CHANGES IN PHASIC EVOKED ACTIVITY OF CORTICAL NEURONS PRODUCED BY IONTOPHORETIC APPLICATION OF GLUTAMATE, GABA, AND ATROPINE

B. N. Bezdenezhnykh and V. B. Shvyrkov

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Recent investigations have shown that the individual phases of responses of neurons discharging in connection with particular components of evoked potentials (EP) are incorporated into various processes of the functional system of the behavioral act and are caused by activation through different synaptic inputs [5, 6]. The temporal structure of the single unit response to the same stimulus can vary during changes in the integral behavioral response [9], thus confirming the dynamic organization of receptive fields of central and peripheral neurons [7]. From the standpoint of the theory of the functional system [2, 3], the organization of the receptive field and the temporal structure of the unit response are explained by the method of incorporation of the neuron into overall integration which, by changing the metabolism and chemical sensitivity of the subsynaptic membranes, makes the neurons selectively sensitive only to certain synaptic inputs and makes the formation of nonspecific responses less likely.

The object of this investigation was to test this hypothesis and to discover whether methods of incorporation of single cortical neurons into the functional system of the defensive behavioral act can be varied by changing the chemical processes in the neurons through microiontophoretic application of biologically active substances. Experiments were carried out on seven waking rabbits fixed in a stereotaxic apparatus. Electric shocks (square pulses 20-100 V, 1-500 msec) were applied at intervals of 20-50 sec through needle electrodes implanted subcutaneously in the area of the receptive field of the recorded neuron. Unit activity of 23 somatosensory cortical neurons was recorded and the drugs were applied to them by means of four-channel glass microelectrodes. The recording channel was filled with 3 M KCl and the other channels with 2 M solutions of L-glutamate, GABA, and atropine. For iontophoretic application of all drugs a current of 5-20 nA was applied (in the outward direction for atropine and GABA, inward for L-glutamate) for 10-15 min. Each neuron was investigated in conjunction with several parameters of electrical stimulation. Unit activity, cortical surface EPs, and EMG activity of the forelimb muscles were amplified and recorded on magnetic tape. EPs were averaged and poststimulus histograms constructed with the NTA-512B analyzer from the tape recording.

Ten neurons were areactive; of the 13 reactive cells substantial changes in the temporal structure of the discharge were detected in seven; these changes could consist of abolition of one phase of the response, the rest being preserved, or the appearance of new components. For example, in one neuron, instead of a response consisting of a phase of discharge at the time of a negative component and a phase of discharge at the moment of the late positive component of the EP, after application of L-glutamate (10 nA) a primary response and a discharge at the time of the negative component of the EP appeared but the late activation disappeared. Different drugs caused different changes in the structure of the unit response. Figure 1 shows the response of a neuron in which activity was observed during stimulation of the contralateral forelimb (30 V) only during the late positive component of the EP. On application of L-glutamate (10 nA) or atropine (10 nA) to this neuron, it generated primary responses, so that the response became biphasic, whereas after iontophoretic application of GABA (10 nA) the original late activation disappeared, but a response appeared during the primary positive component of the EP.

Since changes in the parameters of electrical stimulation lead to changes in the integration of cortical neurons [1], this procedure was used to vary the method of incorporation of the neuron into the system. If the response of a neuron was changed by a change in the parameters of electrical stimulation, indicating a different form of incorporation of the neuron into the new system [5], changes were also observed in the effect of

P. K. Anokhin Institute of Normal Physiology, Academy of Medical Sciences of the USSR. Institute of Psychology, Academy of Sciences of the USSR, Moscow. Translated from Neirofiziologiya, Vol. 8, No. 2, pp. 192-195, March-April, 1976. Original article submitted September 20, 1974.

