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I. V. Danilov and N. N. Kudryatseva

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EFFECT OF RHYTHMIC PHOTOSTIMULATION ON MONKEYS WITH HYPERKINESIS OF POSTENCEPHALITIC GENESIS

I. V. Danilov and N. N. Kudryatseva

Laboratory of Experimental Central Nervous System Pathology
USSR Academy of Medical Sciences, Leningrad

The effects of rhythmic photostimulation on monkeys (macaca rhesus) with postencephalitic hyperkinesia were studied. It was established that a reaction opposite to that occurring in healthy monkeys developed -- specifically, disappearance of hyperkinesia during the use of 3, 9, 18, 20, and 25 hz frequency light as a stimulus. The significance of rhythmic excitatory cycles in the interrelationships between various structures in the brain are discussed. /511*

Intensive study of human brain activity during the administration of rhythmic sensory stimulation has brought to light a number of phenomena associated with important general regularities in brain operation, such as the adoptions and transformations of the rhythm of applied stimuli, provocations of violent motor responses in functionally healthy people, and seizures in epileptics [18-21].

Analogous data were obtained from long-term experiments on dogs [1, 5, 6, 10] and monkeys [7, 13, 14]. Study of the brain's perceptions of sensory stimulation leads to questions about the mechanisms of perception and the brain's treatment of sensory information, especially the significance of the time factor. Two working hypotheses about this are most widely circulated in the literature today: one of them proposes the existence in the brain of certain "critical excitability cycles" which serve to measure time and transmit arriving sensory information for processing by the brain; the second hypothesis is linked to the assumption that there is a special "central scanning mechanism" in the brain which also groups arriving sensory data together in time (for a critical review of these hypotheses, cf. [12]). All

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*Numbers in the margin indicate pagination in the foreign text.

of the aforementioned demonstrates this problem's practical and theoretical interest.

Observations made in experiments on dogs ([1], etc.), which showe: ;hat the provocative strength of intermittent sensory stimuli (light and sound) abates as the experiments continue, served as the premise of the present research study. However, the fact that removal of the responsible stimulus led to a more acute manifestation of the evoked pathology (hyperkinesias) forces us to think that we should speak not of simple "habituation" to the operative stimulus, but rather of the change in the role of the provoking factor associated with the altered functional status of the brain. In order to verify this assumption, we carried out a study of the effects of intermittent photostimulation on monkeys with chronic postencephalitic hyperkinesia, i.e., on animals known to have an altered functional condition of the higher c. n. s. following encephalitis.

Methodology /512

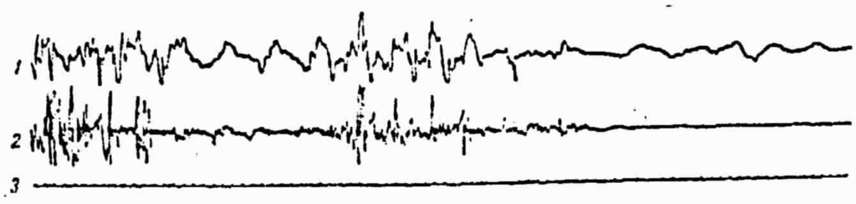
8 monkeys (macaca rhesus) with evident experimental postencephalitic hyperkinesia of the extermities, trunk, and head were used for observation.

Encephalitis was produced by intracerebral injection of Russian tick-borne encephalitis virus [8]. 30-40 days after the acute period had lapsed, continual violent and aimless athetoid movements with varying degrees of intensity appeared in the animals, the most acutely pronounced movements being in the upper and lower extremities. In some cases the movements occurred only in the fingers, while in others they involved an entire extremity, the neck muscles, and the face. If the observed motor disorders are compared with those in man, they would most probably be ascribed to the group of hyperkinesias chiefly involving sub-cortical levels [9].

