EFFECT OF ELECTRICAL STIMULATION ON ACTIVITY OF NEURON POPULATIONS OF HUMAN SUBCORTICAL BRAIN STRUCTURES

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UDC 612.826.014.424

Tests were carried out on patients with parkinsonism treated by the method of long-stay implanted electrodes. The character of responses of the subcortical neuron populations to stimulation by single pulses was recorded extracellularly during therapeutic and diagnostic procedures. The thalamic nuclei had the highest level of excitability, followed by the strio-pallidary complex and, finally, by nuclei of the brain stem. Threshold pulses evoked spike activity only in the region of stimulation. Supraliminal pulses evoked a local decrease in unit activity together with simultaneous but varied distant changes in activity in the neuron populations elsewhere in the subcortex.

KEY WORDS: parkinsonism; subcortical nuclei; effect of electrical stimulation.

Experimental studies of the effect of an electric current on the brain and responses of the motor and autonomic systems accompanying this effect [1, 5, 8, 19] have provided the theoretical basis for the therapeutic and diagnostic application of electric currents to deep brain structures in patients under treatment by the method of long-stay implanted electrodes [3, 4]. Yet experimental observations, however complete, require further study under clinical conditions.

The object of this investigation was to study the level of excitability and responses of the basal ganglia of the human brain to electrical stimulation.

EXPERIMENTAL METHOD

Unit activity (UA) of neuron populations (NPs) was recorded in the deep brain structures of six patients with chronic postencephalitic parkinsonism, into each of whom 30-36 long-stay intracerebral electrodes had been implanted for therapeutic and diagnostic purposes [2]. Activity of 130 units was analyzed.

The brain electrodes were 80-100 μ in diameter, insulated throughout with fluoroplast except for the contact surface of the tip, 1 mm in length, and connected into bundles with six electrodes in each bundle. Because of the large contact surface of the electrodes the record of unit activity was a "tuft" of discharges, and only spikes with the highest amplitude were analyzed. It was assumed that in that case the activity of neurons located closest to the recording surface of the electrode would be obtained [6].

To isolate spikes with an amplitude of a specified value an amplitude discriminator was used; pulses at its output were counted with the aid of the PS-100 counter over intervals of 15 sec or they were led into integrators of an MN-7 analogue computer and recorded on a multichannel potentiometer as a function of current frequency. Where spike activity was counted with the PS-100 counter the results were displayed as graphs with the number of discharges plotted along the ordinate and their dynamics under the influence of electrical stimulation along the abscissa. Bipolar electrical stimulation of NPs was carried out with single biphasic pulses. The stimulus duration was 0.1 msec throughout the investigations and the voltage varied, depending on the specific purpose of the investigation, from 4 to 16 V.

Department of Human Neurophysiology, Institute of Experimental Medicine, Academy of Medical Sciences of the USSR, Leningrad. (Presented by Academician of the Academy of Medical Sciences of the USSR S. V. Anichkov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 79, No. 2, pp. 3-6, February, 1975. Original article submitted March 25, 1974.

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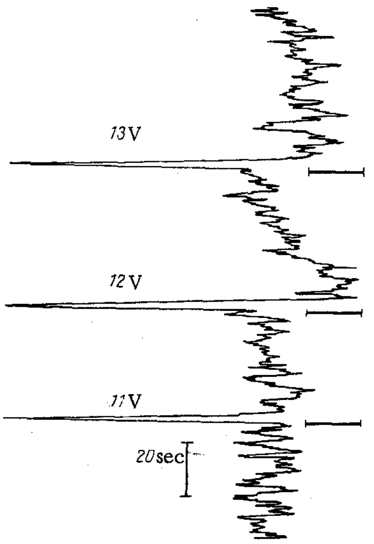

Fig. 1. Determination of threshold of stimulation in region of red nucleus. Integrated record (reading from bottom to top) of unit activity of neuron population of red nucleus in response to single pulses of 11, 12, and 13 V. Time of stimulation marked by straight line. Shift of curve to the right denotes increase in firing rate; spike-shaped shift of curve to the left denotes automatic inactivation of pen of instrument at moment of stimulation.

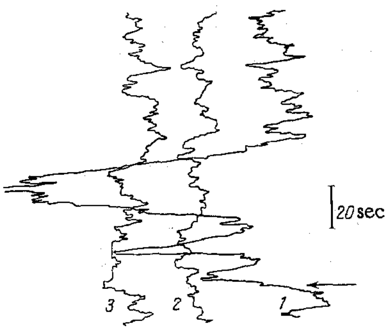

Fig. 2. Multichannel integrated recording (read from bottom to top) of unit activity in ventro-lateral nucleus (1) and centrum medianum (2) of thalamus and also in region of medial component of globus pallidus (3) at time of application (arrow) of a single pulse of 6 V, threshold level for ventro-lateral nucleus. Shift of curves to the left denotes a decrease, to the right an increase in firing rate.

