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CORTICAL ELECTRICAL ACTIVITY OF HUNGRY DOGS WITH NORMAL AND DISTURBED GASTRIC INNERVATION

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KEY WORDS: electrocorticogram; peristaltic movements of the stomach; hunger motivation.

Chronic experiments on hungry waking dogs in an ordinary laboratory situation have revealed a periodic increase in activation of the cerebral cortex which corresponds to periods of gastric contractions [4, 9, 12]. Under conditions of relative isolation from external stimuli activation of the electrocorticogram (ECoG) in such dogs was found only during periods of gastric contractions, whereas at rest slow-wave high-amplitude activity predominated [6, 8].

The level of nutrient substances in the blood, controlled by subcortical structures of the food center [11], and interoceptive impulses from the stomach and intestine [1, 2, 5] are considered to be the trigger stimuli which modify electrical activity of different parts of the cortex in hungry animals.

Considering the possible role of the vagus nerves in regulation of the level of hunger motivation, the dynamics of changes in cortical electrical activity was analyzed in dogs with intact and disturbed gastric innervation, and in a state of prolonged physiological hunger.

EXPERIMENTAL METHOD

Altogether 700 electrocorticograms obtained in chronic experiments on six hungry dogs were analyzed. All the dogs had fistulas of the gastric fundus, and bipolar electrodes implanted symmetrically into the cranial bones on the right and left sides. Automatic analysis of ECoG frequencies was carried out with an MAF-4 analyzer connected with an encephalograph (Nihon Kohden, Japan), with electrodes corresponding to projections of the motor cortex of the right and left hemispheres (RH and LH respectively) in two channels simultaneously. ECoG frequencies were analyzed in five bands: 2-4, 4-8, 8-12, 12-20, and 20-30 Hz, which will subsequently be called bands I, II, III, IV, and V. During continuous monitoring of peristaltic movements of the stomach (PMS) on a kymograph, 3-5 ECoGs were recorded during contractions and 6-8 ECoGs during rest of the stomach. In experiments which lasted from 10 a.m. to 6 p.m., 4-6 cycles of PMS and no fewer than 30 RCoGs, each in 3-5 10-sec epochs, were recorded. The dogs were fed at 11 a.m. on the previous day but not on the day of the experiment.

Selective distal vagotomy (SDV) was performed on two of the six dogs 5 months before the experiments [3, 10]. A full description of the method, the experimental conditions, technique of the SDV operation, and analysis of the results will be found elsewhere [3, 6, 8, 10].

The results were subjected to statistical analysis in two versions. In the first (190 ECoGs obtained in experiments on three healthy dogs and 230 ECoGs in experiments on two dogs after SDV) ECoGs of RH and LH were grouped together, without reference to PMS, during each

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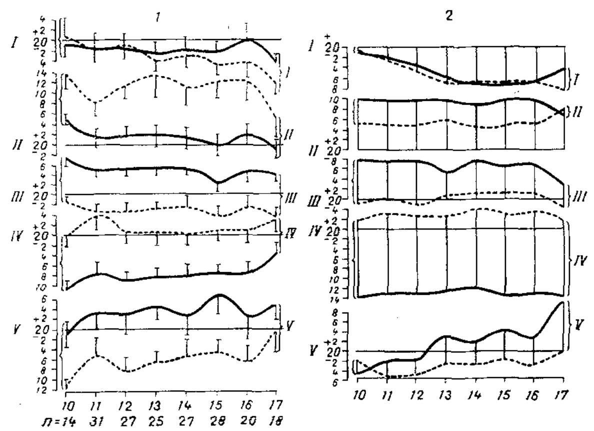

Fig. 1. Combined hourly time course of cortical electrical activity of the right and left hemispheres in dogs with normal (1) and disturbed (2) gastric innervation. From top to bottom: mean weighted coefficients of contributions of frequency bands I-IV to total cortical electrical activity of right (continuous line) and left (broken line) hemispheres. Abscissa, time of day. Coefficients counted on vertical time scale from a contribution of 20%, which corresponds to the "null" hypothesis.

hour of the experiment. With these results it was possible to assess in its general form the dynamics of ECoG frequency spectra in the right and left hemispheres throughout the period of the experiment. The second version consisted of grouping ECoGs according to periods of work and rest for each consecutive cycle of PMS separately [6, 8]. Cycles were counted from the beginning of the first period of gastric contractions. Altogether 470 ECoGs obtained in experiments on four healthy dogs and 230 ECoGs from dogs with preliminary SDV were analyzed.

