and by an increase in the blood urea concentration to 8.4 ± 0.3 mM ($p < 0.001$) was observed 3 months after injection of the immunogen into the rats. The nephrotic syndrome was accompanied by a prethrombotic state, demonstrated by a 4.5-fold increase in the concentration of soluble fibrin-monomer complexes ($p < 0.001$) and an acquired antithrombin III deficiency. The plasma antithrombin III activity was reduced by 30% ($p < 0.01$). Compared with intact animals, the thrombus formation time in rats with the nephrotic syndrome was reduced by 30% ($p < 0.001$; Table 1). Under these conditions unfractionated heparin prevented thrombus formation for 30 ± 0.5 min ($p < 0.001$). Compared with the commercial preparation, LMH increased the thrombus formation time in the shunt by 45% ($p < 0.001$).

These results are evidence that LMH, with its predominantly inhibitory action on factor Xa, is a more effective antithrombotic agent both when the antithrombin III level in the body is normal and when it is lowered. The high antithrombotic activity of LMH is combined with a long period of its retention in the blood stream, so that the dose of the preparation required for the prevention of thrombosis can be reduced.

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NEUROPHYSIOLOGICAL STUDY OF EFFERENT–AFFERENT INTERACTION ON PARIETAL ASSOCIATION CORTICAL NEURONS IN CATS

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KEY WORDS: parietal cortical neurons; pyramidal tract; convergence of excitations; learning.

In the modern view the parietal association cortex not only is involved in the realization of afferent functions of interanalyzer synthesis, but also participates in programming of the efferent, motor functions of the brain [2-4, 8]. Integrated afferent information is transmitted from the parietal to the motor cortex along channels of direct communication between the neuron complexes of the parietal cortex and the neuron pools of the motor cortex, controlling the corresponding peripheral effectors [7, 9].

The aim of the present investigation was to look for the presence of feedback between the motor and parietal areas of the brain. The morphological substrate for this feedback could be recurrent collaterals of axons of cortical motoneurons. The discovery of feedback between the motor and parietal areas and the elucidation of its functional significance could help to revise our interpretation of the neurophysiological status of the integrative neurons of the parietal association cortex in the programming of motor behavioral acts.

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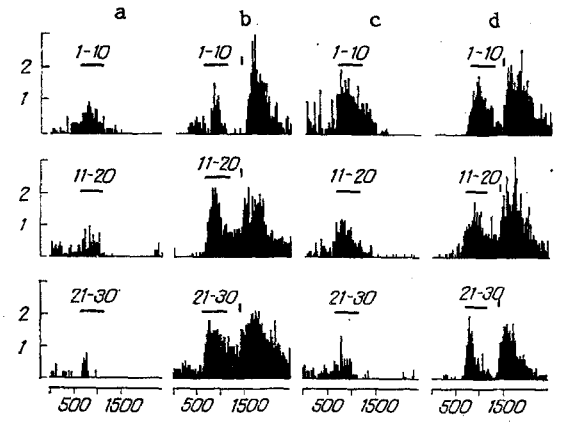

Fig. 1. Time course of responses of neuron to pyramidal tract (PT) stimulation. a) Responses to isolated stimulation of PT; b) reinforcement of stimulation of PT by electrodermal stimulation (EDS); c) extinction of responses; d) secondary learning (PT + EDA). Numbers of averaged realizations indicated above histograms. Markers of stimulation: horizontal line — PT, vertical line — EDS. Abscissa, time (in msec); ordinate, number of spikes in 25 msec.

EXPERIMENTAL METHOD

Experiments were carried out on cats weighing 3-4 kg. During the preliminary stage the animals were scalped, and a burr-hole 5-7 mm was drilled above the middle suprasylvian gyrus, at a point corresponding to the projection of area 5, and the dura was removed. The hole was filled with warm wax.

