EFFECT ON GASTRIC AND INTESTINAL INTEROCEPTIVE CONDITIONED REFLEXES AFTER EXTIRPATION OF THE CORTICAL REPRESENTATION OF THE VAGUS NERVE

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Modern methods of recording electrical activity in the central nervous system have made it possible to determine the cortical representation of the viscera. Many studies have been made [3, 4, 5, 9, 11,12] of cortical interoceptive representation by means of electroencephalography, and the first satisfactory results have been obtained in this way.

The recording of the primary cortical response represented a great step forward in the study of cortical visceral representation, and it has enabled a large number of projection areas of organs innervated by the vagus splanchnic, and pelvic nerves to be determined [7, 15, 16].

Attempts to study cortical visceral representation by means of extirpation have been reported in several articles [1, 2, 6, 8, 10]. By this means it was possible to demonstrate that comparatively large cortical areas, chiefly in the motor and premotor cortex, were concerned in the reception of impulses originating from several of the viscera. However, until now, electrophysiological results have not been in good agreement with those obtained through extirpation. So far as we know, no study has been made of the effect on the interoceptor conditioned reflexes of extirpating the projection areas, as determined by recording the primary responses.

One of us [13] has proposed that the focus of maximal activity in the primary response areas represents the nucleus of the analyzer.

In the present article we have attempted to test this hypothesis by determining the extent to which the vagal cortical projection area is involved in the formation and control of conditioned gastric interoceptor reflexes.

METHOD

The experiments were carried out on three dogs (Ruslan, Sultan, and Jack) in which carotid and gastric fistuli had been established. In Sultan, in addition, there was an intestinal fistula. The work was carried out in a soundproof room using conditioned reflexes of the digestive system. The unconditioned stimulus was a meat preparation. Exteroceptive and interoceptive conditioned reflexes were established in all the animals by presenting the conditioned and unconditioned stimuli at a time interval of 15 seconds. The exteroceptive conditioned stimulus was a bell, and the interoceptive stimulus was applied by inflating a rubber balloon in the empty stomach once per second. In addition, in Sultan, the mechanoreceptors of the small intestine were stimulated by the expansion of a thick-walled rubber balloon introduced through the intestinal fistula.

After developing a set of conditioned reflexes, an operation was performed to remove the cortical vagal area. The anesthetic used was a mixture of chloroform and ether. Two cuts at right angles were made in the dura mater, and the flaps were turned back over the edge of the bone. Using a bent Folkman spoon, a piece of grey matter measuring 1.5 × 1 cm was carefully removed from the postero-inferior portion of the orbital gyrus and from the deep portion of the olfactory groove, areas which corresponded to the projection of the nuclei of the vagus. Because of the small amount of damage to the brain, the dog was again in good condition as early as the 4-5th day. The condition of the exteroceptive and interoceptive conditioned reflexes was again studied.

Also, a control extirpation was carried out in which portions of the parietal cortex of corresponding size were removed from both sides (part of area 7 of the maps by Gurevich and Bykhovskaya).

RESULTS

Ruslan. The conditioned interoceptive reflex to stimulation of the gastric mechanoreceptors was achieved after 25-28 combined applications of the stimuli.

Later, introduction into the experiment of an exteroceptive conditioned stimulus did not change the magnitude of the already elaborated conditioned interoceptive reflex. After the conditioned reflexes to the bell and to gastric interoceptor stimulation had become stable and the variation was less than 5-7 drops, the vagal cortical projection area was removed bilaterally. After 4 days,

the dog was again tested. It was found that the magnitude of the conditioned reflex to gastric mechanoreceptor stimulation had been reduced to half, whereas the exteroceptive conditioned reflex had remained unchanged. After seven days, the saliva yield from the conditioned reflex to mechanoreceptor gastric stimulation gradually returned to 5-6 drops. As a control on the same dog, a second operation was performed in which portions of cortex were removed symmetrically from the parietal areas. No noticeable changes in the extero-or interoceptor conditioned reflexes were noticed. Fig. 1 illustrates the development and the state of the conditioned reflexes before and after the two operations.

