periods and in sleep stages I and II and a decrease in stages III and IV and in rapid-eye-movement sleep periods. These changes, which were more intense at the beginning of the stay, began to decrease from the seventh day of the stay, but the return to control values was recorded only during the decompression at depths below 200 msw. These changes were equivalent to those recorded in other experiments with helium-oxygen mixture in the same range of depths and were independent of the intensity of changes recorded in electroencephalographic activities in awake subjects.

electroencephalogram; high-pressure nervous syndrome; pressure; vigilance

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WHEN HUMAN DIVERS or experimental animals are exposed to high pressure, they develop high-pressure nervous syndrome (HPNS) (4, 5). This syndrome occurs for pressures higher than 1.0 MPa [100 m sea water (msw)] in a He-O_2 breathing mixture. Signs and symptoms of HPNS, such as nausea, vomiting, tremor, myoclonia, increase in slow waves and decrease in fast activities in the electroencephalogram (EEG), decrements in intellectual and psychomotor performance, and sleep disturbances, are factors that reduce diver's ability to work at great depth. Several human deep dives, animal experiments, and neuropharmacological studies have been conducted in an attempt to elucidate the origins and mechanisms of this syndrome, and some methods to counteract it have been used. The methods to prevent HPNS include selection of divers, slow exponential compression in stages, and the use of narcotic gases to antagonize the effects of pressure (2, 4, 18, 21, 23, 24, 26). The latter method has been extensively tested in humans by using increased partial pressure of N_2 (2, 3, 15, 21, 23). Although Bennett et al. (2) concluded that He-N_2-O_2 mixture caused suppression of HPNS, data from Rostain et al. (23) indicated that N_2 caused suppression of only some of the behavioral symptoms of HPNS but that other signs such as EEG changes were similar in He-O_2 and He-N_2-O_2 mixtures. In the present work, we have conducted research to study the effects of He-N_2-O_2 mixture on sleep disturbances classically recorded during dives in He-O_2 mixture (22, 28).

METHODS

Dives

Two dives [Direction des Recherches Études et Techniques (DRET) 79/131 and Entrainement Expérimental (ENTEX) V] were performed to 450 msw, with the divers using the He-N_2-O_2 mixture. The compressions to a depth of 450 msw were carried out as follows (Fig. 1): an exponential-like profile, with speeds decreasing every 100 msw (0.5, 0.4, 0.25, 0.2, and 0.14 m/min), up to the depth of 450 msw; stops of 150 min every 100 msw; and an addition of N_2 before each stop to give a partial pressure of N_2 of 2.2 bar (4.8%) at 450 msw.

The compression was always started at 1400 and lasted 38 h from 0 to 450 msw. The P_{O_2} was 0.4 bar. The humidity was maintained between 50 and 70%, and the temperature was 31 ± 1°C to maintain the thermal comfort of the subjects in He environment.

The subjects spent a 5-day predive period in the same pressure chambers, immediately followed by compression.

Subjects

The divers were from Compagnie Maritime d'Expertise (COMEX) and the French Navy. They were selected from among subjects classified in *groups 0* and *1* according to their susceptibility to HPNS. This classification is based on tests, consisting of fast compressions to 180 msw, as described by Rostain et al. (24) (*group 0*: no increase in EEG theta activities; *group 1*: an increase between 10 and 100%). Twelve subjects (average age 32 ± 4 yr) took part in two experiments (8 subjects in DRET 79/131 and 4 subjects in ENTEX V). During the DRET 79/131, the stay at 450 msw lasted 2 days. During ENTEX V dive, the stay at 450 msw lasted 12 days. Decompression performed with a P_{O_2} of 0.5 bar lasted 14 days.

Neurophysiological Analysis

EEG activity was measured by using either fishhook electrodes (Etudes et Constructions Electromécaniques et Médicales, Paris, France) (DRET 79/131) or platinum-wire electrodes (ENTEX V). In all cases, the electrodes were attached to the scalp for the duration of the dive, implanted in the frontopolar, central, midtemporal, and occipital areas of the right hemisphere. The EEG recordings were made, with the subjects awake, several times a day on an electroencephalograph and analog magnetic tape by twin bipolar leads (frontal-central, central-temporal, and temporal-occipital). The tests lasted 10–15 min and were carried out simultaneously in all subjects during the dive.

The EEG traces were interpreted, and the data, recorded on magnetic tape, were analyzed by computer (Digital PDP11)

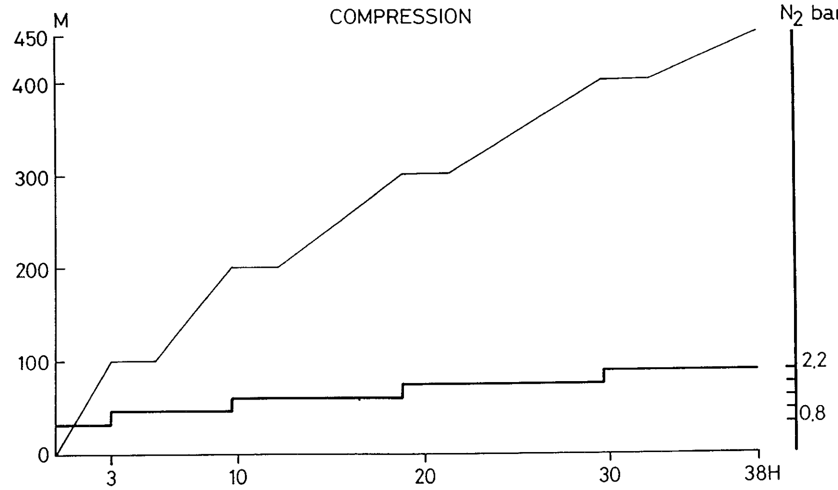

Fig. 1. Profile of compression and of N_2 addition used in 2 experiments.

to give the power spectra, according to the method described by Gourret et al. (8). The computer analysis was carried out simultaneously on three channels, for each subject, on 8-s sequences of EEG recordings meeting the criteria for spectral analysis (i.e., epochs with stationary EEG activities with eyes closed or eyes open without artifact) with low-pass filtering at 40 Hz. The power spectra were calculated for each sequence. The statistical calculations (mean ± SD in each EEG frequency band) were carried out for every five frequency bands (delta 1–4 Hz; theta 4–8 Hz; alpha 8–14 Hz; $beta_1$ 14–22 Hz; $beta_2$ 22–40 Hz) using the mean of several power spectra corresponding to 10–15 min of recording. The differences of the power between the surface values and those recorded under pressure were expressed as percent difference.

