# PARTICIPATION OF THE STEM PORTIONS OF THE BRAIN IN REALIZING THE EFFECT OF CERTAIN PHARMACOLOGICAL AGENTS ON THE PERIODIC CONTRACTIONS OF THE STOMACH

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The significance of the central nervous system, and specifically its stem portion, in the mechanism of periodic activity is confirmed by data recently obtained in experiments with separation of the stomach from the central nervous system at different levels, with transection of the sympathetic and vagus nerves, with reflex action on the centers, and also with direct stimulation of various divisions of the brain.

The results of a pharmacological study of the effect of centrally acting agents on the periodic contractions of the stomach, performed in the laboratory under the direction of S. V. Anichkov, serve as important proof of the central nature of periodic activity. Observations showed that pharmacological blockade of the vegetative ganglia, as well as the action of the central cholinolytics at the synapses of the higher portions of the central nervous system, leads to cessation of the contractions of the empty stomach. In addition, substances acting predominatntly on the stem formations of the brain (aminazine, barbiturates, diphenine, korazol, antifein) manifest a clearer action on the periodic activity than substances of "cortical" activity: caffeine, uretane, chloralhydrate [2, 3, 8, 12, 13).

## Study of the Effects of Centrally Acting Pharmacological Substances When Injected into the Brain Stem of the Dog

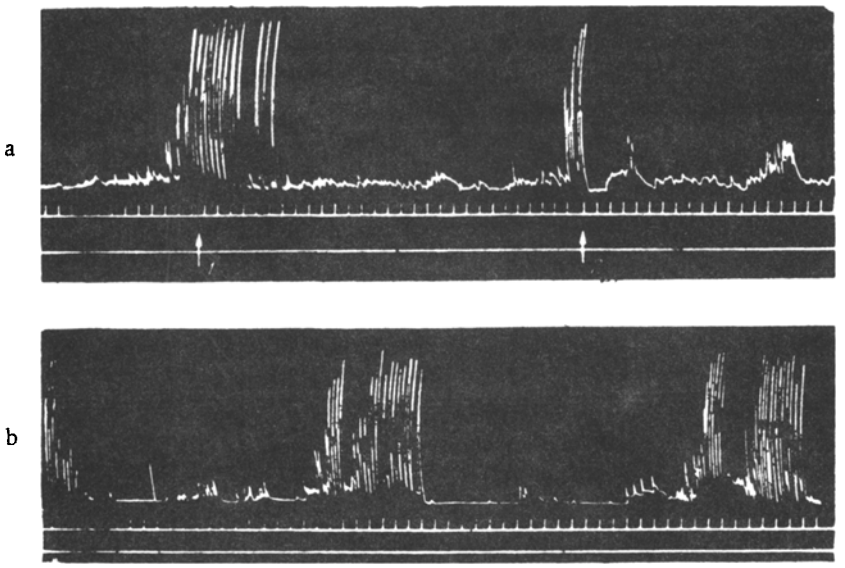
### EXPERIMENTAL METHOD

The substances were injected into dogs via the vertebral artery, through a polyethylene catheter, under long-term experimental conditions, following the method developed in the laboratory under the direction of S. V. Anichkov [11]. In essence, the substance injected into the artery of the brain, passing through the blood supply region and being absorbed there, acts directly on the centers. Histological investigation of the region of distribution of a stain within the brain following its injection into a cerebral artery has confirmed this hypothesis.

It has become possible to differentiate the peripheral action of a substance from the central: a centrally acting material, in doses that do not yield any effect when injected intravenously, showed a marked effect in the same doses when injected directly into an artery of the brain. The experiments were carried out on 4 dogs with catheters in the vertebral arteries.

The Effect of Morphine and Apomorphine. In 2 dogs that were operated on for these experiments intravenous injection of a small dose of morphine (0.06 mg/kg) and apomorphine (0.03 mg/kg), as a rule, caused extra contractions of the empty stomach. However, when these doses were injected into the vertebral artery such contractions did not arise, and the next period of stomach contractions was inhibited. When the same dose was injected into the artery of the brain stem, it proved to be too large, and caused a pessimal reaction of the centers. This became obvious after the doses of these substances were decreased by 15 times. After injection of 0.004 mg/kg of body weight into the vertebral artery there immediately arose an extra period of stomach contractions. When injected intravenously this dose did not cause any effect.

The Effect of Methyldiazil. Methyldiazil, a teriary ammonium compound, shows a marked inhibitory influence on the motor dynamics of the gastrointestinal tract [10], owing to its cholinolytic action. Following our method of injecting this preparation via different routes, we confirmed the central nature of its action on stomach contractions.




The effect of methyldiazil in a dose of 0.005 mg/kg (a) and adrenalin in a dose of 0.02 mg/kg (b), injected intravenously (1) and into the vertebral artery (2).

Doses of 0.003-0.005 mg/kg of body weight did not show an observable effect on the periodic contractions of the stomach when injected intravenously (see figure, a). When these doses were injected into the brain stem via the vertebral artery the stomach contractions immediately ceased, and subsequent periods of work were inhibited for a long period of time.

