# PRIMARY CORTICAL REACTION ZONES UNDER THE INFLUENCE OF THE RECEPTOR APPARATUS OF THE CORONARY VESSELS AND PERICARDIUM

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Many experimental and clinical findings show that excitation of interoceptors reaches the cerebral cortex. Connections between the cortex and the heart have been discovered by the method of conditioned reflexes [2, 7, 15]. During stimulation of interoceptors, bursts of impulses are recorced in the corresponding afferent fibers [4, 5, 16]. A flow of impulses in the afferent nerves of the heart has been observed in different phases of the cardiac cycle when the heart was exposed to the action of various drugs and also after ligation of the coronary arteries [1, 13, 24].

Various authors [3, 4, 9, 10, 11] have shown that when impulses from the interoceptors reach the cortex, they change the character of its bioelectrical activity. These changes were especially clearly marked in the premotor and parietal areas of the cortex.

A flow of afferent impulses also modifies the EEG in man. It has been observed that the EEG undergoes considerable modification when there are pathological changes in the internal organs. In previous research, the author in conjunction with A. V. Meshcheryakova [12], showed that in the course of an attack of angina pectoris, confirmed clinically and electrocardiographically, there was an increase in the frequency and amplitude of the electrical waves, and asynchronous peak waves appeared. Similar changes were recorded in different areas of the cortex, although in the premotor areas of the cortex they either appeared earlier or were most in frequency and amplitude, and in some cases they were limited to these areas.

In order to investigate the representation of the extero- and interoceptors in the cortex, in recent years the method of primary responses has been successfully used. Galambos and Davis [23] defined the auditory zone by this method, Bishop and O'Leary [22] the visual zones, Amassian [20] the representation of the splanchnic nerve, and so on. In a series of researches by Chernigovskii and Kullanda [17] data were obtained relating to the representation of the pelvic and pudendal nerves in the cortex of cats and dogs, and a detailed summary was given of work on representation of the internal organs.

Amassian [20], Kullanda [6] and others studied the primary responses or, more accurately, the primary reactions to adequate stimulation of the internal organs. These reactions cannot be called primary responses, for under the conditions of stimulation of the receptor apparatus it was not possible to determine their latent period, which is a fundamental index of the primary nature of the response. Nevertheless they must be classed as primary as opposed to secondary and generalized reactions, for localization of the cortical zones is typical of primary reactions.

As a result of the reports in the literature and of our own findings, we considered it necessary to investigate, by means of the method of primary responses, whether localized zones exist in the cortex to which afferent impulses proceed from the heart when the coronary circulation is experimentally disturbed.

### EXPERIMENTAL METHOD

Experiments were carried out on 15 cats under intravenous urethane (70-80 mg/kg body weight) or chlora-lose (80-100 mg/kg body weight) anesthesia. With the aid of artificial respiration the thorax was opened and the pericardium incised. Under the left descending coronary artery was passed a ligature with an attachment for frequent stopping and restarting of the blood flow. The pericardium was stimulated mechanically. Since the manipulations were carried out on the heart, and the animal's head was directed downward at this time, in some cases we used a special electrode holder for the EEG leads. Four revolving plexiglass half-rings, fitted with silver electrodes 0.5 mm in diameter, were attached by screws to both temporal bones of the skull. Action potentials were tapped from the exposed cortex. The recordings were made on an ink-writing electroencephalograph from the Experimental Factory of the AMN SSSR, with visual observation on the screen of an oscilloscope. The ECG was recorded at the same time by a semi-direct lead.

## EXPERIMENTAL RESULTS

Without anesthesia or under light ether anesthesia ligation of the coronary arteries or stimulation of the pericardium caused groups of rapid waves to appear in the cortex, more marked in the anterior divisions of the cortex. After prolonged anesthesia, when the background cortical activity was imperceptible, in response to ligation, removal of the ligature, and stimulation of the pericardium, two and sometimes three zones were found in the cortex where a response was recorded in the form of a biphasic wave, with a first positive phase or group of 2-3 waves.

