Effects of Electrical Stimulation of the Hunger Center in the Lateral Hypothalamus and Food Reinforcement on Impulse Activity of the Stomach in Rabbits under Conditions of Hunger and Satiation

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Stimulation of the lateral hypothalamus in preliminary fed animals in the presence of the food is associated with successful food-procuring behavior, accompanied by regular generation of high-amplitude slow electrical waves by muscles of the lesser curvature, body, and antrum of the stomach, which was reflected in the structure of temporal organization of slow electrical activity in the form of unimodal distribution of slow wave periods typical of satiation state. Despite increased level of food motivation caused by stimulation of the lateral hypothalamus, the additional food intake completely abolished the inhibitory effects of hunger motivation excitement on slow electrical muscle activity in the lesser curvature, body, and antrum of the stomach of satiated rabbits. Changes in slow electrical activity of the stomach muscles in rabbits deprived of food over 24 h and offered food and associated food-procuring behavior during electrical stimulation of the lateral hypothalamus have a two-phase pattern. Despite food intake during phase I of electrical stimulation, the downstream inhibitory effect of hunger motivation excitement on myogenic pacemaker of the lesser curvature of stomach abolishes the stimulating effect of food reinforcement on slow electrical muscle activity in the lesser curvature, body, and antrum of the stomach. During phase II of electrical stimulation, the food reinforcement decreases inhibitory effect of hunger motivation excitement on myogenic pacemaker of the lesser curvature that paces maximal rhythm of slow electrical waves for muscles activity in the lesser curvature, body, and antrum of the stomach, which is reflected by unimodal distribution of slow electrical wave periods. Our results indicated that the structure of temporal organization of slow electrical activity of the stomach muscles reflects convergent interactions of food motivation and reinforcement excitations on the dorsal vagal complex neurons in medulla oblongata.

Key Words: *hunger center in the lateral hypothalamus; electrical stimulation; stomach; myoelectrical activity; hunger; satiation*

According to pacemaker theory of motivation [4], the hunger center in the lateral hypothalamus (LH), being the initiative motivation generating center, exerts ascending influences on limbic structures and cortex, and thereby forms searching and food-procuring behavior in animals. Along with ascending activating influences, the hunger center in LH may exert descending stimulating influences on neurons of the dorsal vagal complex in the medulla oblongata [6,7,11] that regulate stomach myoelectrical activity and motor function [6-8, 10]. Afferent impulsation from food reinforcement was proved to flow to neu-

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rons of the dorsal vagal complex as well [5,12,13]. One may assume that food motivation and reinforcement excitations are addressed to the same neurons of dorsal vagal complex of the medulla oblongata. It this connection, it appeared interesting to investigate the reflection of convergent interactions of food motivation and reinforcement excitations on dorsal vagal complex neurons in the myoelectrical activity of the stomach.

Electrical stimulation of the hunger center in LH in preliminary fed rabbits allows investigation of artificially provoked food motivation on myoelectrical activity of the stomach, whereas LH stimulation in food-deprived animals enables detection of patterns of myoelectrical activity of the stomach typical of artificially increased food motivation.

The objective of the study was to investigate effects of electrical stimulation of the hunger center in LH and food reinforcement on stomach myoelectrical activity in rabbits under the conditions of hunger and satiation.

MATERIALS AND METHODS

Myoelectrical activity of stomach lesser curvature, body, and antrum was registered using chronically implanted electrodes in freely moving animals, preliminary subjected to 24-h food deprivation or fed before the experiment [2], with the food offered during stimulation of the hunger center in LH for 1 h. In control experiments, effects of LH stimulation on stomach myoelectrical activity were investigated in rabbits without food offered. Electrical stimulation of LH was performed using bipolar nickel-chromium electrodes implanted as directed by the approach of "travelling electrode"[3] according to stereotaxic atlas coordinates [9]. The following parameters of electrical stimulation were used: frequency 20-30 Hz, pulse duration 0.2 msec, voltage 2.5-3 V. Simultaneously, web-cam registered animal behavior. The experiments were conducted in accordance to main bioethics regulations. Automatic analysis of temporal parameters of stomach myoelectrical activity was performed using AcqKnowledge software. The data were statistically processed using Statistica 6.0 software. Significance of differences was assessed using Mann–Whitney *U* test ($p<0.05$).

