Role of Different Types of Adrenoreceptors of the Lateral Hypothalamus in the Mechanisms of Natural Excitation Due to Food Motivation

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Following microiontophoresis of propranolol, a β-adrenoblocker, and prasosine, an α_1-adrenoblocker, rearrangements of the impulse flows are observed in a number of neurons of the lateral hypothalamus, which manifest themselves in the development of regular activity with a monomodal distribution of interspike intervals.

Key Words: *lateral hypothalamus; hunger motivation; neurons; propranolol; prasosine*

The experimental model for recording neuronal activity in food behavior is based on evidence [5,6] indicating that the motivational state, notably hunger motivation, manifests itself in the specific organization of the spike pattern of the majority of neurons in the central nervous system (CNS), which is characterized by the predominance of two or three types of interspike intervals (ISI) in the impulse flow of a neuron. Such an organization of the pattern corresponds to a bi- and trimodal distribution of ISI on interval histograms with the prevalence of interval lengths of 1-30, 100-400, and >1000 msec. It has been established that when hunger motivation is satisfied by food intake, the impulse activity of the neurons involved in alimentary motivational excitation becomes transformed into regular activity with the predominance of ISI uniform in duration. This manifests itself in a monomodal distribution of the interval histograms and in the predominance of interval spectrum values varying in the range 10-40 and 100-200 msec [5,6]. Adrenoblockers, which competitively bind to adrenoceptors, have been chosen as the acting factor, since the noradrenergic component is among the leading ones in the neurochemical mechanisms of hunger motivation [2,3,7].

The objective of this study was a comparative analysis of the contribution of α_1- and β-adrenoceptors to structural rearrangement of the impulse flow of the "hunger center" neurons of the lateral hypothalamus (LH) for natural alimentary motivation in rabbits. The dynamics of the impulse activity of the LH neurons was analyzed in hungry rabbits for free behavior, adrenoblockers being introduced by microiontophoresis (MIP) and alimentary motivation being naturally satisfied.

MATERIALS AND METHODS

The experiments were carried out on 10 male chinchilla rabbits weighing 2.5-3.5 kg after a 24-h food deprivation under conditions of free behavior. The experiments were performed as follows: 1) the baseline activity was extracellularly recorded for one neuron of the LH; MIP was then performed in the same neuron with a 0.1 M NaCl solution (2), a saturated solution of the β-blocker propranolol (PROP) (3), 0.1 M NaCl (4), and a satu-

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rated solution of the α_1-blocker prasosine (PRAS) (5); 6) the impulse activity of the neuron was recorded during food delivery and intake. The method was described in detail elsewhere [2,5,7]. The data for each neuron were processed by calculating the mean interspike interval (M), the variance (G), the coefficient of variation (CV), and the mean impulse frequency (P). The interval histograms were plotted using a piecewise-nonuniform and logarithmic scale and by the method of logarithm intervalograms.

RESULTS

The baseline activity of 47 neurons of the LH was recorded for free behavior of rabbits after a 24-h deprivation of food. MIP of PROP was performed in 28 neurons and MIP of PRAS in 21 neurons. We also studied the activity of 5 neurons during food delivery and intake. The main results are shown in Table 1.

Analysis of the baseline activity showed that neurons with an ISI distribution typical of the state of hunger accounted for 59.5% (28 out of 47 neurons; groups 1 and 5) (Table 1), this being consistent with published data [5,6]. MIP of NaCl caused no reliable changes.

In the majority of neurons we observed rearrangements of the impulse activity after MIP of PROP, which manifested themselves as regular activity with a monomodal distribution of ISI (groups 1, 2, and 3). The number of neurons with a monomodal distribution of ISI reliably increased as compared to the baseline level: 57.2% (16 out of 28 neurons). Similar changes were observed after MIP of PRAS. Neurons with a monomodal distribution of ISI comprised 47.5% (10 neurons out of 21; groups 1 and 2), but the number of neurons with a predominance of ISI in the range 100-200 msec was higher than after MIP of PROP (19 and 10.7%, respectively). The effects of the adrenoblockers were short-lived (5-15 sec), after which the impulse activity reverted to the baseline pattern.

During food delivery and intake, the activity of neurons of the LH became regular with monomodal interval characteristics. In 3 out of 5 neurons, the predominant ISI intervals were in the range of 5-25 msec, and in 2 neurons in the range of 30-69 msec.

