AN ELECTROPHYSIOLOGICAL INVESTIGATION OF THE STATE OF THE CENTRAL NERVOUS SYSTEM IN EXPERIMENTAL BRUCELLOSIS

I. I. Polyakov and K. M. Mokhin

From the Laboratory of Pathophysiology (Head – Candidate of Medical Sciences K. M. Mokhin) of the Rostov Scientific-Research Antiplague Institute (Dir. – Candidate of Medical Sciences A. K. Shishkin) of the USSR Ministry of Public Health
(Presented by Active Member of the Akad. Med. Nauk SSSR N. N. Zhukov-Verezhnikov)
Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 53, No. 2, pp. 52-57, February, 1962
Original article submitted February 17, 1961

It is known, from numerous clinical observations, that the brucellosis infection is associated with well defined pathological phenomena, related to disturbances in the activity of the nervous system. Investigations, employing clinico-physiological methods, have indicated the presence of profound functional disturbances in the cerebral cortex associated with brucellosis [1, 8, 9, 10]. However, clinical observations do not make it possible to study the complete dynamics of the functional changes in the cerebral cortex of patients with brucellosis, nor the effect of different therapeutic methods on the upper divisions of the central nervous system.

Our goal was to study the state of the central nervous system in brucellosis, using the method of electroencephalography.

EXPERIMENTAL METHOD

Electrodes made of Nichrome wires 0.25 mm in diameter were set in place in the occipital division of the cerebral cortex of guinea pigs. The distance between electrodes was equal to 4 mm. Fixation of the electrodes was accomplished by the use of dental phosphate - cement. Recording of the bioelectric potentials was carried out on a phototape, using a loop encephalograph. The apparatus permitted passage of frequencies within the diapason of 0.3 to 500 cycles per second. The electroencephalograms were photographed on a film moving a rate of 50 mm/sec.

The experiments were performed on 20 guinea pigs, inoculated subcutaneously with Br. melitensis, strain No. 1098, using a dose of 500 microbial cells. The injection was administered 3 weeks after implantation of the electrodes. The biopotentials were recorded before the inoculation, and during the development of the infectious process.

At the same time, another group of animals (14 guinea pigs), inoculated at the same period and with the same dose of brucella, were used for determinations of the immunobiological reactivity (the reactions of Heddleson and Wright, the Bjorne test, opsono-phagocytic activity of the leukocytes) and the bacteriology of the infectious process.

Regular measurements of the rectal temperature were carried out in both groups of experimental animals, using an electrothermometer.

EXPERIMENTAL RESULTS

A temperature reaction in the animals began to be observed on the 15-20th day following the inoculation. Immunological reactions began to appear 10 days after the inoculation, in the following order: the Heddleson reactions, the Wright reactions, opsono-phagocytic activity, and 20 days after the inoculation, the allergic skin test. At 30 days after the inoculation the indicated reactions attained their most positive levels.

Up until the 10th day after the inoculation, the brucellae were manifested only in the regional lymph nodes. Subsequently (10th-15th day), brucellae were observed in distant nodes and in the spleen. At 20 days after the inoculation, brucellae were grown out of seedings from the majority of organs, i.e. the infection became generalized in character. After 50-80 days, the number of positive seedings from the organs, as well as the number of brucella colonies that grew out, decreased markedly. Analysis of the electroencephalogram (EEG), recorded prior to inoculation of the animals, showed that the bioelectric activity of the brain in the healthy guinea pigs was represented basically by waves with a frequency of 8-14 per second, and an amplitude of 18-25 microvolts, sometimes interrupted by slower waves (3-7 per second) with an amplitude of 40-50 microvolts. In a series of experiments, the basic bioelectric activity was expressed in low amplitude (10-15 microvolts), rapid waves with a frequency of 25-40 pe. second. A repeat recording of the biopotentials showed that the bioelectric activity was relatively stable for each experimental animal.