RESULTS

Threshold stimulation of the hunger center in LH of preliminary fed and food-deprived (24 h) rabbits with the food offered resulted in uniform behavior reaction, manifested in unceasing successful food-procuring behavior. In addition, states of satiation and hunger that served as the background for LH electrical stimulation determined different nature of food reinforcement effect on stomach myoelectrical activity.

When the hunger center in LH is stimulated in pre-fed animals during food consumption, regular generation of high-amplitude slow electrical waves (SEW) by muscles of the lesser curvature, body, and antrum of the stomach (Fig. 1) is preserved with a frequency 4.48 cycles/min (Table 1), which is reflected in the structure of temporal organization of slow electrical activity in the form of unimodal distribution of SEW periods (Fig. 2) typical of the satiation state. Regular pattern of SEW generation by muscles of the lesser curvature, body, and antrum of the stomach during food-procuring behavior during LH electrical stimulation in satiated animals is demonstrated by unimodal distribution of SEW periods (Fig. 2) and by low values of coefficient of variation (7, 8, 9%, respectively). Moreover, the structure of temporal organization of spike activity of stomach muscles retains bimodal pattern of interpulse interval distribution (Fig. 3). Described peculiarities of stomach myoelectrical activity are typical signs of satiation [1].

During successful food-procuring behavior induced by LH stimulation in satiated animals, the myogenic pacemaker in the lesser curvature of the stomach continues regular generation of frequent high-amplitude SEW that propagate without decrement to the distal parts and attain the pyloric sphincter, which determines regular pattern and high frequency of SEW generation by muscles of stomach body and antrum in accordance with the main electrical rhythm paced by myogenic stomach pacemaker (Fig. 1).

In control experiments with electrical stimulation of LH in satiated rabbits in the absence of food, unimodal distribution of SEW periods generated by the body and antrum of the stomach changes for bimodal distribution typical of hunger following 24-h food deprivation. The food motivation, artificially induced by LH electrical stimulation in satiated animals in the absence of food is reflected in the structure of temporal organization of spike activity in muscles of stomach body and antrum in terms of shift from bimodal distribution of interpulse intervals to the trimodal distribution. Transfer from satiation to the hunger induced by LH stimulation in pre-fed animals in the absence of food can be explained by descending inhibitory influences of food motivational excitation on myogenic pacemaker of the lesser curvature of the stomach [1], which is in line with the date presented elsewhere [8,10], where the inhibiting effects of LH stimulation on myoelectrical activity and motor function of the stomach was reported.

These findings suggests that despite increased level of food motivation, produced by LH stimulation,

