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Quantitative EEG during progressive hypocarbia and hypoxia. Hyperventilation-induced EEG changes reconsidered

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Summary To investigate the role of cerebral hypoxia as a causative factor in the alteration of the qEEG during hyperventilation, qEEG changes caused by progressive hypocapnia were compared with qEEG changes due to progressive normobaric hypoxia in two parallel groups of 12 and 10 healthy male subjects (age 20–27 years), respectively.

In the first group, qEEG records were obtained before and during hyperventilation to pCO_2 levels of 4.0, 3.0 and 2.0 kPa. In the second group, the qEEG samples were taken before and during hypoxia with hemoglobin oxygen saturations of 80, 70 and 60%. In both groups, blood flow velocity in the middle cerebral artery was also recorded.

Hyperventilation caused an exponential increase in slow activity and a decrease in alpha power. No shift in the alpha mean frequency and alpha peak frequency was observed, except with the pCO_2 level of 4.0 kPa, which caused an increase in both variables. Hypoxia with a hemoglobin oxygen saturation of 60% caused a much less pronounced increase in slow activity. No change in total power in the alpha band was found, but both the alpha peak frequency and alpha mean frequency decreased. Lesser degrees of hypoxia caused only minimal EEG changes. Blood flow velocity was decreased by hyperventilation but increased by hypoxia.

It is concluded that the EEG changes observed during hyperventilation must mainly or totally be attributed to factors other than cerebral hypoxia.

Key words: Hyperventilation; Cerebral hypoxia; Cerebral blood flow; qEEG

Hyperventilation (HV) decreases arterial pCO_2, leading to vasoconstriction of precapillary arterioles and, as a consequence, to a reduction in cerebral blood flow (CBF) (Kety and Schmidt 1946; Wasserman and Patterson 1961). The EEG response to HV in young normal subjects consists in an increase in slow activity and a decrease in alpha activity (Berger 1934; Davis and Wallace 1942; Gibbs et al. 1942). These changes resemble those observed in cerebral hypoxia and ischemia (Meyer and Waltz 1960; Kraaier et al. 1988b). A widely accepted explanation is that the EEG slowing observed during hypocapnia is due to cerebral ischemic-hypoxic changes secondary to a decreased cerebral blood flow together with the Bohr effect (decreased dissociation of oxyhemoglobin with increased pH) (Davis and Wallace 1942; Kety and Schmidt 1946; Meyer and Gotoh 1960). It has been demonstrated that the EEG changes of hypocapnia occur below a threshold of decreased cerebral tissue pO_2: the anoxic threshold (Gotoh et al. 1965).

However, there are also data that are not consistent with this hypoxia theory. Wasserman and Patterson (1961) could demonstrate no decrease in cerebral oxygen consumption during HV. In addition, no changes in cerebral adenosine triphosphate (ATP) or phosphocreatine (PCr) concentrations were found, indicating that oxydative phosphorylation was adequate (Granholm et al. 1969; Young and Yagel 1984; Van Rijen et al. 1989). Thus, the exact physiological mechanism underlying the EEG response to HV remains a source of dispute.

This study was designed to investigate the role of cerebral hypoxia as a causative factor in the alteration of the qEEG during HV. To this end, qEEG changes caused by progressive hypocapnia were compared with qEEG changes caused by progressive normobaric hypoxia. Changes in both slow activity and alpha activity were studied. Special attention was paid to the alpha peak and mean frequencies because these variables have been shown to be sensitive to minor degrees of cerebral ischemia (Van Huffelen 1980; Van Huffelen et al. 1984).

Methods

Subjects

The effects of hypocapnia were studied in 12 healthy, drug-free male subjects (mean age 23.4 years; S.D. 1.3

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years; range 21.2–24.8 years). Hypoxia was induced in another group of 10 healthy, drug-free male subjects (mean age 23 years; S.D. 2.2 years; range 20.3–27.3 years). The subjects were informed about the procedures and gave their consent.

