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Reversibility of the Chronic Post-Stroke State

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SUMMARY Forty patients with cerebral infarction associated with occlusion of the internal carotid artery (ICA) or the middle cerebral artery (MCA) were treated with hyperbaric oxygenation (HO). EEG analyses were performed regularly in order to assess the course of the cerebral lesion. Patients in an early post-stroke stage (III B) and patients in a chronic post-stroke stage (IV) had the changes in EEG analysis and neurological findings distributed evenly between these two groups.

In 27% of the cases, the improvement was considerable, 53% had

moderate improvement, and 20% showed no change of condition. The improvement mainly consisted of an increase of alpha-wave and beta-wave activity over the affected brain region. We were able to show this fact clearly by means of the EEG-analysis-system applied. The results show that (a) hyperbaric oxygenation therapy (HOT) has a very favorable influence upon the course of disease, and (b) simultaneous application of HOT and EEG analysis allows for a differentiation between reversible and irreversible post-stroke changes in brain tissue.

Introduction

ELECTROENCEPHALOGRAPHY is helpful in showing changes in patients with cerebral damage. Noting the findings of others¹⁻³ we used EEG several years ago to detect the effect of hyperbaric oxygenation (HO) in cases of brain trauma and cerebral infarction.⁴⁻⁶ We also applied HO at pressures of 2 to 3 ata* with a length of exposure of at least one hour, and often for a longer period of time.

After we demonstrated by comparative clinico-neurological evaluation and biochemical examinations of the cerebral glucose metabolism that inspiratory oxygen pressure (IOP) above 1.5 ata results in a disturbance of the oxidative glucose, respectively, of the energy metabolism of the injured human brain,⁷ we applied HO only at pressures up to 1.5 ata and a length of exposure of approximately 40 minutes. This dosage of oxygen was applied not only once but repeatedly in all cases so that the hyperbaric oxygenation therapy (HOT) consisted of a series of individual HOs.

The electrical brain activity improved in a large number of cases. The conventional EEG examination and evaluation, however, complicated this task because of the rapidly increasing amount of data. We therefore used an automatic EEG-interval-analysis-system which is keyed to the visual evaluation of the EEG curve; the system proceeds by measuring and counting, provides quantifiable and reproducible results, and permits an interpretation of the findings by means of customary EEG concepts.⁸

Methods

Forty patients (24 men and 16 women between the ages of 8 and 68; average age, 46.9 years) were studied; 20 patients with occlusion of the internal carotid artery (ICA) and 20 with an obstruction of the middle cerebral artery (MCA). Twenty of these 40 patients were in the post-stroke stage, III B (stroke without or with only a partial improvement within the first four weeks), and 20 were in the chronic post-stroke stage, IV (permanent neurological symptoms beyond the fourth week).^{9, 10}

After identification of the brain artery occlusions by angiography, each patient had a series of 10 to 15 HOs,

which were performed daily. The duration of time between the maximum neurological deficit and the first HO treatment averaged eight days, with a range of one to 14 days, in the group of patients in Stage III B, and averaged three months, with a range of one to 16 months, in the group of patients in Stage IV.

HOT was applied under spontaneous respiration of oxygen at a pressure of 1.5 ata and a period of exposure of about 40 minutes in a specially constructed hyperbaric chamber. At the same time, frontal, parieto-occipital and temporal EEGs were recorded simultaneously from the hyperbaric chamber in bipolar form on six channels in order to diagnose the artifact, and stored on magnetic tapes. These EEG-analytical tests occurred before the phase of pressure under spontaneous respiration of air, twice during respiration of oxygen under 1.5 ata (in each case after 15 and 30 minutes), after lowering the pressure to 1 ata under respiration of oxygen, and finally 15 minutes after the change from oxygen to air respiration. They were performed as often as possible, particularly at the beginning, middle and conclusion of the HOT.