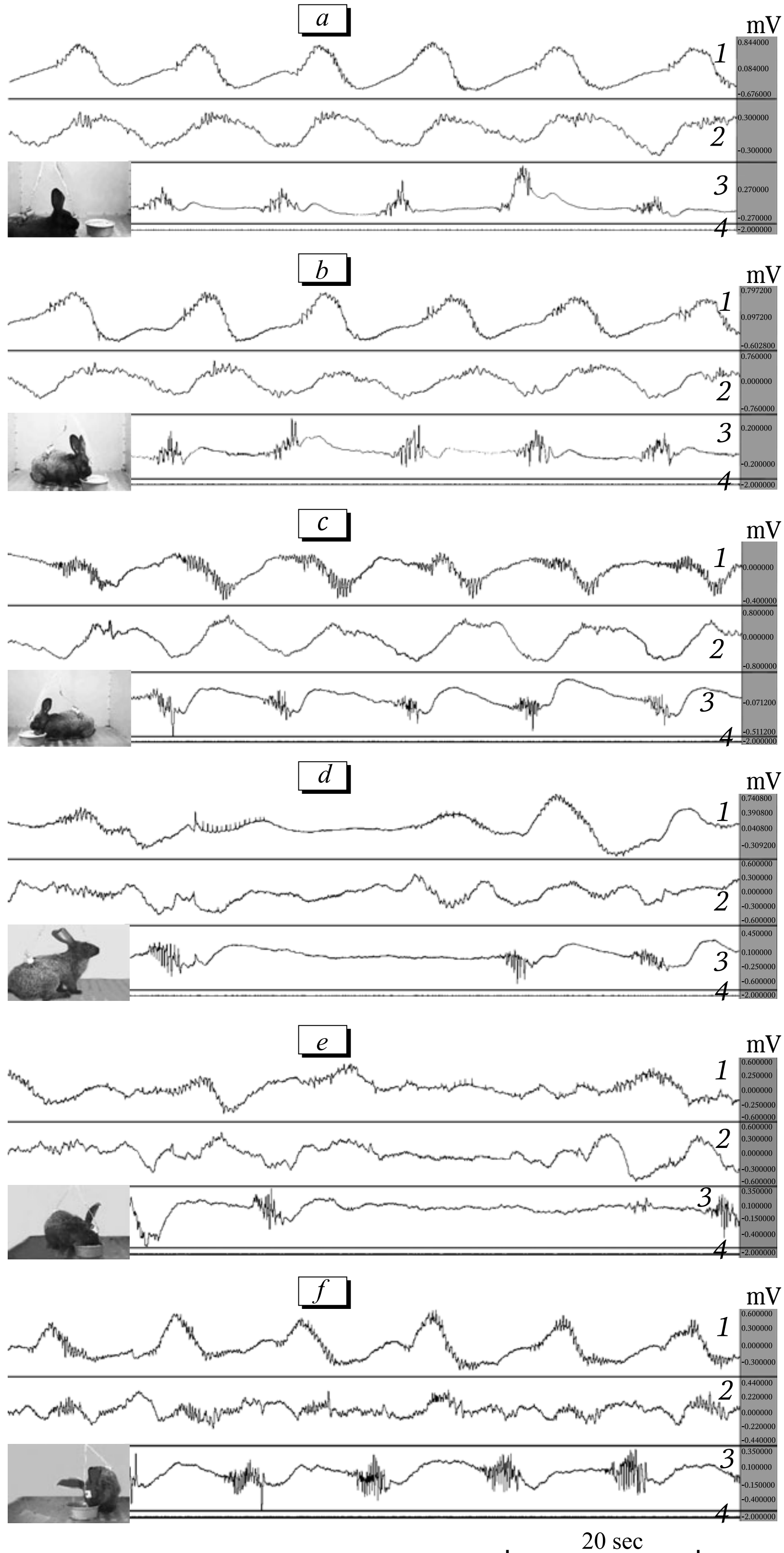

Fig. 1. Myoelectrical activity of the lesser curvature (*1*), body (*2*), and antrum of the stomach (*3*) in preliminary fed rabbit in the presence of the food before LH stimulation (*a*) and on minutes 5 (*b*) and 40 (*c*) of LH stimulation and accompanying successful food-procuring behavior and under conditions of 24-h food deprivation in the absence of food before LH electrical stimulation (*d*) and on minutes 5 (*e*) and 40 (*f*) of LH electrical stimulation and accompanying successful food-procuring behavior. *4*: electrical stimulation of LH

TABLE 1. Statistical Parameters of Myoelectrical Activity of Stomach (sec) in Preliminary Fed Rabbits before Electrical Stimulation of LH, during Successful Food-Procuring Behavior, that Emerges during LH Electrical Stimulation and in the Course of Natural Food Consumption

