Undersea Biomedical Research, Vol. 16, No. 1, 1989

EEG power spectra in rats during compression and during pentobarbital infusion at pressure

R. URSIN, K. FURSET, and L. AANDERUD

Departments of Physiology and Anesthesiology, University of Bergen, Bergen, Norway

Ursin R, Furset K, Aanderud L. EEG power spectra in rats during compression and during pentobarbital infusion at pressure. Undersea Biomed Res 1989; 16(1):41–51.—The EEG of rats was studied with power spectrum analysis under compression to 71 ATA with He-O_2 and during constant rate infusion of pentobarbital at 71 ATA and at surface. During compression the 1–4 Hz delta activity was increased, and 8–11 Hz alpha, 12–14 Hz spindle, and 16–10 Hz low beta activities were reduced compared to control animal recordings. During the course of pentobarbital infusion at 71 ATA, this picture changed: the delta activity was reduced while alpha and spindle activities (barbiturate spindles) increased, considerably more than in the rats studied at surface pressure. The findings may only in part be explained by pressure reversal of anesthesia.

hyperbaric
anesthesia
pressure reversal
EEG
pentobarbital
barbiturate spindles

It is well known that the effect of anesthetic agents may be reduced at high ambient pressure. This so-called "pressure reversal of anesthesia" has been observed in many species and with a variety of anesthetic agents, but the cause is not known. Although a direct antagonism of pressure on the effect of anesthetics is possible, an increasing amount of data indicate that the interaction of anesthetics and pressure is complex and may involve several mechanisms of direct as well as indirect antagonism (1, 2).

In earlier work (3, 4) we studied anesthetic effects under high pressure of two barbiturates, thiopental and pentobarbital, using EEG burst suppression (5) as the criterion for anesthesia. During the course of barbiturate infusion, apparent differences were observed in the EEG in animals subjected to high ambient pressure, compared to the control animals. The present paper is a further study of the EEG effects of compression to 71 ATA (7.2 MPa), and of the EEG effects of pentobarbital infusion at 71 ATA and at surface pressure.

METHODS

Animals, housing, and training

Male Møll-Wistar rats (Møllegaard, Denmark), weighing 230–330 g at the time of the experiments, were used. The experiments were run in 2 series. In the first, pharmacokinetic studies were also performed (4), and complete EEG data were obtained from 7 experimental but only 3 control animals. Series 2 was run 15 mo. later with 3 experimental and 5 control animals. Identical procedures were used in the 2 experiments. For treatment of the results from the 2 series, *see* section on data reduction and statistics.

The animals were housed in individual cages and had free access to food and water. They were maintained on a 12/12 light/dark schedule with lights on at 0600 h.

As a preparation to the hyperbaric chamber experiments the animals were individually restrained and habituated to the chamber. The adaptation started by handling the animals and ended with training the rats to be restrained in a Plexiglas tube in the hyperbaric chamber, to become accustomed to the experimental procedure, the noise of the fan, and the gas inlet. The purpose of this procedure was to minimize the stress reaction to the experimental situation and thereby keep the experimental conditions as constant as possible.

Electrode and catheter implantation

Two weeks before the experiments started the animals were anesthetized with a mixture of Hypnorm Janssen-Dormicum Roche diluted with equal amounts of distilled water (the mixture contained fentanyl, 0.05 mg/ml; fluanizone, 2.5 mg/ml; and midazolam, 1.25 mg/ml). Stainless steel screw electrodes were implanted bilaterally according to a method described earlier (6), frontal electrodes 2 mm anterior to the bregma and 2 mm lateral to the midline, and parietal electrodes 2 mm frontal to the lambda and 2 mm lateral to the midline. Presoldered wires attached the electrodes to a miniature connector that was fastened to the skull with acrylic cement.

One day before the experiment the animals were again anesthetized, and a PE-50 catheter was inserted into the right femoral vein. The catheter was led subcutaneously to a pocket under the skin on the back, filled with heparinized saline, and sealed. Bilateral paracentesis of the tympanic membrane was performed to avoid ear pain during compression.

Compression procedure

A 4-liter chamber system was used (7). It was equipped with a high-pressure pump, and syringe for drug infusion. The chamber temperature was kept at 33° ± 0.5°C and the animals' rectal temperatures were maintained at 37.5° ± 0.5°C during the experiments. The animals were compressed with helium at a rate of 0.3 ATA/min. Before the compression oxygen partial pressure was raised to 0.6 ATA. Oxygen was added to keep its partial pressure at 0.4 ATA. Gas mixing was ensured by a fan circulating the atmosphere through soda lime to keep CO_2 concentration below 0.01 vol/vol. The P_{CO_2} was invariably found to be below this limit. The animals could be observed through the front port of the chamber.