Description of the EEG-Analysis System

The EEG-signal is placed directly or by intermediate storage on analog tape into the analysis system. Distribution into the four classical EEG-frequency ranges occurs by filter. Then the four filter exits are conveyed to an analog-digital-converter over a multiplexer. The interval time is determined with an exactitude of ± 1 ms from the zero passes for every individual wave by means of a tact generator† controlled by quartz. The events are classified by a computer into the respective interval class and added up over an optional measured time between one and five minutes. The incidence of events is determined for five interval classes per EEG range; hereby the class graduation within the beta-range amounts to 2 Hz (23 to 13 Hz), within the alpha-range and theta-range to 1 Hz (13 to 8 Hz, 8 to 3 Hz) and within the delta-range to 0.5 Hz (3 to 0.5 Hz).

In addition to printing the incidence of events (a) in the respective interval class, the following characteristic measures were determined and printed out (fig. 1). The incidence of sums (b) results by adding the incidence of events of

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*ata = atmospheres absolute.

†An electronic device to determine very accurately short time intervals.

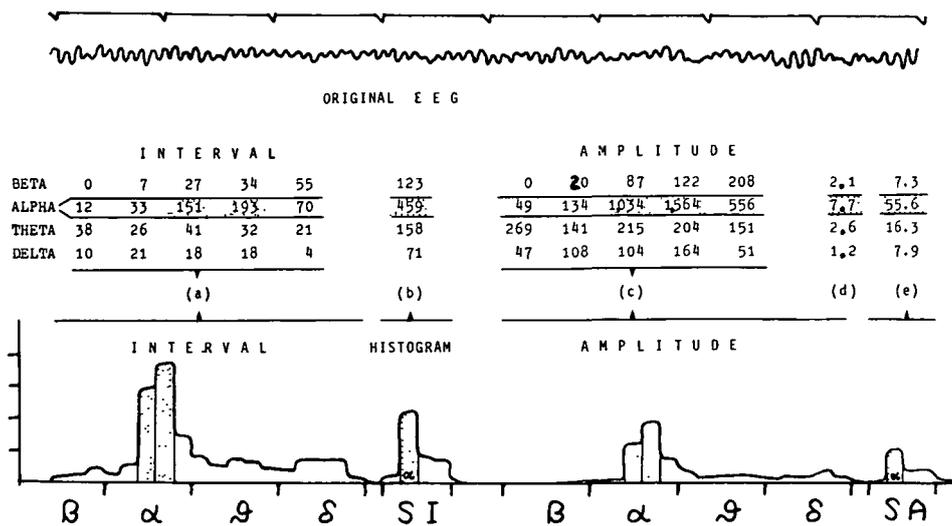


FIGURE 1. EEG recording and analysis of a normal person.

the five interval classes of every EEG-range during the analysis time. The mean frequency (d) is obtained by dividing the incidence of sums by the analysis time in seconds. The amplitude information (c), adjoined to the respective interval class, results from measuring the positive and negative amplitude of every half-wave and listing them into grades of 16, the sum being a function of the positive and negative absolute values of the total wave. The interval-amplitude-histogram, developed from these values, connects frequency and amplitude and reveals the main range of activity. In order to obtain values for the electrical brain activity, which were independent of the duration of analysis, we determined the electrical power equivalent (EPE) (e) as an index value. The EPE results from adding up the amplitude information in an EEG-range and dividing it by the measured time; it constitutes a mean amplitude value per unit of time. This quantity has an informational substance comparable to the power spectrum.

Results

If you subject healthy test persons to HO and analyze their EEGs during this time, the following observations are typical. The normal initial EEG of a 24-year-old person shows an alpha-rhythm of 9 to 10 waves per second (fig. 1). The analysis of this derivation reflects this fact clearly in the data protocol and in the pertinent histogram. Here we find the largest number of incidence of events within the alpha-range, i.e., in the interval classes of the 9 to 10 per second waves. The incidence of sums is accordingly the highest within the alpha-range. Since the amplitude information is adjoined to the respective interval class, we also find the highest amplitude values in the 9 to 10 Hz interval class. The EPE value or the mean amplitude value per time unit for the alpha-range also predominates. By recording the determined EPE values for each of the four wave-ranges and the sum of four EPE values, which constitutes a quantity for the electrical brain activity, during the period of HO, it is possible to show the actual alterations (fig. 2). In the case of the test persons, the alpha activity and beta activity remain more or less unchanged. There are no changes of EPE values for the

