SEPTAL NUCLEI IN MECHANISMS OF LATERAL HYPOTHALAMIC SELF-STIMULATION IN RABBITS

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The morphological basis of the self-stimulation (SS) phenomenon is an extensive region of the brain connected mainly with the medial forebrain bundle. The nerve fibers of this bundle pass through the lateral hypothalamus and connect the mesencephalon with several limbic and cortical structures [7]. It has been shown that unilateral destruction of various components of this complex leads to changes in SS behavior, induced from the lateral hypothalamus [5, 9]. However, the importance of individual limbic zones in the mechanism of hypothalamic SS has not yet been adequately studied. In this context, because of its extensive afferent connections and its efferent connections with the hypothalamus, the septum pellucidum is the most interesting of these structures. Electrical stimulation of the septum has been shown to induce stable SS in rats [2, 8] and preliminary stimulation of the septum activates hypothalamic SS [6].

The aim of this investigation was to study effects of destruction of the septal nuclei on SS induced in rabbits by electrical stimulation of the lateral hypothalamus.

EXPERIMENTAL METHOD

Experiments were carried out on 14 Chinchilla rabbits weighing 3-3.5 kg. On the 2nd day after scalping of the animals, bipolar nichrome stimulating electrodes were inserted into the region of the lateral hypothalamus (P-2, L-2, H-15-16 mm) by the "floating electrode" method [1]. During the experiments the rabbits were kept in a chamber with a fixed metal ring and allowed free access to water and food. The freely moving animals, on touching the metal ring with their nose and lips, thereby closed an electric circuit, stimulating the hypothalamus, and on this basis they were quickly trained in SS. Parameters of the current stimulating the brain were: volleys of square pulses with a frequency of 100 Hz, duration 0.3 sec, current 40-60 mA, duration of a single pulse 1.4 msec. Two electrodes were implanted unilaterally in eight rabbits into the medial and lateral septal nuclei (A-3, L-0.5 and 0.8, H-9; A-3, L-1 and 1.5, H-8 and 10 mm, respectively); in six rabbits the electrodes were implanted bilaterally. Sessions of SS were given daily for 10-14 days. The frequency of SS in a 5-min interval was investigated every 10 min for the duration of an experiment lasting 2 h in the experiment, 3 days before coagulation, and 10-14 days after coagulation of the septal nuclei. Coagulation was carried out by passing a direct current of mA for 30 sec. After the end of the experiments the animals' brain was fixed for 5-7 days in 10% formalin solution. The brain was then frozen and frontal sections 30 μ thick were cut. The experimental results were subjected to statistical analysis by Student's t test.

EXPERIMENTAL RESULTS

The experiments showed that unilateral destruction of the septal nuclei (eight rabbits) gave opposite effects on SS induced by the lateral hypothalamus ipsilateral and contralateral relative to the coagulation structures. In cases when coagulation of the septal nuclei was carried out ipsilaterally and affected the medial septal nucleus and the dorsal, intralaminar, and ventral parts of the lateral nucleus, the frequency of SS of the lateral hypothalamus was reduced on the 2nd and 3rd days after destruction on average by 25-32%. These changes did not reach the level of statistical significance. On the 4th day after the operation the frequency of SS returned to its background level, and remained virtually unchanged for the

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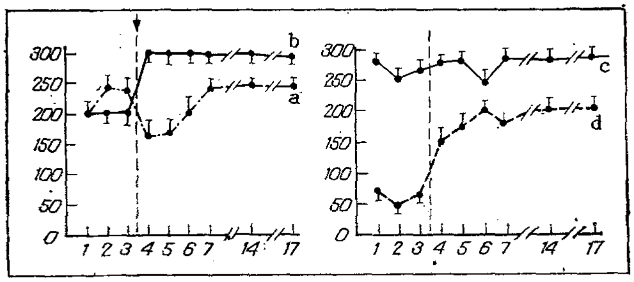

Fig. 1. Changes in frequency of SS after coagulation of the septal nuclei. Arrow indicates moment of coagulation. a) Frequency of SS after ipsilateral destruction (medial septal nucleus, dorsal, intralaminar, and ventral parts of lateral nucleus); b) frequency of SS after contralateral destruction (intralaminar part of dorsal nucleus, medial nucleus, intralaminar and ventral parts of lateral nucleus); c) bilateral destruction (intralaminar part of dorsal nucleus, medial nucleus, intralaminar and ventral parts of the groove of the stria terminalis), with a high background frequency of SS; d) bilateral destruction (intralaminar parts of dorsal nuclei, medial nuclei, dorsal, intralaminar, and ventral parts of lateral nuclei), with a low background frequency of SS. Abscissa, days of experiment; ordinate, frequency of SS.

next 10-14 days of the experiment (Fig. 1a). Contralateral destruction of the septum (intralaminar part of the dorsal nucleus, medial nucleus, intralaminar and ventral parts of the lateral nucleus) led to an increase of 35-40% in the frequency of SS of the lateral hypothalamus ($p < 0.05$). The frequency of SS remained increased during the next 10-14 days (Fig. 1b).