EEG

Silver/silver chloride electrodes were attached to the skin with collodion. The P4O2 and F4C4 derivations were selected for spectral analysis. Only the right-sided derivations were used, thereby permitting simultaneous transcranial Doppler sonography on the left side. The electroencephalograph had a bandwith of 0.26–30 Hz (−3 dB). Artifacts due to blinking, movement or muscle activity were reduced to a minimum by proper instruction of the subjects. Moreover, rejection of 2.5 sec epochs contaminated by artifacts could be accomplished on line by the technician. The EEG signal was digitized with a 12-bit analog-digital converter at a sampling frequency of 100 Hz after filtering with an anti-aliasing filter (cut-off frequency 40 Hz, 36 dB/oct). Before each session the system was calibrated with a sinusoidal signal of known amplitude which was fed into the pre-amplifiers. Mean auto-spectra were calculated over 20 epochs of 5.12 sec (total duration 102.4 sec). Convolution with a spectral window (triangular, three points) was performed, resulting in an effective bandwith of 0.59 Hz (Dumermuth and Molinari 1987).

Blood flow velocity, pCO_2 and hemoglobin oxygen saturation

BFV. Blood flow velocity in the left middle cerebral artery (MCA) was measured with a 2 MHz pulsed Doppler apparatus (TC 2-64, EME) according to the method described by Aaslid (1986). The part of the MCA giving the highest Doppler velocity was chosen for recording of the BFV.

pCO_2. An infra-red gas analyser was used for capnographic control. Exhaled gas was sampled continuously at a flow rate of 500 ml/min via a side tube (140 cm length) of the mouthpiece. The nose was closed with a noseclip.

$HbSaO_2$. During the hypoxia study, hemoglobin oxygen saturation ($HbSaO_2$) was monitored continuously with a finger oxymeter (Ohmeda, model 3700); in the 60–100% range the accuracy was ±2.4%.

Design of the studies

Hypocapnia. The hypocapnia study consisted of 3 separate recording sessions. In the first, the end-tidal pCO_2 was decreased from baseline to 4.0 kPa, in the second to 3.0 kPa and in the third to 2.0 kPa. The sessions took place at the same time of the day, at 1 week intervals.

During the experiments, the subject was lying comfortably on a bed, with the eyes closed. To obtain baseline data, the subject first breathed at his normal speed and depth through a mouthpiece. After a short period of familiarization, the baseline pCO_2 was noted. A 102.4 sec EEG sample was taken for spectral analysis (baseline spectrum) and the BFV was recorded concurrently.

The subject then increased his frequency of ventilation to a rate indicated by a metronome (20/min when an end-tidal pCO_2 of 4.0 kPa was required and 30/min when an end-tidal pCO_2 of 3.0 or 2.0 kPa was required). A supervisor, who read the capnogram, instructed the subject on the appropriate ventilation depth so that the required pCO_2 value was reached within 2 min and maintained throughout the HV phase, resulting in a steady-state pCO_2. A 102.4 sec EEG sample was taken 4 min after the subject had started to hyperventilate (HV spectrum). The BFV was recorded in the sixth minute after starting HV. After 6 min the subject was asked to breathe normally again. A third 102.4 sec EEG sample was taken 5 min after the subject had stopped hyperventilating; the BFV was recorded in the seventh minute after cessation of HV.

Hypoxia. The hypoxia study also consisted of 3 separate recording sessions. In the first, the $HbSaO_2$ was reduced from baseline to 60%, in the second to 70% and in the third to 80%. The sessions took place at the same time of day, at intervals of at least 1 week. During the experiments, the subject was lying comfortably on a bed, with the eyes closed.

To obtain baseline data, the subject first breathed normal air through a mouthpiece. After a short period of familiarization, the baseline $HbSaO_2$ was noted and a 102.4 sec EEG sample was taken for spectral analysis (baseline spectrum); the BFV was recorded concurrently.

The mouthpiece was then adjusted to a rebreathing circuit. The subject breathed in a gas mixture consisting of oxygen and nitrogen. CO_2 was filtered out with a carbon dioxide-absorbing by-pass. The concentration of oxygen inspired during rebreathing was varied with an adjustable oxygen supply such that the inspired $HbSaO_2$ was reached within 5 min and maintained for another 17 min. Sixteen minutes after the introduction of hypoxia a 51.2 sec EEG sample was taken (hypoxia spectrum) and the BFV was recorded. During the experiment, the end-tidal pCO_2 was monitored continuously. To prevent HV, a supervisor instructed the subject on depth and frequency of breathing such that the pCO_2 did not fall below 4.5 kPa. After 22 min the subject was re-oxygenated by allowing him to breathe oxygen-enriched air until his $HbSaO_2$ reached baseline levels.

qEEG variables

The qEEG variables used in this study are shown in Table I. Subtraction spectra were made by subtracting

TABLE I

qEEG variables used in this study.