theta-range and delta-range discernible after 15 minutes of continuous respiration of oxygen under a pressure of 1.5 ata. After 30 minutes under an IOP of 1.5 ata, however, there is a slight decrease of the delta-wave and theta-wave activity observable. Therefore, the sum of the EPE values also slightly decreases. During respiration of oxygen under normal pressure and after changing from oxygen to renewed respiration of air, the theta-wave activity increases again slightly, so that the sum of the EPE value increases again slightly. A comparison between the initial and the final values of the EEG analysis shows no appreciable change. Contrary to this reaction of electrical brain activity, we found, in the case of patients having occlusions of cerebral arteries, the following alterations under HO, as presented by the EEG-analysis findings of three typical cases.

Case 1

A 34-year-old woman had had four transient ischemic attacks (TIA) in the form of headaches, vertigo and a slight hemihypesthesia and hemiparesis since 1969. A considerable hemiparesis, hemihypesthesia and an incomplete aphasia suddenly occurred at the beginning of March, 1975. During medical treatment the hemiparesis and the hemi-

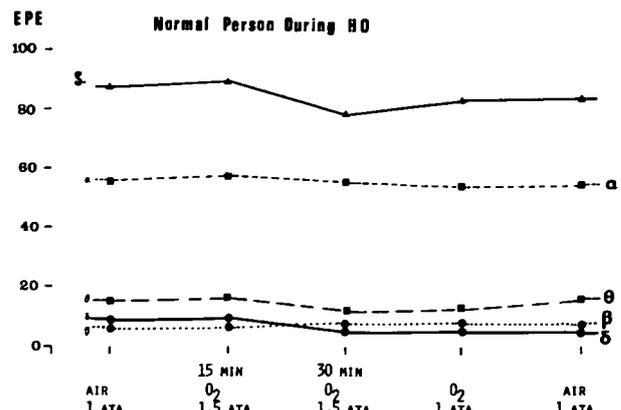


FIGURE 2. EPE values of a normal person subjected to HO.

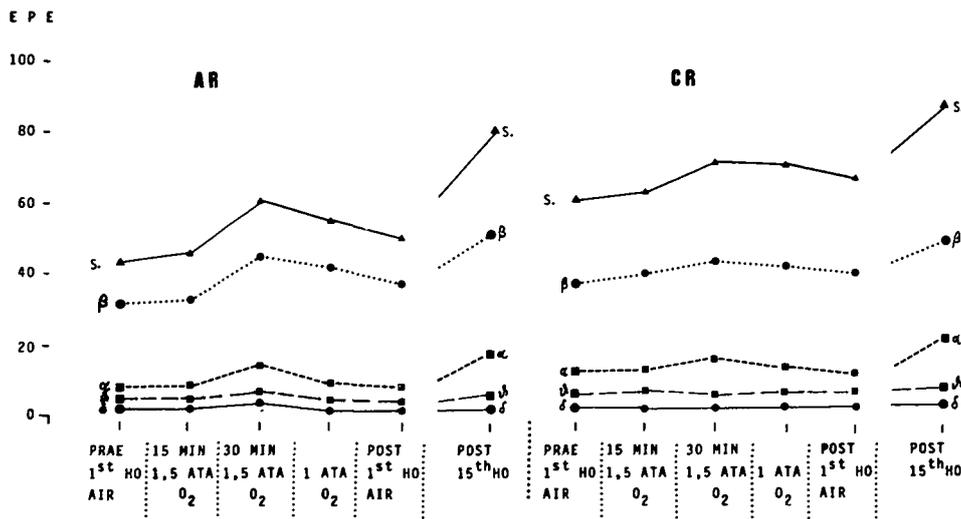


FIGURE 3. Changes of EPE values in Case 1 during the first HO treatment and at the end of HOT. AR = affected region, CR = contralateral region.

hypesthesia improved slightly in the first two weeks after the stroke. From then on the symptomatology remained unchanged. When the patient was admitted to the hospital following her stroke, we found a distinct hemisympmatology and an incomplete aphasia. The EEG showed a moderate change temporoparietally and the angiogram revealed occlusion of a main branch of the left MCA immediately behind the bifurcation, which caused an extensive temporoparietal avascular region. We began HOT seven and one-half weeks following the onset of stroke.