Parameter	LC of the stomach				Stomach body				Stomach antrum			
	IPI in PP burst	duration of PP burst	IBI	period of SEW and/or burst-like PP rhythm	IPI in PP burst	duration of PP burst	IBI	period of SEW and/or burst-like PP rhythm	IPI in PP burst	duration of PP burst	IBI	period of SEW and/or burst-like PP rhythm
Satiation before electrical stimulation of LH												
n	16 143	1080	1080	1080	9050	1065	1065	1065	13 152	1054	1054	1054
M	0.33	4.93	8.59	13.52	0.43	3.66	9.73	13.39	0.20	2.44	11.65	14.09
Me	0.31	4.75	8.66	13.41	0.34	3.48	9.68	13.14	0.18	2.34	11.57	14.01
σ	0.19	1.12	1.16	1.11	0.31	1.12	1.62	1.59	0.08	0.59	1.09	1.09
m	0.001	0.03	0.04	0.03	0.001	0.03	0.05	0.05	0.001	0.02	0.03	0.03
As	2.23	1.22	-0.46	0.84	1.96	1.04	0.26	0.39	1.97	0.88	0.72	0.53
σ_{As}	0.02	0.07	0.07	0.07	0.03	0.07	0.07	0.07	0.02	0.08	0.08	0.08
Ex	9.25	2.22	0.81	2.40	4.62	1.04	-0.22	-0.23	8.06	0.82	1.27	1.07
σ_{Ex}	0.04	0.15	0.15	0.15	0.05	0.15	0.15	0.15	0.04	0.15	0.15	0.15
25%	0.19	4.15	8.02	12.79	0.23	2.75	8.60	12.22	0,13	2.03	10,92	13.42
75%	0.41	5.42	9.24	14.13	0.52	4.29	10.78	14.43	0.24	2.84	12.27	14.68
Food-procuring behavior during electrical stimulation of LH (satiated state)												
n	17 964	1024	1024	1024	14 394	1008	1008	1008	12 080	1004	1004	1004
M	0.32	5.61	7.78	13.39	0.31	4.48	8.90	13.38	0.21	2.49	10.83	13.33
Me	0.30	5.61	7.68	13.31	0.25	4.29	8.94	13.25	0.18	2.44	10.65	13.16
σ	0.17	0.73	1.05	0.94	0.21	1.33	1.50	1.16	0.11	0.51	1.21	1.19
m	0.001	0.02	0.03	0.03	0.001	0.04	0.05	0.04	0.001	0.02	0.04	0.04
As	1.98	0.12	0.73	0.38	2.78	0.20	0.21	0.98	2.22	0.38	1.44	1.21
σ_{As}	0.02	0.08	0.08	0.08	0.02	0.08	0.08	0.08	0.02	0.08	0.08	0.08
Ex	7.27	-0.03	1.55	1.74	10.55	-0.55	-0.10	3.97	7.63	0.76	4.43	3.18
σ_{Ex}	0.04	0.15	0.15	0.15	0.04	0.15	0.15	0.15	0.04	0.15	0.15	0.15
25%	0.20	5.16	7.01	12.80	0.20	3.55	7.89	12.67	0.13	2.14	10.03	12.59
75%	0.39	6.05	8.48	13.96	0.36	5.36	9.77	14.02	0.24	2.82	11.30	13.87
Natural food-procuring behavior with no electrical stimulation of LH												
n	18 944	825	825	825	12 680	818	818	818	11 887	804	804	804
M	0.28	6.37	6.38	12.76	0.31	4.83	8.66	13.49	0.20	2.89	10.74	13.63
Me	0.24	6.13	6.46	12.69	0.25	4.72	8.82	13.38	0.17	2.80	10.64	13.53
σ	0.17	1,43	1,57	0,91	0,23	1,39	1,74	1,18	0,09	0,71	1.05	0.91
m	0.001	0.05	0.05	0.03	0.001	0.05	0.06	0.04	0.001	0.02	0.04	0.03
As	2.88	0.42	-0.03	0.01	2.82	0.32	-0.04	0.38	2.01	0.45	0.47	0.38
σ_{As}	0.02	0.09	0.09	0.09	0.02	0.09	0.09	0.09	0.02	0.09	0.09	0.09
Ex	15.98	-0.69	-0.90	-0.90	10.86	-0.71	-0.51	0.49	7.03	-0.65	0.12	0.08
σ_{Ex}	0.04	0.17	0.17	0.17	0.04	0.17	0.17	0.17	0.04	0.17	0.17	0.17
25%	0.16	5.25	5.09	12.20	0.17	3.73	7.29	12.72	0.13	2.28	10.01	12.97
75%	0.36	7.45	7.60	13.36	0.35	5.80	9.94	14.24	0.24	3.40	11.41	14.20

Note. Here and in Table. 2: LC: lesser curvature, IPI: interpulse interval, IBI: interburst interval, PP: peak potentials.