For the study of the sleep EEG, each night the subject fixed cutaneous electrodes (silver disks, 1.2-mm diameter) with adhesive tape to each side of his eyes to record the ocular movements. Amplitude and frequency of respiration were recorded with bucconasal thermistors and with an abdominal strap equipped with an extensiometer and electrodes to measure the variations of thoracic impedance. Oral temperature was measured morning and evening with thermistors (Yellow Springs 420 series) placed under the subject's tongue.

The EEG activities were recorded on an electroencephalograph (Alvar) in twined bipolar derivation (frontopolar-central, central-midtemporal, midtemporal-occipital). The sleep EEGs were recorded each night during the predive period and during the dive. The subjects had regularly scheduled daytime activities and regularly scheduled nocturnal sleep times. Because the daytime workload was heavy, both during the compression and the stay at depth, divers were unable to take naps during the day.

During all experiments (predive and dive), the lights were off no later than 2230 and on at 0630. The divers slept in conventional beds and, in all cases, were able to isolate themselves in their beds by a curtain. The noise was controlled so that the background level was equivalent to that of a conventional bedroom and was the same during the predive period and during the dive.

The analyses of the sleep traces were carried out in two stages. First, the EEG traces were read visually. They were interpreted in analyzed sections of 20 s (corresponding to one page of polygraph paper) to determine the five conventional sleep stages according to the criteria reported by Gourret et al. (8) and Rostain et al. (22), with the addition of the intermediate phases defined by Lairy et al. (11). Our population of divers showed sleep periods corresponding to all these phases. We decided to include these phases and to follow their development during the dives. Sleep duration is expressed in number of pages, with each page corresponding to a section of 20 s. The results (stages and number of pages) were then entered manually and stored on disks as described previously (8, 22). The programs reproduced sleep development as a hypnogram and calculated the duration of the various stages [waking periods; stages 1, 2, 3, 4; rapid-eye-movement (REM) sleep periods; intermediary stage (IS)], percentage of total time spent in these stages, duration of sleep, frequency of occurrence of each stage, average duration of each stage, inter-REM intervals, and number of cycles of sleep. These analyses were carried out for each sleep cycle and for the entire night. They were done each night for each subject, for groups of nights, and for groups of subjects in identical situations so as to compare mean values; e.g, those obtained on the surface and those obtained during a stay at a specific depth. The last three nights of the predive period were taken as references.

For statistical analysis, the results for each subject were averaged for each dive for control nights and for nights spent at a constant depth. These values were assumed to be paired (same subjects in two different situations), and the Wilcoxon paired test was used (7). Averages were also obtained for all subjects at 450 msw. For these comparisons, the Mann-Whitney *U*-test was used (7). The significance was calculated on two-tailed test.

Sleep quality was evaluated by the ratio of the durations of the stages 3 + 4 and stages 1 + 2 and by the ratio of the durations of REM periods and non-REM (NREM) sleep.

RESULTS

Sleep and Stage Durations

During the compression. A slight decrease in sleep duration was observed the second night of the compression in the two dives, i.e., between 400 and 450 msw when compared with that recorded at atmospheric pressure (Table 1). The mean decrease was ~60 min (15%) for DRET 79/131 and ~40 min (11%) for ENTEX V dive.

The mean duration of each stage calculated for the eight subjects of the DRET 79/131 dive indicated a significant increase in awake period durations and a decrease in stage 3 duration (−33%) for the first night of compression, between 175 and 250 msw, and a decrease in REM period (−36%) the second night. The mean duration calculated for each stage for the four divers of ENTEX V dive indicated an increase in stage 2

Table 1. *Mean duration of total sleep by night for experiments DRET 79/131 and ENTEX V*

Depth of Dive, m	DRET 79/131, h:min ($n = 8$)	ENTEX V, h:min ($n = 4$)
0	6:36 ± 0:39	6:11 ± 0:55
175	6:13 ± 0:16	7:30 ± 0:07*
400	5:39 ± 0:26*	5:30 ± 0:19
450	6:08 ± 0:54	6:45 ± 0:25
450	5:22 ± 1:04*	6:34 ± 0:36
450		6:37 ± 0:46
450		6:20 ± 1:03
450		5:42 ± 1:14
450		6:14 ± 1:08
450		5:03 ± 0:48
450		6:57 ± 0:45
450		6:15 ± 1:26
450		6:39 ± 1:13
450		7:08 ± 0:33
450		6:13 ± 0:32
400	6:38 ± 0:42	7:33 ± 0:14*
350	6:29 ± 1:16	6:51 ± 0:55
300	7:05 ± 0:49	5:35 ± 0:25
260	7:04 ± 0:37	6:42 ± 0:54
210	7:08 ± 0:24	6:52 ± 0:20
180	6:50 ± 0:25	6:19 ± 0:47
140	7:30 ± 0:17	6:59 ± 0:53

Values are means ± SD; *n*, no. of subjects. *$P < 0.05$.

duration (+33%) for the first night and a decrease in REM period duration (−60%) for the second night when compared with those recorded at atmospheric pressure (Figs. 2 and 3).

The duration of various stages expressed as percentage of total sleep time indicated changes only in stage 3 for the first night of the compression of DRET 79/131 dive and in REM periods during the second night of the compression of ENTEX V dive (Figs. 4 and 5).

During the stay at 450 msw. In DRET 79/131, the duration of the sleep did not show significant decrease during the two nights of the stay when compared with that recorded at atmospheric pressure; however, there was an increase in the variability among individuals, indicated by the increase of the SD. Also, no significant change was recorded for the duration of total sleep during the stay at 450 msw in the second dive; an increase of the variability among individuals was recorded during the stay (Table 1).