It should be mentioned that, in addition to 59.5% of neurons with types of ISI distribution characteristic of alimentary motivational excitation, there were small groups of neurons whose baseline activity exhibited other patterns of impulse flow

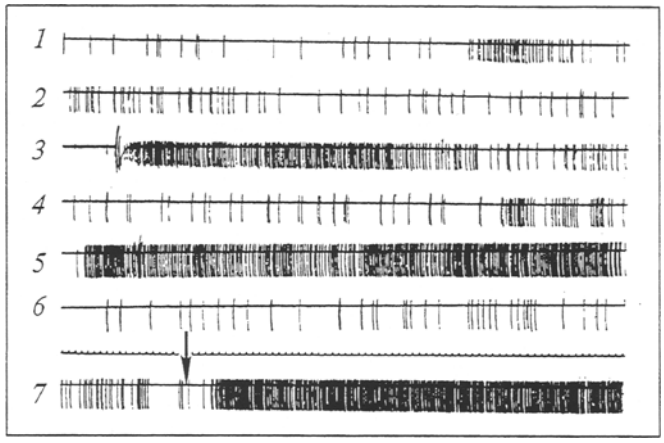

Fig. 1. Dynamics of impulse activity of a LH neuron in the course of experiment. *1*) baseline activity; *2*) after MIP of NaCl; *3*) after MIP of PROP; *4*) initial pattern recovery after MIP of PROP and before MIP of PRAS; *5*) after MIP of PRAS; *6*) initial pattern recovery after MIP of PRAS and before food delivery; *7*) activity during food delivery and intake, start of eating marked by an arrow; time mark 100 msec.

structure. This was probably due to the fact that a multitude of excitations, generated by diverse neurochemical mechanisms which are triggered by a constant dynamic interaction between motivational excitation and environmental afferentations, undergo a process of integration at each point in time in the neurons of the LH (which is one of the most important motivatiogenic zones in the CNS), and this allows the entire organism to adapt effectively to changes of environmental conditions [1]. This being so, it is appropriate to analyze the structural changes of the impulse flow of neurons, since this is one of the accessible indexes of the integration processes during selective blocking of different types of adrenoceptors.

The dynamics of the impulse activity of LH neurons in hungry rabbits during the experiments (Figs. 1, 2) and integral analysis of the statistical parameters (Table 1) attest to transformation of the ISI distribution typical of the state of hunger into a distribution with indexes typical of food intake. PROP and PRAS had unidirectional, but somewhat different effects. PROP initiated more brief changes than PRAS: 3-5 and 5-15 sec, respectively; MIP of PRAS triggered regular impulse activity with both short (10-30 msec, 28.5% of neurons) and long (100-200 msec, 19% of neurons) ISI; on the other hand, in the case of MIP of PROP the majority of neurons exhibited a monomodal distribution of ISI with the predominance (46.5% of neurons) of short (1-30 msec) intervals, while neurons with predominantly long (100-200 msec) intervals comprised 10.7%. It may be assumed that both α_1- and β-adrenoceptors to a certain extent contribute to the regulation of the

TABLE 1. Analysis of Impulse Activity of Neurons in the LH

Distribution of ISI	Group №	Number of neurons and % of total count	Range of predominant values of ISI in SI histograms		Mean ISI, SI	Variance	Coefficient of variation, %	Mean impulse frequency, cps
			piecewise-nonuniform scale	logarithmic scale				
Baseline values (47 neurons)								
Bimodal			1–20	2.5–25	55–287	64–448	110–280	3.5–18
	1	23 (48.9%)	100–400	63–398				
			20–40	25–63				
	2	8 (17%)	100–200	100–158	62–144	65–159	105–226	6.9–16
			40–60	39–63				
	3	4 (8.5%)	100–200	100–158	121–144	139–226	114–152	6.7–8.2
		10–20	10–15					
	4	1 (2.1%)	>1000	>1000	383.4	855	223.1	2.6
Trimodal	5	5 (10.6%)	1–20	3.9–39	324–581	424–1276	125–249	1.7–3.1
			100–200	100–158				
			>1000					
	6	1 (2.1%)	1–5	3.9–6.3	184.6	232.9	126.1	5.4
			40–50	39–63				
			100–200	158–251				
Monomodal	7	1 (2.1%)	10–20	10–15	35	53.3	152	28.6
	8	2 (4.2%)	100–200	100–158	173–295	200–641	115–217	3.4–5.7
Polymodal	9	2 (4.2%)	5–1000	6.3–1000	191–335	327–459	136–171	3–5.2
After MIP of PROP (28 neurons)								
Monomodal	1	1 (3.6%)	1–10	3.9–6.3	11.7	94.4	807	85.5
	2	12 (42.9%)	10–30	10–39	20–70	10–197	79–382	14.5–49.5
	3	3 (10.7%)	100–200	63–158	67–119	59–146	88–150	8.4–14.9
Bimodal	4	2 (7.1%)	1–5	2–6	180–242	239–370	132–153	4.1–5.6
			100–300	100–398				
	5	6 (21.4%)	30–60	39–63	105–177	100–243	95–148	5.6–9.3
			100–200	63–158				
	6	1 (3.6%)	1–5	2–4	835	1809	216	1.2
			>1000	>1000				
Trimodal	7	1 (3.6%)	10–20	15–25	810	1193	147	1.2
			400–500	398–630				
			>1000	>1000				
Polymodal	8	2 (7.1%)	5–1000	6.3–1000	347–524	514–614	117–148	1.9–2.9
After MIP of PRAS (21 neurons)								
Monomodal	1	6 (28.5%)	10–30	10–25	18–58.7	12–116	52–199	24.2–56.6
	2	4 (19%)	100–200	63–158,	145–290		132–535	91–184
3.4–6.8								
Bimodal	3	3 (14.3%)	1–10	2.5–6	151–225	185–358	122–186	4.4–6.6
			100–200	63–251				
	4	1 (4.8%)	50–60	39–63	125.7	110.9	88.9	8
			100–200	158–390				
Trimodal	5	5 (23.8%)	1–20	2–25	346–612	467–1085	125–177	1.6–2.9
			100–300	251–630				
			>1000	>1000				
	6	2 (9.5%)	1–5	2–4	205–285	278–340	135–240	4.9–5.2
			10–30	25–63				
			100–200	251–398				