Bipolar metal electrodes for stimulating axons of the pyramidal tract were inserted into the medullary pyramids through the base of the occipital bone. The electrodes were definitively arranged to take account of the amplitude characteristics of the antidromic evoked potential recorded in the zone of the anterior sigmoid gyrus during stimulation of the pyramidal tract by single square pulses.

All operative maneuvers were performed under pentobarbital anesthesia (30-40 mg/kg, intraperitoneally). When the animal recovered consciousness the fixation sites of the animals in the stereotaxic apparatus were infiltrated with 0.5% procaine solution, the animals were intubated, immobilized with muscle relaxants, and artificially ventilated. Unit activity began to be recorded 8-10 h after completion of the preliminary manipulations.

Flashes from a gas-discharge tube, clicks, and electric shocks applied to the skin of the footpads through metal plates (0.3 msec, 30-50 V, 100 Hz, 50 msec) and electrical pulses applied to pyramidal tract axons (0.05-0.1 msec, 4-8 V, 200 Hz, 500 msec) were used as stimuli.

Single unit activity was recorded extracellularly by the use of glass microelectrodes filled with 3 M NaCl solution. The resistance of the electrodes in physiological saline varied from 10 to 20 MΩ.

For visual monitoring and recording of the processes observed a universal electrophysiological system was used. The time course of the neuronal responses was evaluated by plotting peristimulus histograms, normalized for the number of realizations, on a microcomputer of the "Élektronika DZ-28" type. The bin width of the histograms was 25 msec and the epoch of analysis 2500 msec.

EXPERIMENTAL RESULTS

Activity of 164 neurons was investigated. Of that number, 64 responded to stimulation of axons of the pyramidal tract. In 45 cases (70%) the discharge of the neurons was strengthened, in eight cases (13%) an inhibitory effect was observed, and 11 neurons (17%) gave responses of mixed type. The minimal latent periods of response of the different neurons varied from 25 to 50 msec and the maximal from 150 to 200 msec. Compared with visual cortical (area 17) responses described previously [5], the neuronal responses in area 5 of the parietal association cortex to pyramidal tract stimulation were stronger and relatively more stable. Of the

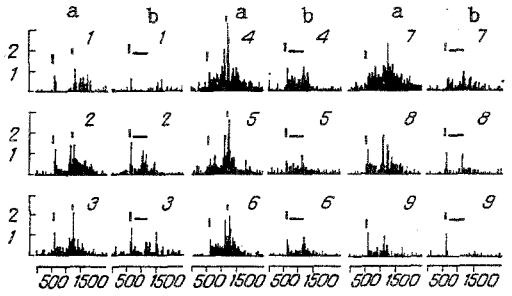

Fig. 2. Time course of neuronal responses to simple and combined conditioned stimuli. a: 1-6) Responses to combined acoustic and electrodermal stimulation; 7-9) increase in frequency of responses; b) responses to combined stimulus of clicks + PT. Histograms in series plotted consecutively by averaging of 10 realizations. Markers of stimulation: short vertical line — clicks, dots — EDS, horizontal line — stimulation of PT. Remainder of legend as to Fig. 1.

group of neurons in the parietal cortex which responded to pyramidal tract stimulation, 56 (87%) modified their firing pattern in response to electrodermal stimulation and 39 neurons (61%) responded to flashes or clicks.

Changes in the firing patterns of neurons during isolated stimulation of pyramidal tract axons and in response to combined repetitive stimulation of the pyramidal tract and nociceptive electrodermal stimulation (interval between stimulations 40-60 sec) were analyzed.

In the case of isolated stereotyped stimulation of the pyramidal tract a phenomenon of partial habituation was observed most frequently (46 neurons, 72%), and was manifested as a decrease in strength of the initial responses and shortening of their duration. Recovery of the response parameters and subsequent dynamic changes in the pattern of spontaneous and evoked unit activity were recorded to a combination of pyramidal tract stimulation and nociceptive reinforcement. An example of changes in evoked unit activity in response to combined stimulation is shown in Fig. 1. The successive change in the firing pattern of the neuron, in the first place to pyramidal tract stimulation, and reaching peak intensity with the 20th combination, will be noted. The determined character of the observed change in firing pattern is emphasized by the procedure of extinction of the response and also by the secondary learning by the neuron.