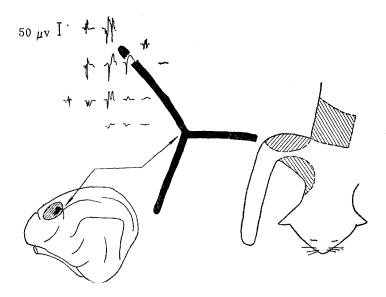


Fig. 1. The first zone of representation of the receptors of the heart in the posterior cruciate gyrus. The primary reactions are superimposed on a schematic chart of the cortex. It can be seen that this zone is covered by the zone of the splanchnic nerve and by the somatic zone from the forepaws and chest (Adrian [19]).

The first zone (Fig. 1), situated in the posterior cruciate gyrus, is in the first zone of somatic sensation, partially covering the zone of representation of the splanchnic nerve. The variations in potential which we then marked on the brain chart corresponding to the point at which they appeared were similar, in their general features (sequence, duration and amplitude), to those observed simultaneously on the oscilloscope, although they differed slightly in shape on account of the inertia of the ink-recording system. The amplitude of the maximum response was of the order of 100  $\mu$ v (individual observations gave a response greater than 200  $\mu$ v). The duration

of the first phase in those cases when the response had a clear biphasic form was 20-30 msec. The focus of maximum response and the limits of the zone, as also the form of the response, changed slightly in the course of the experiment but in the different experiments, however, as a rule it did not extent beyond the limits of the limb area of the first zone of somatic sensation.

It must be pointed out that in certain experiments under deep anesthesia we were able to record the primary response during tactile stimulation of the forepaws and chest in the same zone as during stimulation coming from the heart. The areas of the cortex given in the scheme in the work of Adrian [19] also show coincidence of the somatic zone (from the chest and paws) and the visceral zone obtained by us.

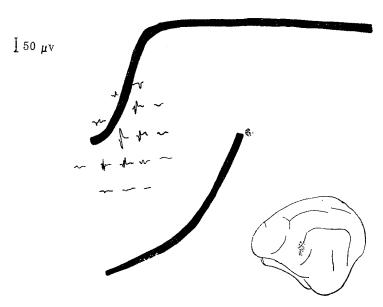


Fig. 2. Second zone of representation of the receptors of the heart in the anterior ectosylvian gyrus, falling within the second zone of somatic sensation of the limbs.

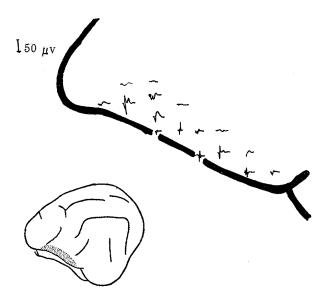


Fig. 3. Third zone of representation of the receptors of the heart in the orbital gyrus (within the zone of representation of the vagus nerve).

In Fig. 2 we depict the second zone obtained under the same conditions. It is situated in the anterior ecto-sylvian gyrus, in the second zone of somatic sensation, and also covering or coinciding with the second zone of the splanchnic nerve. This zone is smaller in extent, and the amplitude of its maximum response is lower than in the first zone (about 50-70  $\mu$ v), and we were not able to record clear primary reactions in this zone in all the experiments. The results obtained by Amassian [20] relating to the representation of the splanchnic nerve show the opposite picture. The second zone in the ectosylvian gyrus was much greater in amplitude than the first. It must be pointed out that after ligation of the coronary artery both these zones were much more clearly apparent than during stimulation of the pericardium. Similar primary responses in roughly the same areas were recorded by Kullanda [6] during stimulation of the pericardium.

In Fig. 3 we show the third zone, stiuated in the orbital region of the cortex. This zone falls completely within the vagus nerve zone identified by Bailey and Bremer [21]. As a rule, however, it was smaller in extent. Considerable variations in the amplitude of the maximum response (20-150  $\mu$ v), the presence of two, and sometimes three maximum responses, and the variability of its extent are especially characteristic of this zone. The clear coincidence between the primary reactions and the moment of clamping and releasing the coronary arteries suggests that it is associated with excitation of the receptor formations in the adventitia of the coronary vessels. The temporary clamping of the cornary artery without subsequent ischemia confirmed this hypothesis.

