PHYSIOLOGICAL STUDY OF FUNCTIONAL PECULIARITIES OF THE NERVOUS SYSTEM OF GASTRIC CANCER PATIENTS

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(Received March 7, 1954. Presented by N. N. Petrov, Member of the Acad. Med. Sci. USSR).

Over the past few years it has been shown that considerable disturbances of the functional sections of the nervous system are to be found in persons with malignant or benign tumours. However, many of the essential features of the nervous mechanisms associated with the initiation, formation, and development of tumors still await elucidation. We have in this connection undertaken a systematic study of the functional features of the nervous system in various gastric diseases.

We here present the results obtained from the study of 57 men, 33 of whom had a diagnosis of stomach cancer, 12 of "precancerous" conditions (gastric polyposis, achlorhydric atrophic or hypertrophic gastritis), and 12 of other diseases of the gastro-intestinal tract (gastric and duodenal ulcer, gastritis with normal acidity).

Every patient was subjected to a thorough physiological-clinical examination on admission to the Institute and on discharge (usually after operation). Further examinations were made 2,6,12, and 18 months after discharge, so that in all the patients were under our observation for about 2 years.

As in our earlier researches, we applied encephalography to the study of the central nervous system (cortical and subcortical regions of the brain), and the methods of accommodometry and chronaximetry to examination of the peripheral nervous system. The electrical activity of the cerebral cortex was registered in the frontal, parietal, temporal, and occipital regions of each hemisphere, by a bipolar method, and of the subcortical regions using a basal electrode introduced through the posterior aperture of the nose into contact with the base of the skull.

The functional state of the peripheral nervous system was tested at each examination of our patients, by determining the accommodation indices and the chronaxie at the so-called motor points of the median and radial nerves of the arm, and of the flexor and extensor muscles of the fingers served by these nerves. Clinical and X-ray examination of the patients was performed at the same time.

The general physiological picture of the functional parts of the nervous system in gastric cancer patients conforms fully to our previously published results, disturbance of function of all parts of the nervous system being found. Encephalography data show that changes in the activity of the cerebral cortex consist in lowering of the magnitude of all the bioelectric potentials, in particular of the alpha-waves. The absolute frequency of the alpha-waves falls to 7 1/2 or even 7 per second (minimum). In functional tests (reaction to light) a lowering of cortical reactivity is also found.

A second specific feature of encephalograms from gastric cancer cases is the presence of slow waves, of a frequency of about 2-3 per second, which become more accentuated as the disease progresses, and are most marked in very advanced, inoperable cases (Fig. 1).

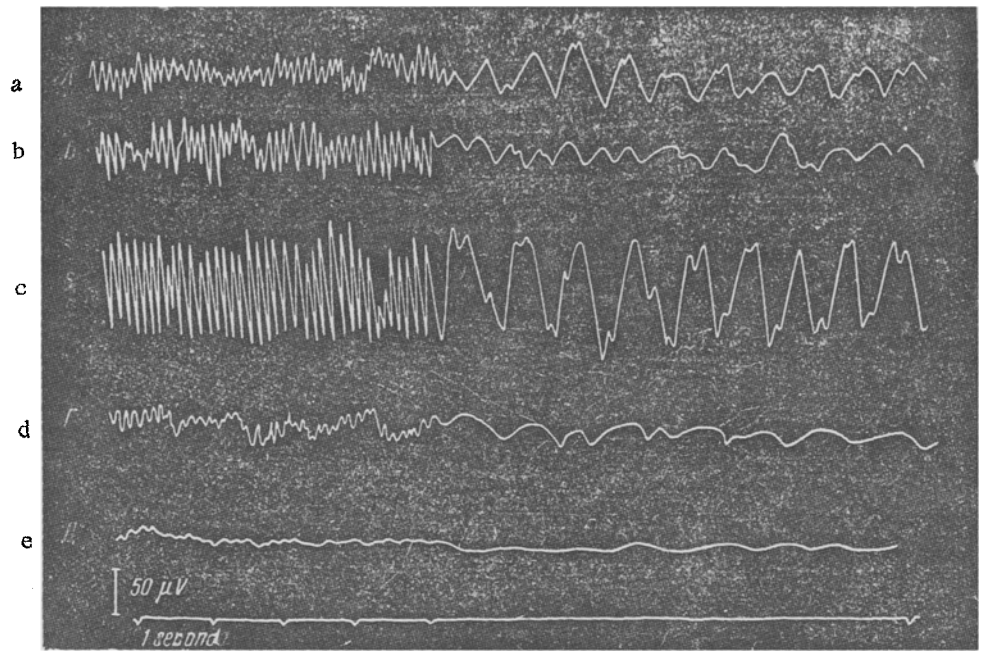

Fig. 1. Electrical activity of the cerebral cortex (right occipital region) of patients with diseases of the stomach. A) electroencephalogram of a healthy person. B) from a case of gastric ulcer. C) from a case of polyposis D) stomach cancer, stage I-II E) stomach cancer, stage IV. Lowest tracing is the time base (seconds).

