Effect of Caffeine and Phenazepam on the Quantitative Parameters of the EEG and Ultraslow Electrical Processes in the Brain

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Abstract—A comparative study of the power and coherence of the ultraslow phasic processes (USPPs) of the brain in the frequency range 0.05–0.5 Hz and the EEG (1.5–50 Hz) at rest with the eyes opened or closed before and after the administration of caffeine and phenazepam, a benzodiazepine tranquilizer, was performed. Caffeine and phenazepam caused similarly directed changes in the EEG pattern. The differences between the effects of these drugs were expressed in a different topography of changes in the EEG pattern. Different locations of such changes are supposed to reflect differences in the behavioral effects of drugs (stimulating or sedative). According to the USPP data, the differences in the drug effects are accompanied not only by a different topography of changes in the USPP pattern, but also by an opposite direction of these changes. This fact makes it possible to suppose that, during pharmacological tests, the differential sensitivity of USPPs as an indicator of CNS sensitivity may be higher than that of the EEG, in view of the closer relationship between the behavioral and electrographic changes.

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Ultraslow brain activity, the frequency of which is lower than the classical EEG range (1.5–70 Hz), has been a subject of investigation for several decades [1–4]. However, despite the works carried out, this type of brain activity has not been studied well enough compared to the EEG. In particular, the quantitative parameters of these processes in relation to a simultaneously recorded EEG have been poorly investigated.

In this study, we performed simultaneous recording of the brain ultraslow phasic processes (USPPs) in the range of oscillations with periods of several seconds [4] and the EEG during the action of two drugs with antagonistic effects on the CNS activity, caffeine and the tranquilizer phenazepam.

Twenty-five subjects, men and women aged 18–28 years, participated in the study. The USPPs (0.05–0.5 Hz) and the EEG (1.5–50 Hz) were recorded from 19 areas of the head surface (in accordance with the international 10–20 system) simultaneously with monopolar derivations. Recording was performed with specially prepared Ag/AgCl electrodes [5] using a Mitsar-EEG electroencephalograph (OOO Mitsar, Russia) with a discretization frequency of 250 Hz. Linked earlobe electrodes served as a reference electrode. Drugs (0.1 g of caffeine sodium benzoate or 0.001 g of phenazepam) were administered orally. Recording of the USPPs and EEG was performed under the conditions of quiet wakefulness with the eyes closed for 5–7 min twice for each subject: before the administration of a drug (control) and 50–65 min after it. The recordings of the USPPs and EEG were analyzed visually. Sections of recordings free of artifacts were used for further analysis. The mean absolute power and coherence function of processes were calculated for each subject in a specific state. We assessed the USPPs; the integrated EEG (1.5–50 Hz); and the EEG in the spectral ranges $\Delta$ (1.5–4 Hz), $\theta$ (4–7 Hz), $\alpha_1$ (7–10 Hz), $\alpha_2$ (10–13 Hz), $\beta_1$ (13–18 Hz), $\beta_2$ (18–30 Hz), and $\gamma$ (30–40 Hz). The coherence function and spectral power parameters were calculated with analysis epochs of 2 s for the EEG and 64 s for the USPPs. The arrays of data were averaged for every subject in each state and normalized via the transforms $Y = \log X$ for the power and $Y = \log(X^2/(1 - X^2))$ for the coherence function.

Statistical analysis included comparison of the mean values of the EEG and the USPPs in different derivations or pairs of derivations using ANOVA for individual comparisons. We estimated the effect of the interaction between the factors state and topography with the Greenhouse–Geisser correction. Statistically significant differences for numerous comparisons were determined using Fisher’s LSD test. Differences with a probability of error less than 0.05 were considered statistically significant.

Analysis of the EEG pattern after the administration of caffeine and phenazepam (Fig. 1) showed that both drugs decreased the power of the integrated EEG in the parietooccipital areas and increased the coherence in almost all areas of the cortex.

Analysis of USPPs showed that the effect of caffeine was accompanied by a decrease in the USPP power in temporal areas of both hemispheres and a
EFFECT OF CAFFEINE AND PHENAZEPAM ON THE QUANTITATIVE

decrease in the USPP coherence in almost all areas of the cortex. On the contrary, the effect of phenazepam was accompanied by an increase in the power in the right temporal areas; an increase in the coherence in the right anterior temporal area; and a decrease in coherence in some zones of the central, frontal, and parietooccipital areas.

The EEG spectral analysis also showed (Fig. 2) that the power in the $\beta_2$ EEG band increased after the administration of either caffeine or phenazepam (over the greater part of the cortical surface in the case of phenazepam and in the temporal derivations $F_8$ and $T_3$ in the case of caffeine). In the $\alpha_1$ band, the power decreased (in derivations from the temporal arch for