SPECTRAL ANALYSIS OF THE EFFECT OF SYDNOCARB ON THE RAT EEG

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In recent years there has been undiminished interest in psychostimulants, as substances optimizing behavior, eradicating fatigue and sleepiness, and increasing physical and mental working capacity. In the former USSR original psychostimulants of the sydnoneimine series (sydnocarb, sydnofen), differing from classical phenylalkylamines in their lower toxicity, shorter action, and weaker sympathomimetic effects, have been created [1]. Experiments on curarized cats and rabbits have shown that sydnocarb causes changes in brain potentials of animals characteristic of an activation reaction: high-frequency and low-amplitude waves were found in cats in different regions of the cortex, whereas in rabbits, low-amplitude fast activity also predominated in the sensomotor cortex, but a low-amplitude regular theta-rhythm was recorded in the motor and parietal regions of the cortex and the mesencephalic reticular formation [2, 7]. The aim of this investigation was to make an accurate quantitative evaluation of EEG changes in unrestrained animals under the influence of sydnocarb and allowing for the pharmacologic action of the solvent on the EEG.

EXPERIMENTAL METHOD

Experiments were carried out on 29 noninbred male albino rats weighing 180-250 g. Under pentobarbital anesthesia (50 mg/kg, intramuscularly) nichrome electrodes were inserted stereotactically into the rats 5-6 days before the experiments began, to record the EEG under chronic conditions in the sensomotor cortex of the left and right hemispheres, the dorsal hippocampus, and the lateral hypothalamus of the left hemisphere. A more detailed description of this procedure was given previously [3-5]. On the day of the experiment, the rats were accustomed for 1-1.5 h to the experimental setup in the chamber, after which the brain potentials of the rats were recorded simultaneously on an electroencephalograph and tape recorder ("O.T.E. Biomedica," Italy), in rats in the waking state before (background) and 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, and 5.0 h after peroral administration of 9 g/kg of polyethyleneglycol 400 (PÉG-400, from "Loba Feinchemie," or peroral administration of 10 mg/kg of sydnocarb, dissolved in PÉG-400. The potentials were recorded during 5-min time intervals. After the experiments the tape recordings were processed by a "Berg-Fourier Analyzer" (O.T.E. Biomedica). Power spectra of the EEG were averaged during 4 min 08 sec [3]. The results were subjected to statistical analysis by the nonparametric signs test [8].

EXPERIMENTAL RESULTS

Spectral analysis of the action of the solvent PÉG-400 showed it to have a definite effect on the Fourier power spectrum of the EEG of the sensomotor cortex, dorsal hippocampus, and lateral hypothalamus of the rat brain (Table 1). For instance, PÉG-400 led to a decrease in the total power and the absolute power of several frequency bands in these brain structures. In the cortex it affected the structure of the power spectrum of the EEG, leading to

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TABLE 1. Quantitative Analysis of EEG Power Spectra (PS) of Different Brain Structures of Unrestrained Rats After Administration of PÉG-400 (9 g/kg, perorally)

Brain structures	Parameter of power spectra							
	absolute power of spectral bands (Hz)					total power 0-32	amplitude of dominant peak	frequency of dominant peak
	0—4 δ	4—8 θ	8—13 α	13—20 β_1	20—32 β_2			
Left cortex	−29,8±20,8	−37,0±20,0*	−29,8±19,0*	−29,4±23,9*	−18,4±14,8	−29,8±18,6*	−42,8±19,7*	−0,9±0,8
Right cortex	−16,5±19,1	−39,6±19,2*	−31,3±25,8	−36,1±19,3*	−18,6±17,2	−31,5±20,5*	−39,1±25,4*	−0,9±0,6*
Hippocampus	−25,1±11,3*	−36,2±20,1*	−36,3±21,3	−28,6±23,4	−24,2±10,4*	−32,3±18,2*	−42,3±8,2*	−1,2±0,4*
Hypothalamus	−27,4±13,9	−37,2±20,0	−7,6±18,6	−33,6±17,5	−29,8±8,8	34,6±15,5	−40,0±14,9	−1,4±0,2

Brain structures	Relative power of spectral bands (Hz)					Ratio of parameters (index)		
	0—4	4—8	8—13	13—20	20—32	$\frac{\theta}{\delta}$	$\frac{\theta}{\alpha}$	$\frac{\theta}{\beta_1+\beta_2}$
Left cortex	0,0±25,0	−10,0±14,0	−0,6±3,1	−1,4±7,0	+20,6±16,0*	−7,4±26,0	−0,2±29,2	−16,4±20,9
Right cortex	+41,8±61,0	−14,2±9,9	−7,8±7,4	−7,8±7,7	+25,3±11,3*	−32,8±27,4	−13,3±12,0	−19,8±15,9
Hippocampus	+14,5±19,3	−8,8±9,8	−8,3±5,0	+7,6±11,8	+16,6±18,4	−18,0±17,5	+6,2±11,8	−17,3±16,3
Hypothalamus	+14,0±13,7	−7,8±10,4	−8,4±6,3	+2,6±13,2	+10,0±27,4	−14,4±17,2	+1,4±18,5	−8,0±19,6

Legend. Value of each parameter in background (before administration of PÉG-400) is 100%. Mean values ± standard deviation are shown. *p < 0.05 for nonparametric signs test.

