SYNAPTIC RESPONSES OF SENSORIMOTOR CORTICAL NEURONS TO DIRECT CORTICAL STIMULATION

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The inhibitory postsynaptic potential in the response of sensorimotor cortical neurons to direct stimulation consists of two components, presumably generated by different parts of the neuron.

Although responses of cortical neurons to direct stimulation of the surface of the cortex have frequently been investigated, including by intracellular recording methods [11,12,14,15,17], the writer's experiments have revealed some unusual features of these responses which merit special description.

EXPERIMENTAL METHOD

Experiments were carried out on unanesthetized rabbits by the method described previously [1,2]. The surface of the sensorimotor cortex was stimulated with single (less frequently than 1/sec), short (0.1-0.5 msec) pulses (5-15 V) through silver bipolar electrodes touching the pia mater. The stimulating electrodes were less than 1 mm apart and from the site of insertion of the glass recording microelectrode, which was filled with potassium citrate.

EXPERIMENTAL RESULTS

During intracellular and quasi-intracellular recording, in most cases (55 of 71 cells) an ordinary response was observed (Figs. 1A, $2A_1$), consisting of a primary excitatory postsynaptic potential (EPSP) followed by an inhibitory postsynaptic potential (IPSP). If the strength of stimulation was strong enough, the EPSP gave one (less commonly two) spike(s) (Fig. 3c,j). In neurons with low (10-30 mV) membrane potential (MP), because of damage by the microelectrode (40 cells were recorded), as a rule the response began with a primary IPSP (Figs. 1C,D, 3d,e,k,l).

In many neurons (Fig. 1B), and this was particularly obvious in a large number of the damaged cells (Figs. 1C, $2A_4$, B_3), the IPSP consisted of two components: a first of relatively short duration (15-30 msec) and a second, longer component (over 80 msec). During gradual injury to the neurons (Figs. 1B, 2A) the primary component of the IPSP increased from the early stages of injury (Fig. $1B_2$) then decreased slightly, while the secondary component at first showed little change, and then decreased so that the separation into two components became more obvious (Figs. $1B_{2,3}$, $2A_1$).

Changes in the PSPs during passage of a polarizing current through the recording intracellular microelectrode by means of a bridge circuit were investigated in four neurons. In control tests (without the current) hyperpolarization consisting of two components was observed (Fig. $2B_3$). Component I showed a distinct increase against the background of the depolarizing current and fell steeply, changing its sign with the current in the opposite direction (Fig. 2B,C). Component II was virtually unchanged during artificial hyperpolarization and decreased slightly during passage of the depolarizing current.

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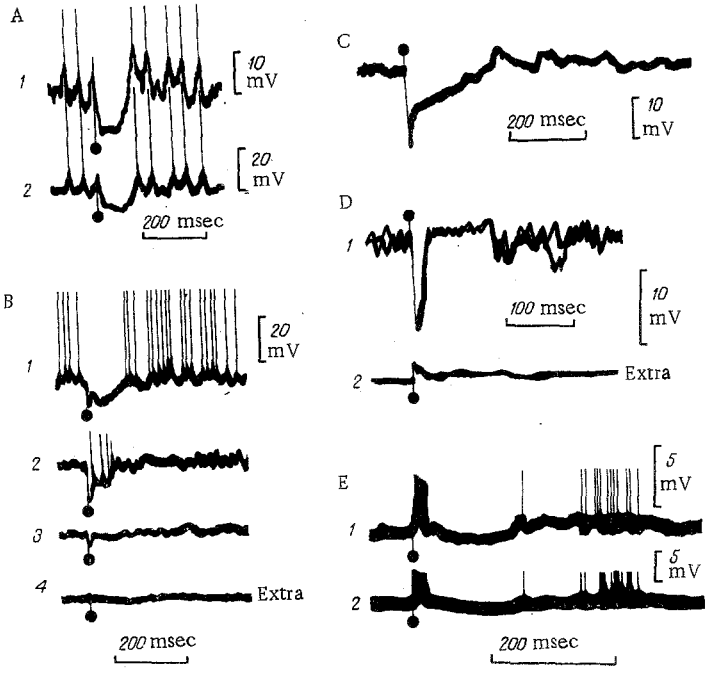

