CORRELATION BETWEEN BRAIN ELECTRICAL RESPONSES AND LIPID PEROXIDATION DURING PATHOLOGICAL AGING

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Lipid peroxidation (LPO) of biological membranes is one of the leading factors in the development of age disturbances, including normal and pathological aging of the brain [1, 5, 6]. The influence of free radical processes is manifested, in particular, as a decrease in the electrical resistance of membranes of nerve and glial cells, and this affects the electrical reactions of these cells [1, 2]. Direct correlation was demonstrated previously in experiments on animals between accumulation of LPO products in the brain and the level of the steady brain potential (SBP), an integral parameter of membrane potentials of nerve and glial cells [3]. It can be tentatively suggested that LPO also influences other electrophysiological parameters.

The aim of this investigation was to look for correlation between LPO processes and electrical activity of the brain, in order to elucidate the role of free radical reactions in disturbances of neuronal electrogenesis during pathological aging.

EXPERIMENTAL METHOD

Altogether two groups of subjects were tested. Group 1 (12 women) consisted of patients with atrophic diseases of the brain, namely Alzheimer's disease and senile dementia. The ages of the patients ranged from 49 to 82 years. Control group 2 consisted of normal subjects (six persons: four men and two women) aged 17-29 years. The intensity of LPO was compared with the electrophysiological characteristics of brain activity before and after mild stressor stimulation, produced by prolonged clicks, 20 min in duration, 90 dB in intensity, and with an average frequency of 2 stimuli/sec.

This type of stimulation was chosen because, according to data in the literature [1], stress causes changes in the level of LPO. The character of the changes in LPO linked with electrical activity of the brain could therefore be revealed better than in a resting state. Moreover, it can be tentatively suggested that even mild stressor stimulation can induce different changes in patients and normal subjects, and the study of this problem could shed light on some aspects of the pathogenesis of pathological aging.

The intensity of LPO was assessed with the aid of a noninvasive method developed previously, based on measuring the quantity of endogenous n-pentane in the expired air by gas chromatography. It was postulated after a preliminary study that the pentane concentration in the expired air reflects LPO processes chiefly in the brain [2].

After determination of the basic (before stimulation) electrophysiological parameters the subjects were placed in a chamber into which air free from pentane was passed. Samples of expired air were taken 20 min later, electrophysiological parameters were measured, and acoustic stimulation applied. Further air samples were then taken and the electrophysiological parameters recorded.

The electrophysiological investigation comprised measurement of the SBP and visual evoked potentials (VEP). SBP was recorded by a monopolar technique using Ag/AgCl electrodes with adjustable potential difference of 1-2 mV and a dc amplifier with input resis-

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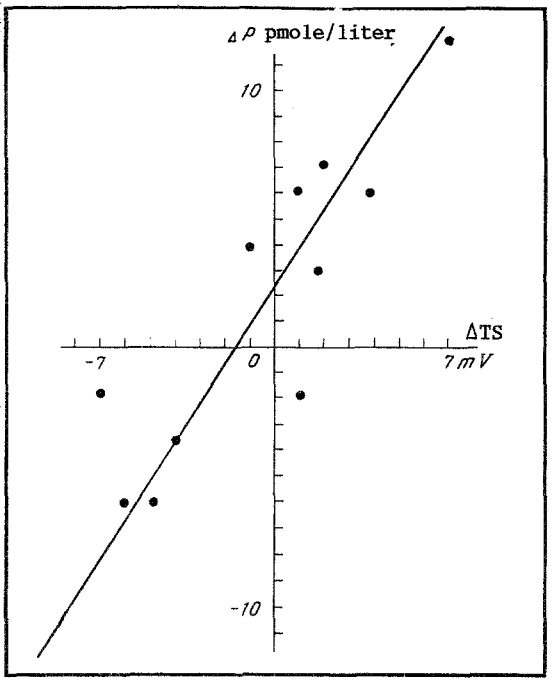

Fig. 1. Correlation between changes in VEP and intensity of LPO under influence of acoustic stressor stimulation in patients with senile dementia and with Alzheimer's disease. Points correspond to experimental data recorded in different patients. Abscissa, shift of steady potential level into left temporal region (ΔTS, mV); ordinate, change in pentane level (ΔP, pmole/liter).

tance of 10^7 Ω. The reference electrode was located on the wrist, the active electrodes along the sagittal line, in the frontal, central, and occipital regions, and also in the right and left temporal regions (points F_{pz}, C_z, O_z, T3, T4). Fuller details of the technique of recording SBP were described previously [4].