TABLE 2. Quantitative Analysis of EEG Power Spectra (PS) in Different Brain Structures of Unrestrained Rats After Administration of Sydnocarb (10 mg/kg, perorally), Dissolved in PÉG-400

Brain structures	Parameter of power spectra							
	absolute power of spectral bands (Hz)					total power 0-32	amplitude of dominant peak	frequency of dominant peak
	0—4 δ	4—8 θ	8—13α	13—20 β_1	20—32 β_2			
Left cortex	−30,5±19,7*	−35,6±13,8*	−32,8±17,0*	−23,0±12,7*	−21,8±20,1*	−29,0±15,4*	−36,2±13,1*	−5,3±10,9
Right cortex	−30,6±23,2*	−33,4±19,0*	−30,6±21,1*	−24,8±17,0*	−19,8±18,4	−27,6±16,1*	−38,8±12,0*	−3,6±16,8
Hippocampus	−18,6±16,0	−26,0±12,2*	−31,5±14,1*	−23,0±10,8*	−14,2±7,9*	−24,3±9,4*	−26,1±8,1*	−7,8±9,2
Hypothalamus	−12,4±13,8	−28,0±9,1*	−28,2±10,8*	−22,8±6,3*	−20,0±13,7*	−26,4±15,5*	−37,4±21,3*	−10,8±7,5*

Brain structures	Relative power of spectral bands (Hz)					Ratio of parameters (index)		
	0—4	4—8	8—13	13—20	20—32	$\frac{\theta}{\delta}$	$\frac{\theta}{\alpha}$	$\frac{\theta}{\beta_1+\beta_2}$
Left cortex	−2,6±26,9	−12,4±3,2*	−7,4±9,3	+6,2±6,0*	+17,6±11,6*	−4,4±27,2	−3,4±6,5	−25,2± 9,9*
Right cortex	−5,4±16,4	−8,4±13,2	−3,8±11,6	+3,9±6,9	+20,8±21,5	−0,2±24,6	−3,2±10,6	−16,2±19,3
Hippocampus	+8,5±22,9	−1,5±12,3	−10,0±8,3*	+2,8±9,6	+13,6±9,1*	−5,5±24,3	+10,1±16,5	−23,3±3,0*
Hypothalamus	+2,3±19,0	−8,5±8,8	−10,7±10,9	−2,0±5,1	+17,0±12,3*	−15,7±18,2	+5,0±15,1	−12,7±9,8*

Legend. Value of each parameter in background (before injection of preparation) is 100%. Mean values ± mean standard deviation shown. *p < 0.05 for nonparametric signs test.

an increase in the contribution of fast-wave $beta_2$-activity. It is significant that PÉG-400 caused reduction of the amplitude of the dominant peak of the EEG spectra and shifted it into the region of slower frequencies, evidence of reduction of the amplitude and slowing of the dominant theta-rhythm. The action of PÉG-400 lasted 4-5 h after its administration. Besides the facts described above, PÉG-400 also was found to abolish seizure EEG activity in those rats in which seizure discharges were discovered in the course of spontaneous brain electrical activity.

Sydnocarb, dissolved in PÉG-400, had a stronger effect on the EEG power spectra of the brain structures studied, and in particular, on the structure of the spectra (relative power and indices) (Table 2). Compared with the action of PÉG-400, sydnocarb significantly reduced the absolute power of the delta and $beta_2$ frequency bands, and modified the structure of the EEG power spectra of the cortex, toward an increase in the contribution of $beta_{1,2}$-components. In the hippocampus, sydnocarb, unlike PÉG-400, reduced the alpha- and $beta_1$-bands and modified the structure of the EEG spectra, by reducing the alpha- and increasing the $beta_2$-component. In the hypothalamus sydnocarb did not affect the absolute power of the delta-band, but reduced it in all other frequency bands and increased the contribution of the fast-wave $beta_2$-band. Essentially, in the cortex and hippocampus sydno-

carb did not significantly reduce the frequency of the dominant peak. Thus sydnocarb possesses a marked effect of its own on the EEG, which is partly concealed by the action of PÉG-400; despite this, however, it is clearly manifested also against the background of the action of the solvent.

It can evidently be concluded from the facts described above that the solvent PÉG-400 is not an agent that is totally neutral in relation to the CNS, but it has an intrinsic physiological activity and can endow substances dissolved in it with additional properties, as other workers have noted [6, 9-11, 14]. On the neurophysiological level, PÉG-400 depresses slow-wave activity and causes a shift of the dominant peak by 1-1.5 Hz toward lower slow-wave frequencies, and has an anticonvulsant effect. It can accordingly be postulated that PÉG-400 has a certain depressant action on the CNS, which is similar in some respects to the effect of tranquilizers [15].

So far as the action of sydnocarb is concerned, the experiments showed that its effect is partly masked by the solvent, but its own intrinsic effect on the EEG, distinguished by quantitative spectral analysis, namely reduction of the amplitude of all components and an increase in the contribution of fast-wave activity, evidently suggests that sydnocarb causes activation of the CNS.

Under the influence of many psychostimulants, desynchronization develops in the EEG of certain brain structures, and is characterized by reduction of the amplitude of slow-wave rhythms and by predominance of the fast beta-rhythm [1, 2, 5, 7]. By spectral analysis it was found that under the influence of psychostimulants the absolute power of all frequency bands falls [12, 13], and this is accompanied by an increase in the relative power (contribution) of the $beta_{1,2}$-bands [5]. The neurophysiological changes observed under the influence of sydnocarb, in all probability suggest that the drug can raise the level of wakefulness (consciousness) of animals within optimal limits, and that this effect may lie at the basis of its psychostimulant action, leading ultimately to optimization of behavioral functions and to enhancement of physical and mental working capacity.

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