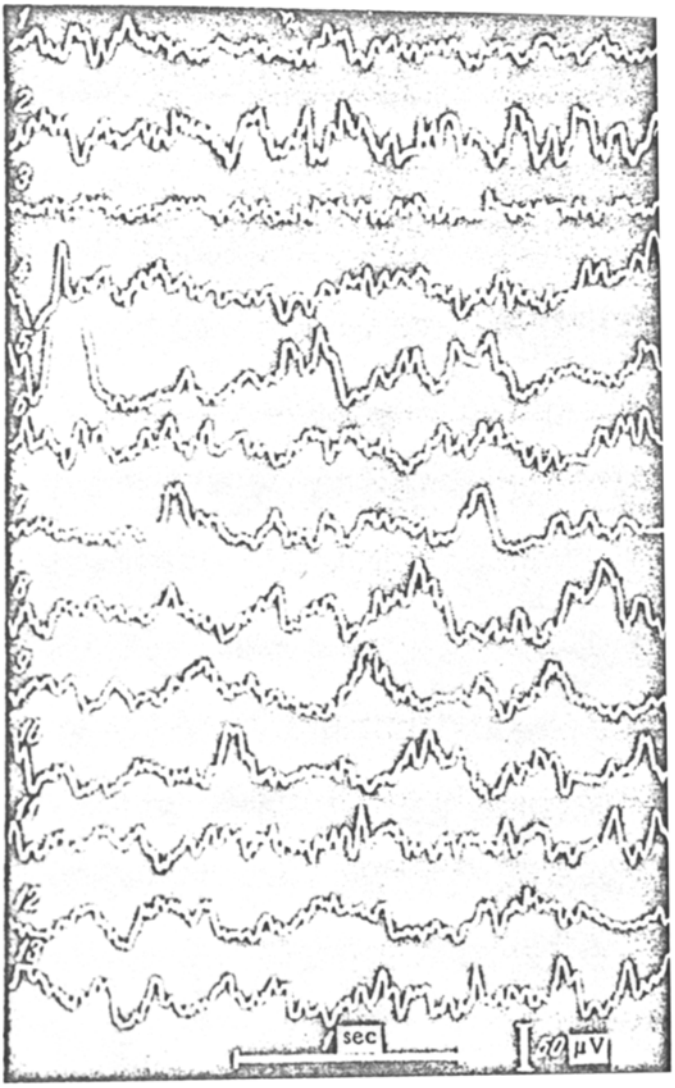

Fig. 1. Electroencephalograms from guinea pig No. 4325, inoculated with brucella. 1) Before inoculation; 2-13) after inoculation; 2) after 5 days; 3) after 10 days; 4) after 14 days; 5) after 17 days; 6) after 23 days; 7) after 26 days; 8) after 28 days; 9) after 31 days; 10) after 34 days; 11) after 38 days; 12) after 43 days; 13) after 57 days.

In the majority of cases, a topographical change in the bioelectric activity of the guinea pigs' cerebral cortex occurred as early as the 1st-3rd day after the inoculation. These changes expressed themselves by a shift in the frequency spectrum toward the slower side, and an increase in the amplitude of the biopotentials. The tendency toward similar changes in the biocurrents of the brain subsequently increased, and by the 5th day, we recorded slow (2-4 per second), high waves with an amplitude of 60-100 microvolts in all the experimental animals.

This reaction of the bioelectric activity to implantation of a virulent strain of brucella into the organism occurred only in the first 5-6 days after the inoculation; it was then replaced by a depression of the bioelectric activity. When the biopotentials were recorded on the 10th-11th days, their intensity was lower than it was in the normal state. In the majority of cases, the depression was observed during the following 3-8 days. Beginning with the 17-25th days after the inoculation, after the depression of the bioelectric activity, there again occurred an intensification in the