The mean duration of each stage for the DRET 79/131 dive indicated an increase in awake period durations (around +50%) during the 2 nights at 450 msw and a significant decrease in stages 3, 4, and REM period durations the second night at 450 msw (−29, −86, and −46%, respectively). The changes were more consistent during the longer stay of the ENTEX V dive. Indeed, there was an increase of the duration variability of awake periods, indicated by the increase of SD, a significant increase of stage 1 sleep during a great part of the stay (up to +150%), an increase in stage 2 duration, especially during the first 6 nights of the stay (up to +60%), with a decrease of stage 3 duration during the same period (up to −68%), a decrease of stage 4 duration and even a disapearence of this stage, and a decrease in REM period durations at the beginning of the stay at 450 msw (up to −60%) (Figs. 2 and 3).

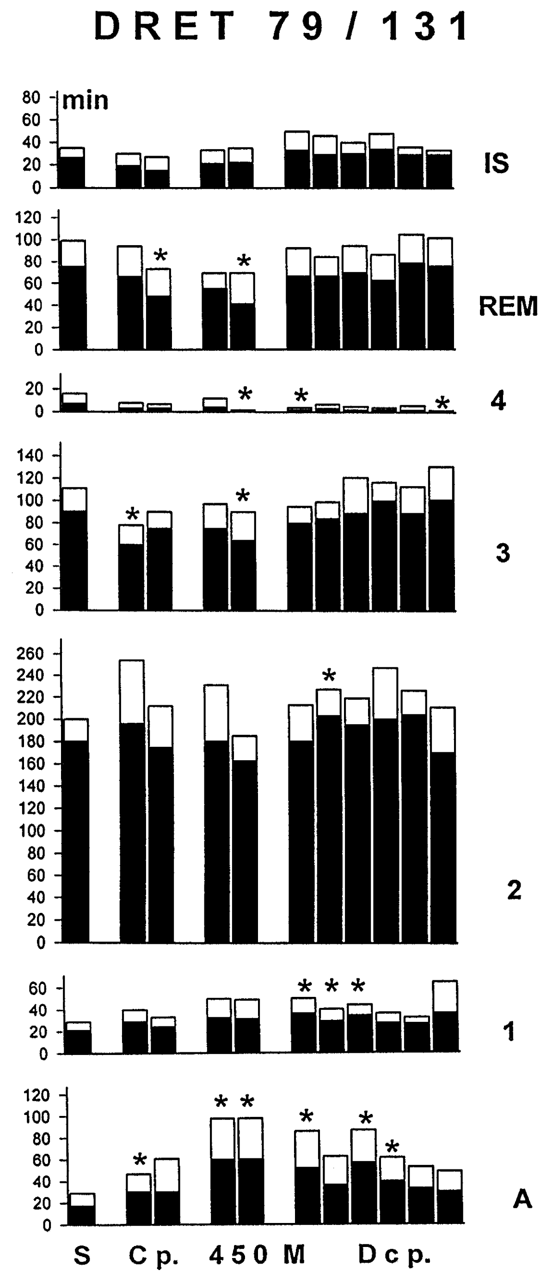

Fig. 2. Mean duration of each stage of sleep for 8 subjects from experiment DRET 79/131. S, control value for all 8 subjects; Cp, results from 2 nights during compression; 450 m, sleep duration during stay at 450 m sea water (msw); Dcp, sleep duration during 6 nights of decompression. *Bottom* to *top*: awake periods (A); sleep stages 1, 2, 3, and 4; rapid-eye-movement (REM) sleep periods; and intermediary stage (IS). *Significant difference with Wilcoxon test ($P < 0.05$).

The duration of various stages expressed as percentage of total sleep time calculated for the DRET 79/131 dive indicated an increase in awake periods and a decrease in stages 3 and 4 and REM period the second night of the stay. For ENTEX V dive, the percentage increased significantly for stages 1 and 2 essentially during the first 6 nights of the stay. It decreased for stages 3 and 4 and REM period for the same nights (Figs. 4 and 5).

The duration and the percent duration of each stage indicated a progressive improvement during the last 6

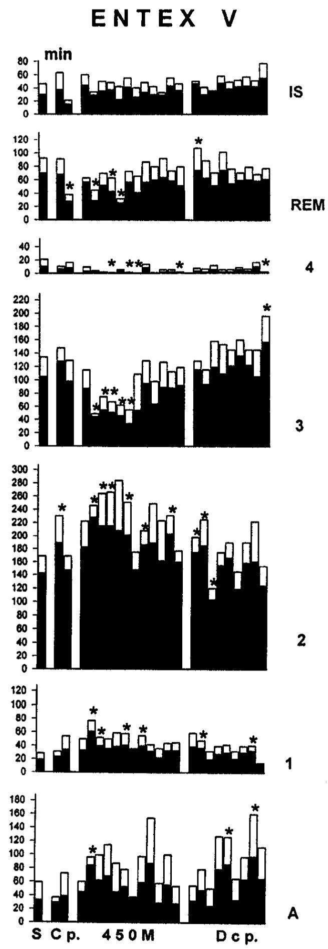

Fig. 3. Mean duration of each stage of sleep for 4 subjects from experiment ENTEX V. S, control value for all 4 subjets; Cp, results from 2 nights during compression; 450 m, sleep duration during 12-day stay at 450 msw; Dcp, sleep duration during 9 nights of decompression. *Significant difference with Mann-Whitney *U*-test ($P < 0.05$).

nights of the stay, with a periodic increase or decrease according to the nights and the stages, without return to control values.

During the decompression. The duration and the percentage of sleep returned to values similar to those recorded during the predive values, except for stage 4, which stayed lower than control.

Sleep Quality, Respiration, and Temperature

The analysis of the ratio of stages 3 + 4 to stages 1 + 2 for the subjects of the dive DRET 79/131 indicated a reduction from 0.42 during the control nights to 0.32 and 0.30 during the compression and the stay at 450 msw (Fig. 6). Recovery was recorded during the decompression. The REM/NREM ratio calculated for all subjects indicated a decrease from 0.33 at atmospheric pressure to 0.26 and 0.25 during the compression and the stay at 4.5 MPa. A recovery was recorded during the decompression.