The EEG analyses, performed prior to the first HO, showed a lower alpha-wave, beta-wave and theta-wave activity over the affected brain region than over the contralateral brain region (fig. 3). After 30 minutes of continuous respiration of oxygen at 1.5 ata, the alpha-wave and beta-wave activity increased distinctly over the affected brain region and only slightly over the contralateral brain region.

This caused a rise in the sum of EPE values and showed an improvement of the electrical brain activity above the affected region, in particular. After reducing the IOP to 1 ata and after changing from oxygen to air respiration, the alpha activity and beta activity slightly decreased again. Comparison between the initial and final EPE values showed an increase of beta-wave activity on both sides. At the end of HO, the value of EPE sums was above the initial value, and the difference was more distinct over the affected brain region. This typical reaction continued during the further course of HOT, so that after the fifteenth HO there was considerable improvement of electrical brain activity. This improvement was on both sides of the brain, and consisted of a conspicuous increase of alpha-wave and beta-wave activity, which was more distinct over the affected brain region. Nevertheless, the electrical brain activity over the affected brain region remained slightly reduced as compared to the contralateral side. This corresponded also to the clinico-neurological process because at the conclusion of HOT there was a latent weakness in the right arm and the dysphasia disappeared. These improvements remained.

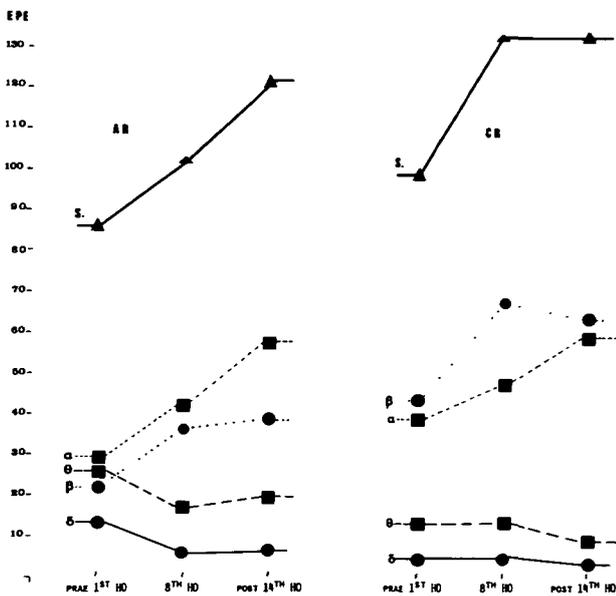


FIGURE 4. Changes of EPE values in Case 2 during HOT.

Case 2

A 39-year-old woman had occlusion of the right MCA. This led to moderate impairment of consciousness and severe left hemiparesis. Six days later the first HO treatment was given. Corresponding to the neurological abnormality, the EEG analyses performed prior to the first HO showed a distinctly reduced alpha activity and beta activity and a considerable increase of theta-wave and delta-wave activity as compared to the contralateral brain region (fig. 4). After the eighth HO treatment, there was an increase of alpha-wave and beta-wave activity, coinciding with a decrease of theta-wave and delta-wave activity, so that the theta-wave and delta-wave activity practically reached the level of the contralateral side. There was also a distinct increase of alpha and beta activity on the contralateral side. During further HOT, the alpha activity, in particular, continued to increase over the affected and contralateral regions of the brain. At the end of HOT, there was considerable bi-

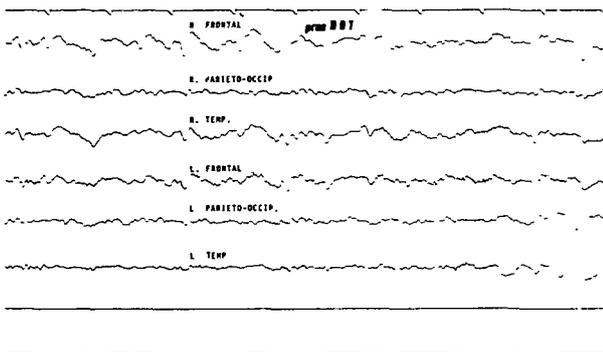


FIGURE 5. EEG of Case 3 at the beginning of HOT.