MPD	Mean logarithmic power density in the delta band (1.3–3.0 Hz) in dB
MPT	Mean logarithmic power density in the theta-1 band (3.0–6.0 Hz) in dB
MPA	Mean logarithmic power density in the alpha band (7.7–12.4 Hz) in dB
MFA	Mean frequency of the alpha band (7.7–12.4 Hz) in Hz
PFA	Peak frequency of the alpha band (7.7–12.4 Hz) in Hz
TP	Total power of the 0.1–22.9 Hz spectrum in μV^2
MP_{tot}	Mean frequency of the total spectrum (0.1–22.9 Hz) in Hz

the baseline spectrum from the spectrum recorded during HV or hypoxia, as described previously (Kraaier et al. 1988a).

Statistics

The computed variables had a sufficiently normal distribution to justify the use of parametric statistics. The differences in the computed variables were tested with *t* tests.

Results

Subjects

For the HV experiments with pCO_2 values of 4.0 and 2.0 kPa, EEG data from one subject had to be rejected for technical reasons. In the hypoxia study data from one subject were excluded during the 70% $HbSaO_2$ session and from another subject during the 60% $HbSaO_2$ session because in both cases the pCO_2 fell below 4.5 kPa. All other EEG samples were used for statistical analyses.

BFV, pCO_2 and $HbSaO_2$

Table II shows the mean BFV values at rest, during HV at pCO_2 levels of 4.0, 3.0 and 2.0 kPa, and after recovery in each HV experiment. The baseline pCO_2 and baseline BFV of each subject were slightly different in each experiment, but a multivariate analysis of variance with both variables did not reveal a statistically significant difference between the experiments. The mean baseline pCO_2 and BFV were calculated for each subject. The mean baseline pCO_2 for all subjects and all stages was 5.5 kPa (S.D. 0.4 kPa); the mean baseline BFV was 66 cm/sec (S.D. 10 cm/sec). No significant correlation between pCO_2 at rest and BFV at rest and during HV was found. During HV the BFV decreased in relation to the reduction in pCO_2, which suggests that vasoconstriction occurred (Fig. 1).

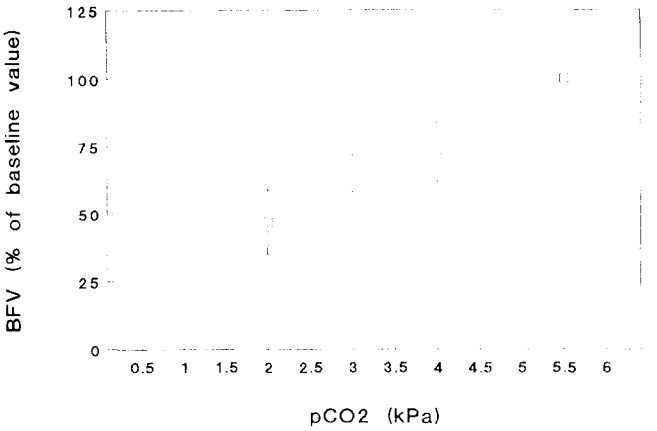

Fig. 1. Relative change in blood flow velocity (BFV) in the middle cerebral artery (hyperventilation/baseline) during hyperventilation to 4.0, 3.0 and 2.0 kPa pCO_2 (mean values and S.D.s).

Table III shows the mean baseline percentage $HbSaO_2$ and the mean BFV at rest and during hypoxia with $HbSaO_2$ percentages of 80, 70 and 60%. As during HV, the mean baseline BFV was calculated for each subject. The mean baseline BFV for all subjects and all stages was 67 cm/sec (S.D. 13 cm/sec), which did not differ significantly from the baseline BFV value found during HV. In contrast to during HV, during hypoxia the BFV increased in relation to the reduction in $HbSaO_2$, due to vasodilatation, thereby compensating for hypoxia.

Baseline EEG spectra

No significant difference between the baseline spectra obtained in the HV and hypoxia studies was found, which allows the EEG changes during HV and hypoxia to be compared.

