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CORRECTION OF RESPIRATORY DISORDERS BY ELECTRICAL STIMULATION OF STRUCTURES OF THE RESPIRATORY CENTER

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The problem of correction of respiratory disorders is urgent from both theoretical and practical viewpoints. Its successful solution is intimately bound with clear and precise ideas on the site of generation of respiratory rhythmic activity. Disturbances of normal breathing are of many different kinds, as are the principles and conditions producing them. It is not surprising that different methods have been suggested for their correction. Methods of artificial ventilation of the lungs and electrical stimulation of the peripheral part of the nervous system of the respiratory apparatus have been widely used under both experimental and clinical conditions [1-4]. "Inspiratory" and "expiratory" areas, stimulation of which can be used to regulate the rhythm of the respiratory neurons and to restart arrested breathing in cats, have been discovered in the medial and lateral zones of the respiratory center [5, 6].

To study the properties of the central bound rhythm and restoration of respiratory function in cats which have stopped breathing by application of square pulses of current, in the investigation described below the "inspiratory" and "expiratory" areas of the gigantocellular nucleus, tractus solitarius, and nucleus ambiguus and nucleus retroambiguus were stimulatedm as described earlier [5, 6].

EXPERIMENTAL METHOD

Experiments were carried out on 61 cats weighing 2.5-3.8 kg anesthetized with pentobarbital (40 mg/kg, intraperitoneally). Preparation of the animal and the method used to stimulate structures of the respiratory center and to derive activity of the respiratory neurons were described previously [6]. During consecutive stimulation of the "inspiratory" and "expiratory" areas, taking stereotaxic coordinates from the atlas [7], two stimulating electrodes were inserted: One was fixed securely in the occipital bone, and the other, which could be moved, was fixed in the aiming head of the SEZh-3 stereotaxic apparatus and so could be inserted into different structures of the respiratory center. In four experiments electrodes were inserted without preliminary aspiration of the cerebellum. The experiments were divided into two series. In the experiments of series I an arbitrary rhythm was "bound" on respiration by stimulating one of the "inspiratory" areas or by consecutive repetitive stimulation of the "inspiratory" and "expiratory" areas. In the experiments of series II attempts to correct various disturbances of respiration, or to restore respiration if it had ceased, were made by stimulation of the "inspiratory" areas. In 12 experiments respiratory arrest was induced by additional intravenous injection of pentobarbital (20-50 mg/kg) into the animal.

EXPERIMENTAL RESULTS

Responses of unit activity of 113 respiratory neurons to stimulation of the "inspiratory" and "expiratory" areas of the respiratory center were studied. The strongest stimulating effect was obtained by stimulation of the "inspiratory" and "expiratory" areas of the gigantocellular nucleus. About 80% of inspiratory and expiratory neurons of the "ventral and dorsal respiratory nuclei" responded with rhythm binding to stimulation of structures of the gigan-

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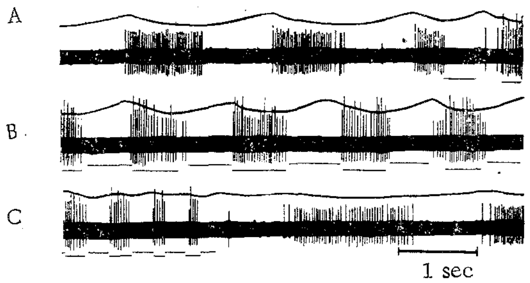

Fig. 1

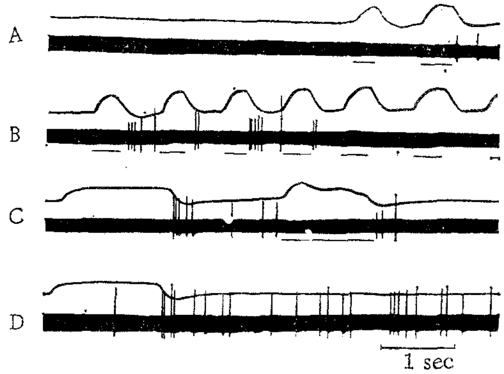

Fig. 2

Fig. 1. Control of spike activity of "complete" expiratory neuron by stimulation of "inspiratory" and "expiratory" areas of the gigantocellular nucleus. A, B, C) Respiration and spike activity of "complete" expiratory neuron before, during, and after electrical stimulation of "inspiratory" area respectively (coordinates: 4 mm rostrally to obex, 0.5 mm laterally to midline, depth 3.5 mm from dorsal surface) and "expiratory" area (coordinates: 2.5 mm rostrally to obex, 1.5 mm laterally to midline, depth 3 mm). Top trace is pneumogram, bottom trace unit activity.

