ELECTRICAL ACTIVITY OF THE CEREBRAL HEMISPHERES AFTER SECTION OF THE BRAINSTEM (BREMER'S METHOD) IN DOGS OF VARIOUS AGES

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In previous investigations in our laboratory we found that there are great differences between the electrical activities of the two cerebral hemispheres of young puppies and mature dogs. In the young puppies the most characteristic feature is the low frequency during the waking state and the absence of that alteration of the EEG rhythm which is characteristic of adults during natural sleep, or under the influence of aminasin or small doeses of barbiturate (sodium amytal and medinal). When in this condition, there were no indications of a state of anesthesia. An increase of the sodium amytal or medinal doses in the young puppies caused an early collapse associated with a gradual depression of electrical activity, which disappeared completely within two hours of the injection [1-5,8].

We share the modern view of the role of the ascending activating reticular system of the brainstem and the nonspecific nuclei of the thalamus in controlling the electrical activity of the adult cerebral cortex (whether in the waking state or in natural or barbiturate sleep) [9,12-16]; in order to analyse the laboratory results we decided to investigate the EEG of dogs of various ages after transverse section of the brainstem at various levels corresponding to Bremer's encéphale isolé and cerveau isolé preparations.

EXPERIMENTAL METHOD

We have studied puppies at ages when the characteristic features of the electrical activity were most marked. The first group consisted of 20 puppies aged between 4-5 and 8-9 days, and the second of 11 puppies of 18-20 to 26-27 days and the third of 9 pups aged 2-3 months. In previous investigations we have found that at the age of 2-3 months the EEG comes to resemble closely that of the adult animal. In each puppy we made a series of transections at both levels of the central nervous system. The animals were not fixed to the stand. To maintain the temperature constant the young puppies were placed on a heated slab. The animals were rendered motionless for the required time (while artificial respiration was maintained) by intravenous injection of 0.01-0.02% myorelaxin given in an amount sufficient to ensure an effect for 10-15 minutes. Cortical electrical activity was recorded from the frontal leads by means of needle electrodes; the recordings were made immediately after the injection of myorelaxin, and after the two transections. Then, in the encéphale isolé preparation the EEG was recorded until a clear manifestation of the "waking head" was obtained. As a further indication of the animal's condition we simultaneously recorded the ECG (lead II).

To obtain the encéphale isolé preparation we dissected out the atlanto-occipital membrane, and to make the cerveau isolé we trepanned an opening in the occipital region (close to the midline). To avoid damage to the brain the dura was divided as close as possible to the edge of the cerebral hemisphere. The transection was made by a spatula of a size appropriate to the age of the animal; the spatula curved round the edge of the cerebral hemisphere, passed along the tentorium as far as the corpora quadrigemina. Confirmation of the site of the transection was made after each experiment by opening the cranium.

EXPERIMENTAL RESULTS

Bremer originally found that after bulbospinal transection cortical activity in the cat retained a typical waking pattern, whereas transection at midbrain level caused an alteration of the rhythm to the sleep pattern. In the first case the behavior was that of the "waking head," while in the second the condition was one of sleep [10]. Further studies