Sultan. After 12-15 combined applications of the stimuli, the conditioned reflex was developed to the bell (6-7 drops) and after 18-20 applications, the interoceptive reflex to mechanoreceptor gastric stimulation reached a steady level at 5-6 drops. Next, in the same dog, after 28-30 combined applications of the stimuli, a conditioned reflex was developed to stimulation of the mechanoreceptors of the intestine (3-5 drops). In the great majority of cases, conditioned gastric mechanoreceptor stimulation produced 1-2 drops more than did stimulation of the intestinal mechanoreceptors.

After the conditioned reflexes had become stable within the limits described, the vagal cortical representation was extirpated bilaterally. Tests of conditioned reflex activity 4 days after the operation showed that the conditioned responses to the bell and to stimulation of the intestinal mechanoreceptors had undergone no change, and remained within the previous limits. The conditioned response to gastric stimulation had become reduced, and only after 8-10 days gradually returned to the preoperative level (Fig. 2).

Jack. To determine the part played by the afferent vagal pathways, in the dog Jack, it was decided to divide the vagus below the diaphragm at the same time as the fistula was established. In this way it was thought that the afferent vagal pathway would be largely eliminated. As in the previous animals, conditioned exteroceptor and interoceptor reflexes were developed. During the formation of these reflexes, several special features were noticed, and it was found that they developed much more slowly than in the other two dogs, and that the response was phasic. Whereas in Ruslan and Sultan the gastric conditioned reflex appeared after 18-22 combined presentations of the stimuli, and remained stable, in Jack, it did not develop until 38-40 presentations, and then disappeared and did not return until the 54-56th stimulation.

After the vagal cortical areas had been extirpated, the interoceptive conditioned reflex was considerably reduced, and whereas 5 drops had been obtained before operation, only 1 was obtained afterward. The feature of this period was the greater time taken for the recovery of the reflex compared with the corresponding period in dogs in whom the stomach had not been denervated. Just as in Ruslan and Sultan, the exteroceptive conditioned reflex underwent no important change (Fig. 3).

At present there is no agreement as to what is the functional structure of the cortical interoceptor representation [2, 14].

The results described here confirm the idea that the cortical areas determined by recording primary responses are the cortical nuclei of the interoceptors. This conclusion is supported by the fact that after the vagal cortical areas had been removed, the interoceptive conditioned reflex to mechanoreceptor gastric stimulation was impaired in 2 out of the 3 dogs. Also, it remained reduced for 11-17 days, and in Jack, after subdiaphragmal vagotomy, the reduction lasted for 40-45 days. The difference in the extent of the reduction of the conditioned reflexes and the times at which they returned

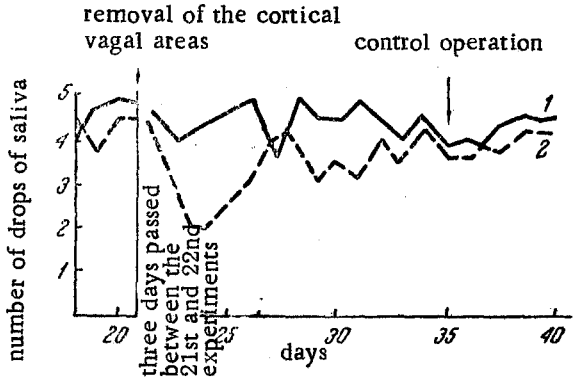

Fig. 1. A conditioned reflex activity in the dog Ruslan before and after removal of the vagal cortical representation. 1) Response to bell; 2) response to gastric stimulation.