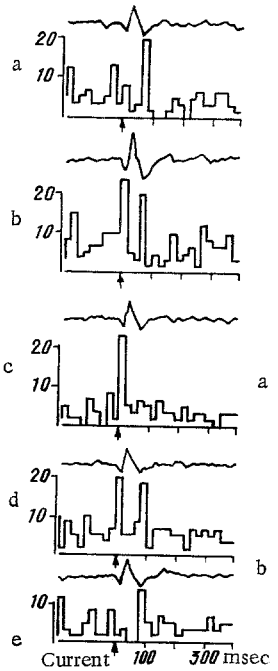

Fig. 1

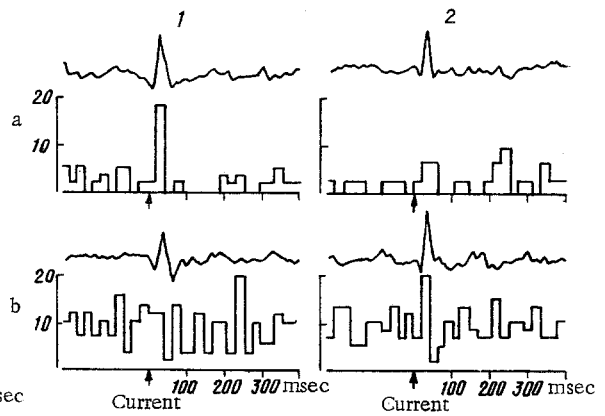

Fig. 2

Fig. 1. Changes in neuronal response pattern on iontophoretic application of various drugs. a-e) Above, averaged evoked potentials (n = 20); below, poststimulus histograms of unit responses. Abscissa, time, msec (channel width 24 msec); ordinate, total number of spikes in channel (n = 20); a) original response; b) response after application of L-glutamate (10 nA); c) of GABA (10 nA); d) of atropine (nA); e) control, response without microiontophoresis.

Fig. 2. Changes in effect of L-glutamate on activity of same neuron depending on location of electrical stimulation: 1, 2) responses to stimulation of contralateral forelimbs and hind limbs (40 V) respectively; a) original response; b) response after application of L-glutamate (10 nA). Remainder of legend as in Fig. 1.

the drugs on that neuron. The response of a neuron which exhibited activity during the negative component of EP in response to stimulation of the contralateral forelimb, but was inactive in response to stimulation of the hind limb, is illustrated in Fig. 2. In the first case application of L-glutamate abolished the response, in the second case it evoked a response.

The results suggested that not only single neurons [4], but also the separate components of their responses possess chemical specificity. The opportunity presented by the iontophoretic method of acting selectively on individual phases of the neuronal response confirms that different components of the response are linked with activation of the neuron through different synaptic inputs [6]. On the other hand, this fact can also be regarded as an argument in support of the neurochemical nature of changes in receptive fields of central neurons on their incorporation into one system or another; different biologically active substances act specifically on the individual groups of synaptic inputs that form the receptive field of the central neuron [8, 10]. Other evidence in support of this hypothesis is the inconstant effect of the same drug on responses appearing in a neuron when incorporated by different methods into the system. Different systems evidently use different synaptic inputs of the neuron and the variation of its sensitivity to particular substances observed in these cases shows that the change in the receptive field of the neuron when it is incorporated first into one, then into another system, are based on neurochemical mechanisms.

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DIRECTION-SENSITIVE NEURONS IN THE FROG VISUAL SYSTEM

S. L. Kondrashev and O. Yu. Orlov

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Direction-sensitive ganglion cells have been found in the frog retina [10], but it is not yet known to which visual centers of the brain information from them is sent. In the Anura there are several visual centers of the brain which receive fibers from the retina [2, 7]. No directional elements have been discovered in the tectum or medulla of frogs and toads, whereas they are found in these parts of the brain in representatives of all other classes of vertebrates [1, 4, 5, 9]. The writers suggest that the only place to which axons could run from these directional ganglion cells of frogs, and where neurons with directional properties could be found, is the nucleus of the basal optic tract (n. opticus tegmenti) [2].

To test this hypothesis the properties of neurons of the basal optic tract and adjacent regions of the brain of Rana temporaria L. were investigated electrophysiologically. The frog was immobilized with tubocurarine and craniotomy was performed from the ventral aspect, i.e., through the mouth. Electrical activity was recorded with platinized electrodes in the usual way [3]. To determine the location of the brain region concerned, the atlas of the frog's brain [6] and the results of an investigation by Nomokonova [2] were used.

In order to obtain access for the microelectrode to the region where the oculomotor nerve leaves the ventral surface of the brain, the hypothalamus was displaced in the rostral direction after removal of the meninges (Fig. 1).

Experiments were carried out on 25 frogs in the fall and winter.

Visual stimuli (long strips of black paper, 2 cm wide, and dark disks 1-2 cm in diameter) were presented against a light background at a distance of about 20 cm from the eye.

Responses of direction-sensitive neurons were recorded in the region of n. opticus tegmenti (Fig. 2). For the overwhelming majority (47) of neurons the direction of preference of stimulus movement was "from

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