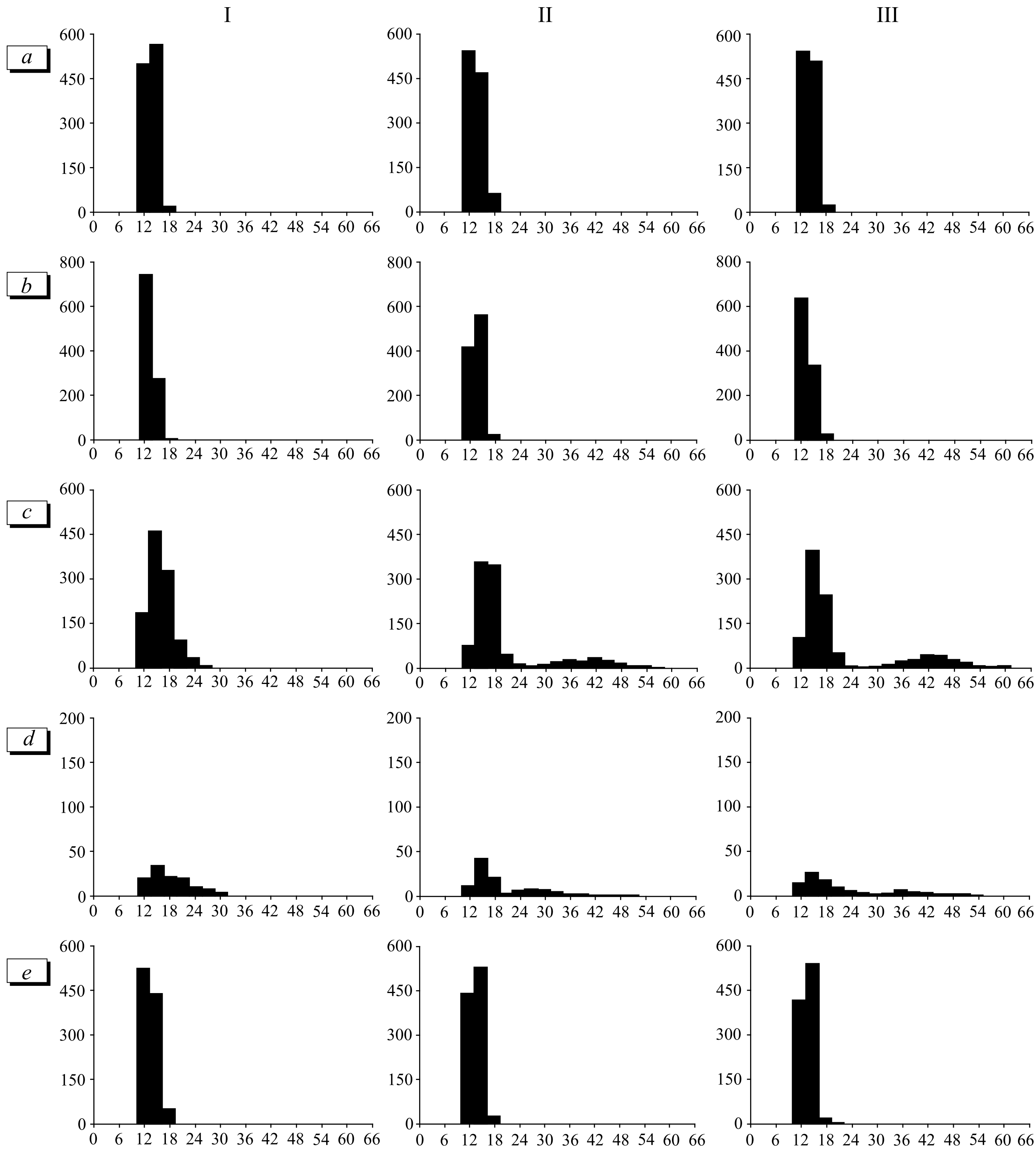

Fig. 2. Histograms for distributions of SEW periods generated by stomach muscles in the lesser curvature (I), body (II), and antrum (III) in preliminary fed rabbits before (*a*) and during LH electrical stimulation (*b*) in the presence of food and accompanying successful food-procuring behavior and under conditions of 24-h food deprivation before LH electrical stimulation in the absence of food (*c*), during phase I (*d*) and II (*e*) of LH electrical stimulation in the presence of food and accompanying successful food-procuring behavior. Abscissa: SEW periods (sec); ordinate: absolute frequency of SEW periods.

additional food intake completely abolishes the inhibitory effects of hunger motivational excitement on slow electrical activity of muscles in lesser curvature and distal parts of the stomach of fed rabbits.