The control animals stayed in the same chamber and for the same amount of time as the experimental animals, but the chamber was not completely closed and not pressurized. Instead, air was blown through the opening and the fan was on continuously as in the pressure experiments.

Drug administration

After 1 h of adaptation at 71 ATA, pentobarbital was infused at the constant rate of 5 mg/min until the appearance of the "silent second," a 1-sec EEG burst suppression (3, 5). After the experiment the animals were killed by an overdose of pentobarbital.

EEG recording and analysis

Frontoparietal EEG was recorded on a Grass polygraph, filtered between 1 and 60 Hz, and written on paper at a speed of 10 or 15 mm/sec, and to analog tape. A baseline recording was performed before compression started. During compression, EEG was recorded for at least 3 min for each 10 ATA increase in pressure. In the control animals, EEG samples were recorded at similar intervals. The control animals had a tendency to fall asleep between recordings, so all animals were aroused before each recording by knocking at the chamber window with a pencil to ensure similar background EEG under the two conditions. At 71 ATA, EEG was recorded at the beginning and end of the 1-h adaptation period, and in the control animals before and after an equally long interval. During pentobarbital infusion, EEG was recorded continuously. The paper record served as basis for identifying the anesthesia criterion of 1-sec burst suppression and as a check of the quality of the recordings.

At a later date the analog tape was played back to a PDP 11-23 computer, digitized at a rate of 100 samples/sec, and subjected to Fourier Transform on 1-sec data epochs, with frequency resolution of 1 Hz. Intensity in μV^2/(cycles/sec) for each 1-Hz band was averaged per 1 min. Intensity ("power") per 1 min in the frequency bands of delta (1–4 Hz), theta (5–7 Hz), alpha (8–11 Hz), spindles (12–14 Hz), and low beta (16 Hz and higher) was computed by adding power of the respective 1-Hz frequency bands.

Data reduction and statistics

The EEG power data were computed in the form of percent of total power to reduce variance caused by difference in the range of absolute power between animals.

The results from the 2 series were generally overlapping. The anesthesia induction doses for the 2 control groups were 9.4 ± 0.8 (mean ± SEM; SD 2.0) and 8.5 ± 0.5 (SD 1.2), and for the experimental groups 13.83 ± 0.3 (SD 0.8) and 12.39 ± 1.7 (SD 3.6). The corresponding results were not significantly different, and the results from the 2 series were pooled in the further data reduction.

As mentioned above, there were 10 experimental animals (pressurized up to 71 ATA) and 8 control animals (surface, 1 ATA) in the experiment. However, the baseline EEG data from 3 of the 10 experimental animals had to be excluded because of EEG artifacts. Thus, for the baseline data analysis (Fig. 1), n for experimental animals was = 7, and n for control animals was = 8. From 1 of the 8 control animals

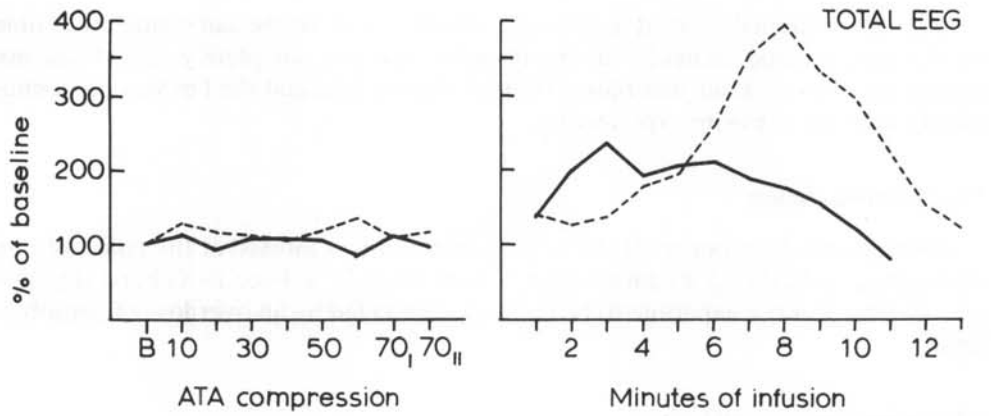

Fig. 1. Total EEG activity in percent of total EEG activity of the baseline recording, at each 10 ATA compression and equal time surface control *(left)*, and during pentobarbital infusion at 71 ATA He-O_2 and control conditions *(right)*. *Solid line*, control condition; *broken line*, experimental (high pressure) condition.

no compression control data were obtained. For the compression data analysis (10–71 ATA) therefore, experimental animal n was = 10, control animal n was = 7. Finally, data from one experimental animal had to be excluded from the infusion EEG data analysis because of EEG artifacts. For the infusion data analysis then, experimental animal n was = 9, control animal n was = 8.