It must be pointed out that in the course of the experiment the disturbance of the coronary circulation increased in severity, as a result of both the duration of the experiment and the frequent applications of the ligature (on the average 10-15), leading to ischemia, which was apparent during the recording of the ECG. During this time the foci of maximum response were displaced, the configuration of the responses was altered, the response more rarely preserved its proper biphasic form and was replaced by a monophasic type, and often the zone grew in size. In addition, in the intervals between stimulation, and especially at the time when the blood flow in the coronary artery was arrested, biphasic waves of the primary response type or groups of waves, sometimes of considerable amplitude, appeared.

When recordings were taken of the zones described above, the following relationship was observed: during ligation of the coronary artery the first and second zones were more marked than the orbital. During stimulation of the pericardium the opposite relationship held good. After division of the vagus nerves in the neck the primary reactions in the orbital zone diminished or disappeared. These findings are in agreement with those of Bailey and Bremer [21] concerning the representation of the vagus nerve. There is morphological evidence [8] that the myocardium of the atria and the pericardium are innervated by the sympathetic and vagus nerves, whereas the myocardium of the ventricles has a purely sympathetic innervation.

The physiological observations of Shakhbazyan [18] and Rodionov [14] show that the pain reception of the heart is associated with excitation of the endings of nerves passing in the composition of the sympathetic trunks. Clinical data concerning the development of angina pectoris during compression of the stellate and cervicular sympathetic ganglia also confirm this hypothesis indirectly. It is also known that pain impulses cause a diffuse excitation of the first zone of somatic sensation in both hemispheres. Ligation of the coronary artery in unanesthetized animals, like spasm or thrombosis of the artery in man, causes strong pain stimulation.

These observations evidently give grounds for considering that the first and second zones defined in our experiments are the consequence of excitation of the endings of nerves passing in the composition of the sympathetic trunks, whereas the zone in the orbital region reflects the result of excitation of the endings of the vagus nerve.

It was pointed out previously that in the course of a prolonged experiment, as increasing ischemia develops as a result of the frequent ligation, primary reactions or groups of waves are observed in the cortex, unconnected with the moment of ligation or of stimulation of the pericardium. These waves appear especially often when the coronary artery is covered.

It may be suggested on hypothetical grounds that the receptors of the myocardium possess a higher threshold than the nerve endings in the coronary vessels, and signals are received from them after a higher intensity of stimulation. The coincidence of the first and second zones of afferent impulsation from the heart and the somatic zones of the forepaws and chest appears to be important because irradiation of pain and a zone of hyperalgesia in the upper limbs and chest are characteristic of angina pectoris. It is generally considered that irradiation of pain and hyperalgesia are determined at the level of the spinal cord, but it is evidently possible (and our

findings confirm this) that the cortex also plays a part in these phenomena. In this connection it is interesting to note that, according to statistical evidence, reflex angina pectoris is encountered much more often in neuritis of the nerves of the upper limbs than in neuritis of the nerves of the lower limbs. The overlapping of the first and second zones of representation of the receptors of the heart by the zone of representation of the splanchnic nerve may also provide a morphological basis for the reflex angina pectoris accompanying gastric ulcer, cholecystitis, duodenitis and other diseases of the internal organs.

## SUMMARY

Experiments on cats established the presence of 3 primary cortical reaction zones responding to the stimulating action exerted on the receptor apparatus of the coronary vessels and pericardium. The first of them is located in the cruciate gyrus in the first zone of somatic sensation, partly overlapping the zone of the splanchnic nerve. The second zone is located in the ectosylvian gyrus in the second zone of somatic sensation. The site of the third one is the orbital region, in the zone of the vagus nerve.

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