Changes in slow electrical activity of the stomach muscles in rabbits deprived of food over 24 h in the presence of food and emerging food-procuring behavior during electrical stimulation of LH have a

TABLE 2. Statistical Parameters of Myoelectrical Activity of the Stomach (sec) in Hungry Rabbits before Electrical Stimulation of LH, during Successful Food-Procuring Behavior during LH Stimulation

Parameter	LC of stomach				Stomach body				Stomach antrum			
	IPI in PP burst	duration of PP burst	IBI	period of SEW and/or burst-like PP rhythm	IPI in PP burst	duration of PP burst	IBI	period of SEW and/or burst-like PP rhythm	IPI in PP burst	duration of PP burst	IBI	period of SEW and/or burst-like PP rhythm
State of hunger before electrical stimulation of LH												
n	18 171	1117	1117	1117	12 874	1031	1031	1031	12 010	1024	1024	1024
M	0.38	6.16	9.65	15.81	0.43	5.42	14.90	20.31	0.23	2.65	18.92	21.57
Me	0.33	6.17	9.09	15.57	0.32	5.49	11.16	16.64	0.19	2.58	13.64	16.29
σ	0.26	2.10	3.34	2.98	0,32	1.68	9.89	9.81	0.14	0.61	11.88	11.88
m	0.001	0.06	0.10	0.09	0.001	0.05	0.31	0.31	0.001	0.02	0.37	0.37
As	2.17	0.01	1.38	0.74	2.03	0.06	1.79	1.82	3.12	0.73	1.52	1.52
σ_{As}	0.02	0.07	0.07	0,07	0,02	0.08	0.08	0.08	0.02	0.08	0.08	0.08
Ex	7.02	-0.49	2.46	1.20	4.55	-0.86	2.10	2.18	16.70	0.45	0.83	0.86
σ_{Ex}	0.04	0.15	0.15	0.15	0.04	0.15	0.15	0.15	0.04	0.15	0.15	0.15
25%	0.19	4.76	7.35	13.94	0.24	3.99	9.13	14.93	0.14	2.20	11.91	14.60
75%	0.47	7.64	10.94	17.32	0.52	6.73	13.90	18.80	0.27	3.01	17.37	20.11
Food-procuring behavior in phase I of LH electrical stimulation (hunger)												
n	2869	118	118	118	1313	112	112	112	1258	107	107	107
M	0.31	7.58	9.27	16.85	0.51	6.02	13.78	19.88	0.26	2.96	19.56	22.52
Me	0.26	7.37	8.79	16.52	0.47	6.24	10.50	16.40	0.21	2.90	15.25	18.41
σ	0.19	1.94	3.24	3.33	0.34	1.93	8.50	8.63	0.17	0.75	11.11	11.10
m	0.001	0.18	0.30	0.31	0.01	0.18	0.80	0.82	0.001	0.07	1.07	1.07
As	2.14	0.25	0.65	0.33	1.22	-0.04	1.35	1.50	2.44	0.02	1.11	1.10
σ_{As}	0.05	0.22	0.22	0.22	0.07	0.23	0.23	0.23	0.07	0.23	0.23	0.23
Ex	7.96	-0.20	-0.42	-0.57	1.76	-0.97	0.94	1.96	9.24	-0.38	0.08	0.09
σ_{Ex}	0.09	0.44	0.44	0.44	0.13	0.45	0.45	0.45	0.14	0.46	0.46	0.46
25%	0.18	6.32	6.72	14.39	0.24	4.48	7.85	14.75	0.15	2.35	11.35	14.39
75%	0.40	8.91	12.11	19.50	0.69	7.60	19.58	25.37	0.31	3.50	27.01	29.31
Food-procuring behavior during phase II of LH electrical stimulation (hunger)												
n	21 627	1012	1012	1012	15 175	993	993	993	11 546	982	982	982
M	0.30	6.41	7.02	13.43	0.35	5.40	7.95	13.35	0.22	3.21	10.15	13.36
Me	0.26	6.27	7.04	13.16	0.29	5.50	7.86	13.25	0.18	3.22	9.92	13.19
σ	0.18	1.44	1.29	1.22	0.24	1.75	1.67	1.24	0.12	0.53	1.17	1.09
m	0.001	0.05	0.04	0.04	0.001	0.06	0.05	0.04	0,001	0.02	0.04	0.03
As	2.55	0.09	0.44	0.95	2.67	0.07	0.05	0.43	2.54	-0.01	1.34	1.19
σ_{As}	0.02	0.08	0.08	0.08	0.02	0.08	0.08	0.08	0.02	0.08	0.08	0.08
Ex	12.54	-0.32	0.44	1.94	9.90	-1.13	-1.00	1.38	10.68	-0.12	4.48	5.97
σ_{Ex}	0.03	0.15	0.15	0.15	0.04	0.16	0.16	0.16	0.05	0.16	0.16	0.16
25%	0.17	5.39	6.01	12.78	0.21	3.75	6.50	12.67	0.14	2.86	9.47	12.79
75%	0.39	7.50	7.83	13.92	0.41	6.95	9.51	13.87	0.26	3.55	10.65	13.87