TABLE II

pCO_2 and blood flow velocity (BFV) in the middle cerebral artery at rest and during and after hyperventilation (HV) to pCO_2 values of 4.0, 3.0 and 2.0 kPa. Mean values and (S.D.). N = 12.

pCO_2 during HV (kPa)	4.0	3.0	2.0
Baseline pCO_2 (kPa)	5.4 (0.4)	5.6 (0.4)	5.4 (0.5)
Baseline BFV (cm/sec)	66 (12)	68 (11)	64 (11)
BFV during HV (cm/sec)	48 (10)	43 (7)	31 (11)
BFV after HV (cm/sec)	65 (13)	74 (14)	68 (14)
Relative change BFV	−0.27 (0.11)	−0.35 (0.07)	−0.53 (0.12)

TABLE III

Blood flow velocity (BFV) in the middle cerebral artery at rest and during hypoxia with hemoglobin oxygen saturations ($HbSaO_2$) of 80, 70 and 60%, and baseline $HbSaO_2$ percentages. Mean values and (S.D.).

Hypoxia $HbSaO_2$ (%)	80	70	60
	(N = 10)	(N = 9)	(N = 9)
Baseline $HbSaO_2$ (%)	96 (1)	95 (3)	96 (1)
Baseline BFV (cm/sec)	67 (12)	68 (17)	66 (9)
Hypoxia BFV (cm/sec)	73 (16)	82 (15)	92 (14)
Relative change BFV	0.08 (0.11)	0.21 (0.16)	0.39 (0.12)

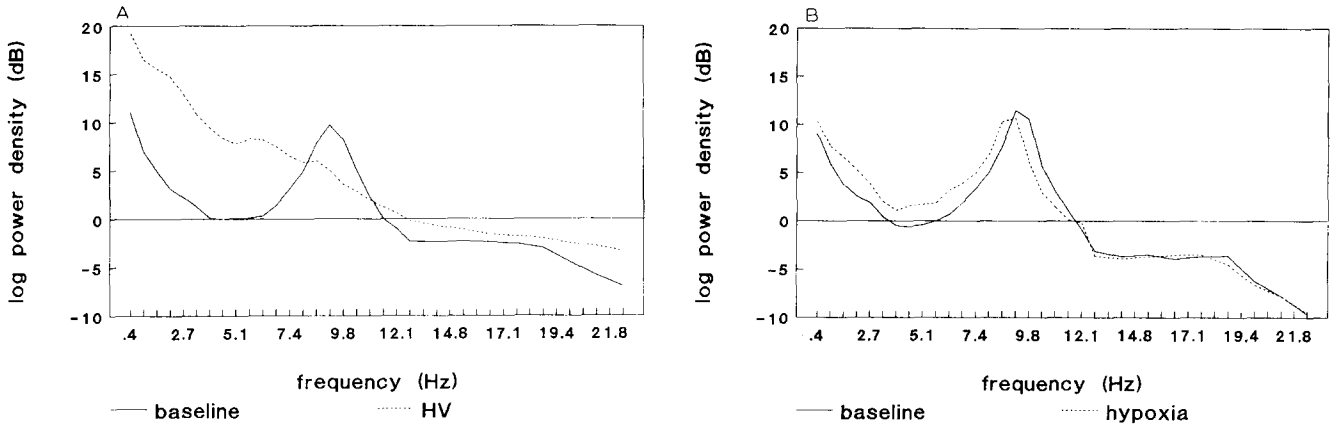

Fig. 2. A: mean baseline and hyperventilation (HV) spectra of absolute logarithmic power density for derivation P4O2 during HV at 2.0 kPa pCO_2. N = 11. B: mean baseline and hypoxia spectra of absolute logarithmic power density for derivation P4O2 during hypoxia with a hemoglobin oxygen saturation of 60%. N = 9.

HV and hypoxia EEG spectra

In Fig. 2A the mean baseline and 2.0 kPa HV spectra for derivation P4O2 are shown. In Fig. 2B the mean baseline and hypoxia spectra are presented for hypoxia with an $HbSaO_2$ of 60%. These figures show a large difference between HV and hypoxia-induced spectral changes.