afferentations involved in the development of alimentary motivational excitation. This speculation is corroborated by data on a reliable reduction of food intake after microinjections of α- and β-adrenoblockers in the LH of hungry animals [9], as well as by the fact that after MIP of norepinephrine (NE) the structure of the impulse flow of LH neurons in food-satiated rabbits is transformed into a pattern typical of the state of hunger [7].

As is well known, α_1- and β-adrenoceptors contribute to the regulation of different Ca- and

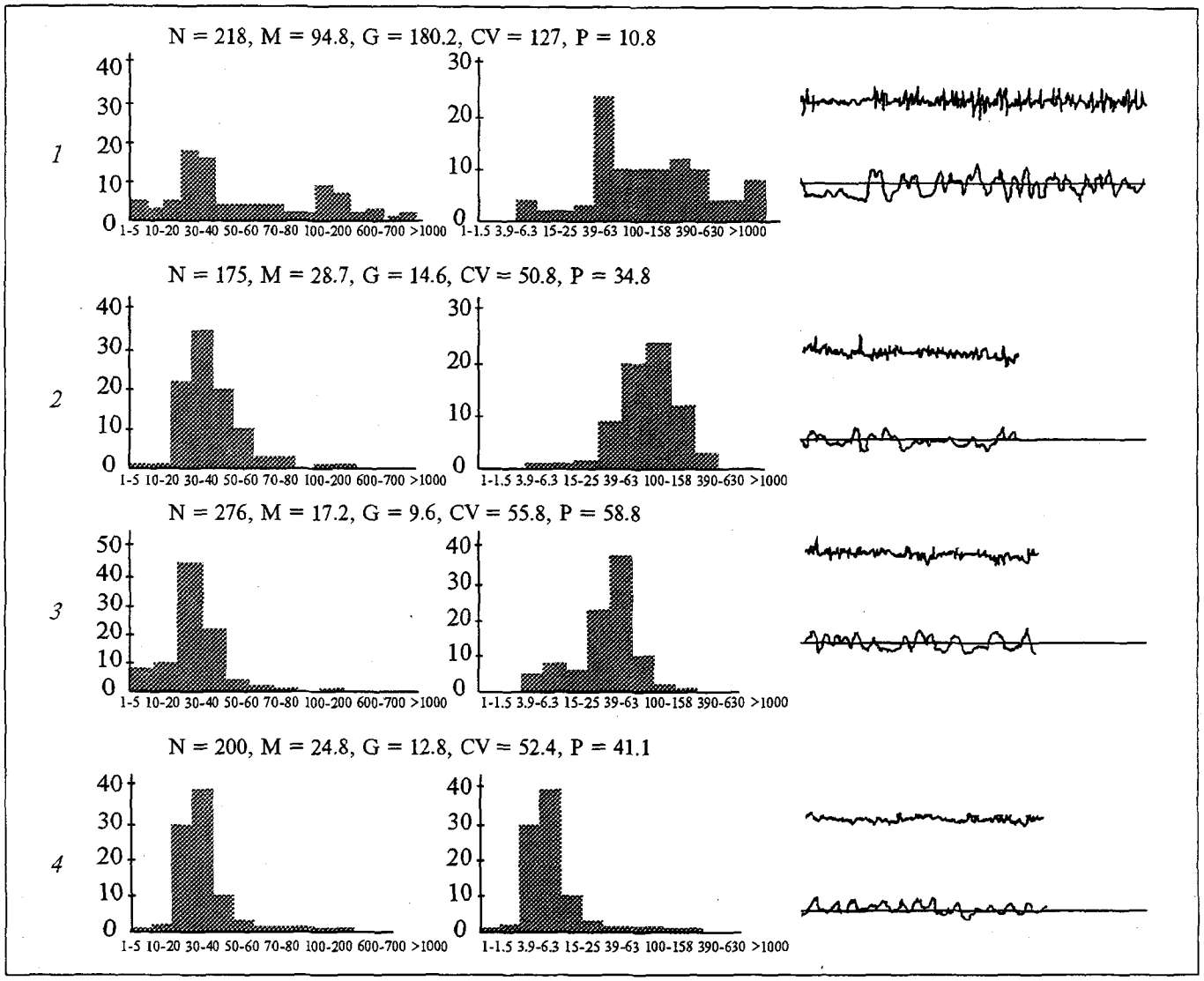

Fig. 2. Dynamics of statistical parameters reflecting structure of impulse flow of the neuron presented in Fig. 1. From left to right: interval histograms with piecewise – nonuniform and logarithmic scale; logarithmic intervalogram (top) and curve of dynamic nonuniformity (bottom). *1*) baseline activity; *2*) after MIP of PROP; *3*) after MIP of PRAS; *4*) during food intake. N: number of neurons; other designations are explained in MATERIALS AND METHODS.

cAMP-dependent mechanisms; therefore, the role of the noradrenergic component in the formation of alimentary motivational excitation is nonuniform, since the latter is a process of integration of interactions involving a number of neurotransmitters and neuropeptides at the neurochemical level [2,4,7]. Some studies imply that within the LH NE may act independently of opioid peptides [8] and may modulate the regulatory effects of cholecystokinin fragments [2,7] and neuropeptide Y [3]. On the one hand, NE evidently regulates the membrane mechanisms underlying conformational changes and expression of the receptors for neuropeptides and other neurotransmitters, which is a kind of "input adjustment" in neurons and which, to a certain extent, determines the subsequent integrative processes; on the other hand, metabolism in the cytoplasm and genome functions may also be regulated by NE. The combination of these processes partly accounts for the neuronal integrative functions, one of the manifestations of which is the structure of the impulse flow.

It may be speculated that the regulatory effects of NE differ within the LH in cases of its interaction with α_1- and β-receptors and are exhibited in the generation of spikes with varying frequency in one neuron, because long (100-200 msec) intervals mostly disappear for blocking of the β-receptors, while blocking of the α_1-receptors in a number of cases (19%) results, along with the above effect, in the disappearance of short (1-30 msec) intervals, this being consistent with other data [2]. Evidently, in the state of hunger one of the neurochemical mechanisms underpinning the