Two-way analyses of variance (ANOVAs) for repeated measures (8) were run to compare EEG power in the different bands during compression and control, with compression from 10 ATA to 71 ATA as repeated measures. Two-way ANOVAs were also run for the infusion period data, with minutes of infusion (1–11) as repeated measures. One-way ANOVAs and post-hoc t tests were run where ANOVAs showed significant changes. The t test results are presented only in the figures. Reported values are means ± SEM unless otherwise stated. All significance levels are two-tailed.

RESULTS

Means of total power under the different conditions are given in Fig. 1. A report of an increase or decrease in a frequency band is relative and must be compared with the data for total power if one wants to get an impression of absolute power changes.

Baseline

The composition of the baseline EEG recording (recordings done before the compression or the control procedure started; Fig. 2, *left*) was not significantly different in the 2 groups of animals. Experimental animal delta activity was 48.44 ± 3.19%; control animal delta activity was 41.08 ± 0.94% of total, $P < 0.10$. For the other frequency bands the differences were smaller.

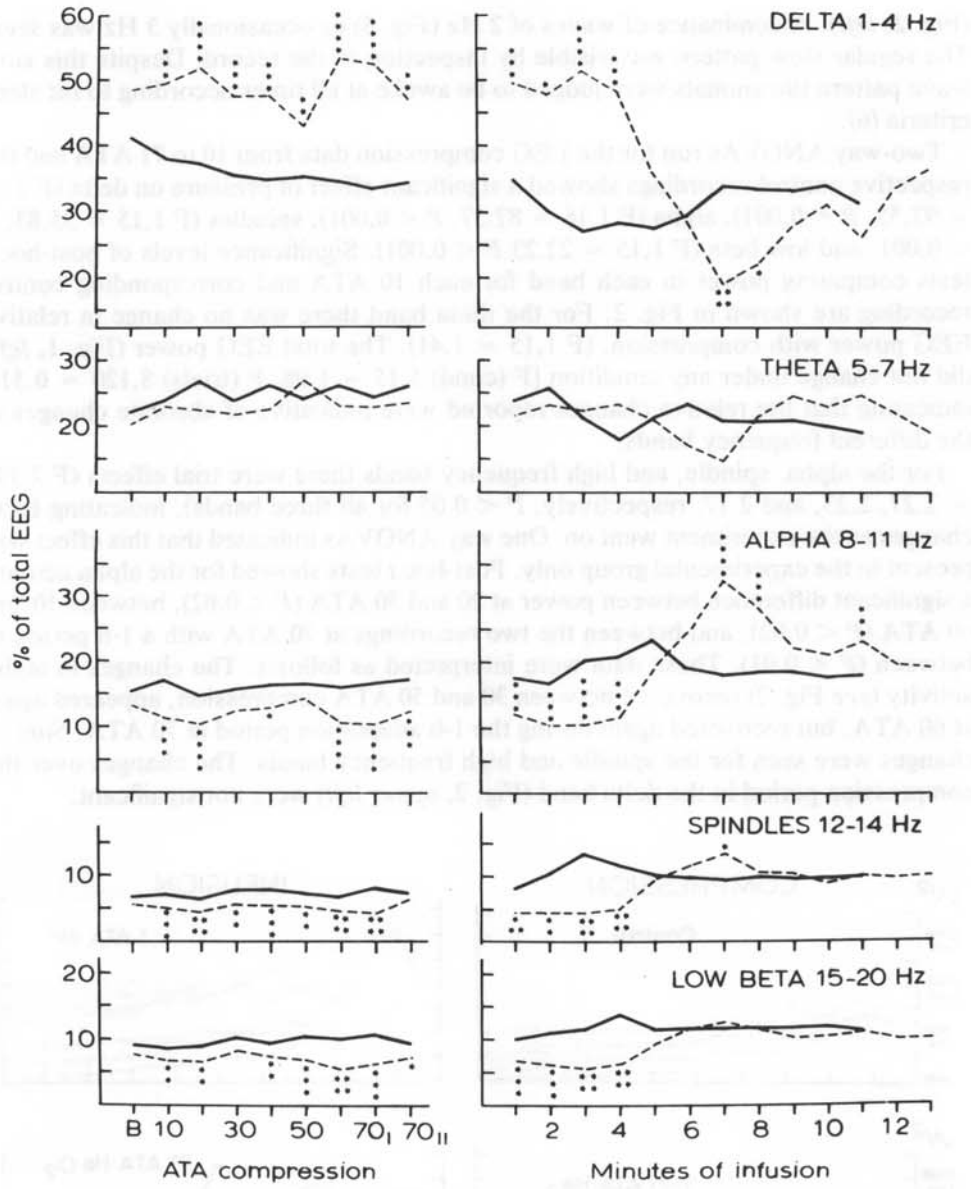

Fig. 2. Relative power (percent of total EEG power) in the delta, theta, alpha, spindle, and low beta frequency bands; *left*, at each 10 ATA during compression to 70 ATA *(broken line)* and during equal time at surface *(solid line); right*, during pentobarbital infusion at 71 ATA He-O_2 and at surface conditions. *Asterisks* indicate significance levels of differences between the high pressure condition and the surface condition; ****, ***, **, * indicating $P < 0.001$, 0.01, 0.02, and 0.05, respectively.

Compression

A relative increase (increased percent of total EEG) of the delta frequency band and a decrease in alpha activity, spindles, and high frequency components of the EEG were seen in the animals under compression compared to animals at surface