EXPERIMENTAL RESULTS

Data on the time course of combined cortical electrical activity of the right and left hemispheres in healthy dogs and dogs with SDV are given in Fig. 1. Definite asymmetry of the contribution of frequencies of bands II-IV to combined cortical electrical activity of RH and LH was found. In healthy dogs (Fig. 1, 1) the contribution of frequencies of band II on the right side corresponded to a mean weighted coefficient of 20%, but on the left it was about 30%. Band III accounted for 25-26% of total activity in RH, but only 16-18% in LH. Band IV was more strongly represented in the cortex of LH, band V in the cortex of RH. The major contribution to cortical activity in RH of the hungry dogs was thus made by bands III and V (α- and β_2-rhythms), and in the cortex of LH by bands II and IV (θ- and β_1-rhythms). The contribution of band I (δ-rhythm) was the same on right and left sides. It declined toward the end of the experiment, especially in the cortex of LH, while at the same time the contributions of fast components of the ECoG in band V increased (Fig. 1, 1).

In dogs with SDV (Fig. 1, 2) the contribution of band II in RH was increased, whereas in LH it was reduced compared with that in normal dogs, so that asymmetry was absent. Asymmetry of band IV was increased. The combined time course of relations between fast and slow components of ECoG during the experiment did not differ in principle from that in normal dogs. There was s tendency for an earlier and deeper decline in the contribution of band I to total electrical activity accompanied by an increase in the contribution of band V, especially in the cortex of LH. Redistributions of the frequency spectrum of RCoG after SDV in the right and left hemispheres are difficult to explain at present.

Since at each point 12-14 ECoGs for normal dogs and at least five ECoGs for dogs with SDV were used during grouping of the ECoGs by phases of the cycles, all details of the ECoG frequency spectrum curves deserve attention. It will be clear from Fig. 2 that cortical electrical activity in band I in normal hungry dogs changed similarly in RH and LH. Its minimal contribution to total electrical activity corresponded to periods of gastric contractions and coincided with peaks of maximal contribution of frequencies in band V (Fig. 2, I and V). Contributions of bands II and III are similar in principle to that of band I. The dynamics of changes in band IV was similar to that of band V.

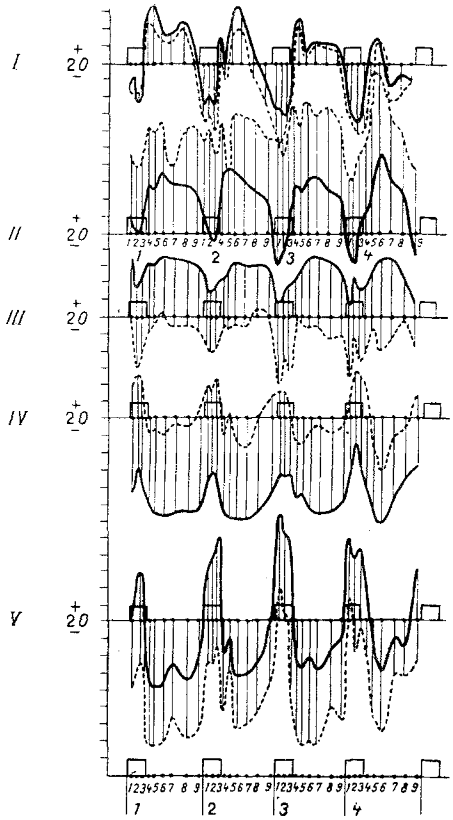

Fig. 2. Time course of changes in ECoG frequency spectrum during phases of consecutive cycles of PMS in healthy dogs. From top to bottom: frequency bands I-V of cortical electrical activity of right (continuous line) and left (broken line) hemispheres. Parameters of their dynamics (mean weighted coefficients) grouped together for all bands on a common base for consecutive cycles of PMS. Horizontal lines (I-V) show the same scheme of PMS cycles on a time scale. Periods of contractions are outlined by squares, and ECoG grouping points 1-3 on band II and below correspond to them. Duration on time scale is 20 min. Rest period — horizontal lines: ECoG grouping points 4-9 correspond to them, duration 70 min. Total duration of each cycle 90 min. Mean data given for four consecutive cycles (1, 2, 3, 4 — the numbers in large type below and on band II). Thin vertical lines connecting curves of ECoG dynamics in right and left hemispheres correspond to ECoG grouping points for phases of the cycles. Vertical scale as in Fig. 1.

The fact that the slow and fast components of the ECoG are so clearly opposite in phase, together with the "random" differences in details for phases of the cycles, as it appeared previously, was observed in a general form in an earlier investigation [8]. These details deserve special examination in view of the aim of the present communication.