The analysis of the ratio of stages 3 + 4 to stages 1 + 2 for the subjects of the ENTEX V dive indicated a reduction from 0.7 to 0.26, 0.18, 0.34, and 0.43 during the nights S1, S2, S3, and S4 of the stay at 4.5 MPa, respectively (Fig. 7). Recovery was recorded during the decompression. The REM/NREM ratio indicated a decrease from 0.37 at atmospheric pressure to 0.27, 0.26, 0.28, and 0.31 during the group of nights called S1, S2, S3, and S4 of the stay, respectively. Recovery was also recorded during decompression (Fig. 7).

During both experiments, no significant changes in respiration and temperature relative to control were recorded. Oral temperature was between 36.5 and 35°C, and respiration frequencies were between 10 and 20 breaths/min, depending of the divers and the stages of sleep.

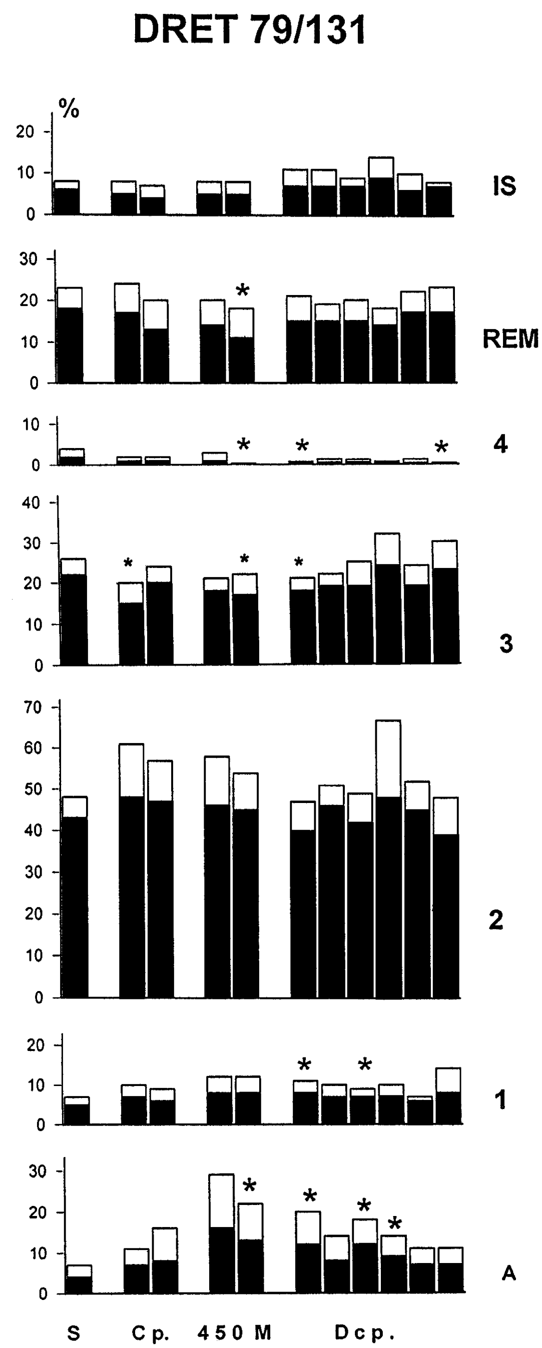

Fig. 4. Mean duration of each stage expressed as %total sleep time for 8 subjects during experiment DRET 79/131. Symbol definitions as in Fig. 2. *$P < 0.05$.

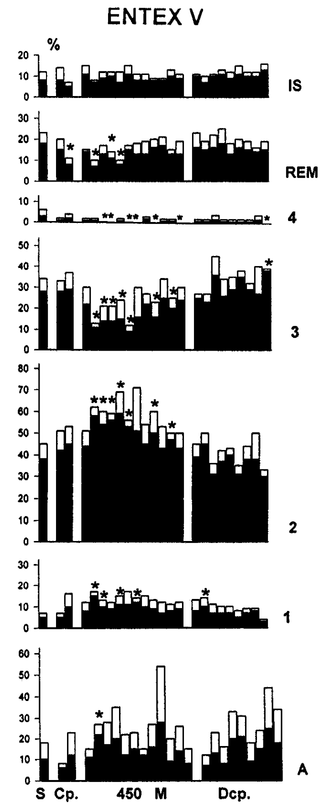

Fig. 5. Mean duration of each stage expressed as %total sleep time for 4 subjects during experiment ENTEX V. Symbol definitions as in Fig. 3. $^{*}P < 0.05$.

EEG Changes

Changes in awake-state EEG activities have been recorded during both experiments. The analyses of EEG trace and of power spectra indicated a decrease in alpha frequencies in all subjects, which occurred from 100 msw (1 MPa), and an increase in theta frequencies, which occurred in frontal area in most of the subjects at ~200 msw (2 MPa).

The decrease of the power in alpha frequencies persisted during the compression and the stay at 450 msw; it reached 50–80%, depending on the subject.

The increase in theta frequencies varied from 50 to 1,300%, depending on the subject (Fig. 8). During the DRET 79/131 dive, the maximal increases were recorded in seven subjects during the first 24 h of the stay. A consequent decrease was recorded on the second day of the stay. No increase in theta waves was recorded in one subject. During the second dive (ENTEX V), we recorded different patterns in the development of the increase in slow waves. In two subjects, the maximum values were recorded at the end of the compression (~300%), followed by a decrease to 100% and then an oscillatory development between 100 and 300% during the 12 days of the stay. In a third subject, we recorded a progressive increase from the first day to the last day of the stay at 450 msw. In the fourth subject, no significant increase was recorded.

During decompression, changes in the power of fast activities disappeared at depths between 250 and 100 msw. The increase in slow waves disappeared between 100 and 50 msw.

Comparison Between Awake EEG Changes and Sleep Disturbances

The comparison between the awake-state EEG changes and the sleep disturbances in the subjects in whom the increase of slow waves was high and in the two subjects in whom the increase in slow waves was not recorded indicated no fundamental changes in sleep disturbances; the increase in stages 1 and 2 and the decrease of stages 3 and 4 were analogous in all subjects (Figs. 9 and 10).