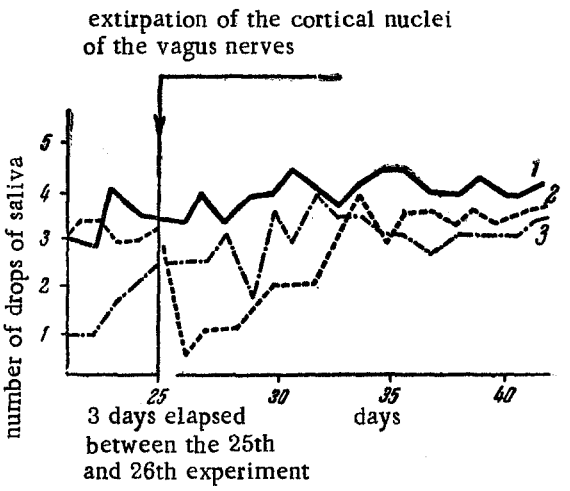

Fig. 2. Conditioned reflex activity in Sultan before and after extirpation of the vagal cortical representation. 1) Response to bell; 2) response to gastric stimulation; 3) response to intestinal stimulation.

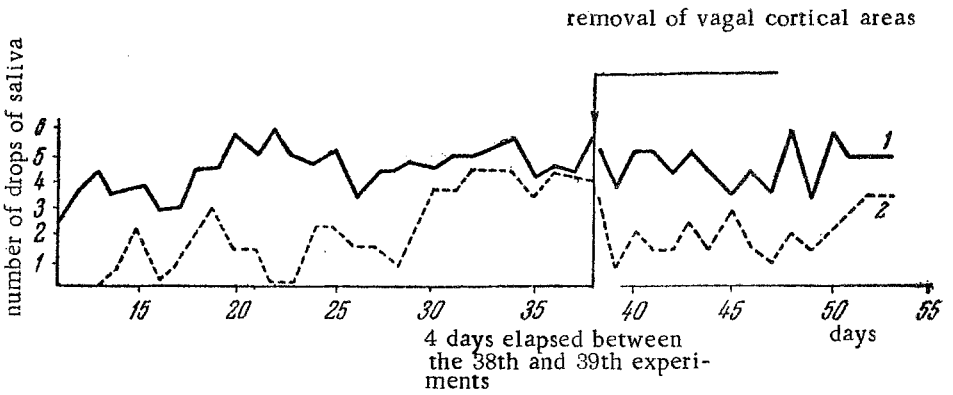

Fig. 3. Conditioned reflex in Jack before and after extirpation of the vagal cortical areas. 1) Response to bell; 2) response to gastric stimulation.

suggests that removal of the cortical areas in which the vagus nerve is represented makes it more difficult to establish conditioned reflexes from organs innervated by this nerve. The fact that after these areas have been removed there was no essential change in a conditioned reflex developed in response to intestinal stimulation gives reason to suppose that these areas are related particularly to the stomach, which is innervated by the vagus. The absence of any change in reflexes from the intestine may be attributed to their innervation chiefly by the splanchnic nerves, whose cortical representation was not impaired.

Thus, removal of the cortical areas where the greatest amplitude is recorded from vagal stimulation leads to a reduction in the interoceptive gastric reflex, which lasts for a time depending on the extent of the extirpated portion and its distance from the nucleus.

At present, we interpret the results of the experiments on Jack as follows: Subdiaphragmal division of the vagus is not an operation which completely destroys the afferent gastric innervation mediated by sensory vagal fibers. Also, there is no doubt that some sensory innervation is supplied by fibers of the splanchnic nerve. There was, therefore, no complete gastric denervation, but only a considerable reduction in the number of afferent fibers. In our opinion, it was on this account that it remained possible to develop a conditioned gastric interoceptive reflex, which showed the features which we have already described. In view of this, it is also understandable that after the cortical areas have been extirpated, the reflex first disappeared, and then reappeared, but considerably later than in the animals in which the gastric afferent innervation was preserved.

SUMMARY

The experiments were performed on three dogs. The extero- and interoceptive conditioned reflexes were studied before and after extirpating the vagal cortical areas. The extirpation caused a disturbance of conditioned reflexes associated with gastric stimulation, but had no effect on those which depended on stimulation of the intestine, which is innervated by the splanchnic nerve. A control operation, in which a portion of a parietal lobe was extirpated, was performed on one of the dogs, and caused no changes in the conditioned reflexes in which an association was made between stimulation of the extero- and interoceptors. Removal of the sensory vagal cortical centers in dogs in which the stomach had been denervated caused a prolonged and fluctuating disturbance of the gastric interoceptive reflexes.

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