pattern of neuronal activity with two predominant lengths of ISI (1-30 and 100-200 msec) is the integration of interactions between NE and both α_1- and β-adrenoceptors.

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The Invertor Mechanism of Changes in the Plasma Membranes of Hepatocytes during Induction of Microsomal Monooxygenases in Adult and Old Rats

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Age-specific changes of some parameters of the state of the plasma membrane are studied for genetic induction of enzymes of microsomal oxidation. Changes of the state of plasma membrane of hepatocytes are shown to be associated with the synthesis of a specific intracellular regulator (invertor).

Key Words: *plasma membranes; microsomal oxidation; phenobarbital; aging*

In our previous studies hyperpolarization of the plasma membrane was shown to develop during activation of protein biosynthesis caused by different factors (action of a number of hormones, regeneration, blood loss) [7]. It has been established that, during exposure to insulin and testosterone, the development of hyperpolarization results from activation of Na,K-ATPase and is governed by the synthesis of specific intracellular genome-controlled regulators, which have been defined by us as invertors [8,10,11]. In the course of aging the pattern of the plasma membrane response to activation of protein biosynthesis alters [11]. A genetic induction of microsomal oxidation enzymes in the liver causes pronounced shifts in protein biosynthesis [1,4]. There are numerous reports that the pattern of genetic induction of microsomal monooxygenases markedly changes in the course of aging [5,12]. The aim of the present study was to investigate age-related specificities of changes of some parameters of the state of the plasma membrane for genetic induction of enzymes of microsomal oxidation and to elucidate the possible mechanism of these shifts.

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MATERIALS AND METHODS

The experiments were carried out on certificated male Wistar rats (6-8 months). Phenobarbital (PB)

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