The VEP were recorded on a "Neuropack II" analyzer (Japan). Bipolar derivation of VEP was used. The active electrodes were located in the occipital regions (points O_1, O_2) and the reference electrodes in the central regions (points C_3, C_4), on the 10 × 20 system [7].

The biochemical and electrophysiological data were processed on the IBM-PC computer, using standard statistical programs.

EXPERIMENTAL RESULTS

Before acoustic stimulation the greatest differences in the electrophysiological parameters between the groups of subjects studied were found for the latent period (LP) and amplitude of the main components of VEP. For instance, LP of the N_1 wave in the right and left hemispheres was 69.6 ± 1.7 and 68.2 ± 1.2 msec in normal subjects and 103.7 ± 5.6 and 101.0 ± 4.7 msec for the patients, respectively ($p < 0.001$). The amplitude of the same component in normal individuals was 3.9 ± 0.5 and 4.8 ± 1 mV, but 12.5 ± 1.5 and 12.9 ± 1.4 mV, respectively in the patients ($p < 0.001$). Highly significant differences between the mean values of LP and amplitudes also were observed for the subsequent P_2 and N_2 components. Thus, LP and the amplitude of most components of VEP in the patients were significantly greater in value than the corresponding parameters in normal subjects. Mean values of SBP and of the pentane content per unit of body weight did not differ in the two groups. The pentane concentration was of the order of 0.22 ± 0.01 pmole/liter/kg.

The pentane concentration in the expired air in groups of patients and normal subjects correlated with LP of the P_1 component of VEP ($r = 0.63$ and 0.83, respectively, $p < 0.05$), and also with the amplitude of components P_1 and P_2 of VEP ($r = 0.65$ and -0.67, respectively) of the normal subjects only.

Under the influence of acoustic stimulation, SBP and the pentane concentration could both be either raised or lowered, but their mean values were constant. After acoustic stimulation, LPO naturally followed a different course in different brain formations in the normal subjects and patients. LPO products evidently accumulate predominantly in the cortical projection areas in normal subject, for differences of the constant potentials between the right temporal and frontal derivations and also between the left temporal region and the same derivation correlate ($p < 0.05$; $r = 0.85$ and 0.80, respectively) with the pentane concentration in the expired air. In patients with atrophic brain damage LPO products accumulate probably in the better preserved structures of the brain stem, for the potential difference between the central and occipital derivations, located on the sagittal line, correlate ($r = 0.68$) with the pentane concentration.

Acoustic stimulation caused a decrease in amplitude of the first negative component of VEP in the patients by 2.7 ± 1.1 and 3.1 ± 1.1 μV for the right and left hemispheres, and in the normal subjects there was only a tendency for the amplitude of this component to increase; the positive shift of this component on VEP averaged 4.2 ± 1.8 and 2.0 ± 1.2 μV for the right and left hemispheres, respectively. Correlation between the pentane level and LP of VEP was observed only for components P_1 and N_1 of VEP, namely 0.82 and 0.76, respectively for patients with Alzheimer's disease and with senile dementia, whereas no such dependence could be demonstrated for normal subjects.

In response to stressor stimulation qualitative differences between the two groups of subjects were discovered by the study of correlation between the change in the pentane concentration and the shift of the electrophysiological parameters taking place under the influence of the weak stressor stimulus. In normal subjects no such correlation could be found. In the patients, correlation was discovered between the rise of the pentane concentration and the change in SBP in all derivations: frontal, central, occipital, and right and left temporal, for which the values of the coefficients of correlation were as follows: 0.61, 0.71, 0.79, 0.70, and 0.71 (Fig. 1). In patients with a shift of the pentane concentrations, changes in the CBP difference between the frontal and occipital derivations ($r = 0.61$) and the amplitudes of the first negative component of VEP recorded in the right hemisphere ($r = -0.61$) were found to be significantly correlated.

Thus, besides the general rules connecting LPO processes and electrophysiological parameters in the two groups, significant differences also were found, and were manifested after stressor stimulation, evidently as a result of damage to the antioxidant systems of the brain during pathological aging.

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