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FUNCTIONAL LINKS IN THE BRAIN CORTEX OF KINDLED RATS EVALUATED AT DIFFERENT STAGES OF KINDLING SEIZURES PRECIPITATION

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Annotation: The work investigated the relationships between brain structures established in different periods of pentylenetetrazol (PTZ)-induced kindled seizure precipitation. As structures for investigations, the cortical ones of both hemispheres and the paleocerebellar cortex (VI-VII lobules) were chosen. Usage of these structures was explained by the well-known role of cortical neuronal population in spike-wave rhythm generation as well as the 'antiepileptic' properties of paleocerebellum.

Key-words: brain cortex, kindling, seizures, mathematical model

To 2-months old Wistar rats (6 animals) under Nembutal anesthesia (40,0 mg/kg), electrodes were implanted into frontal (AP=3,2; L=1,8) [Paxinos, Watson, 1982], occipital (AP=-7,8; L=2,5), and temporal (AP=- 7,8; L=7,0) zones of the cortex of both hemispheres. Experimental observations started in 7 days from the moment of operation. Bipolar registration was performed with a time constant of 0,3- 1,0 sec. The next leads were used for registration in the left hemisphere: front-temporal (marked in Fig 1 with N1), temporal-occipital (N2), and front-occipital (N3). A similar system of leads was explored for the cortex of the right hemisphere, which is marked with N4, N5, and N6 in Fig. 1 correspondently). With N7, the paleocerebellar lead is marked. Early and fully developed stages of EEG-kindling manifestations were registered in 3-6 and 17-21 administrations of PTZ (35,0 mg/kg, i.p.) correspondently. EcoG registration was performed with a frequency of discretization of 256 samples/sec in free-moving rats.

For mathematical model creation, the self-prepared software was explored. The average amplitude of the EcoG signal determined for 10 sec period of registration was used. Altogether 30 such periods were used for the final calculation. The formation of a mathematical model was performed employing multiple linear regression and correlation. With the aim of creating mathematical models of each of the amplitude indices under investigation, we obtained the Y -plotted characteristic marked later on in equations (1.1.-1.7.) with YAlk, Y A2k, Y A3k, Y A4k, Y A5k, Y A6k and Y A 7k - figures that were in good correspondence to above-mentioned number order of bipolar leads. Y -data was calculated based on other variable amplitudes in the other six leads (X-plotted ones, marked as ax I, bx2, cx3, dx4, ex5, fx6, and gx7). The resultant data permit us to identify the direction and type of proper influence and to depict it with the corresponding arrow on the multigraph.

As a result of such a process, equations pertinent to multiple linear regression and which were used regularly (based on false-rotation) in our analysis received a typical form:

$$YA1k=Bo+bx2+cx3+dx4+ex5+fx6+gx7 \quad (1.1)$$

$$YA2k=Bo+axI+cx3+dx4+ex5+fx6+gx7 \quad (1.2)$$

$$YA3k=Bo+axI+bx2+dx4+ex5+fx6+gx7 \quad (1.3)$$

$$YA4k=Bo+axI+bx2+cx3+ex5+fx6+gx7 \quad (1.4)$$

$$YA5k=Bo+axI+bx2+cx3+dx4+fx6+gx7 \quad (1.5)$$

$$YA6k=Bo+axI+bx2+cx3+dx4+ex5+gx7 \quad (1.6)$$

$$YA7k=Bo+axI+bx2+cx3+dx4+ex5+fx6 \quad (1.7)$$

Where Bo is a constant factor, coefficients "a," "b," "c," "d," "e," "f', and "g" reflect the level of the influence upon the index, which is under the analysis of the rest of the members of equation (xi; x2; x3; x4, x5, x6, x7). The regression coefficients indicate the amount of influence of a particular electrode on each of the other electrodes. The significance of regression coefficients was determined by the standard deviations of coefficients of regression, and the efficacy of regression as a whole (positive and negative links) was estimated by calculating the square coefficient of multiple correlations. In this way, positive and negative links were identified between leads (structures), as well as their direction. The level of statistical significance was accepted at 0,05 (when one-way directed influence was determined) and 0,1 (when two-way directed influences were determined).

Geometrical presentation of the equations of MLR was performed in the form of polycyclic multigraphs containing directed positive and negative influences marked with arrows when they were significant. The error calculation was connected with the evaluation of the "power" of corresponding relations. The multigraph analysis consisted of the following steps: A. Creation of polycyclic multigraphs on the basis of the relationship of average amplitudes of signals registered in every lead, with the consequent determination of a) Number of mutually positive (a) and negative (b) intrahemispheric links; b) Number and character of links between hemispheric structures and the cerebellar paleocortex.

The comparison of this multigraph with the EcoG registered in control Wistar rats administered with 0,9% NaCl solution showed that in Wistar rats, structures of each hemisphere are far from being encompassed in the whole entity: between structures, one-side less numerous influences were identified. The intensive mutual negative influences were present between hemispheres. The absence of influences from the cerebellar cortex on hemispheres also was characteristic of control Wistar rats (**Fig. 1**).