The Effect of Adrenalin. The ability of adrenalin to stop the periodic contractions of the stomach temporarily was described a comparatively long time ago [1], but the mechanism of this action is not sufficiently clear. It is known that adrenalin has a depressive peripheral action on the smooth musculature of the gastrointestinal tract. At the same time, the central, inhibitory effects on the stomach are exerted via the sympathetic (gastric) nerves, and the role of the adrenergic system of the central nervous system in stomach contractions has not been proven [4, 5].

In our experiments, following intravenous injection of 0.02 mg of adrenalin/kg of body weight the contractions of the stomach were inhibited for a course of 4-6 min. When this dose was injected into the vertebral artery the effect did not increase, and occurred in the same manner as regards duration and strength of inhibition of the motor activity (see figure, b). Subthreshold doses of adrenalin (0.003 mg/kg), which did not show any effect on the motor activity when injected intravenously, also failed to show an effect when injected into the brain stem. Thus, the inhibitory effect of adrenalin on the motor activity of the stomach is chiefly caused by its peripheral action.

## The Bioelectric Activity of Stem Formations of the Brain During Periodic Contractions of the Stomach and Under the Influence of Centrally Acting Neurotropic Agents

### EXPERIMENTAL METHOD

The EEG of the cortex and upper divisions of the brain stem were obtained in dogs simultaneously with baloonographic recording of the stomach contractions. The cortical electrodes were set in the mid-parietal region, the subcortical in the rostral divisions of the recticular formation of the brain stem at the level of the pons. The electrodes were inserted according to an atlas of the dog's brain (O. S. Andrianov, 1959), by means of calculations based on bone orientations following measurements of the cranium. In the experiment, we used 2 dogs with chronically attached

electrodes, specially selected according to characteristics of behavior and accustomed to a many-houred, stationary stance in the chamber. The potentials were conducted bipolarly through a cathode four-chambered amplifier, and recorded on an ink-writing apparatus.

The electrocardiogram was recorded simultaneously. A total of 26 observations were carried out. We failed to find any data in the literature on the character of the EEG during different phases of periodic activity of the stomach.

In comparing the nature of the EEG during the stomach's periods of "rest" and "work", in 20 of the 26 experiments we observed a clear difference in the bioelectrical activity of the brain. In the "work" period, the biopotentials of the stem divisions markedly increased their rhythm and intensified their amplitude. This intensification was most clearly observed at the beginning of the "work" period, often disappearing before its conclusion. The high-frequency, low-amplitude potentials were intensified on the EEG of the brain stem during the "work" period. The difference in the EEG for the periods of "rest" and "work" was expressed very clearly in certain experiments, while sometimes it consisted of only a minimal increase in the amplitude of the potentials. In the EEG of the cortex we did not observe any regular difference between the periods of "rest" and "work", although in certain experiments changes in the potentials occurred in the same direction as in the subcortical electrodes.

We demonstrated analogous changes in the character of the EEG (increase in frequency and amplidtude of the potentials) for the brain stem during the extra period of "work" for the stomach caused by the injection of small doses of morphine (0.06 mg/kg).

The injection of methyldiazil in doses of 0.1-0.2 mg/kg of body weight stopped the periodic contractions of the dogs' stomachs for several hours. Simultaneous with this, the EEG of the brain stem and cortex registered slow waves of high amplitude. In the period that the motor activity of the stomach was depressed by methyldiazil, the EEG retained the character typical for this action. We did not observe changes in the EEG even at the time when, according to calculations, a sequential period of stomach contractions was due to arise.

The neurotropic agents studied by us, both stimulatory (morphine, apomorphine) and inhibitory (methyldiazil) to the motor activity of the empty stomach, accomplish their effect on the medulla oblongata. Their action on motor activity appears to be central. In contrast to this, the inhibitory effect of adrenalin is peripheral.

Action by the central neurotropic agents directly on the brain stem can cause stomach contractions, or inhibit contractions that have already arisen. This is evidence that in the stem portions of the brain there are sensory formations, directly related to the periodic contractions of the stomach. Changes in the periodic contractions of the stomach under the influence of central neurotropic agents may be regarded as an index of the action of these substances on the subcortical, stem formations of the brain.

The biolectrical activity of the brain stem periodically changes. These changes occur simultaneously with the periodic contractions of the stomach, and principally at the beginning of them. Such changes in the biopotentials can be caused by the injection of morphine in doses that stimulate motor activity. By the injection of methyldiazil these changes can be eliminated for a long period of time.

## SUMMARY

Chronic experiments were performed on dogs. Pharmacological agents were injected into the vertebral artery of these animals. As demonstrated, substances stimulating the motor activity (morphine), as well as those inhibiting the motor (methyldiazil) proved to be several times more potent than when injected intravenously.

The bioelectric activity of the brain stem changed periodically simultaneously with periodic contractions of the stomach. The same changes in biocurrents could be induced by morphine administration or could be arrested for a long time by methyldiazil. The data obtained were a new confirmation of the idea of the central mechanism for the appearance and regulation of periodic body activity.

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