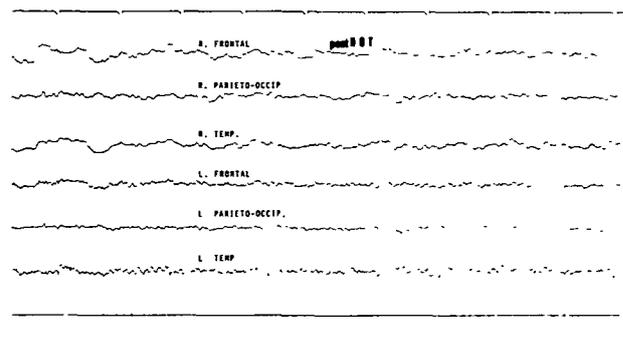


FIGURE 7. EEG of Case 3 at the conclusion of HOT

lateral improvement of electrical brain activity, which was particularly distinct in the affected brain region. There was simultaneous clinical improvement.

Case 3

A 56-year-old patient had occlusion of the right ICA. There were severe left hemiparesis and clouding of consciousness. The patient was treated medically and physically in the hospital. Considerable spasticity developed in the paretic extremities. Eight weeks passed before the beginning of HOT. The conventional EEG-derivation (fig. 5) showed moderately severe general alterations. The EEG registered a

basic rhythm consisting primarily of six to seven per second theta waves and of grouped one to three per second delta waves, distinctly accentuated on the right, and scarce beta-wave and alpha-wave activity. Between the right temporal and fronto-precentral regions, there was a focus of dysrhythmia with delta-wave activity.

Before the first HO treatment, the EEG analysis (fig. 6) showed a distinctly reduced total activity with predominant theta activity over the affected side of the brain. The alpha-wave and beta-wave activity were markedly reduced in relation to the delta activity. There were greater alpha activity and beta activity over the contralateral side of the brain. The alpha activity was predominant, but the theta-wave activity also was increased and above the beta-wave activity. After every HO treatment, the alpha-wave and beta-wave activity increased on both sides, so that we could register a distinct increase in these wave regions after the eleventh HO treatment. Whereas the alpha activity just surpassed the theta-wave activity on the side affected, the contralateral side showed that the alpha-wave and beta-wave activity were distinctly more than the decreased theta activity and delta activity. The extent of change in EEG findings, which was based mainly upon the increase of alpha-wave and beta-wave activity, was considerable. The conventional EEG showed an increase of alpha-wave and beta-wave activity and a reduction of slow waves after the conclusion of HOT (fig. 7). After the conclusion of HOT, the hemiparesis improved.

Forty patients with stroke caused by occlusion of cerebral arteries, similar to the cases previously described, were treated and observed. These 40 cases were divided into three groups (table 1). Group 1 (11 patients) showed considerable improvement of electrical brain activity, corresponding to an increase in EPE values of more than 30% of the initial value. Group 2 (21 patients) showed an increase of the elec-