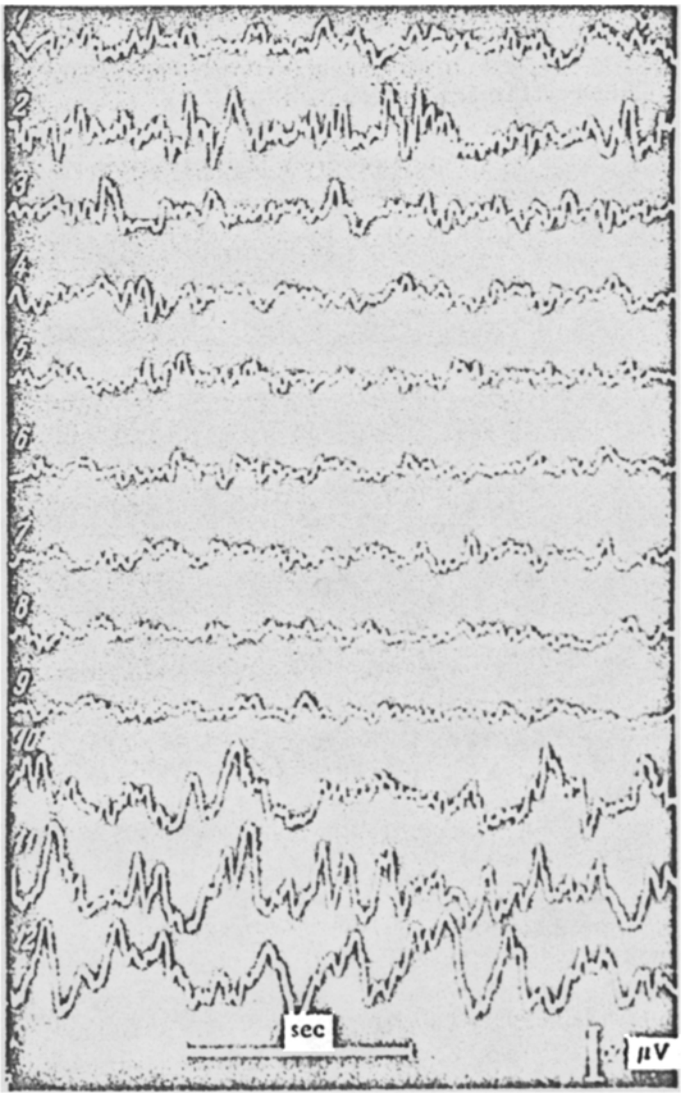

Fig. 2. Electroencephalograms of guinea pig No. 4324, inoculated with brucella. 1) Prior to inoculation; 2-12) after inoculation; 2) after 5 days; 3) after 14 days; 4) after 17 days; 5) after 21 days; 6) after 25 days; 7) after 28 days; 8) after 31 days; 9) after 34 days; 10) after 38 days; 11) after 43 days; 12) after 57 days.

majority of the pigs (15 out of 20). During this period, slow pathological waves, with a frequency of 2-5 per second and an amplitude of 80-130 microvolts, were dominant (Fig. 1). Along with these waves, we sometimes noted rapid, isolated bursts, or low (10-15 microvolts), high frequency waves.

In 5 of the animals, lowering of the bioelectric activity was observed up until the 30-35th day of the infectious process; then the activity was intensified sharply, with the appearance of slow, high, waves (Fig. 2).

It is interesting to note that, within the dynamics of the brucellosis infection, the EEG sometimes showed alternation of the slow waves with periods of marked depression of the bioelectric activity.

Thus, it is apparent from the data presented that during the period of generalized infection there is an appreciable disturbance of the brain's bioelectric activity, manifested by the appearance of slow, high-amplitude waves or a sharp depression of the bioelectric activity.

As the infectious process developed and crossed into the chronic form (50-80 days after the inoculation), the dominant wave of the EEG in all experiments became the high (100-150 microvolts), slow (2-5 per second) oscillations, sometimes interrupted by low, rapid-frequency waves. In a number of the experiments, the most pronounced changes in the bioelectric activity were recorded during this period (Fig. 2 and 3).