DISCUSSION

The major objective of this study was to research the effects of He-N_2-O_2 mixture on sleep organization of the divers exposed to pressure of 4.5 MPa.

Sleep disturbances occurred during the compression period; they cannot be attributed to a new environmental effect, since each subject slept in the same bed and in the same pressure chamber for several nights during the predive period, just before the start of compression. During compression, these disturbances consisted of a decrease of total duration of sleep and a slight decrease

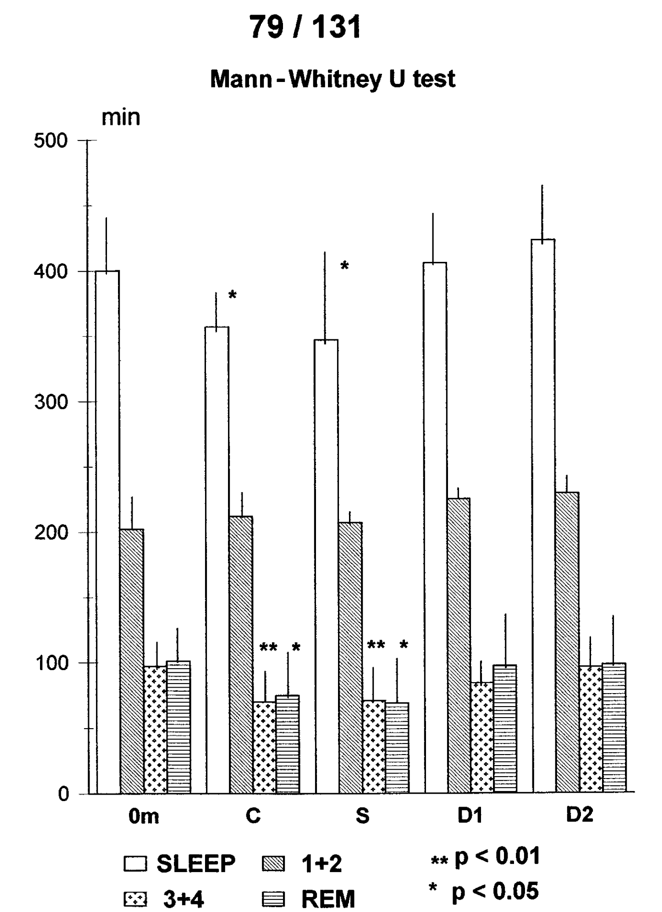

Fig. 6. Mean duration of total sleep, stages 1 + 2, stages 3 + 4, and REM periods calculated for 8 subjects of dive DRET 79/131 for 2 nights of predive periods (0m); 2 nights of compression (C); 2 nights of stay (S); and during decompression for the 1st 2 nights (D1) and the following 2 nights (D2).

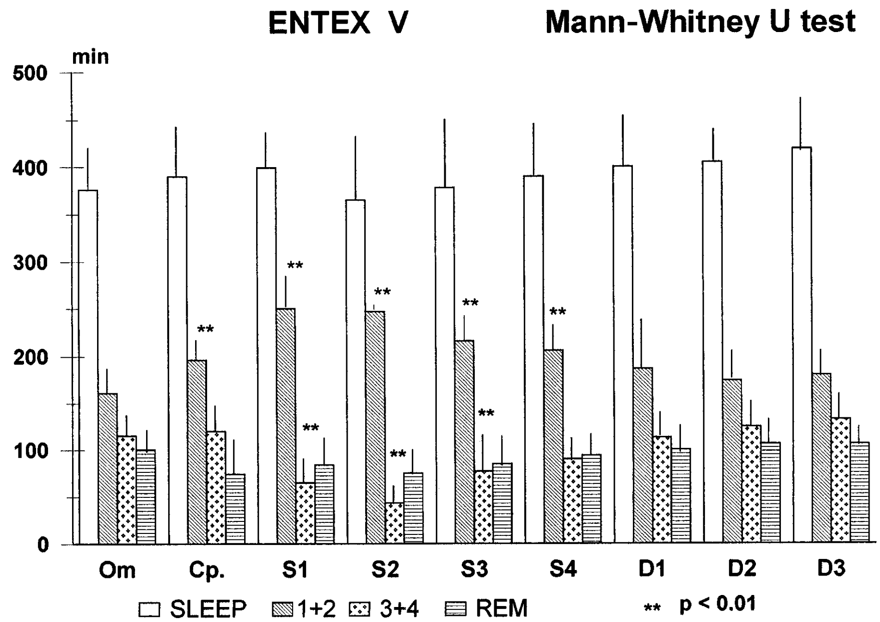

Fig. 7. Mean duration of total sleep, stages 1 + 2, stages 3 + 4, and REM periods for 4 subjects of dive ENTEX V calculated for predive period nights (0m), 2 nights of compression (Cp), 12 nights of stay grouped by 3-night periods (S1-S4), and 9 nights during decompression grouped by 3-night periods (D1, D2, D3).

in REM periods, especially the second night of compression. According to the dive, we recorded either an increase in stage 2 or a decrease in stage 3. The disturbances increased at 4.5 MPa during the first night of the stay, especially in the ENTEX V dive; they consisted of an increase of awake periods and of stages 1 and 2, a decrease in stages 3 and 4 and even a disappearence of this last stage, and a decrease of the REM periods. A progressive improvement was recorded from the seventh night of the ENTEX V dive, but a total recovery was only recorded during decompression.

