The reasons for the difference in the action of individual drugs belonging to the analgesic group and the benzodiazepine derivatives are not absolutely clear and are difficult to explain at the present time. The possibility cannot be ruled out that the differences are connected with their influence on different mediator mechanisms of the antinociceptive effect [12].

**LITERATURE CITED**

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**EFFECT OF INTRAVENOUS DIAZEPAM ON CORTICAL UNIT ACTIVITY IN RABBITS**

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Changes in single unit activity were studied by a microelectrode technique in the sensomotor cortex of rabbits at different times after a single intravenous injection of diazepam (1-5 mg/kg). A few seconds after the injection of diazepam marked depression of spontaneous activity and of activity evoked by sciatic nerve stimulation was observed, together with an increase in the duration of the inhibitory pause in responses of the neurons to afferent stimulation and to direct stimulation of the cortical surface. These changes were considerably reduced 15-60 min after injection of diazepam. The results were compared with those of other workers who studied the clinical and pharmacokinetic effects of the benzodiazepines. It is concluded that the depressant effect of diazepam on cortical activity is connected with its sedative, amnesic, and anticonvulsant effect, and also that GABA plays an important role in the mechanism of these effects.

KEY WORDS: diazepam; sensomotor cortex; dynamics of depression of unit activity.

In a series of articles devoted to the benzodiazepines the effect of these drugs on electrical activity of nerve cells in different parts of the CNS is described [2, 6, 7, 11, 14]. The data given are not only episodic, but also sometimes contradictory in character. As yet no systematic study has been made of changes in the activity of brain neurons in the course of time after injection of benzodiazepines.
Fig. 1. Changes in different types of electrical activity of two neurons of rabbit sensomotor cortex with time after intravenous injection of diazepam, 1 mg/kg. A, B) one neuron; C, D) another neuron. A, C) Spontaneous activity; B) responses of neuron to electrical stimulation of sciatic nerve (1.50 V). D) Response of neuron to electrical stimulation of cortical surface (3.15 V). Abscissa, time (in msec); ordinate, number of action potentials. C) Control of unit activity before injection of diazepam. Numbers by curves show time after injection of diazepam (in min). Vertical lines on curves show duration of inhibitory pause. Remainder of explanation in text.

The object of the present investigation was to study the temporal pattern of changes in sensomotor cortical unit activity after a single intravenous injection of diazepam. The need for such an investigation has arisen primarily because of the marked effect of benzodiazepines on cortical inhibition recently demonstrated in the writer's laboratory [1, 2, 16]. Moreover, the world literature now contains a wealth of data on the pharmacokinetics of the benzodiazepines and on the temporal course of their clinical effects. It seemed important to compare these data with the results of a dynamic study of changes in cortical unit activity after parenteral injection of benzodiazepines.

EXPERIMENTAL METHOD

Experiments were carried out on 13 adult rabbits weighing 3-4 kg. Sensomotor cortical unit activity was recorded extracellularly by glass microelectrodes filled with 3 M NaCl solution at the focus of maximal activity, identified by stimulation of the sciatic nerve with square pulses (0.1 msec, 0.2-10 V). Besides responses of single neurons to afferent stimulation, their responses to electrical stimulation of the cortical surface (0.1 msec, 5-10 V) through bipolar nichrome electrodes (diameter 0.1 mm, interelectrode distance 0.2 mm) also were studied. The spontaneous unit activity was recorded first (60 sec) followed by 30 responses of the neuron to stimulation of the sciatic nerve or cortical surface (60 sec, 0.5 Hz); this was followed by intravenous injection of diazepam (Seduxen, Gedeon Richter, Hungary) in a dose of 0.5-5.0 mg/kg at the rate of 1-2 mg/min). At various times after injection of diazepam, unit activity was again recorded by the scheme described above. To analyze the data, standard voltage quanta were formed from the neuronal discharges. By summation of each successive quantum with its predecessor, unit activity was represented as a function of voltage with time. Synchronous summation of 30 cuts of spontaneous and evoked activity (640 or 1280 msec) was carried out by