Bilateral destruction of the septal nuclei (intralaminar part of the dorsal nucleus, medial nucleus, intralaminar and ventral parts of the sulcus of the stria terminalis) caused virtually no change in the frequency of SS of the lateral hypothalamus in the rabbits, if its background (control) values were high enough: 258 ± 26 closings of the electric circuit during 5-min intervals (mean data for four rabbits, Fig. 1c). A different picture was observed if the background frequency of SS was low. In two rabbits in which the background frequency of SS during 5-min intervals was 55.8 ± 18, for instance, and also was ambivalent in character – having stimulated themselves twice or 3 times, the rabbits ran into the corner of the cage, struck the floor with their hind limbs 4 or 5 times, and returned again after 8-10 sec for further self-stimulation – the frequency of SS 24 h after bilateral destruction of the septal nuclei was increased to 109.0 ± 22.8; the number of times they struck the floor with their hind limbs was reduced. After 48 h the frequency of SS became even greater (163.5 ± 23.6 closings of the electric circuit during 5-min intervals; $p < 0.05$); the animals did not strike the floor with their hind limbs and became quieter. The frequency of SS remained high throughout the 14 days of the experiment (Fig. 1d). The histological control showed that destruction in these rabbits extended to the intralaminar parts of the dorsal nuclei, and the dorsal, intralaminar, and ventral parts of the lateral nuclei.

These results showing the opposite effects of destruction of the septal nuclei in ipsilateral and contralateral self-stimulation of the lateral hypothalamus are evidence that different mechanisms are involved in these effects. This is shown also by the fact that effects observed after ipsilateral destruction are reversible: The frequency of SS fell only in the first 2 days after coagulation, then recovered, whereas in the case of contralateral destruction SS increased and remained high throughout the 14 days of the experiment. It has been shown [2] that removal of the anterior zones of the cortex acts only on contralateral SS; the authors cited suggest that effects on SS in the case of ipsilateral lesions depends on subcortical structures, but both cortical and subcortical structures are involved in contralateral effects. Possibly in contralateral lesions nerve fibers running from one hemisphere into the other and giving an inhibitory effect [2] are damaged, and as a result, intensification of SS is observed. Moreover, injury to the structures of one brain hemisphere may perhaps stimulate activity of the contralateral hemisphere. We know [3], for example, that in the case of unilateral injury to the subtantia nigra, secretion of dopamine is reduced in the ipsilateral, but increased in the contralateral corpus striatum. The present experiments showed that effects of bilateral destruction of the septal nuclei depend on the initial level of SS. The frequency of self-stimulation was virtually unchanged after destruction if the background level of SS was high. In animals with a low background frequency of SS and with aggressive behavioral components, bilateral destruction of the septal nuclei led to a marked increase in the frequency of SS and to disappearance of the aggressive behavioral components. These findings are in agreement with existing reports [4] that aggressiveness is reduced after destruction of the septum.

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EFFECT OF DEATH OF A SINGLE NEURON ON FUNCTIONAL ORGANIZATION OF THE NEURON NET OF *Hirudo medicinalis*

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Division of or injury to axon bundles has been shown to lead to anatomical and physiological reorganization of the nervous system in both vertebrates and invertebrates: the amplitude and shape of the postsynaptic potentials (PSP) are modified [7], regions of innervation of residual neurons are widened [5, 9, 12], increased sensitivity to mediator appears in the extrasynaptic region [8], and changes are observed in the topography of synaptic junctions [14, 15]. Meanwhile, a process of natural death of nerve cells is known to take place constantly in the CNS [4, 6]. There is no information in the literature on whether any restructuring of the nervous system takes place in response to this. The question of whether the neuron net is a dynamic and constantly changing structure or whether it is a system with an excessive number of elements, for which death of a neuron is simply an "imperceptible" loss of a structural unit, remains open.

The after-effects of death of single neurons can be studied on nerve nets containing a small number of large and easily identifiable cells. The nervous system of the leech *Hirudo medicinalis*, distinguished by relative simplicity and accessibility for experimental procedures in vivo [3], is a convenient model for such investigations.

An assembly of cells responsible for reflex acts of the "mechanical stimulation of the skin – contraction of the body wall" type in the segmental ganglion of the leech has been described in detail. Altogether 14 mechanosensory cells, belonging to three modalities, have been identified: four cells of N-type, four cells of P-type, and six cells of T-type [10]. All mechanosensory neurons, moreover, form monosynaptic junctions with motoneurons of the same segmental ganglion, including with two AE-motoneurons [13]. Mechanosensory cells have contact through interganglionic connectives with motoneurons in neighboring ganglia also [2, 7]. According to electron-microscopic data, mechanosensory neurons of one modality make contact with each other [11], whereas no functioning synapses between them can be discovered by electrophysiological methods.

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