Effects of HV and hypoxia on EEG subtraction spectra

The EEG subtraction spectra for derivation P4O2 during HV are shown in Fig. 3A; there was an increase in slow activity (1.3–7.7 Hz) and in activity in the low beta range (12.4–17.7 Hz) and a decrease in alpha power (7.7–12.4 Hz). The changes in slow activity were greatest for the change from 3.0 to 2.0 kPa, and smallest for the change from the resting condition to 4.0 kPa pCO_2.

EEG subtraction spectra for the P4O2 derivation during hypoxia are shown in Fig. 3B. Hypoxia with $HbSaO_2$ percentages of 80% and 70% caused no or only minimal spectral changes. Hypoxia with an $HbSaO_2$ of 60% gave rise to an increase in slow activity together with an increase in power in the low alpha range (7.7–9.2 Hz) and in contrast a decrease in activity in the high alpha range (10.4–12.4 Hz). No changes were seen in the low beta range.

Changes in alpha activity can be studied in detail by means of subtraction spectra of frequency bands centered on the individual alpha peak frequency (Schwibbe et al. 1981). In these subtraction spectra, which are presented in Fig. 4A for HV and in Fig. 4B for hypoxia, substantial differences between the two conditions were observed. During HV, the decrease in alpha power was greatest in the frequency band comprising the alpha peak frequency. HV at pCO_2 levels of 4.0 and 3.0 kPa also reduced alpha power in frequency bands below the alpha peak frequency. HV at a pCO_2 level of 2.0 kPa caused a more or less symmetrical

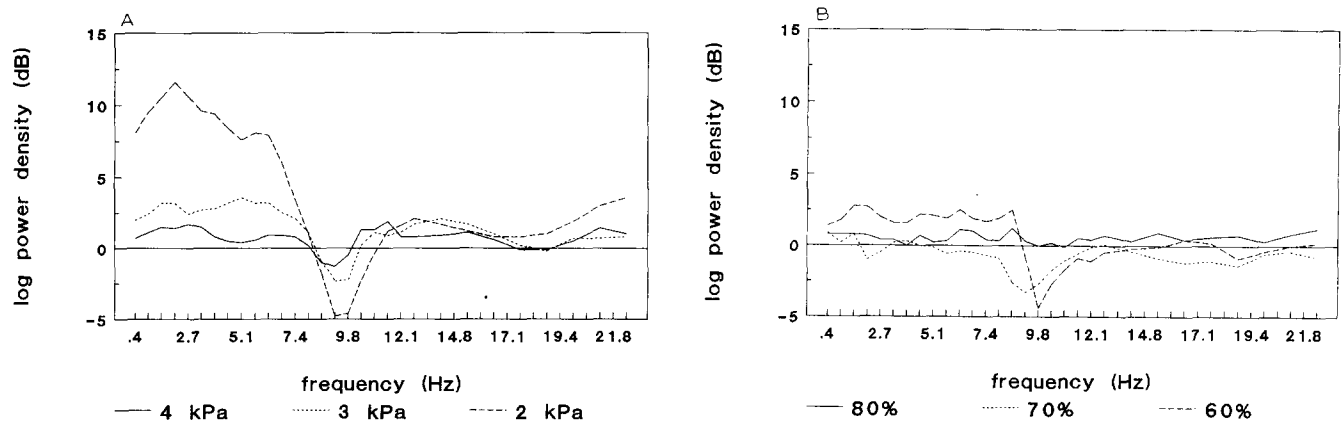

Fig. 3. A: subtraction spectra of absolute logarithmic power density for the P4O2 derivation during hyperventilation (HV) to pCO_2 values of 4.0, 3.0 and 2.0 kPa. N = 11, 12 and 11, respectively. B: subtraction spectra of absolute logarithmic power density for the P4O2 derivation during hypoxia with hemoglobin oxygen saturations of 80, 70 and 60%. N = 9, 10 and 9, respectively.

TABLE IV

Mean differences (S.D.) between qEEG parameters under baseline conditions and during hyperventilation (HV) at 4.0, 3.0 and 2.0 kPa pCO_2. Values for the P4O2 derivation are shown on every first line; on every second line values for the F4C4 derivation are presented. The significance of the values is indicated by *** ($P < 0.001$); ** ($0.001 < P < 0.01$) or * ($0.01 < P < 0.05$).