(Fig. 2, *left*). A dominance of waves of 2 Hz (Fig. 3) or occasionally 3 Hz was seen. The regular slow pattern was visible by inspection of the record. Despite this slow wave pattern the animals were judged to be awake at all times according to rat sleep criteria (6).

Two-way ANOVAs run for the EEG compression data from 10 to 71 ATA and the respective control recordings showed a significant effect of pressure on delta ($F\ 1,15 = 97.55$, $P < 0.001$), alpha ($F\ 1,16 = 87.57$, $P < 0.001$), spindles ($F\ 1,15 = 35.83$, $P < 0.001$, and low beta ($F\ 1,15 = 22.23$ $P < 0.001$). Significance levels of post-hoc *t* tests comparing power in each band for each 10 ATA and corresponding control recording are shown in Fig. 2. For the theta band there was no change in relative EEG power with compression. ($F\ 1,15 = 1.41$). The total EEG power (Fig. 1, *left*) did not change under any condition [F (cond) $1,15 = 1.98$, F (trials) $8,120 = 0.51$], indicating that the relative changes reported were indicative of absolute changes in the different frequency bands.

For the alpha, spindle, and high frequency bands there were trial effects ($F\ 7,105 = 2.27$, 2.23, and 2.17, respectively, $P < 0.05$ for all three bands), indicating EEG changes as the experiment went on. One way ANOVAs indicated that this effect was present in the experimental group only. Post-hoc *t* tests showed for the alpha activity a significant difference between power at 20 and 50 ATA ($P < 0.02$), between 50 and 60 ATA ($P < 0.02$), and between the two recordings at 70 ATA with a 1-h period in between ($P < 0.01$). These data were interpreted as follows: The changes in alpha activity (*see* Fig. 2) recovered between 30 and 50 ATA compression, appeared again at 60 ATA, but recovered again during the 1-h adaptation period at 70 ATA. Similar changes were seen for the spindle and high frequency bands. The changes over the compression period in the delta band (Fig. 2, *upper left*) were not significant.