We have previously described the conditions under which experiments are conducted on monkeys and the methodology of electrode-implanting operations [7]. Electrodes were implanted in the cortices (visual and motor areas) and subcortical structures (caudate nucleus, globus pallidus, putamen, and thalamus) of three monkeys. The experiment used intermittent light with frequencies of 3, 7, 9, 18, and 25 flashes per second and flash intensities of 0.3 joules. The duration of the experiments varied from 30 minutes to 1.5-2 hrs. Stimulation was repeatedly applied, and the time of stimulation totaled 5 to 25 minutes. Movements were recorded using a specially constructed sensor affixed to the extremities.

Results

The tests we conducted indicated that intermittent rhythmic light with frequencies of 3, 7, 9, 18, and 25 flashes per second weakened, and often completely relaxed, violent movements while they were flashing (fig. 1). The monkeys sometimes closed their eyes and fell into a somnolent state under the influence of the stimulus. The rapidity of onset of the "tranquility" or total motor "rest" after the moment of turning on the photostimulus varied from 1-2 seconds to several minutes, while, as a rule, violent movements intensified at the beginning of the light's operation. In the presence of the light, the hyperkinesias



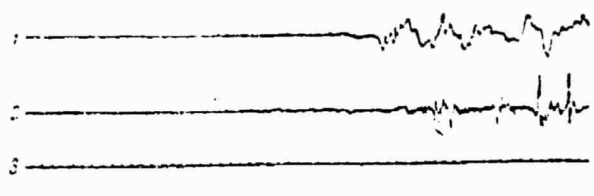


Fig. 1. Actogram recorded before and during relaxation of hyperkinesia under the influence of rhythmic photostimulation with a frequency of 20 flashes/second.

1 -- left upper extremity; 2 -- left lower extremity; 3 -- recorded stim.

disappeared more quickly if the animal's head was rigidly fixed. The duration of periods of "diminution" or "total motor rest" in certain animals was also quite varied -- from 2 sec. to 3.5 min. over the course of a 5 minute photostimulation. Repeated application of the light did not essentially change the animal's response. Lower stimulation frequencies -- 3, 7, or 9 per sec. -- had the most prolonged effect in decelerating or relaxing the pathological movements. Whereas the indicated light frequencies removed violent responses for 2-2.5 min. over the course of 5 minutes of operation, light with 18-25 flashes per second did this for only 35-40 sec. At the same time, it became quite apparent that, as a rule, after ceasing operation of any frequency of light, there occurred a period of "tranquility" which sometimes lasted up to 3.5 minutes (observation time: 5 min.), then the usual motor response returned.

The nature of the EEGs and electrocerebrocorticograms [ECCGs] for /514 the monkeys with implanted electrodes changed during the periods of diminution and "total motor rest". Slow, high-amplitude oscillations were registered from all leads, or the phenomenon of rhythm adoption appeared in the visual cortex, and sometimes in all other deep structures as well (fig. 2,B). It should be noted that the phenomena of rhythm transformation or restoration of background activity were virtually never observed during the photostimulation period.

The nature of the response depended to a considerable extent on the general functional condition of the animal. In some experiments, when the monkey was very agitated (strong motor excitation), the "calming" response to intermittent light was less acutely pronounced. Environment (noise, human speech, etc.) also changed the response, decreasing the positive effect of photostimulation.

Discussion of Results

Therefore, the results obtained clearly show that rhythmic photostimulation, which in healthy monkeys causes hyperkinesia, and in certain particularly light-sensitive individuals even results in photomyoclonic