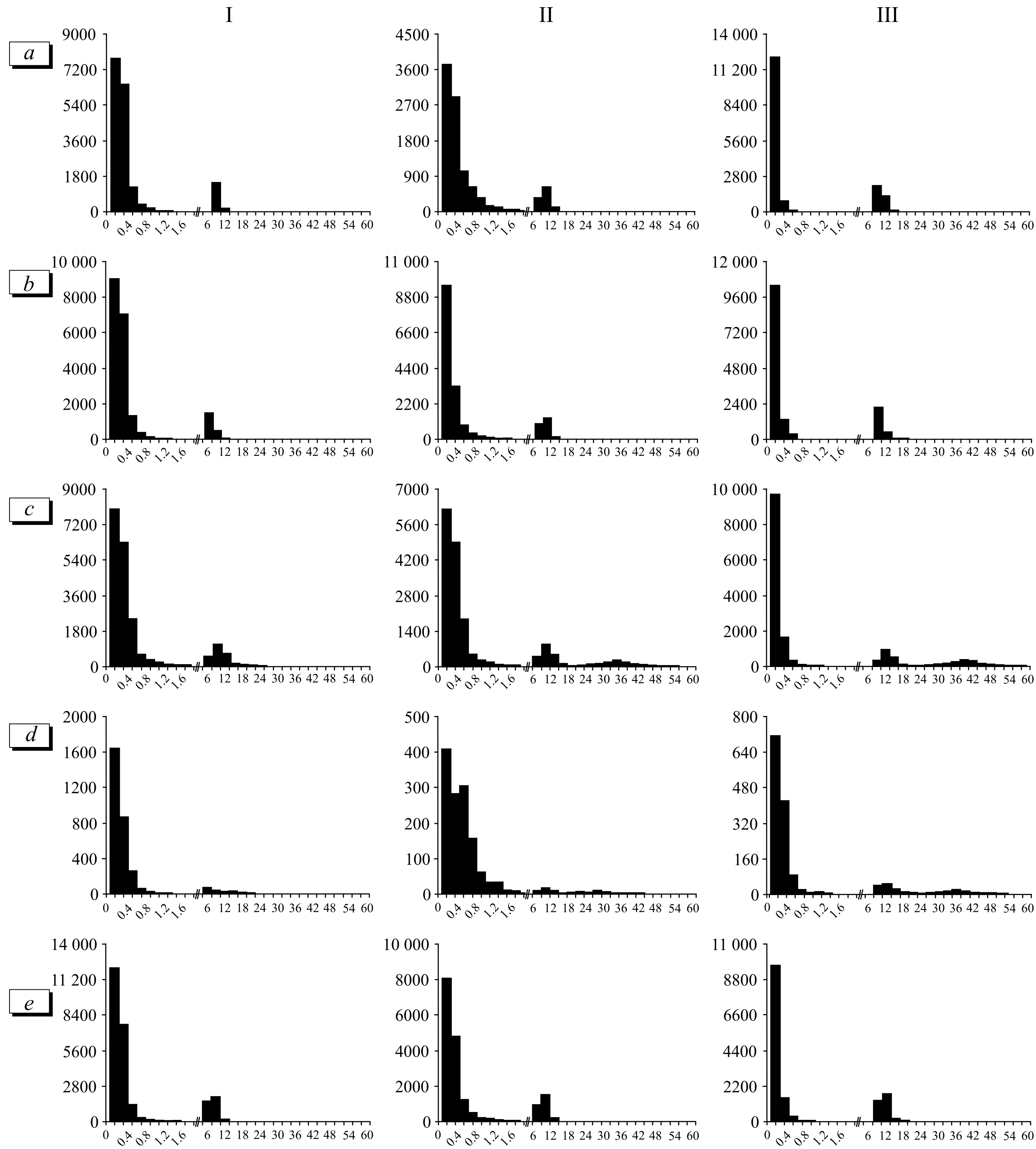

Fig. 3. Histograms for distributions of interpulse intervals of spike muscle activity in the lesser curvature (I), body (II), and antrum (III) in preliminary fed rabbits before (*a*) and during LH electrical stimulation (*b*) in the presence of food and accompanying successful food-procuring behavior and under conditions of 24-h food deprivation before LH electrical stimulation in the absence of food (*c*) and during phase I (*d*) and II (*e*) of LH electrical stimulation in the presence of food and accompanying successful food-procuring behavior. Abscissa: interpulse intervals (sec); ordinate: absolute frequency of interpulse intervals.

biphasic pattern. At the initial stage of food-procuring behavior in hungry rabbits (0-13 min of hunger center stimulation in LH), high dispersion of period values for SEW generated by stomach body and antrum muscles is preserved (Fig. 1), as is seem from coefficient of variation (43 and 49%, respectively) and bimodal pattern of SEW period distribution (Fig. 2), typical of 24-h food deprivation. In addition, frequency of SEW generation by muscles of the stomach body and antrum was 3.01 and 2.66 cycles/min, respectively (Table 2). Structure of temporal organization of impulse activity of body and antrum stomach muscles retains trimodal pattern of interpulse interval distribution in hungry rabbits during feeding behavior appearing in phase I of LH stimulation (Fig. 3). Irregular pattern of SEW generation by body and antrum stomach muscles at the initial stage of successful food-procuring behavior can be explained by inhibitory influences of food motivational excitement on myogenic stomach pacemaker, as indicated by presence of low-amplitude slow potentials, which propagate to distal parts with decrement, among high-amplitude SEW, generated by lesser curvature muscles (Fig. 1).