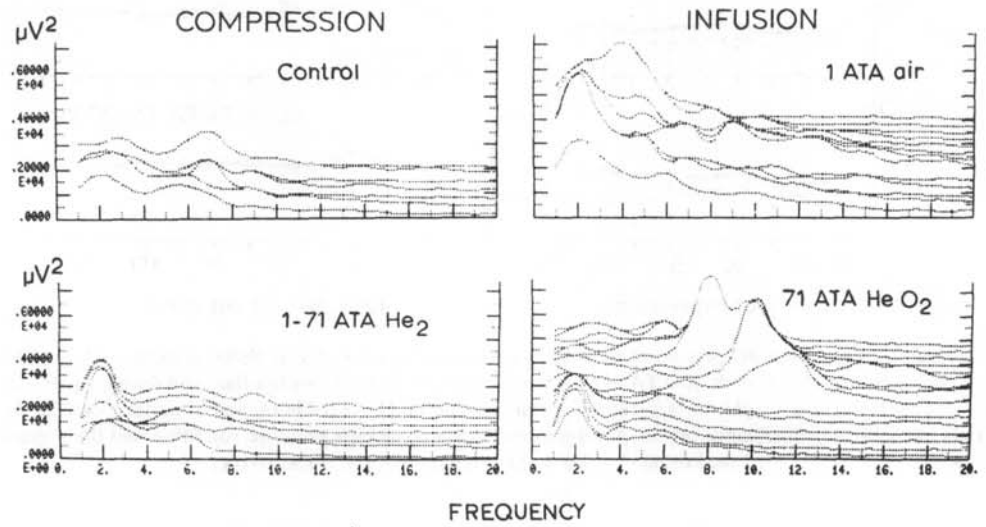

Fig. 3. *Left*, activity at various frequencies from 1 to 20 Hz, in μV^2/(cycle/sec), in 1-min samples per 10 ATA compression or equal time control. *Right*, spectra during pentobarbital infusion under 71 ATA He-O_2 and control conditions. In all plots, each minute is represented by one line, and the lines are plotted successively above each other, suppressing hidden lines. Data from one control animal *(top)* and one experimental animal *(bottom)* are shown.

Pentobarbital infusion

Samples of the EEG record during pentobarbital infusion are presented in Fig. 4.

Comparison with baseline

The absolute power changes during pentobarbital infusion, total EEG power in percent of baseline power per minute of infusion, are shown in Fig. 1, *right*. Peak EEG power in the control situation at 1 ATA was reached during the 3rd min of infusion, whereas peak power was reached during the 7–8th min of infusion at 71 ATA. The peak at high pressure was significantly higher than at surface (control group min 3 = 235.8 ± 34.5%; 71 ATA group min 8 = 395.8 ± 45.8% of baseline, $P < 0.01$).

Changes in relative composition of the EEG

The changes in each frequency band in percent of total EEG power throughout the infusion period are illustrated in Fig. 2, *right*. Two way ANOVAs for each frequency band showed no total condition effect for delta, theta, and alpha, but differences at 71 ATA vs. surface for the spindle ($F_{1,15} = 5.11$, $P < 0.05$) and low beta ($F_{1,15} = 8.50$, $P < 0.025$) bands. A trial effect for all bands except the theta band indicated changes in the EEG pattern as the infusion went on ($F_{10,150} = 8.13, 13.03, 5.93, 8.22$; $P < 0.001, 0.001, 0.01$, and 0.001 for the delta, alpha, spindle, and low beta bands, respectively). Highly significant condition-trial interactions in the delta, alpha, spindle, and low beta bands ($F_{10,150} = 9.74$–31.55; $P < 0.001$ in all four bands) suggested that the EEG changes over time differed between the experimental and control groups. One-way ANOVAs run separately for the 1 ATA group and the 71 ATA group infusion data confirmed that the trial effects were almost exclusively due to the changes during infusion at 71 ATA ($F_{12,96} = 12.2, 15.79, 13.73$, and 14.52 for the delta, alpha, spindle, and low beta band, respectively, $P < 0.001$ for all four bands).

During the first 4 min of infusion the differences between the 2 groups were similar to those seen during compression: increased delta activity and decreased alpha,

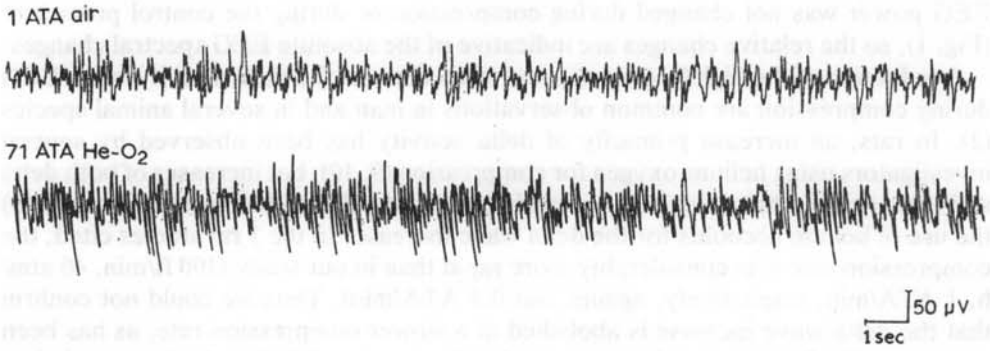

Fig. 4. Recording of pentobarbital-induced EEG activity at a time when around one half of anesthesia induction dose had been infused; *top*, control animal; *bottom*, animal at 71 ATA.