The basic, qualitative aspect of the functional changes was the same for all the cortical areas of our cancer patients.

Characteristic changes also appear in the electrical activity of the subcortical regions of cancer patients. Stage I and II cancers give clearly expressed intensification of subcortical activity, while in stages III and IV the height of the potentials falls progressively.

The frequency of the subcortical waves in early gastric cancer is relatively high, and is variable; it diminishes as the disease progresses to the III and IV stages (Fig. 2).

Considerable increase in accommodation (100 msec and more) is found in stages I and II, leading to a flattening of the accommodation curves. In the more advanced stages of cancer the changes in accommodation bear a qualitatively different character; the lambda values diminish (to 20 m sec or less), and the inflexed accommodation curves become convex. The change from the first to the second type passes through a more or less prolonged transition stage, through a zero level at which the accommodation indices are numerically identical with those for healthy subjects; we found that this transition stage usually occurs in stage III cancers.

It thus appears that the changes in accommodation and in subcortical activity during development of cancer manifest themselves as a regular diphasic process. The second phase is found with great regularity in advanced cancer, and may provide an indication for an unfavorable prognosis (Fig. 3).

It should be noted that transition from the first to the second phase of accommodation changes may be encountered at different stages of progress of the disease in different patients. Even in a particular patient the transition does not take place simultaneously for different innervational systems; its onset is earlier in less stable systems.

Diphasic changes are observed in the magnitude of the so-called subordinational accommodation index during the course of gastric cancer. During stages I and II it rises to values of up to three times the normal.

This is succeeded by reversion to unity, indicating equalization of accommodation of antagonistic innervational systems. Since the magnitude of the subordinational index reflects the activity of the brain stem, these findings are additional evidence of the diphasic development of changes in activity of the subcortical regions of the human brain during the course of stomach cancer.

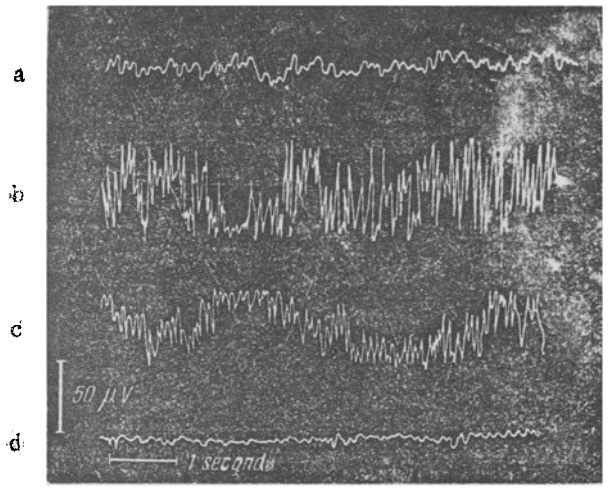

Fig. 2. Electrical activity of subcortical regions of the brain of persons suffering from gastric diseases. A) electrogram taken from a healthy person B) from a polyposis patient C) I-II stage gastric cancer D) stage IV cancer. Time scale: 1 second.

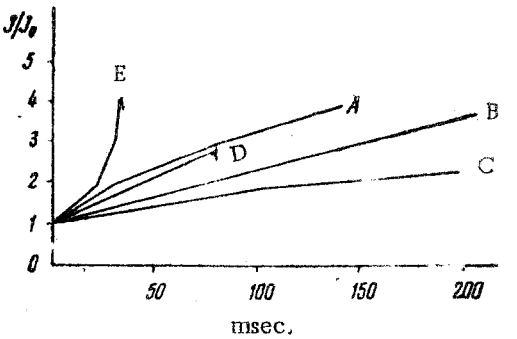

Fig. 3. Accommodation of the nervous system in patients with gastric disease. A) indices for healthy persons B) for gastric polyposis patients C) for stage I-II cancers D) for stage III cancer E) for stage IV cancer.

Changes in chronaxie are not so clearly defined; it can only be said that there is a tendency toward increase during the course of cancer.