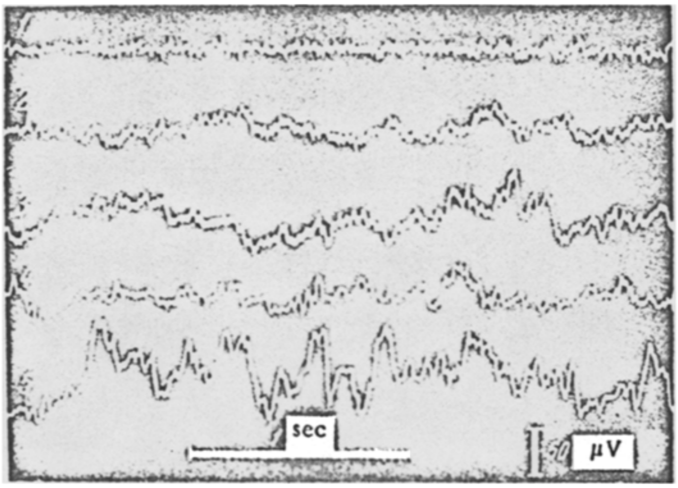

Fig. 3. Electroencephalograms of guinea pig No. 1363, inoculated with brucella. 1) Prior to inoculation; 2-5) after inoculation; 2) after a day; 3) after 33 days; 4) after 65 days; 5) after 80 days.

Comparison of the dynamics in the changes of the brain's bioelectric activity with the immunobiological, bacteriological, and temperature indices showed a high sensitivity of the central formations of the nervous system to the introduction of the pathogens of brucellosis into the organism. While the changes in the brain's bioelectric activity were noted as early as the 1st day, and especially were topographical by the 5th day after the inoculation, shifts in the immunobiological reactivity and temperature reaction were not yet observed at that time, and the brucellosis pathogen was still found either at the site of injection or in the nearest regional node. It must be postulated that the reaction of the central nervous system to introduction of brucella into the organism, is, at this time, the result of stimulation of receptor formations, located in the tissue at the site of localization of the injected brucellae. The possibility cannot be excluded, however, that it is also caused by passage of small doses of antigenic substances included in the composition of the brucella microbe, from the site of injection into the general blood stream causing stimulation of receptor formations in the vascular system and other links in the neuroreflex arc.

With multiplication of the brucellae and increase of the degree of antigenic stimulation, the functional state of the central nervous system also changed, which was reflected by the onset of a depression of the biocurrents on the 10-11th days. With further development of the infectious process, when the major changes start to occur in the immunobiological reactivity, including patent sensitization of the organism and increase in the intensity of antigenic stimulation secondary to generalization of the infection, more pronounced functional changes are noted in the central nervous system. These changes involve the vegetative functions of the organism, and in particular, lead to shifts in thermoregulation. At this time, the EEG shows high, slow waves, or marked depression of the bioelectric activity.

This electrophysiological picture accompanies the entire period of the infectious process, becoming especially topographical in appearance with transition of the disease to the chronic stage.

According to contemporary viewpoints, these types of disturbances in the bioelectric activity may be regarded as a sign of the development of inhibitory processes in the central nervous system [2-7, 11].

It must be noted that the appearance of pathological, slow waves in our experiments was not related to a temperature reaction in the organism, but was rather a reflection of the toxic effect of certain substances formed in association with the brucellosis infection.

Thus, the presented, comparative investigations of the functional state of the central nervous system, immunobiological reactivity, bacteriology of the infectious process, and temperature state in guinea pigs inoculated with brucella showed that with introduction of brucella into the organism the first changes that occur are noted in the central nervous system, and then afterward there occur corresponding shifts in the immunobiological reactivity and thermoregulation. The most marked changes in the activity of the cerebral cortex of the guinea pigs inoculated with brucella were observed during the chronic stage of the disease.

SUMMARY

Experiments were performed on guinea pigs infected with Br. melitensis strains. Cerebral biocurrents and immunobiological reactivity were studied in dynamics. Already on the 3rd-5th day after the injection the presence of an electrophysiological reaction of the brain cortex was noted in the form of marked activation of the biopotentials; on the 10th-11th day it was replaced by depression of biocurrents. Later, in the majority of experiments there was a considerable increase of the biocurrent amplitude with the appearance of slow waves (2-5 per sec.). Such EEG shifts are the most marked at the chronic stage of the disease. Comparative investigation of the functional CNS state, immunobiological reactivity, infectious process bacteriology, and body temperature in brucellosis infected guinea pigs have demonstrated that the first response to invasion of brucella into the organism were changes in the central nervous system, followed by corresponding shifts in immunobiological reactivity and thermocontrol.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