spindle, and beta activity in the experimental group compared to the control group. During the 5th and 6th min, a drastic change took place in the spectral bands in the experimental animals. This is evident when comparing *left* and *right* sides of Fig. 2. The relative delta power decreased to values significantly lower than control values, whereas relative alpha and spindle power increased correspondingly (*see* significance level of the post-hoc *t* tests in Fig. 2). The increase was particularly prominent for the alpha band. The changes peaked during min 7 and then leveled off. The values of the delta, alpha spindle, and low beta activity from min 5 on and throughout the rest of the recording period were significantly different from the first minute of infusion for all frequency bands ($P < 0.05$–0.001).

In the control condition only alpha activity changed during the infusion ($F_{10,70} = 2.74$, $P < 0.05$). Compared to min 1 values, the alpha activity was increased during min 3–5 ($P < 0.05$–0.02), then went back to min 1 levels. The peak of the alpha activity was significantly higher in the 71 ATA group than in the surface group (32.5 ± 2.1 vs. 23.6 ± 1.4% of total EEG, $P < 0.01$).

Induction dose

The mean time from infusion start to the anesthesia criterion of 1-sec burst suppression was 8.95 ± 0.51 min in the control group and 13.35 ± 0.64 min in the experimental group. This corresponds to induction doses of pentobarbital of 44.8 ± 2.6 mg/kg at surface and 66.8 ± 3.2 mg/kg at 71 ATA, a 49.1% increase at high pressure, significant at $P < 0.001$.

It is evident from Fig. 2, *right,* that the EEG spectral values were fairly similar in the 2 conditions at the time the anesthesia end point was reached (min 9 in the control condition and min 13 in the experimental condition).

DISCUSSION

The relative increase of low frequency, 1–4 Hz delta activity and decrease of the higher 8–11 Hz alpha, 12–14 Hz spindles, and 16–20 Hz low beta activities in the experimental group during compression indicate a general slowing of the EEG. Total EEG power was not changed during compression or during the control procedure (Fig. 1), so the relative changes are indicative of the absolute EEG spectral changes.

A reduction of the high frequencies and an increase of the theta activity in the EEG during compression are common observations in man and in several animal species (2). In rats, an increase primarily of delta activity has been observed by several investigators using helium-oxygen for compression (9, 10), but increases of both delta and theta activity have also been reported (11). According to Bennett and Dossett (9) the use of helium accounts for the delta wave increase. In the 3 rat studies cited, the compression rate was considerably more rapid than in our study (100 ft/min, 40 atm/h, 1 ATA/min, respectively, against our 0.3 ATA/min). Thus we could not confirm that the delta wave increase is abolished at a slower compression rate, as has been suggested (9). Our data tend to support the observation (12) that the increased slow wave activity is an effect of the compression procedure rather than of the high pressure per se. Changes were seen at 10 ATA and did not progress much at higher

pressures. Rather, there was some recovery during the 1-h adaptation period at 71 ATA.

During the first minutes of infusion the differences in the EEG pattern between the 1 ATA and the 71 ATA groups were similar to the differences during compression. After 5 min of pentobarbital infusion the pressure-induced EEG changes in the 71 ATA group had been abolished (*see* Fig. 2). In both groups, after approximately one third of the anesthetic dose had been infused, the EEG pattern shifted toward dominance of the 8–11 Hz and 12–14 Hz activity bands.

Activity in the 8–11 Hz range under some circumstances may be of hippocampal origin (high frequency theta activity) (13). However, in pentobarbital-treated rats, neither spontaneous nor midbrain tegmental stimulation-elicited hippocampal theta activity could be observed (13). In the present study, activities in the 8–11 and 12–14 Hz bands are termed alpha and spindle activity, respectively, and are considered to correspond to the so-called barbiturate spindles (14) or barbiturate EEG activity, which is a thalamic rhythmic activity. It is due to the powerful recurrent inhibition in the thalamic neuronal system with oscillating depolarization in inhibitory interneurons, creating hyperpolarization and rebound sequences in the thalamic projection cells (15). The inhibitory cells are probably γ-aminobutyric acid (GABA)-ergic (16). The ability of barbiturates to enhance thalamic rhythmic activity may be due to the postulated GABA-like or GABA-enhancing effects of barbiturates (17, 18). The rhythmic activity is also dependent on an optimal, moderate, excitatory input to the thalamic projection cells. An increase in afferent impulses will tend to desynchronize the rhythm, whereas a too low level of excitation will silence the thalamic cells (15).