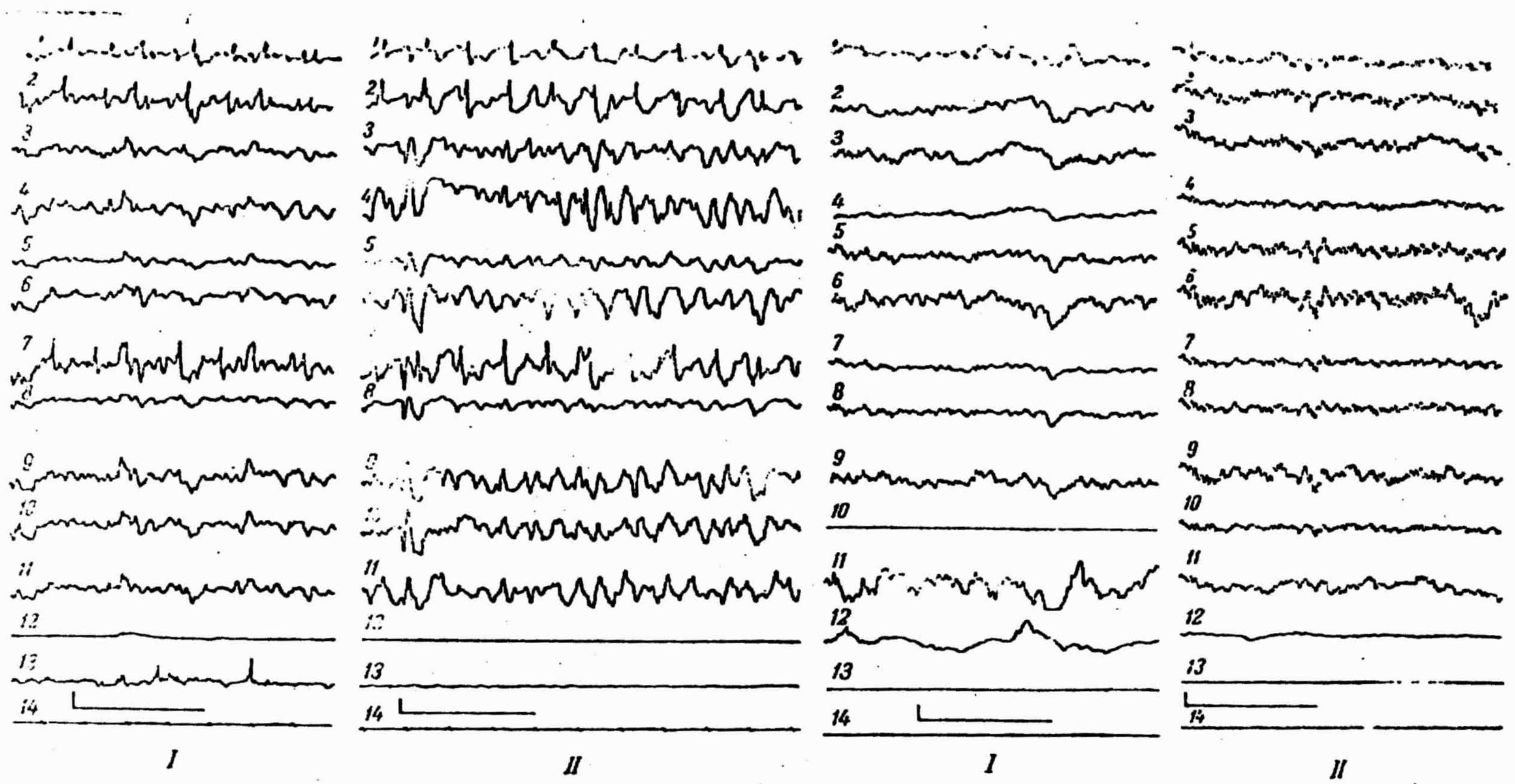


Fig. 2. EEGs and ECCGs of monkeys during cessation of violent movements under the influence of periodic photostimulation.

A: I-- EEG and ECCG during hyperkinesia (background). 1,2--visual cortex from right and left; 3,4--motor areas from right and left; 5,6--caudate nucleus from right and left; 7--thalamus (medial regions) from right; 8,9--globus pallidus (medial segment) from right and left; 10,11--putamen from right and left; 12,13--actogram of right upper and lower extremities; 14--recorded stimuli. II--EEG and ECCG during relaxation and motor rest; symbols same as in I.

B. I-- background. 1,2--visual cortex from right and left; 3,4--motor cortex, right and left; 5,6--putamen, right and left; 7,8--caudate nucleus, right and left; 9,10--thalamus, (medial parts), right and left; 11--globus pallidus (medial segment) from right; 12, 13--actogram of left upper and lower extremities; 14--recorded stimuli.
II-- EEG and ECCG during relaxation of violent movements; symbols same as in I.

seizures, has a diametrically opposite effect when applied to animals with chronic postencephalitic hyperkinesia, i.e., temporary relaxation of violent movements.