EXPERIMENTAL RESULTS AND DISCUSSION

The results showed that the subcortical structures investigated can be subdivided on the basis of the threshold of stimulation into three main groups. The first group consisted of thalamic nuclei, in whose NPs stimulation by pulses of 6-7 V led to an initial dynamics of spontaneous UA. The threshold of stimulation of the nonspecific nuclei was 1 V higher than that of the specific, namely 7 V.

The second group of nuclei was the strio-pallidary complex. The threshold of stimulation in these structures was a little higher than in the thalamic nuclei, namely 10 V. Finally, the structures with the highest threshold of stimulation of all that were tested were nuclei in the brain stem (group 3). The threshold of stimulation of these structures was 12 V.

Threshold pulses evoked a different pattern of spontaneous UA in all NPs of the subcortical structures. In some formations (thalamic nuclei) the number of unit discharges decreased immediately after the spike by a substantial amount, sometimes to 59% of the initial value. In other structures (red nucleus, substantia nigra), on the other hand, immediately after stimulus the firing rate increased (Fig. 1). These changes were of short duration (of the order of several tens of seconds), after which UA of the NP studied returned to its initial level. Stimulation by threshold pulses for a given NP led to the dynamics of spontaneous UA described above in the region of stimulation only, and no changes in UA were induced either in distant NPs functionally connected with the NP studied or in populations lying next to the region stimulated (in the zone of the neighboring electrode 2 mm away) (Fig. 2).

In another part of the investigation single pulses of supraliminal voltage were used. The supraliminal voltage was obtained by increasing by 25% the threshold voltage characteristic of the particular group of subcortical structures. In response to supraliminal stimulation the spontaneous IA was reduced by a varied degree in all NPs studied. The recovery cycle of UA to its initial level was characteristic of each of the three groups of subcortical structures listed above. The most marked slowing of UA after the stimulus was observed in the thalamic nuclei. Recovery to the original level took place after 3-4 min. In the strio-pallidary region after the stimulus there was a very slight decrease in firing rate; the original level of UA was restored after 1-2 min, but in some cases, having reached its original level, UA climbed to 20-25% above it, to return finally to its initial values in the course of the next 3-4 min. The decrease in frequency of UA was minimal in NPs in the brain stem, with recovery of the original level in the course of 2-3 min. Besides the dynamics of UA described above in the region of application of the stimulus, in the case of supraliminal electrical stimulation a varied change in the UA pattern was observed simultaneously in NPs of other structures connected functionally with the region stimulated. These changes in UA could take the form of either an increase or a decrease in the frequency of the discharges. The functional state of the various subcortical structures could thus be readjusted in

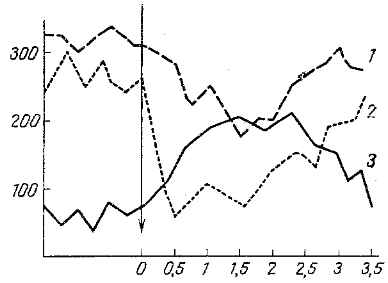

Fig. 3. Averaged graph of dynamics of unit discharge frequency in region of pulvinar (1) and centrum medianum (2) of thalamus and in region of red nucleus (3) after application (arrow) of single supraliminal pulse (10 V) in region of centrum medianum. Abscissa, time (in min); ordinate, number of spike discharges during 15-sec recording intervals.

various ways primarily through a change in the functional state of the region stimulated. The duration of this general retuning did not exceed on the average 4-5 min, after which the frequency of UA in the structures returned to its initial values (Fig. 3).

The results of this investigation, based on recordings of unit activity, a fine and sensitive index of the functional state of the structure investigated, not only demonstrate the different levels of excitability of the basal ganglia, but also predict the conditions of electrical stimulation under which purely local or both local and distant changes in UA will arise.

The results of experimental investigations showing a definite connection between responses of subcortical origin, on the one hand, and the functional level of the subcortical structures and parameters of the electrical stimulation used, on the other hand [7, 9, 11] are complementary to the data described above and they point to the need for a differential approach to the choice by the clinician and neurophysiologist of the parameters of therapeutic and diagnostic electrical stimulation applied to deep brain structures in order to obtain comparable clinical effects. The use of supraliminal single pulses for these procedures leads to physiological irradiation of excitation from the region of stimulation and to a change in the level of excitability of other structures. These distant changes reflect returning of the functions of individual areas and components of the system controlling a particular bodily function that takes place under these circumstances and, in turn, accounts for the complex central mechanism of peripheral responses.

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