In the dynamics of changes in the ECoG frequency spectrum in band V, besides "stationary" and well-defined peaks of activation corresponding to periods of gastric contractions (Fig. 2V), what appear to be additional waves of activation deserve attention. In the first cycle such a wave occurs in the middle of the resting period (Fig. 2, V, point 7). In the second cycle it can be seen at point 5 (10 min after the end of the period of contraction), in the third cycle at point 6 (20 min after the end of the period of contractions). In the fourth cycle waves of this kind are found at point 3 (end of the period of contractions) and at point 7 (middle of the rest period). The additional wave of activation, much weaker than the "stationary" peaks, is thus found in band V in the period of contractions of the fourth cycle and in rest periods of all cycles. If the points of its appearance in rest periods

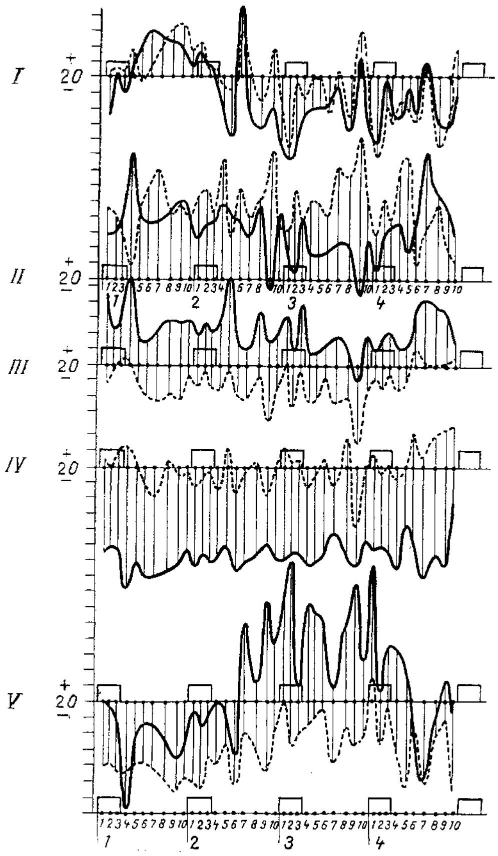

Fig. 3. Dynamics of changes in ECoG frequency spectrum during phases of consecutive cycles in dogs with SDV. Legend as to Fig. 1. Mean duration of cycles 120 min (periods of contractions 30 min, of rest 90 min). Because of longer duration of rest periods ECoGs in this phase of the cycles were grouped for points 4-10 (on band II and below).

are compared (see Fig. 2, V, first cycle — point 7, second cycle — point 4, third cycle — point 6, fourth cycle — point 7) it will be easy to see that it apparently moves along the cycle, and passes through the period of contractions in the course of a one-day experiment. However, in the first and fourth cycles it is found exactly in the middle of the rest periods at point 7 (Fig. 2, V). Its amplitude differs somewhat in the cortex of RH and LH, especially in the third cycle. To distinguish it from the "stationary" peaks, we called this additional wave the "migrating" activation wave (MAW). Whether it is a reflection of a slower rhythm with a period of 270 min or whether it has "split off" the "stationary" peaks of activation is difficult at present to decide. It must be pointed out that its migration is genuine and is one of the most important factors determining individuality of ECoG frequency spectra in a series of consecutive PMS cycles.

For example, the presence of MAW in the second cycle (see Fig. 2, V, point 5) is accompanied by a transient but marked oppositeness of phase of the contributions of frequencies of band II on the right and left, which is not found to this degree in any other cycle. Meanwhile in cycles 1 and 4, where it occurs at point 7, there is a similar decrease in the contribution of band II on the right and left sides. Individuality of the ECoG frequency spectrum in the cycles also reflects relations between frequencies in different bands, which vary in the course of the one-day experiment. The following particular features must receive attention.

The minimal contribution of frequencies of bands II and III to total cortical electrical activity occurs in general during periods of gastric contractions. However, only in the period of contractions of the third cycle did the maximal decrease in the contribution of these bands coincide in time. In cycles 2 and 4 the maximal decrease in the contribution of band III occurred 7-10 min before that of band II. In the period of contractions of the fourth cycle (Fig. 2, III-I) it is particularly easy to see that the contribution of the α-like-rhythm falls first in the cortex of RH (point 1), followed a few minutes later by the contribution of band II (point 2), and a few minutes later still the minimal contribution of band I can be distinguished. These regulatory relations are evidently closely connected with MAW. MAW are found in the time course of changes in band IV in the cortex of RH only at the beginning of the rest period of the third cycle (point 5), a few minutes before the appearance of MAW in band V of RH. Meanwhile in the cortex of LH MAW reflect those of band V in the ECoG of RH almost completely in phase (see Fig. 2, IV, V, first, second, and third cycles).

The increasing oppositeness of phase in the time course of contributions of frequencies of band III on the right and left sides in rest periods, especially in the fourth cycle, is interesting. In that cycle the splitting tendency, i.e., instability of the contribution of band III in the cortex of LH, becomes maximal.