In both control and pressurized conditions the EEG activity increased to a maximum when about half of the anesthetic dose of barbiturate had been infused. In the 71 ATA condition the maximum of the alpha band activity (measured as percent of total power) was significantly higher than maximum alpha activity in the control condition. If the increase in total power is also taken into account (Fig. 1), the increase in alpha activity in the animals under pressure was quite dramatic. This increase in the alpha band plus a lesser increase in the spindle band accounted for the equally dramatic decrease in relative delta power, from higher than control values to lower than control values (Fig. 2, *top left*).

The finding of a difference in the barbiturate EEG activity between the animals at surface and the animals at 71 ATA was quite unexpected and is difficult to interpret. The barbiturate EEG activity shows similarities to the alpha activity preceding normal sleep (15) and to sleep spindles (6), and could be related to the anesthetic effect. This is supported by the time course of the EEG changes with relation to the anesthesia criterion. Maximum alpha activity was seen after approximately one half of the infusion time in both conditions. Also, when the anesthesia criterion was reached, total EEG power and power in the different bands were similar in the two conditions, indicating that the EEG power data depicted similar endpoint conditions. The delay of the alpha maximum in the animals under pressure would then be due to pressure antagonism of the anesthesia. The increase in barbiturate activity, however, cannot easily be explained as a simple pressure antagonism. At the time when the alpha maximum was reached, the animals under pressure had received a higher dose of pentobarbital than the control animals (7- vs. 5-min infusion). We demonstrated earlier that the distribution of pentobarbital in the rat at 1 ATA did not differ from the distribution at 71 ATA (4). Thus, the dose difference may explain the difference

in the size of the alpha maximum under the two conditions, if the drug effects on the EEG were *not* affected by pressure. One interpretation of the difference, therefore, is that the reversal of anesthesia is related to effects of the barbiturate other than the effect that causes the EEG changes.

Although not an antiepileptic drug like phenobarbital, pentobarbital like most barbiturates has anticonvulsant effects in anesthetic doses. The barbiturate EEG activity may be related to the anticonvulsive effect. This is supported by findings that other types of anticonvulsive treatments increase thalamic rhythmic activity. In humans, activities in 8–11 and 12–15 Hz ranges increased as epileptic seizure activity was reduced after conditioning of 12–15 Hz activity (19); in cats and monkeys, increasing 12–14 Hz activity by conditioning reduced seizures (20, 21). Also, antiepileptic drugs like benzodiazepines and diphenylhydantoin increased 12–14 Hz spindle activity in humans (22) and cats (23). However, phenobarbital did not increase this type of activity (23) nor did the anticonvulsant 2-aminophosphonoheptanoic acid (2-APH) (11); thus this activity is not a prerequisite for anticonvulsant effect. The relationship between high ambient pressure and anesthetic and anticonvulsant effects of the barbiturate spindle activity is not clear. The nonanesthetic barbituric acid had some anticonvulsant effect in rats under high ambient pressure (24); however, EEG was not recorded.

In the earlier literature on barbiturates there seems to be a consensus that anesthetic doses have a depressant effect directly on the thalamic relay nuclei for every sensory modality, with the general effect of reducing arousal (25, 26). The animal under high ambient pressure is subjected to physiologic stresses and altered sensory feedback, which may increase arousal levels and contribute to the counteraction of high pressure on anesthesia. The present data are compatible with the idea that the drug, before it had any anesthetic effect, had to counteract arousing effects of the hyperbaric situation. After the first 5 min (Fig. 2) the anesthetic effect was apparent also in the animals under pressure. Increase in alpha and spindle activity then would be an effect of the higher dose the animals had received when the anesthetic effect of the drug became apparent. The present data thus are consistent with the hypothesis that pressure reversal of anesthesia may be due to an antagonism not only on a pharmacologic level, but also on a physiologic level via increased sensory feedback under high pressure. Further research is necessary to verify this hypothesis.