Of the total number of neurons studied by the use of combined stimulation, changes in firing pattern were found in 42 cases (66%). The most widespread type of change was an activation response to pyramidal tract stimulation in the form of a phasic or phasic—tonic increase in firing rate, accompanied by a phasic or phasic—tonic increase in firing rate in response to electrodermal stimulation. Restructuring of evoked neuronal responses to combined stimulation usually proceeded parallel with analogous restructuring of spontaneous activity, although some neurons whose spontaneous activity was unchanged, or in certain cases even reduced, were recorded.

The results of a series of experiments in which changes in the firing pattern of a neuron were investigated during presentation of simple and combined conditioned reflexes to the animal are shown in Fig. 2. The simple stimulus (clicks) was reinforced by painful electrodermal stimulation, and the combined stimulus (clicks + repetitive pyramidal tract stimulation 100 msec later) was presented without reinforcement. As analysis showed, in these experiments changes in unit activity characteristic of conditioning followed a parallel course for simple (positive) and combined (differential) stimuli only during the first 30-50 combinations. Later, evident differences were observed in the quantitative characteristics of responses to reinforced and unreinforced stimuli within intervals of random stimulation of pyramidal tract axons. The activated state of the neuron under these circumstances, corresponding to the quality of the response to the painful electrodermal stimulus, was revealed on presentation of the simple stimulus (clicks). Presentation of the combined (differential) stimulus did not induce any analogous anticipatory change in the firing pattern of the neuron.

The following conclusions can be drawn from the results. Efferent neurons of the motor cortex have an effector influence via recurrent collaterals on parietal cortical unit activity.

The plastic character of this influence, manifested as changes in the structure of collateral responses in response to combinations of pyramidal tract stimulation and electrodermal reinforcement, may be emphasized. This last fact serves as proof of involvement of neurons of the association cortex in the mechanisms of early distinction of reinforcement, on the basis not only of extrinsic afferent information, but also of information on the structure of the pattern of the efferent spike train destined for the peripheral effectors.

Involvement of neurons of the parietal association cortex in processes of afferent synthesis and of extrapolation of the quality of reinforcement as applied to the motor act must therefore be regarded as the product of convergence of triggering afferent, collateral efferent, and also afferent reinforcing excitations, completing the elementary cycle of the motor act, and their interaction on these neurons [1, 6].

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EFFECT OF GLUTAMIC ACID AND GLUTATHIONE ON GASTRIC SECRETORY FUNCTION

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KEY WORDS: glutamic acid; glutathione; γ-glutamyl cycle; potentiating action.

Previous investigations conducted in the writers' laboratory showed that glutamic acid (Glu), injected into the blood stream in a moderately high concentration, strongly inhibits gastric secretion through the sympathicoadrenal system [1, 3]. In the investigation described below an attempt was made to reproduce this effect by injecting Glu into the gastrointestinal tract. According to data in the literature [9, 10], Glu undergoes transamination with pyruvate in the intestinal epithelial cells with the formation of α-ketoglutaric acid and alanine. However, if its concentration is high enough, the limiting velocity of transamination can be exceeded, and some Glu passes unchanged into the blood stream. We were guided by such considerations, but could not observe any after-effects of these interrelations. The first attempts showed that Glu, used for drinking, not only does not inhibit but, on the contrary, strongly potentiates gastric secretion induced by pentagastrin. We give below the results of an investigation to study this problem.

EXPERIMENTAL METHOD

Experiments were carried out on dogs with isolated Pavlov gastric pouches (two dogs) and gastric and intestinal fistulas (two dogs). Glu (from "Reanal") was used as a solution, neutralized by the addition of NaOH to obtain monosodium glutamate (MSG). This solution (4.5% MSG)

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