HV pCO_2 (kPa)	4.0 (N = 11)	3.0 (N = 12)	2.0 (N = 11)
MPD (dB)	1.42 (1.17) ***	2.93 (3.40) *	10.90 (3.50) ***
	1.17 (2.07)	3.69 (3.71) **	14.50 (4.12) ***
MPT (dB)	0.62 (1.72)	3.10 (2.99) **	8.63 (2.64) ***
	0.24 (2.13)	3.14 (3.24) **	11.06 (2.72) ***
MPA (dB)	-0.83 (1.20) *	-2.52 (2.55) **	-4.29 (2.90) ***
	-0.42 (1.77)	0.26 (2.09)	1.25 (3.46)
MFA (Hz)	0.2 (0.2) *	0.1 (0.3)	0.0 (0.3)
	0.0 (0.2)	-0.1 (0.8)	0.1 (0.4)
PFA (Hz)	0.5 (0.6) **	0.2 (0.4)	-
TP (μV^2)	9 (53)	1 (19)	133 (139) ***
	4 (22)	39 (44) ***	398 (291) ***
MF_{tot} (Hz)	0.2 (0.6)	-1.1 (1.6) *	-3.9 (1.6) ***
	0.1 (1.1)	0.0 (2.6)	-2.5 (2.9) *

TABLE V

Mean differences (S.D.) between qEEG parameters under baseline conditions and during hypoxia with hemoglobin oxygen saturation ($HbSaO_2$) percentages of 80, 70 and 60%. Values for the P4O2 derivation are shown on every first line; on every second line values for the F4C4 derivation are presented. The significance of the values is indicated by *** ($P < 0.001$), ** ($0.001 < P < 0.01$) or * ($0.01 < P < 0.05$).

$HbSaO_2$ (%)	80 (N = 9)	70 (N = 10)	60 (N = 9)
MPD (dB)	-0.64 (1.62)	-0.22 (0.83)	2.48 (1.58) **
	0.09 (2.18)	-0.63 (2.46)	1.61 (3.68)
MPT (dB)	-0.31 (1.29)	-0.03 (1.57)	1.86 (1.48) **
	0.14 (1.38)	-0.48 (1.10)	2.11 (2.72) *
MPA (dB)	-0.44 (2.80)	-2.70 (3.71)	0.51 (2.46)
	-0.83 (2.27)	-1.38 (2.86)	0.72 (1.49)
MFA (Hz)	0.1 (0.2)	0.0 (0.4)	0.3 (0.2) **
	0.0 (0.2)	0.0 (0.2)	-0.1 (0.3)
PFA (Hz)	-0.1 (0.3)	0.0 (0.5)	-0.6 (0.6) *
TP (μV^2)	0.39 (1.85)	-2.84 (4.16)	0.21 (1.06)
	-0.28 (2.57)	-0.55 (0.69) *	0.98 (3.01)
MP_{tot} (Hz)	-0.01 (0.82)	-0.40 (0.59)	1.08 (1.07) *
	-0.04 (0.82)	0.71 (2.95)	0.32 (1.97)

decrease in power in a 1.8 Hz frequency band centered on the alpha peak frequency.

Hypoxia with an $HbSaO_2$ of 70% caused a decrease in power in the frequency band comprising the alpha peak frequency and in 2 adjacent 0.6 Hz bands above this frequency. Especially the $HbSaO_2$ of 60% gave rise to spectral changes that differed markedly from those obtained during HV. A reduction in activity in a 1.8 Hz band above the alpha peak frequency and an increase in activity in a 1.8 Hz band below the alpha peak frequency were found, indicating a shift in alpha power to a lower frequency range.

Effects of HV and hypoxia on qEEG variables

The effects of HV and hypoxia on the selected qEEG variables are shown in Tables IV and V, respectively.

Slow activity. From Table IV it is apparent that the power in the delta and theta-1 bands increased more or less exponentially in relation to the decrease in pCO_2 during HV. In the P4O2 derivation the change from 3.0 to 2.0 kPa accounted for 73% and 63% of the increase of power in these bands, respectively. Similar changes in slow activity were observed for the F4C4 derivation.

Although hypoxia with an $HbSaO_2$ of 60% also increased slow activity, this increase was much less pronounced than that observed during forceful HV. No change in slow activity could be demonstrated with higher $HbSaO_2$ percentages.