This research was sponsored in part by the Norwegian Research Council for Science and the Humanities.—*Manuscript received April 1988; accepted October 1988.*

REFERENCES

1. Kendig JJ. Anesthetics and pressure in nerve cells. In: Fink BR, ed. Molecular mechanisms of anesthesia. New York: Raven Press, 1980:59–68.
2. Halsey MJ. Effects of high pressure on the central nervous system. Physiol Rev 1982; 62:1341–1377.
3. Aanderud L, Ursin R, Larsen M. Effect of high pressure on EEG burst suppression dose of thiopental in rats. Undersea Biomed Res 1982; 9:255–261.
4. Aanderud L, Ursin R, Furset K. Anesthetic effect and distribution of infused pentobarbital in the rat at 71 ATA. Undersea Biomed Res 1987; 14:93–99.
5. Wahlstrøm G. Estimation of brain sensitivity to hexobarbitone (Enhexymal NFN) in rats by an EEG threshold. Acta Pharmacol Toxicol 1966; 24:404–418.

6. Ursin R, Larsen M. Increased sleep following intracerebroventricular injection of the delta sleep-inducing peptide in rats. Neurosci Lett 1983; 40:145–149.
7. Aanderud L. A system for pharmacological studies in small animals at high pressure. Undersea Biomed Res 1981; 8:69–74.
8. Bruning JL, Kintz BL. Computational handbook of statistics, 2nd ed. Glenview, IL: Scott, Foresman and Company, 1975.
9. Bennett PB, Dossett AN. EEG activity of rats compressed by inert gases to 700 feet and oxygen-helium to 4000 feet. Aerosp Med 1973; 44:239–244.
10. Kaufmann PG, Bennett PB, Farmer JC Jr. Cerebellar and cerebral electroencephalogram during the high pressure nervous syndrome (HPNS) in rats. Undersea Biomed Res 1977; 4:391–402.
11. Wardley-Smith B, Rostain JC, Meldrum BS, Halsey MJ. Effect of 2-aminophosphonoheptanoic acid on the EEG of rats exposed to high pressure. Undersea Biomed Res 1986; 13:155–163.
12. Albano G, Criscuoli PM, Scaglione GC, Mazzone M, La Monaca G, Burruano G. La sindrome da estreme pressioni ambientali. Rilievi EEG ed ECG su ratti liberi con elettrodi a dimora. Ann Med Nav Trop 1972; 77:11–28.
13. Kramis R, Vanderwolf CH, Bland B. Two types of hippocampal rhythmical slow activity in both the rabbit and the rat: relations to behavior and effects of atropine, diethyl ether, urethane, and pentobarbital. Exp Neurol 1975:58–85.
14. Andersen P, Andersson SA, Lømo T. Some factors involved in the thalamic control of spontaneous barbiturate spindles. J Physiol 1967; 192:257–281.
15. Andersen P, Andersson SA. Physiological basis of the alpha rhythm. New York: Appleton-Century-Crofts, 1968.
16. Steriade M, Deschenes M. The thalamus as a neuronal oscillator. Brain Res Rev 1984; 8:1–63.
17. Polc P, Haefely W. Effects of two benzodiazepines, phenobarbitone, and baclofen on synaptic transmission in the cat cuneate nucleus. Arch Pharmacol (Naunyn Schmiedebergs) 1976; 294:121–131.
18. Nicoll RA. Pentobarbital: differential postsynaptic actions on sympathetic ganglion cells. Science 1978; 199:451–452.
19. Sterman MB, Shouse MN. Qualitative analysis of training, sleep EEG and clinical response to EEG operant conditioning in epileptics. Electroencephalogr Clin Neurophysiol 1980; 49:558–576.
20. Sterman MB. Effects of brain surgery and EEG operant conditioning on seizure latency following monomethylhydrazine intoxication in the cat. Exp Neurol 1976; 50:757—765.
21. Sterman MB, Goodman SJ, Kovalesky R. Effects of sensorimotor EEG feedback training on seizure susceptibility in the rhesus monkey. Exp Neurol 1978; 62:735–747.
22. Johnson LC, Hanson K, Bickford RG. Effect of flurazepam on sleep spindles and *k*-complexes. Electroencephalogr Clin Neurophysiol 1976; 40:67–77.
23. Kaplan BJ. Phenobarbital and phenytoin effects on somatosensory evoked potentials and spontaneous EEG in normal cat brain. Epilepsia 1977; 18:397–403.
24. Rostain JC, Wardley-Smith B, Halsey MJ, Nunn JF. Effect of barbituric acid on the high pressure nervous syndrome in the rat. Undersea Biomed Res 1986; 13:407–411.
25. King EE, Naquet R, Magoun HW. Alterations in somatic afferent transmission through the thalamus by central mechanisms and barbiturates. J Pharmacol Exp Ther 1957; 119:48–63.
26. Domino EF. Sites of action of some central nervous system depressants. Ann Rev Pharmacol 1962; 2:215–250.