Are there other examples of similar diametrically opposed effects of the selfsame influence on sick and healthy animals? The Lee phenomenon [15, 16], the development of temporary stuttering in a normally-speaking human when he perceives his own voice time-delayed, may serve as one of the clearest examples of this. As has been shown by a number of studies, among them one of our own [4], the opposite effect -- temporary remission from stammering -- is observed in stutterers under the same conditions of delayed perception of their own voices. There are in the literature certain works involving the study of the effects of rhythmic photostimulation on pathologic motor responses. Thus, Tasuki et al. [17] describe observations on humans where certain flashes of light caused inhibition of a patient's small tremors. The mechanism of this phenomenon is not analyzed by the authors. Forster and his associates [11] describe the extinguishing of convulsive bioelectric activity which developed with binocular photostimulation during intermittent photostimulation of one eye. Therefore, taking all these facts as a whole, we may conclude that the results we obtained reflect some common regularities associated with the functional organization of the brain and the peculiarities of its response to sensory, and particularly rhythmic, stimulation.

Analysis of the changes in the character of bioelectric activity in various structures of the brains of monkeys with hyperkinesia of postencephalitic origin during rhythmic photostimulation shows their sharply pronounced unidirectionality -- slight and steady adoption and retention of the rhythm of the applied stimulus in both the cortex and deep structures of the brain (sometimes more sharply pronounced in the occipital regions of the cortex). Transformation of the rhythm or return of activity to background form is not observed -- the brain firmly retains the rhythmics of the applied stimuli. Periods of remission from violent motor responses, frequently accompanied by a somnolent (from outer appearances) state, arise upon this backgound. As was shown in our preceding report [3], biolelectric activity in the brains of healthy monkeys during rhythmic photostimulation is characterized by a complex dynamic picture of adoption, transformation, rhythm "by-products", etc. Motor disturbances are not observed under these conditions. Finally, under these identical conditions, hyperkinesias/515 were noted in some monkeys, and photomyoclonic seizures in the particularly photosensitive ones. Thus, three types of responses to rhythmic photostimulation in the monkey brain may be isolated.

Analysis of relations between brain centers in animals with experimental hyperkinesias, enlisting the services of cross-correlation analysis methods [2], has shown that in this case there is a complex reorganization of degrees of association, both between certain deeper structures themselves and between the cortex and deeper structures, i.e., a complex systemic structure of pathological excitation takes shape.

Alterations of degrees of association in some regions of the human brain have also been obtained, as demonstrated by stuttering and disruption of speech in normally-speaking people when perception of their speaking is delayed, and normalization of speech (under the same time-delayed conditions) in persons suffering from stammering [4].

All these statements permit us to regard rhythmic photostimulation as a testing stimulus faciliating judgments about the stability of the systemic relationships between brain centers. By system stability we mean in this case its agility and its range of variability, allowing the implementation of reorganization in connection with arriving information in such a way that the brain can carry out its functions without disruption.

In addition, rhythmic photostimulation within the range utilized by us (3-25 hz) has a stabilizing influence, thrusting forth new types of inter-center relationships (in the case of hyperkinesia provocation, forming a structure of pathological excitation, and in the presence of hyperkinesia -- also forcing new inter-center relationships), thereby temporarily suppressing and disrupting the pathological system of center interrelationships already present.

Conclusions

1. Rhythmic photostimulation (3-25 flashes per sec.) relaxes violent motor responses in monkeys with postencephalitic hyperkinesias.

2. The observations conducted permit us to regard rhythmic photostimulation as a testing stimulation, allowing judgments about the stability of systemic relationships between brain centers to be made.

3. Intermittent photostimulation with the applied range (3-25 hz) has a stabilizing effect, in a certain functional state forming a suitable system of center interrelationships.

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