Fig. 1. Responses to direct cortical stimulation recorded in five neurons from different experiments: A) typical intracellular response consisting of EPSP-IPSP sequence; B) response consisting of two-component IPSP: 1) at beginning of recording; 2,3) at various stages of injury (see text); 4) control focal extracellular potential recorded immediately before recording unit activity; C, D_1) intracellular responses of two depolarized cells; D_2) focal extracellular potential immediately after death of neuron illustrated in D_1; E) response consisting of primary high-frequency discharge. In A and E: 1) recording through ac amplifier (RC = 0.1 sec); 2) the same, through dc amplifier with lower amplification. Here and in Fig. 2, dots denote time of stimulation. In B_2, temporary restoration of inactivated spike activity takes place during development of component II of IPSP.

It cannot be concluded from these findings that the complex appearance of the IPSP is due entirely to superposition of the secondary EPSP on it. It shows that the IPSP consists of two components with different properties. It can be assumed that component I was generated by axosomatic synapses located near to the point of insertion of the microelectrode, while component II was associated with activity of more distant (axodendritic) inhibitory synapses. The decrease in component II during damage to the cell is evidently due to the decrease in input impedance of the neuron body. The slight changes in this component during passage of the current likewise can be explained by changes in membrane resistance. In addition, this component may be connected primarily, not with IPSP generation, but with "disfacilitation" [18], i.e., with a decrease in the background excitatory input. There is a corresponding decrease in amplitude of the background synaptic waves in the corresponding period, which is clearly visible in depolarized neurons (Fig. $1D_1$).

However, "disfacilitation" alone cannot explain the late long-latency hyperpolarization in cortical neurons [16].

The presence of two components of the IPSP has recently been discovered also at other levels of the nervous system [8-10]; they can also be seen in previously published recordings of unit responses from the rabbit and cat cortex to peripheral stimuli [2,3,5].

In the overwhelming majority of extracellular recordings the primary response also consisted of one (Fig. 3B), less commonly of 2-3 spikes, or consisted entirely of inhibition. A short-latency high-frequency (300-600/sec) discharge up to 25-30 msec in duration was generated only in a few cases (in less than 10% of all neurons investigated; Fig. 3a, g).

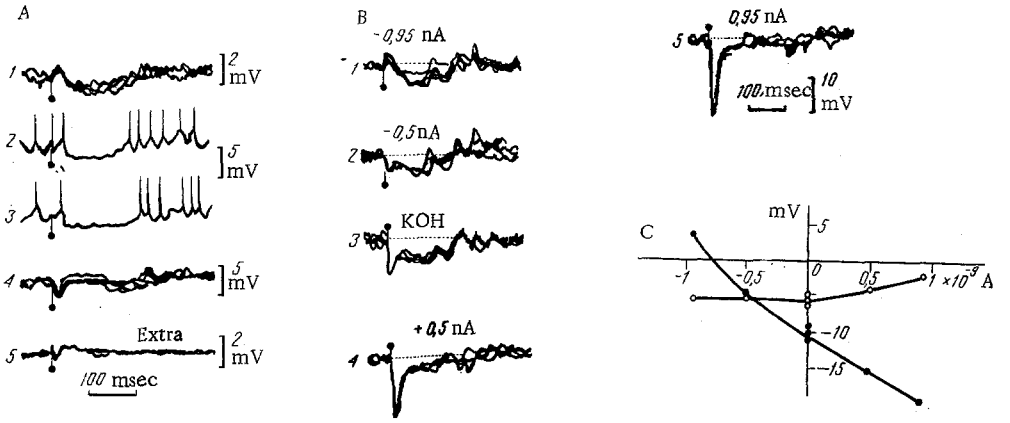

Fig. 2. Changes in response to surface stimulation after injury (A) and during intracellular polarization (B, C). A: 1) Subthreshold unit response during quasi-intracellular recording; 2,3) intracellular recording of activity of same neuron (puncture of membrane caused appearance of background discharges and spike response to stimulation); 4) response of same neuron after depolarization as a result of injury; 5) control extracellular potential after death of cells. B: 1,2,4,5) Responses of another neuron during passage of polarizing current of different strengths; 3) control response without polarization. C) Graph showing amplitude of postsynaptic potential (deviation along ordinate in mV) as a function of strength of current passed intracellularly (deviation along abscissa in nA). Maximal amplitude of primary PSP (black circles) and magnitude of secondary response 120 msec after stimulation (empty circles) measured. Tops of spikes not shown in A_2 and A_3. In A_1 and A_5—ac amplifier; in other records, dc amplifier.