Fig. 2. Restoration of spike discharge of respiratory neuron and respiration by electrical stimulation of "inspiratory" area of gigantocellular nucleus. A) Respiratory arrest during preparation of animal for experiment; B) repetitive stimulation of "inspiratory" area (coordinates as in Fig. 1); C, D) restoration of unit activity and respiration.

tocellular nucleus (Fig. 1). Rhythm binding by the neurons took place in response to the first stimulation. In three of 14 experiments the new "bound" rhythm continued for two to five respiratory cycles after the end of stimulation. A facilitatory effect on respiratory neurons of the lateral zone during stimulation of the gigantocellular nucleus was manifested not only as an increase in the mean discharge frequency in the evoked volleys but also, and more especially, as an increase in the number of functioning respiratory neurons and neuromotor units of the diaphragm and intercostal muscles. Unit activity from eight inspiratory and 11 expiratory cells, which was not present before stimulation (Fig. 1), was recorded in the region of the "ventral respiratory nucleus" as a result of stimulation. The character of activity of the respiratory neurons during stimulation of the "expiratory" and "inspiratory" areas of the gigantocellular nucleus depended on the type of neuron, the time of application of the stimulus, and the latent period of response of the neuron. For instance, in all 11 inspiratory–expiratory and expiratory–inspiratory neurons suppression or inhibition of activity was observed irrespective of the stimulated point. The response of the principal types of respiratory units ("early," "complete," "late") depended on the time of stimulation: The nearer the time of stimulation to the beginning of the next period of bursting activity of the neuron, the more effective the stimulation was and the shorter its latent period. An artificially evoked increase in the frequency of respiratory movements to 36.2 ± 3.7% or a decrease in their frequency to 26.3 ± 4.8% of the original values was accompanied by an increase in the mean discharge frequency of the neurons. With a faster or slower "bound" rhythm the mean firing rate was slower than initially (Fig. 1). During stimulation of the majority of "inspiratory" and "expiratory" areas of the lateral zone, rhythm binding was unstable: "Slipping" of unit activity from the "bound" rhythm of respiratory movements was often observed. More than 30% of respiratory neurons did not give evoked responses. Only stimulation of some areas (for example, 3 mm rostrally to the obex, 3 mm laterally to the midline, at a depth of 2.5 mm from the dorsal surface) was accompanied by rhythm binding in the principal group of neurons, just as to stimulation of structures of the medial zone.

In 33 experiments electrical stimulation was applied to the "inspiratory" areas of the gigantocellular nucleus (coordinates of one of them: 4 mm rostrally to the obex, 0.5 mm laterally to the midline, at a depth of 3.5 mm from the dorsal surface) in cats which had ceased to breath during preparation for the experiment or as the result of respiratory arrest

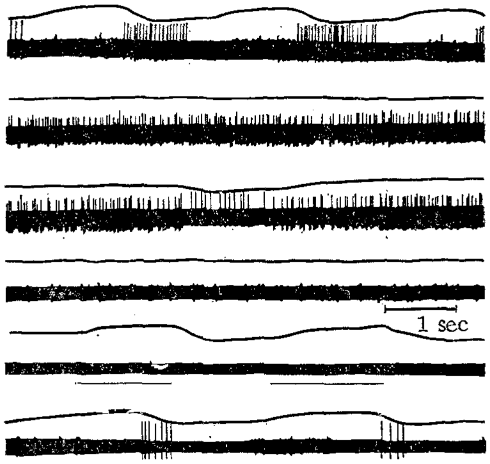

Fig. 3. Respiratory arrest after injection of pentobarbital and restoration of breathing after electrical stimulation of "inspiratory" area of gigantocellular nucleus. A) Initial unit activity of inspiratory and expiratory neurons; B, C) respiration and unit activity 3 min after intravenous injection of 40 mg/kg pentobarbital; D) 10 min later; E) repetitive stimulation of "inspiratory" area; F) restoration of respiratory unit activity after stimulation for 5 min.

induced by injection of pentobarbital. Breathing was restored either when respiratory movements were starting to be depressed, 1-3 min after breathing stopped, but while cardiac activity still continued, or 10-30 sec after the cessation of cardiac activity. The effectiveness of the restorative procedures depended on the functional state of the respiratory and cardiovascular system: In the experiments of the second variant unit activity of respiratory neurons and respiratory movements were restored in 20 animals for a long time (Fig. 2), and respiration could not be renewed in only two animals; in the third variant respiratory movements could be restored in only two of six cats. Stimulation of the "inspiratory" area also had a favorable influence on cardiac activity (the strength of the cardiac contractions and their frequency were increased). No special procedures aimed at restoring cardiac activity were carried out. Intravenous injection of pentobarbital caused pathological types of respiration, chiefly inspiratory apnea, followed by respiratory arrest. Electrical stimulation of the "inspiratory" area of the gigantocellular restored unit activity of respiratory neurons and respiration in 11 cats (Fig. 3). Stimulation of the "inspiratory" area of the nucleus of the tractus solitarius, mentioned above, restored respiratory movements in three of five animals in experiments of the second variant. Attempts to restore respiration by stimulation of other structures of the lateral zone of the respiratory center were nearly always unsuccessful.

It was thus established experimentally that a new rhythm can be imposed on the "respiratory neurons" of the ventral and dorsal respiratory nuclei and on respiratory movements, and arrested breathing also can be restored by stimulation of the "inspiratory" and "expiratory" areas of the gigantocellular nucleus and also of two areas of the nucleus of the tractus solitarius.

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