Alpha power. During HV, the alpha power in the P4O2 derivation decreased in relation to the reduction in pCO_2. In the F4C4 derivation no change in alpha power was observed. However, in view of the location

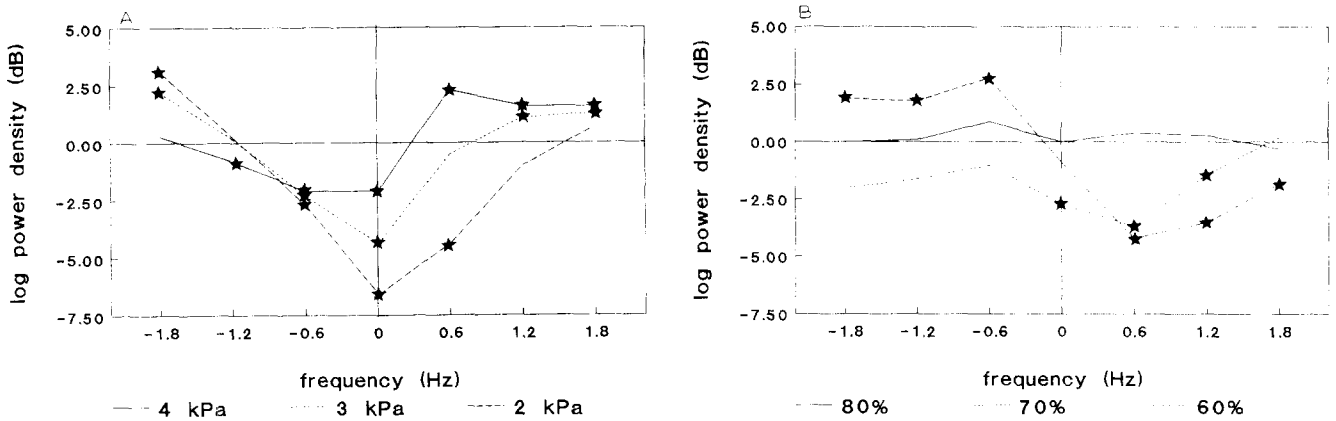

Fig. 4. Subtraction spectra of absolute logarithmic power density of 7 0.6 Hz frequency bands centered on the individual alpha peak frequency for the P4O2 derivation during hyperventilation (A) and hypoxia (B). Symbols indicate significant differences ($P < 0.05$). For N see Figs. 3A and B.

of the alpha rhythm, this derivation should be considered to be inappropriate for the examination of changes in the alpha band. In contrast to HV, hypoxia did not change the power density of the alpha band.

Alpha frequency shift. No shift in the mean frequency of the alpha band was found during HV except for the pCO_2 level of 4.0 kPa for the P4O2 derivation, which gave rise to an increase in this frequency. Hypoxia with an $HbSaO_2$ of 60% caused a decrease of the mean frequency in the alpha band for the P4O2 derivation. Hypoxia with higher oxygen saturations did not lead to a shift in the mean frequency of the alpha band.

Peak frequencies revealed similar differences between HV and hypoxia. These variables were measured only in the P4O2 derivation. Because of the large decrease in alpha activity, no alpha peak frequencies could be detected during HV at a pCO_2 level of 2.0 kPa.In contrast to HV, hypoxia with an $HbSaO_2$ of 60% caused a decrease in the alpha peak frequency by 0.6 Hz.

Total power. In derivation P4O2, no changes in total power were found during HV to pCO_2 values of 4.0 and 3.0 kPa; an increase in total power was found during HV to a pCO_2 value of 2.0 kPa. In derivation F4C4 an increase in total power was already measured during HV to 3.0 kPa. Unlike HV hypoxia did not increase total power.

Frequency shift of the entire spectrum. As a result of the increase in slow activity and a decrease in alpha power, a decrease in the mean frequency of the entire spectrum was found during HV to pCO_2 levels of 3.0 and 2.0 kPa. The mean frequency also decreased during hypoxia with an $HbSaO_2$ of 60%. In accordance with the changes described above, the decrease during forceful HV was far more pronounced than that during hypoxia.

Discussion

There is considerable evidence to support the theory that EEG slowing during HV is due to hypoxic-ischemic changes, resulting from the hypocapnia-induced reduction in cerebral blood flow together with the Bohr effect. It has, for instance, been demonstrated that cerebral tissue pO_2 decreases during HV (Meyer and Gotoh 1960) and that this decrease is corrected by inspiration of 100% oxygen (Kennealy et al. 1980). In other studies however, no measurable decrease in cerebral oxygen consumption could be demonstrated (Wasserman and Patterson 1961).