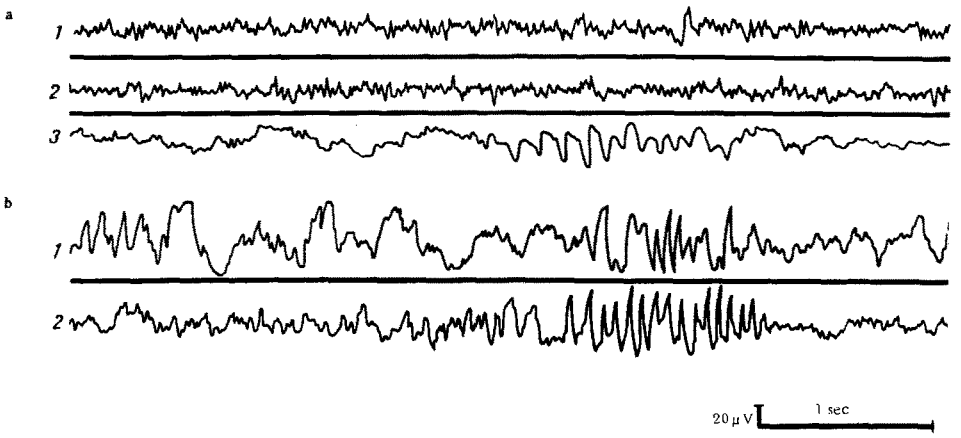

Fig. 1. Electroencephalograms. a) Three-month-old-puppy; 1) in the waking condition; 2) after transection of the spinal cord below the medulla (encéphale isolé preparation); 3) after division of the midbrain (cerveau isolé preparation); b) 2-3 -month-old puppy; 1) during natural sleep; 2) under barbiturate sleep.

[12-16] caused several authors, and Bremer [11] to interpret sleep after mesencephalic transection as a result of separation of the diencephalon from the ascending activating reticular formation of the brainstem which cut it off from the flow of afferent impulses.

In puppies of the third age group transection between the medulla and the spinal cord (encéphale isolé preparation) produced the effect of a "waking head": the eyes were open, the ears in the alert position, and the blink reflex was well shown. In this condition the EEG recorded high frequency electrical activity of the β-rhythm type characteristic of the waking condition at this age (Fig. 1, a, 1, 2).

At the next midbrain transection (most of the divisions were made through the corpora quadrigemina) the effect of a "sleeping head" was obtained: the eyes were closed, there was no blink reflex, and the head and ears hung down limply. In this condition the EEG consisted of slow high-amplitude oscillations of the Δ-rhythm type alternating in many cases with others which resembled the α-rhythm (Fig. 1, a, 3).

The resemblance of the EEG obtained under these conditions to that obtained by Bremer on the cerveau isolé of adult animals. We also observed this kind of electrical activity in animals of the same age in either natural or barbiturate-induced sleep (Fig. 1, b, 1, 2).

A completely different state of affairs was found in the younger group of puppies (first group). Division of the spinal cord below the medulla produced certain indications of the "waking head" (there was a well-marked blink reflex, and head movement); there were however no high-frequency oscillations of the β-rhythm type. In this condition the electrical activity recorded was a similar frequency to the activity found in a younger age group in the waking state, but the amplitude was rather less (Fig. 2, a and b).

The next division of the midbrain produced no consistent picture. The behavior and EEG at this age depended upon the site of the transection. If it was made between the corpora quadrigemina or at the level of the posterior quadrigemina, a condition of deep sleep was produced: the blink reflex disappeared, and the head hung down. In this case the change of rhythm characteristic of the cerveau isolé was not recorded. The electrical activity of the cerebral cortex showed no change in frequency, and was periodic (Fig. 2, c). Under natural conditions we found such periodicity only in puppies during their first three days of life.

Under conditions when transection of the midbrain was made at the level of the anterior quadrigemina, a state of collapse set in resembling the condition found when large doses of barbiturates are given. One of the typical signs in the condition of collapse was that the jaws made stretching and chewing movements while the head was bent back. Under these conditions the chewing movements appeared immediately after the transection. There was no change in the frequency of the electrical activity of the cortex, but it disappeared completely for the first five minutes after the transection, and did not recover during more than one hour of observation, whereas the frequency of the heart beat remained within normal limits (while the body temperature was maintained artificially at 35-36°) (Fig. 2, d).