The increase of stages 1 and 2 and the decrease of stages 3 and 4 and even of REM periods have been

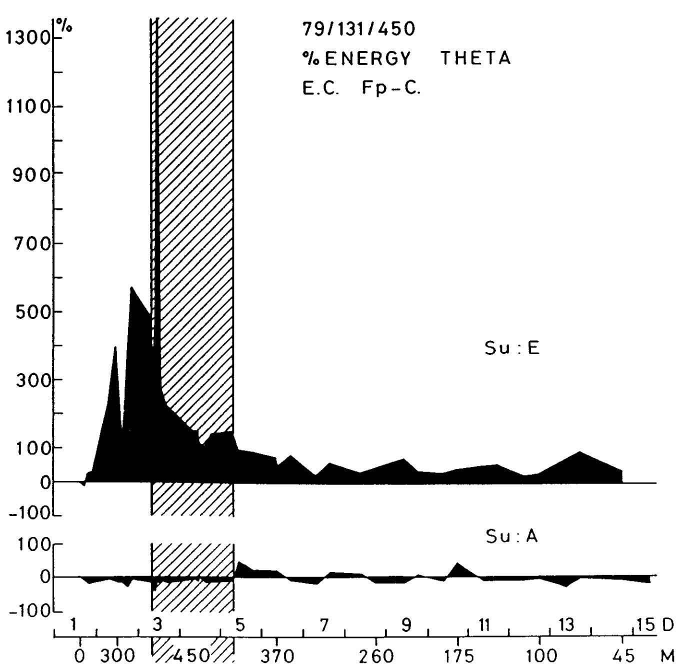

Fig. 8. Power of theta EEG frequency band recorded in frontopolar central lead (Fp-C) expressed as %difference from control value when subjects closed their eyes (EC), measured in 2 subjects (Su A and E) during experiment DRET 79/131. D, days.

reported previously for sleep studies that we have carried out during dives in He-O_2 mixture at 2.5 MPa (25), at 3, 4, and 5 MPa (22, 28), and during compressions up to 6.2 MPa (25). Other authors have also reported sleep disturbances during dives in He-O_2 at 3 and 3.5 MPa (30, 31) or, more recently, at 2 MPa (16). These changes were related to the compression effects (22, 28) and, more specifically, to the speed of compression, since sleep disturbances appeared to be of greater intensity during fast compression. However, these workers also have suggested that the composition of the breathing-gas mixture could play a role in the occurrence of these sleep disturbances (28). Indeed, the use of gas mixture such as He-N_2-O_2 modified the characteristics of the HPNS (4, 15, 21, 23); for instance, neurological symptoms are reduced or even suppressed. In our study, the use of the He-N_2-O_2 mixture with 4.8% of N_2 induces sleep disturbances that were analogous to the results obtained in the same range of pressures with the He-O_2 mixture (28). Indeed, Rostain et al. (22, 28) reported an increase of duration of stage 1 up to +200%, of stage 2 around +50 to 10%, a decrease of duration of stage 3 up to −33%, a disappearance of stage 4, and also a decrease of REM period duration of −50% compared with control nights. Consequently, the increase of stages 1 and 2 and the decrease of stages 3 and 4 appeared to be on the same order as the two different breathing mixtures. Such results have also been obtained with the changes in awake EEG where no significant improvement have been recorded in humans between the He-O_2 mixture and the He-N_2-O_2 mixture (21, 23). Such changes in awake EEG have been recorded in the present study, but no relationships between the intensity of the awake-state EEG changes and the sleep disturbances have been recorded, since subjects who had high increase in awake EEG slow waves and subjects who had few or no increase in awake EEG slow waves presented equivalent sleep disturbances.

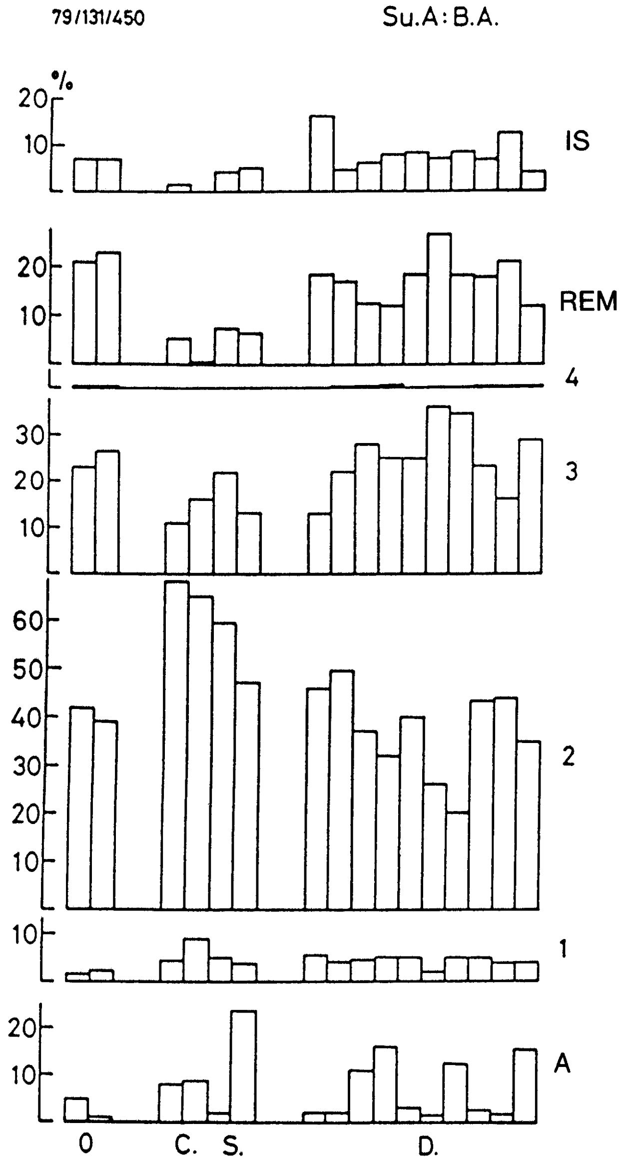

Fig. 9. Mean duration of each sleep stage expressed as %total sleep time for *subject A* during experiment DRET 79/131. C, compression; S, stay; D, decompression.

Moreover, the slight improvement of sleep disturbances recorded from the seventh night of the stay in our experiment has been also reported during long stays in $He\text{-}O_2$ mixture at 3 or 4 MPa (28) and, consequently, cannot be attributed to the $He\text{-}N_2\text{-}O_2$ mixture.

Previous studies (20, 22, 27, 28) have examined the possible role of environmental parameters such as temperature; their authors conclude that the absence of important variation in the subject's body temperature suggests that the temperature was correct and the thermal comfort was respected. Nonetheless, a thermal discomfort must be taken into account in sleep disturbances. The P_{O_2} has been also considered, since it was higher than in atmospheric air (400–500 mbar rather than 210 mbar); it does not seem to affect sleep in our experimental conditions, as reported previously (22, 28), since the same P_{O_2} values have been used during the predive control. Finally, recording of respiration (frequency and amplitudes) did not show abnormalities that might explain sleep changes.