Biochemical support for the hypoxia theory is found in the increase in both the lactate/pyruvate and NADH/NAD + ratios in brain tissue and cerebrospinal fluid at pCO_2 values below 2.7 kPa (Alexander et al. 1968; Granholm et al. 1969). It has, however, been demonstrated that alkalosis per se stimulates glycolysis, resulting in an increased lactate and pyruvate production, due to stimulation of the enzyme phosphofructokinase by increased pH (Lowry and Passoneau 1966). Therefore, the biochemical changes occurring during HV cannot be ascribed to hypoxia alone but must, at least partially, be attributed to the increase in phosphofructokinase activity.

In clinical studies, different effects of cerebral ischemic-hypoxic changes on the EEG have been described. A major subdivision can be made into two patient categories, based on the clinical classification of cerebral ischemia. The first group comprises those patients with more severe forms of cerebral ischemia in which the EEG usually shows abnormalities on visual assessment. The most frequently observed changes in these EEGs are, among others, an absence of or decrease in alpha activity (Gibbs and Gibbs 1941; Strauss et al. 1943), slowing of the alpha rhythm (Farbrot 1954) and an increase in delta activity (Gibbs and Gibbs 1941). However, these changes are not constant; for example an increase in alpha activity has been described as well (Barré et al. 1950).

The second group consists of patients with minor cerebral ischemia (TIA, RIND, PNS). In this group, the visually assessed EEG is most often normal (Birchfield et al. 1959), although the qEEG may reveal slight but consistent abnormalities. In patients with minor unilateral cerebral ischemia and normal EEGs on visual assessment, slowing of the alpha rhythm was found on the affected side. A decrease in the alpha peak frequency proved to be the most sensitive parameter to demonstrate minor cerebral ischemia. In these patients, an increase in delta activity was found, but no change in the power of the alpha band could be detected (Van Huffelen 1980; Van Huffelen et al. 1984).

Concerning the power in the alpha and delta bands, the EEG changes during HV found in the present study resemble to some extent those observed in patients with severe cerebral ischemia. The reduction in BFV in the MCA is also in line with the assumption that ischemic-hypoxic changes occur during HV. However, the slowing of the alpha rhythm which is observed in patients with cerebral ischemia was not found during HV. Despite the observed similarities, this result shows that the EEG changes during HV should not be used as neurophysiological support for the notion that HV gives rise to cerebral ischemic-hypoxic changes.

Hypoxia with an $HbSaO_2$ of 60% resulted in EEG changes similar to those observed in patients with minor cerebral ischemia. These results support the hypoxic-ischemic character of the EEG changes observed in patients with minor ischemia.

The EEG in the present study during both HV and hypoxia showed an increase in slow activity. The increase during moderate and severe HV (at pCO_2 levels of 3.0 and 2.0 kPa) was much more pronounced than that during hypoxia. One might argue that EEG changes similar to those observed during HV will be found during more severe hypoxia. However, extrapolation of the results found during hypoxia did not result in the same changes as observed during HV; the EEG changes clearly have different characteristics.

The differences in qEEG changes due to HV and hypoxia were most marked in the alpha band. The reduction in both alpha mean and alpha peak frequency found during hypoxia was not observed during HV, while one of the features of the EEG changes during HV, the decrease in alpha power, was not seen during hypoxia. It is obvious that these differences plead against a major causative role of cerebral hypoxia in the alteration of the qEEG during HV. The existence of cerebral hypoxia during (forceful) HV, however, cannot be excluded. Hypoxic EEG changes may be overruled by HV-induced EEG changes.

Another hypothesis that has to be rejected on the ground of the present study is the existence of an anoxic threshold for EEG changes during HV. Although the increase in slow activity and the decrease in alpha activity were greatest for the change from 3.0 to 2.0 kPa, changes in both slow and alpha activity were already observed at pCO_2 levels of 4.0 and 3.0 kPa.

In conclusion, this study has demonstrated that the EEG changes during HV cannot simply be explained by cerebral hypoxia, but must mainly or totally be attributed to other causative mechanisms. This implies that the hypoxia theory explaining the EEG effect of HV can no longer be upheld.

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