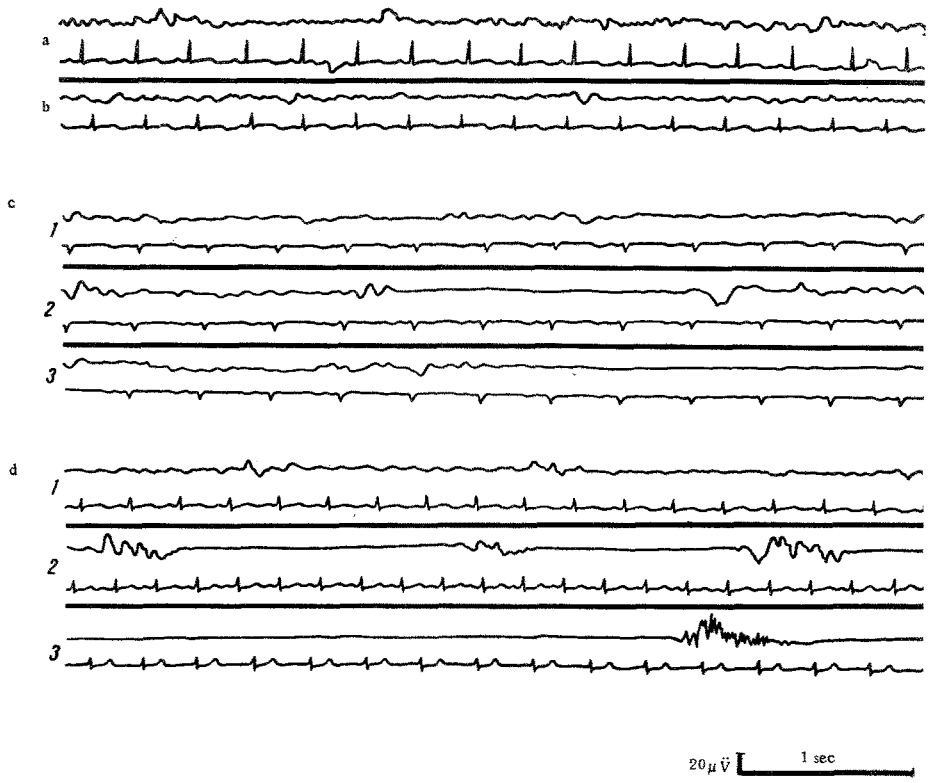

Fig. 2. EEG and ECG of puppies 7 and 8 days old. a) In the waking condition; b) after division of the spinal cord below the medulla; c) after division of the midbrain at the level of the posterior corpora quadrigemina: 1) after 15 minutes; 2) after 30 minutes; 3) after 45 minutes; d) after division of the midbrain at the level of the anterior corpora quadrigemina: 1) after 1-2 minutes; 2) after 5 minutes; 3) after 45 minutes (artifacts due to chewing movements can be seen).

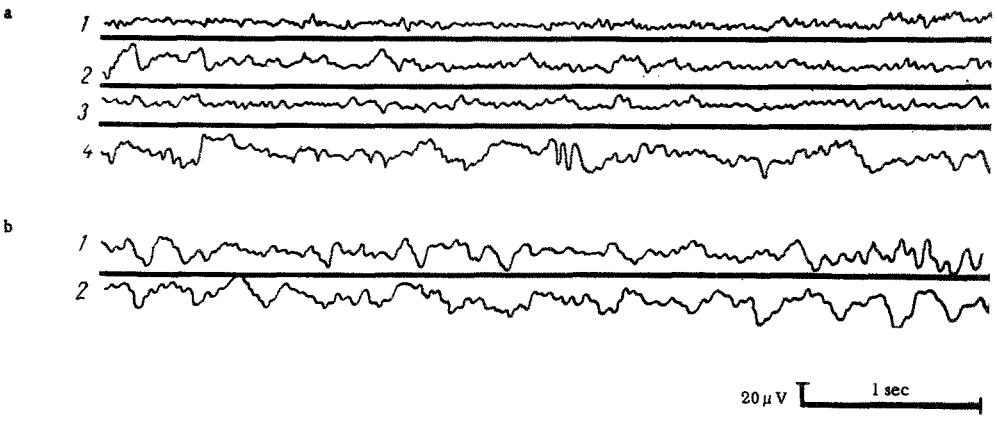

Fig. 3. Electroencephalograms. a) 22-day-old puppy: 1) in the waking condition; 2,3) after transection of the spinal cord below the medulla; 4) after transection of the midbrain; b) puppies of the same age: 1) in a condition of natural sleep; 2) in barbiturate-induced sleep.