These different observations confirm that disturbances of sleep organization make up another one of HPNS symptoms (22, 28) and result from changes in the functioning of the nervous system and of its biochemical mechanisms. Sleep disturbances are probably related to disruption of neurochemical processes implicated in the induction and the regulation of sleep and are induced by pressure more than by gas mixture. Recent results obtained from neurochemical studies performed under pressure conditions indicated that several neurotransmissions seem to be the target of pressure, such as amino acid and monoamine neurotransmissions (1, 12–14, 17, 19, 29, 32). Recent works have demonstrated the implication in the pressure-induced disturbances (9, 10) of the serotoninergic systems, which are known to play a role in the sleep-awake organization. Moreover, some experiments performed with different gas mixtures in animals did not show

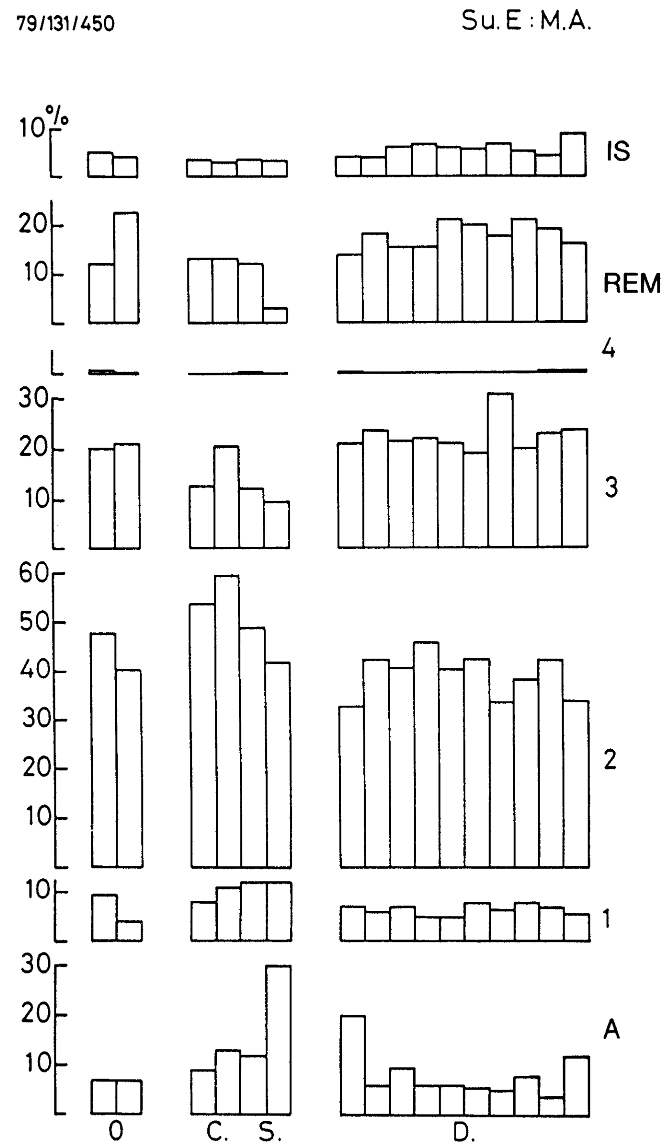

Fig. 10. Mean duration of each sleep stage expressed as %total sleep time for *subject E* during experiment DRET 79/131.

significant increases recorded in some neurotransmitters such as dopamine (19), indicating that the composition of gas mixture did not play a role in these changes.

Consequently, the disturbances of sleep organization recorded in He-O_2 mixture are found again with the He-N_2-O_2 mixture; the addition of 4.8% of N_2 in the breathing-gas mixture did not counteract the effect of pressure on sleep organization. These disruptions, which constitute another symptom of HPNS, since they are independent of most of the neurological problems and of intensity of awake-state EEG changes, are probably related to some neurochemical disturbances reported recently, which include serotoninergic systems.