Deviations from the above described regularities, such as enhancement of electrical activity of the cortex in advanced cancer, have been observed in isolated cases, and these require special consideration.

Cancer progressing to a fatal termination exhibits regularly increasing disturbance of function of the nervous system. The electrical activity of the cortical and subcortical regions of the brain diminishes progressively. Depression of electrical activity of the cortex, with enhancement of subcortical activity and lengthening of accommodation parameters, found in patients with early cancer, is succeeded, as the disease progresses, by depression of subcortical activity and shortening of accommodation parameters, with corresponding change in the accommodation curves, from concave to convex. These changes constitute the second phase of shifts in the functional state of the cortex and subcortical regions. Successive examinations of patients sometimes reveal the transition period from the first to the second phase, during which there is a transient deceptive normalization of individual functional indices of the nervous system.

Radical operative treatment is followed by reversion of the functional condition of the nervous system to normal, and this process is the more marked the earlier the stage of physiological change in nervous activity at which the operation is performed. We have not been able to observe even partial restoration of normal nervous activity in patients operated during the second phase of the process.

Further disturbance of the activity of the nervous system, characteristic of developing cancer, is found regularly soon after operation when this is not followed by improvement in the state of the patient.

We have not encountered full restoration of normal functional relations even after the most radical operations, although partial reversion towards the normal takes place during the subsequent 12 to 18 months.

The physiological findings usually correspond with those of clinical examination. Deviations are generally differences of degree only, indicating the great sensitivity of physiological methods of assessing the condition of patients.

Repeated examinations were made over a period of two years of 24 patients with non-malignant stomach disease; of those 12 had "precancerous" conditions (polyposis, achlorhydric hypertrophic and atrophic gastritis), and 12 suffered from other diseases of the alimentary tract.

The indices of functional state of the nervous system of patients with "precancerous" conditions differed significantly from those for cancer patients (Fig. 3). Depressed electrical activity of the cortex, which is so typical of cancer, was encountered in only 2 of 12 cases, and was of lesser degree. The amplitude of the bioelectric waves was above the normal in 7 cases, while the remaining three gave variable electroencephalograms on different occasions, with mean potentials not differing appreciably from the normal.

The frequency of the alpha-waves is somewhat higher than in cancer (up to 8.5 per second). A characteristic feature of the electroencephalogram in precancerous states is the presence of so-called transitional rhythm of a frequency of 14-17 per second. Such frequencies are only very exceptionally encountered in cancer, in the early stages only. The amplitude of the subcortical electrical activity was found to be slightly raised in half of the precancerous state patients, and not to deviate significantly from normal in the other half. The basic frequency was somewhat higher than in cancer patients.

Changes in accommodation of the peripheral nervous system were similar in nature to those encountered in stage I cancer, but were of smaller degree. The accommodation parameter λ was raised to a smaller extent, and this increase applied only to the functionally more labile innervational systems. Chronaxie of the nervous system is variable in "precancerous" conditions, being not uncommonly smaller than for cancer patients, or even for healthy controls. The subordination indices found in "precancerous" states are somewhat higher than the normal values.

The changes encountered in the functional state of the nervous system of patients suffering from non-malignant disease of the gastro-intestinal tract resemble those of the "precancerous" state, but are of smaller degree.

The data here presented confirm the conclusions made in our earlier publications, and permit of the drawing of further additional conclusions.

The development of malignant tumors of the stomach is associated with progressive changes in the functional sections of the nervous system. These changes appear in the cerebral cortex in the form of progressive depression of its electrical activity. That of the brain stem undergoes a diphasic change during the progress of the disease; raised activity found in the earlier stages is succeeded by depression of activity in the later stages. Changes in the peripheral nervous system are of the same diphasic nature.

The results of clinical examinations of patients are in conformity with our experimental results for transplanted tumors. Our chronic experiments, performed on rabbits and white mice, showed that the growth of transplants is associated with the same typical diphasic changes in activity of the nervous system.

Our study of both of these phases permits us once again to draw the conclusion that the nervous mechanisms of development of malignant tumors are physiologically of the nature of a parabiotic process. Viewed in the light of N. E. Vvedenskii's teachings on parabiosis, the nervous mechanisms of cancerous and precancerous conditions manifest themselves as separate phases and stages of a single process.

Our findings allow us to draw the conclusion that one of the ways to combat cancer should be the introduction of prophylactic and hygienic measures designed to fortify the nervous system, and to raise the functional mobility of nervous processes.