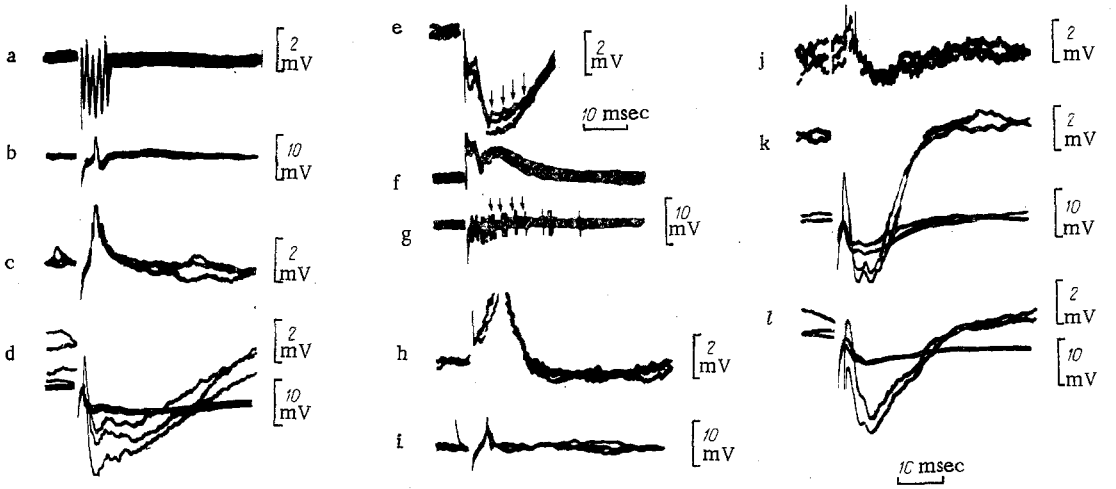

Fig. 3. Responses to methods of stimulation recorded in 11 neurons from same experiment: f) focal extracellular response recorded immediately after death of cell shown in e. Responses consisting of a single spike, similar to response in b were recorded extracellularly in this experiment from another nine neurons not shown in this figure. Records with greater amplification (a, c, e, f, h, j, and also top curves in d, k, *l*) obtained with ac amplifier, while records with lower amplification (b, g, i, lower curves of d, k, *l*) were obtained with dc amplifier. In a-g: same time scale; slightly different scale for h-*l*. Upper parts of curves in c, h, j not shown. Remainder of explanation in text.

In agreement with other workers [4,6,11,13], it can be postulated that a discharge of this type reflects activity of inhibitory cells. This hypothesis was confirmed by observations which revealed waves of high (300-600 Hz) frequency in some neurons in the initial part of the IPSP (Fig. 3d, e, k, *l*).

Attempts to obtain intracellular or even quasi-intracellular recordings from neurons with a prolonged high-frequency initial discharge as a rule led to rapid death of the neurons. This is indirect evidence that cells giving responses of this type are small interneurons. Only in two cases could the microelectrode be brought up to such a position that slow waves corresponding to the intracellular IPSPs appear on the trace. In these cases, an IPSP was observed immediately after the primary EPSP, just as in all other neurons (Fig. 1e).

The high-frequency discharge of the hypothetical inhibitory interneurons (Fig. 3g) readily explains the origin of component I of the IPSP. So far as the long II component of the IPSP is concerned, there are evidently no neurons in the cortex with such a prolonged discharge [4,6,7,11]. It is possible that, just as in many other structures [7], prolonged cortical IPSPs are generated by the relatively short discharge of an inhibitory neuron.

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