Prolonged function of the cardiovascular and respiratory systems while indications of vital function, as indicated by the electrical activity of the cerebral cortex (EEG), were found previously by us in young puppies during protracted collapse induced by various influences, including: staphylococcal and dysenteric poisoning [6,7], and lethal or sublethal doses of barbiturates [4].

Therefore in the young puppies we did not find the situation occurring in many old animals and which is characteristic of the Bremer encephalé isolé and cerveau isolé preparations. The first indications of a relationship between behavior and EEG, as present in the Bremer preparation, was found in puppies which had reached an age of 18-20 days (second age group). As we had demonstrated previously [3,5], the EEG at this stage shows an interruption: there is a progressive increase in the frequency of cortical activity during waking, and the first change consists of an alteration of the rhythm giving rise to a low-frequency high-amplitude potential resembling closely what is found in adults during natural sleep, or in sleep induced by barbiturates or by aminasin.

In puppies of the second age group, transection of the brainstem at the lower border of the medulla caused signs characteristic of the "waking head." The EEG recorded electrical activity close in frequency to what was observed in animals of this age during the waking state (Fig. 3, a, 1, 2, 3). However,as can be seen from the EEG reproduced here, this activity is not maintained, and is replaced by one more in accordance with the sleeping condition. The frequency of oscillation then depends directly on the extent to which the blink reflexes developed.

Transection at midbrain level, usually at the level of the anterior corpora quadrigemina,induces a condition of "sleeping head," and on the EEG there appear slow oscillations characteristic of natural or barbiturate sleep at this age (Fig. 3, a, 4, and b, 1, 2).

These results taken in conjunction with the changes in cortical electrical activity which we found previously in puppies of the earlier age group lead us to suppose that in dogs, up to a certain age, none of those mechanisms are present which, in the adult, give rise to a change of frequency in the EEG and which are related to the functional condition of sleep, waking, and to the influence of barbiturates and aminasin.

The fact that after transection of the brainstem at the level of the anterior corpora quadrigemina the cerebral cortical activity disappeared while the heartbeat remained within normal limits indicated that function of the medial thalamic nuclei, i.e., function at a thalamocortical level, was not established as it is in adult animals. We had previously observed [4] that a state of collapse induced by large doses of barbiturates, and by certain bacterial extracts [6,7] caused the same disappearance of cortical activity while function at lower levels, particularly at a bulbar level, was preserved.

Also, maintenance of electrical activity in the cortex when the transection of the brainstem was made at the level of the posterior corpora quadrigemina indicated the important role of the rostral portion of the reticular portion of the brainstem in the maintenance of this activity, which is characteristic of both sleeping and waking conditions at an early age. The low frequency electrical activity recorded in the young age group in the waking condition and in encéphale isolé preparations indicates also the characteristic functioning of the ascending reticular formation at this age.

The correspondence between the EEG and behavior characteristic of adults as observed after the 18-20th day appears to show that the onset and change of activating function of the ascending reticular formation is related to an increase of afferent impulsation which is,in turn,assocated with activity and reorganization of many of the analyzers at the new level. Then the medial thalamic nuclei take on a function resembling that of the adult animal.

SUMMARY

The EEG was studied in puppies of various ages after the brainstem had been divided at various levels by Bremer's method. In puppies 2-3 months old there was a complete correspondence between the EEG and behavior, just as in encéphale isolé and cerveau isolé preparations of adult dogs. In 8-9-day-old puppies the EEG did not correspond to that found in the two preparations of adult dogs. Division of the midbrain through the anterior corpora quadrigemina which correspond to the cerveau isolé preparation of adults was accompanied in young puppies by the immediate disappearance of electrical activity from the cerebral hemispheres. The first indications of an EEG characteristic of the encéphale and cerveau isolé preparations of adult dogs occurred after the 18-20th day.

Young puppies manifest the characteristic electrical cortical activity found in encéphale isolé and cerveau isolé preparations of adult dogs; the explanation proposed is in terms of the ascending reticular activating system of the brainstem and the absence of any function in the nonspecific nuclei up to a certain stage of development.

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