The most noteworthy feature 5 months after SDV was absence of any clear rhythm and instability of the frequency spectrum of the ECoG during phases of the cycles (Fig. 3). This was manifested particularly clearly in the dynamics of frequencies of bands I and V. Unusual general activation of the ECoG also was noted, starting from point 7 of the second cycle and until point 7 of the fourth cycle (Fig. 3, V). Oppositeness of phase of frequencies of band II in the cortex of RH and LH in healthy dogs was observed in the form of exclusion (see above). After SDV virtually the whole dynamics of the changes in representation of frequencies of this band was opposite in phase in RH and LH (Fig. 3, II). The time course of band III showed some similarity with that in healthy dogs in the form of increasing oppositeness of phase of RH and LH in the course of the experiment (point 7 of the first and third cycles, points 1 and 2 of the fourth cycle). Oppositeness of phase was most marked during rest in the fourth cycle (points 7-10). Unlike the time course of frequencies of band V, which was completely in phase in both hemispheres in intact dogs, after SDV it could be both in phase (Fig. 3, points 6-8 of the first cycle, points 7 and 8 of the fourth cycle), and also clearly out of phase (the remaining points during the cycles). The MAW phenomenon, determining the "individuality" of the frequency spectrum of the ECoG in consecutive cycles, could not be detected clearly after SDV. It can be tentatively suggested that existing disturbances of amplitude differences of the "stationary activation peaks and MAW, and also of regular migration of the latter after SDV are due to changes in the relations between nervous and humoral mechanisms of their regulation. Incidentally the number of activation waves as a whole in each cycle did not exceed three in dogs after SDV, just as in intact dogs (Fig. 3).

The quite unusual combinations of ECoG frequencies at points 9 of the second and third cycles in dogs with SDV also are interesting (Fig. 3, V, II, I): activation of electrical activity of the cortex of RH in band V, opposite changes in the frequencies of band II, and in-phase increases in the representation of frequencies of the I band in RH and LH. No such combinations of ECoG frequencies were observed in healthy dogs. At these same points peaks of minimal representation of frequencies of band III, especially in LH, correspond to those of band II in RH. Peaks of minimal representation of band I were observed only 25 min after these "drops" (Fig. 3, III-I, points 1 in the third and fourth cycles).

It is generally familiar that the stereotype of peristaltic activity of the gastrointestinal tract also includes a number of differences in details in consecutive cycles. The "individuality" of the cycles is manifested particularly clearly in combinations of secretory and motor components of peristalsis in different parts of the digestive tract, whose rhythm does not coincide completely in individual cycles [7]. It was postulated previously that these individual differences between cycles may be one mechanism of regulation of the hunger motivation level from organs of the gastrointestinal tract [7]. A similar combination of periodic stereotype of change in the frequency spectrum of the ECoG and its strictly individual character in consecutive cycles during prolonged physiological hunger confirms this hypothesis. The characteristics of the ECoG in hungry dogs described above evidently reflect central and peripheral neurohumoral regulation of the changing level of hunger motivation (its increasing metabolic and interoceptive stimulation, weakening central depression, and so on). The operation of SDV, which is used in the surgical treatment of peptic ulcer [3], leads to substantial reorganization and destabilization of periodic activity both in organs of the digestive system [10] and in the cerebral cortex. Individuality of the frequency spectrum of the ECoG in the cycles is thereby preserved, like hunger motivation, but they are evidently regulated chiefly by humoral mechanisms with the participation of peptide hormones of the alimentary tract. The physiological significance and mechanisms of the MAW phenomenon require further investigations for their elucidation.

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EFFECT OF INHIBITORS OF PROSTAGLANDIN BIOSYNTHESIS ON RESISTANCE OF MICE TO COOLING: FACT AND HYPOTHESIS

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KEY WORKDS: resistance to cold; prostaglandins; inhibitors of prostaglandin biosynthesis; catecholamines; permissive effect.

Prostaglandins (PG) play an active role in temperature regulation [3]. At low ambient temperatures PGE induce hypothermia after intrahypothalamic, intraventricular, and also intraperitoneal injection [6]. This is basically connected with negative modulation of the function of catecholaminergic systems by PG [3, 6], whose determinative role in protection against cold is well known [1]. PG are unstable substances; they are not stored until required, but are synthesized in response to various stimuli [8]. Intense cooling is a powerful source of such stimuli (hormonal, etc.). Of course the diversity of functions of the prostanoids [8] does not rule out a preventive action of some of these classes in the pathogenesis of hypothermia. However, the usefulness of inhibiting the action of PG in poststress pathological states (postradiation esophagitis, endotoxic shock) has already been demonstrated [9, 12].

In this investigation an attempt was made to increase resistance to cold in acute experiments using inhibitors of PG biosynthesis.

EXPERIMENTAL METHOD

Experiments were carried out on 470 (CBA × C57BL)F_1 hybrid male mice weighing 18-22 g.

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