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REFERENCES

1. **Abraini, J. H., and J. C. Rostain.** Pressure-induced striatal dopamine release correlates hyperlocomotor activity in rats exposed to high pressure. *J. Appl. Physiol.* 71: 638–643, 1991.
2. **Bennett, P. B., G. D. Blenkarn, J. Roby, and D. Youngblood.** Suppression of the high pressure nervous syndrome in human deep dives by He-N_2-O_2. *Undersea Biomed. Res.* 1: 221–237, 1974.
3. **Bennett, P. B., R. Coggin, and M. McLeod.** Effect of compression rate on use of trimix to ameliorate HPNS in man to 686 m (2250 ft). *Undersea Biomed. Res.* 9: 335–351, 1982.
4. **Bennett, P. B., and J. C. Rostain.** The high pressure nervous syndrome in man. In: *The Physiology and Medicine of Diving*, edited by P. B. Bennett and D. H. Elliott. London: Saunders, 1993, p. 194–237.
5. **Brauer, R. W., S. Dimov, X. Fructus, A. Gosset, and R. Naquet.** Syndrome neurologique et électrographique des hautes pressions. *Rev. Neurol.* 121: 264–265, 1969.
6. **Forni, C., and J. C. Rostain.** Effect of helium-oxygen pressure on dopamine detected in vivo in the striatum of hamsters. *J. Appl. Physiol.* 67: 1617–1622, 1989.
7. **Glantz, S. A.** *Primer of Biostatistics*. New York: McGraw-Hill, 1981, p. 353.
8. **Gourret, J. P., J. M. Lagarde, and J. C. Rostain.** Physio: un système d'acquisition et de traitement interactif de signaux électrophysiologiques. *Innov. Technol. Biol. Med.* 5: 425–437, 1984.
9. **Kriem, B., J. H. Abraini, and J. C. Rostain.** Role of 5-HT1B receptor in the pressure-induced behavioral and neurochemical disorders in rats. *Pharmacol. Biochem. Behav.* 53: 257–264, 1996.
10. **Kriem, B., J. C. Rostain, and J. H. Abraini.** Involvement of 5-HT3 receptor in the pressure-induced increase in striatal and accumbens dopamine release and the occurrence of behavioral disorders in free-moving rats. *Neurosci. Lett.* 197: 57–60, 1995.
11. **Lairy, G. C., M. Barros-Ferreira, and L. Goldsteinas.** Les phases intermédiaires du sommeil. In: *The Abnormalities of Sleep in Man*, edited by H. Gastaut, E. Lugaresi, G. Berti Ceroni, and G. Coccagna. Bologna: Auli Gaggi, 1968, p. 275–284.
12. **Meldrum, B. S., B. Wardley-Smith, M. J. Halsey, and J. C. Rostain.** 2-Amino-phosphonoheptanoic acid protects against the high pressure neurological syndrome. *Eur. J. Pharmacol.* 87: 501–502, 1983.
13. **Millan, M. H., B. Wardley-Smith, M. J. Halsey, and B. S. Meldrum.** Effect of NMDA and 2-amino-7-phosphonoheptanoate focal injection into the ventrolateral thalamic nucleus on the high pressure neurological syndrome in the rat. *Brain Res.* 507: 354–356, 1990.
14. **Millan, M. H., B. Wardley-Smith, M. J. Halsey, and B. S. Meldrum.** Brain nuclei and neurotransmitters involved in the regulation of the high pressure neurological syndrome in the rat. *Neuropharmacology* 30: 1351–1355, 1991.
15. **Naquet, R., J. C. Rostain, and X. Fructus.** High pressure nervous syndrome: clinical and electrophysiological studies in man. In: *The Strategy for Future Diving to Depths Greater Than 1000 Feet*, edited by M. J. Halsey, W. Settle, and E. B. Smith. Bethesda, MD: Undersea Medical Society, 1975, p. 62–65. (UMS Report No. WS: 6–15–75)
16. **Ozawa, K., A. Hashimoto, and Y. Nishi.** Psychophysiologic changes in sleep during simulated 200-m heliox saturation dives. *Undersea Biomed. Res.* 18: 397–412, 1991.
17. **Rostain, J. C.** The nervous system: man and laboratory mammals. In: *Effects of High Pressure on Biological Systems*, edited by A. G. Macdonald. Berlin: Springer Verlag, 1993, vol. 17, p. 198–238. (Adv. Comp. Environ. Physiol. Ser.)
18. **Rostain, J. C., J. C. Dumas, B. Gardette, J. P. Imbert, and C. Lemaire.** Effects of addition of nitrogen during rapid compression of baboon. *J. Appl. Physiol.* 57: 332–340, 1984.
19. **Rostain, J. C., and C. Forni.** The effects of high pressures of various gas mixtures on rat striatal dopamine detected in vivo by voltammetry. *J. Appl. Physiol.* 78: 1179–1187, 1995.
20. **Rostain, J. C., X. Fructus, J. Ghata, J. C. Legrand, R. Naquet, and A. Reinberg.** Changes in physiological circadian rhythms during helium-oxygen saturation dives to 500 and 610 m. *Undersea Biomed. Res.* 4: A46–A47, 1977.
21. **Rostain, J. C., B. Gardette, and R. Naquet.** Effects of exponential compression curves with nitrogen injections in humans. *J. Appl. Physiol.* 63: 421–425, 1987.
22. **Rostain, J. C., M. C. Gardette-Chauffour, J. P. Gourret, and R. Naquet.** Sleep disturbances in man during different compression profiles up to 62 bars in helium-oxygen mixture. *Electroencephalogr. Clin. Neurophysiol.* 69: 127–135, 1988.
23. **Rostain, J. C., M. C. Gardette-Chauffour, and R. Naquet.** HPNS during rapid compression of men breathing He-O_2 and He-N_2-O_2 at 300 m and 180 m. *Undersea Biomed. Res.* 7: 77–94, 1980.
24. **Rostain, J. C., C. Lemaire, M. C. Gardette-Chauffour, J. Doucet, and R. Naquet.** Estimation of human susceptibility to the high-pressure nervous syndrome. *J. Appl. Physiol.* 54: 1063–1070, 1983.
25. **Rostain, J. C., and S. Lyagoubi.** Etude électroencéphalographique de la veille et du sommeil sous hyperbarie prolongée en atmosphère hélium-oxygène (opération Janus II). *Rev. EEG Neurophysiol.* 1: 239–241, 1971.
26. **Rostain, J. C., and R. Naquet.** Le syndrome nerveux des hautes pressions caractéristiques et évolution en fonction de divers modes de compression. *Rev. EEG Neurophysiol.* 4: 107–124, 1974.
27. **Rostain, J. C., R. Naquet, and A. Reinberg.** Effects of a hyperbaric situation (500 meters depth, heliox atmosphere) on circadian rhythms of two healthy young men. *Int. J. Chronobiol.* 3: 127–139, 1975.
28. **Rostain, J. C., G. Regesta, M. C. Gardette-Chauffour, and R. Naquet.** Sleep organization in man during long stays in helium-oxygen mixture at 30 and 40 bars. *Undersea Biomed. Res.* 18: 21–36, 1991.
29. **Rostain, J. C., B. Wardley-Smith, C. Forni, and M. J. Halsey.** Gamma amino butyric acid and the high pressure neurological syndrome. *Neuropharmacology* 25: 545–554, 1986.
30. **Townsend, R. E., and D. A. Hall.** Sleep, mood, and fatigue during a 14-day He-O_2 open-sea saturation dive to 850 fsw with excursions to 950 fsw. *Undersea Biomed. Res.* 5: 109–117, 1978.
31. **Wilcox, R. H., J. W. Spencer, and F. Russo.** Sleep at 1200 fsw in the University of Pennsylvania predictive studies IV project (Abstract). *Undersea Biomed. Res.* 3: A45, 1976.
32. **Zinebi, F., L. Fagni, and M. Hugon.** Excitatory and inhibitory amino acids involved in the high pressure nervous syndrome: epileptic activity and hyperexcitability. *Amino Acids (Vienna)* 1: 47–56, 1991.