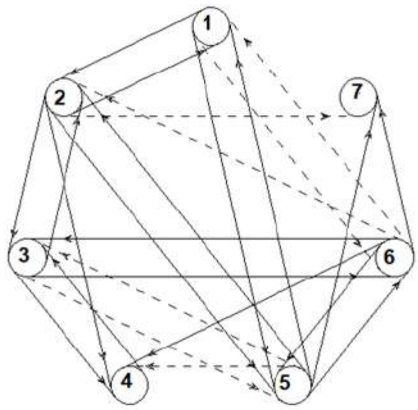

Fig.1. Control rats

Basal activity in the brain cortex of rats at the early stage of kindling was characterized by spike- waves development with a frequency of discharges from 7 to 10 per sec and amplitude from 100 to 450 mcV. The average duration of complexes was 5 seconds (from 1 to 10 seconds). The frequency of appearance of such complexes was from 15 to 20 per hour. The specific behavior of animals during such bursts of precipitation was confined to vibrissa tremor, stereotyped subtle nodding of the head. Besides, animals did not respond to tactile stimuli of skin and vibrissa.

The multigraph, which represents the interaction between brain structures that were under investigation, was characterized by the presence of a number of connections and by the prevalence of positive mutual influences between structures and hemispheres as well (**Fig. 2**). Mutual positive connections encompassed all structures of left hemisphere while between structures of the right hemisphere, few connections were present.

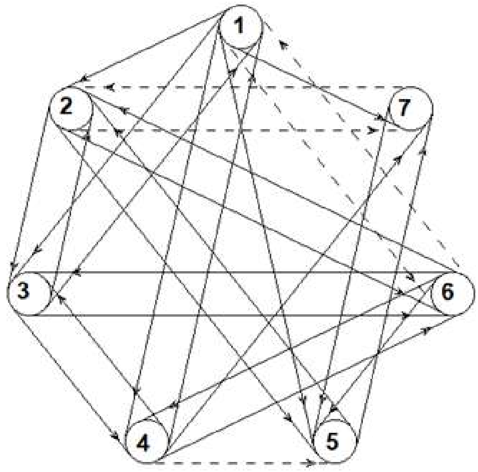

Fig.2 Early stage of PTZ- induced kindling

At the stage of developed generalized seizures, synchronous high amplitude (up to 1,5 mV) spikes generation was observed with a frequency of 11-20 per second. At the period of cessation (suppression) of ictal discharges, the marked reduction of positive influences between structures interhemispherically was observed. (**Fig. 3**). During this period, the sign of interaction of the cerebellar cortex with a fronto-temporal zone of the left hemisphere and frontal-occipital zone of the right hemisphere was changed from positive to negative ones. Simultaneously the negative relations with the frontal-occipital zone of the left hemisphere were established. Altogether, this dynamic might be characterized as a process of substituting interhemispheric relationships from positive to negative.

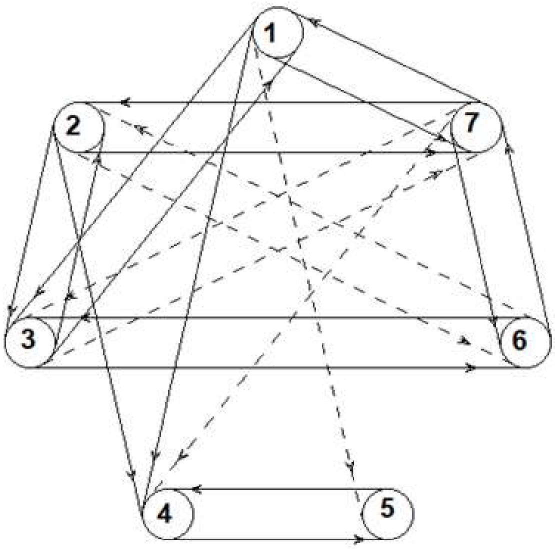

Fig.3. Fully developed generalized clonic-tonic PTZ-kindled seizures

Hence, gained data revealed that the early stage of seizure development is characterized by the strengthening of mutually positive links between brain structures with the reduction of negative ones. Generalized seizure cessation observed at the stage of fully developed kindling is characterized by a reduction of positive links between cortical structures while negative links were preserved. The marked involvement of paleocerebellum was observed at the period of ictal discharge formation and their suppression. Gained results are in correspondence with the neurophysiological mechanisms of PTZ-kindled seizure development [1].

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Retention of radiotracers as a Falling-Flow Phenomenon

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Abstract

The proposed a four-compartmental model describes transport kinetics of 99m-technetium radiotracers with considering radiopharmaceutical accumulation, elimination and radioactive decay and retention of radiotracers at lymph nodes.

Key words

Radiotracers, circulatory system, lymphatic system, sentinel lymph node, ^{99m}Tc-radiotracers, transport kinetics of radiotracers, mathematical model.

Introduction

The dynamics of radiotracers in lymph nodes can be studied using various imaging techniques, such as lymphoscintigraphy, positron emission tomography (PET), or single-photon emission computed tomography (SPECT). These techniques allow for the visualization and quantification of radiotracer distribution within the lymphatic system and lymph nodes. When a radiotracer is injected or administered, it enters the lymphatic system and is transported through lymphatic vessels. The radiotracer may encounter several processes and dynamics within the lymph nodes, including lymphatic uptake, lymphatic transport, lymph node filtration, retention and clearance.