In control series, food motivation in hungry rabbits artificially increased via LH electrical stimulation in the absence of food was reflected in structure of temporal organization of slow electrical activity of body and antrum stomach muscles in terms of shift from bimodal distribution of SEW periods to trimodal distribution, whereas in temporal structure of spiking activity it was reflected by swift from trimodal distribution of interpulse intervals to tetramodal distribution, which are typical of 2 day food deprivation. It can be explained by descending inhibitory influences of hunger motivational excitement on the myogenic pacemaker of lesser curvature of stomach [1]. Our result are in line with the data obtained by other investigators [8,10].

During phase II of LH electrical stimulation, the food reinforcement abolishes inhibitory effects of hunger motivational excitement on lesser curvature myogenic pacemaker, that paces maximal rhythm of SEW generation to stomach body and antrum muscles (4.49 cycles/min) (Fig. 1), which is indicated by unimodal distribution of SEW periods (Fig. 2) and bimodal distribution of interpulse intervals, typical of satiation (Fig. 3).

Thus, structure of temporal organization of slow electrical activity of stomach muscles reflects convergent interactions of food motivation and reinforcement excitations on the dorsal vagal complex neurons in medulla oblongata, which control stomach myoelectrical activity and motor function. In principle, such possibility previously was demonstrated for a number of brain neurons [4].

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