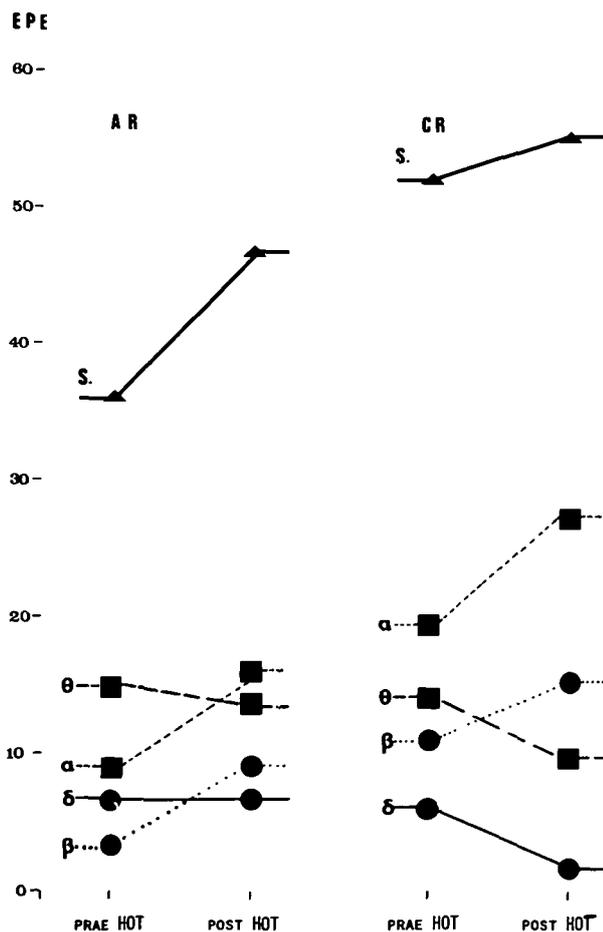


FIGURE 6. Changes of EPE values in Case 3 during HOT

TABLE 1 Changes of EPE in 40 Stroke Patients Treated With HO

Group	EPE value			Stage	
	Definite increase*	Moderate increase†	No change	IIIB	IV
1	11 (27%)			6	5
2		21 (53%)		10	11
3			8 (20%)	4	4

Patients were divided according to the improvement of the electrical brain activity after HOT in relation to the initial EPE values: * > 30% in relation to pretreatment value; † 10% to 30% in relation to pretreatment value.

trical brain activity between 10% and 30%, and Group 3 (eight patients) showed no definite change of the EPE value. These findings correlated well with the cliniconeurological changes. Fifty percent of the patients in each group were in the chronic post-stroke stage. This suggests that the effect of HOT is favorable in either an early or late post-stroke stage.

Discussion

Since these patients had occlusion of the ICA or MCA, the focus of ischemia apparently extended near the cortex of the brain. This caused accentuated changes of the EEG. This was clearly discernible in a comparison of the EEG analyses of Case 1 with Case 3. The improvements of electrical brain activity obtained with HOT (evenly distributed among the cases in the chronic post-stroke stage and the other cases and closely correlated to their clinical course¹¹) may have been caused by the improved oxygen supply of the hypoxic brain. The temporary improvement of electrical brain activity, recorded under increased IOP, is in favor of this. These temporary changes and the differences between the initial and final EPE values after the individual HOs were considerably more distinct in Group 1 than in Group 2. In Group 3 there was only a slight temporary increase of the EPE values under the IOP of 1.5 ata and only rarely were there higher EPE values at the end of an individual HO treatment than the initial values. It appears that the quantity of temporary improvement of electrical brain activity, dependent upon IOP, and the quantity of difference between the initial and final EPE values indicate the extent of still reversible hypoxic alterations of brain tissue and is decisive for the improvement of electrical brain activity. If no appreciable improvement of electrical brain activity and of neurological function occurs under the individual HO or after conclusion of the series of HOs, there must be irreversible cerebral damage. The combined application of HOT and the EEG-analysis system represents a method which permits differentiation between reversible and irreversible hypoxic alterations of brain tissue.

HO applied with a pressure of 1.5 ata improves the oxygen supply within the affected brain tissue. The arterial oxygen pressure rises to approximately 800 to 900 mm Hg. This causes an increase of oxidative metabolism,¹² supplying the cells with much more energy than in the anoxidative metabolism. The increased supply of energy is probably the basis for tissue repair and the resumption of functional performance. Differentiating between functional and perma-

nent ischemic alterations of brain tissue is of great importance in the evaluation of the post-stroke stage. Currently, a number of patients, showing little change in neurological status more than four weeks after their stroke, are classified in the chronic post-stroke stage. Nevertheless, the condition of some of these patients having improved after HOT suggested that surgical reconstruction of arteries might be helpful, while others not subjected to HOT may or may not respond to this treatment.¹³ The method described here assists in separating these two important categories. A separate report will describe such experience.¹⁴

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