ROLE OF PENTAGSTRIN AND OXYTOCIN IN DORSAL HIPPOCAMPAL SINGLE UNIT ACTIVITY DURING RESULTATIVE AND CONFLICT-INDUCING FEEDING BEHAVIOR IN RABBITS

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The presence of pentagastrin in the perineuronal space of the dorsal hippocampus promotes selective involvement of the neurons of this region in the organization of goal-directed feeding behavior [2]. On the basis of P. K. Anokhin's theory of functional systems, it has been postulated that dominant excitation of feeding motivation extracts genetic information from memory by activation of certain regions of the genome of nerve cells coding a peptide factor which has a structure similar to that of gastrin.

We know that processes of information extraction from memory are under the marked influence of hypothalamic neuropeptides — vasopressin and oxytocin [5], which are secreted into the perineuronal space of limbic and mesencephalic structures from peptidergic terminals of neurons of the supraoptic and paraventricular nuclei [4]. It has been suggested that these compounds can induce activity of the genome [1].

The aim of this investigation was to study the effect of pentagastrin and oxytocin on the neuronal mechanisms of dominance of feeding motivation excitation.

EXPERIMENTAL METHOD

Experiments were carried out on 6 noninbred male rabbits weighing 2.5-3 kg. Before the experiment began the rabbits were deprived of food for 72 h. They were then placed in an experimental chamber where, under unrestrained conditions, single unit activity was recorded by means of 4-channel glass microelectrodes from area CA3 of the hippocampus. The recording channel of the electrode was filled with a 3 M solution of sodium chloride, and the second and third channels were used for microiontophoretic application of neuropeptides to the recorded neurons, and contained a 10^{-5} M solution of oxytocin and a 10^{-5} M solution of pentagastrin respectively (both substances were from Serva, West Germany). The fourth channel was filled with a 0.5 M solution of sodium chloride to compensate the current effect. The microelectrodes were inserted into the brain through burr-holes in the cranial bones by means of a micromanipulator, fixed to the animal's head. The experimental program was as follows: Activity of a hippocampal neuron in area CA3 of a hungry rabbit was recorded while the animal was offered carrot, and during the next 3 sec while eating it. After 1 min, carrot was again offered, but when the rabbit tried to eat it, an electric shock (ES) was applied to the right ear (frequency 100 Hz, pulse duration 1 msec, amplitude 3-7 V, duration of stimulation 0.5 sec). The carrot was again offered 1 min later and ES applied when the rabbit attempted to eat it. All these procedures were repeated after a further minute, in the same order, with intervals of 1 min during microiontophoretic application of oxytocin to the neuron, and after yet another minute, during combined application of oxytocin and pentagastrin. The results were analyzed by the construction of frequency histograms, with a controlled reset period of 1 sec. Altogether activity of 30 units was recorded by the complete program.

EXPERIMENTAL RESULTS

When carrot was offered to the hungry rabbits the animals approached it after 1-3 sec and started to eat it. A change in the spontaneous firing rate was observed in 32 of the 39 dorsal hippocampal neurons tested in the course of feeding behavior: 15 neurons increased and 17 de-

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TABLE 1. Changes in Dorsal Hippocampal Unit Activity during Feeding Behavior of Rabbits before and during Microiontophoretic Application of Neuropeptides

Experimental conditions	Activation		Inhibition		No change	
	abs.	%	abs.	%	abs.	%
Background	15	38	17	44	7	18
Oxytocin	23	61	10	23	6	16
Oxytocin + pentagastrin	18	46	17	44	4	10

TABLE 2. Changes in Dorsal Hippocampal Unit Activity during Conflict-Inducing Feeding Behavior of Rabbits before and after Microiontophoretic Application of Neuropeptides

Experimental conditions	Activation		Inhibition		No change	
	abs.	%	abs.	%	abs.	%
Background:						
1st combination	17	44	11	28	11	28
2nd combination	9	24	13	33	17	43
Oxytocin:						
1st combination	12	31	13	33	14	36
2nd combination	11	28	14	36	14	36
Oxytocin + pentagastrin:						
1st combination	15	40	14	36	10	24
2nd combination	14	36	17	44	8	20

creased their firing rate. Microiontophoretic application of oxytocin, and later of pentagastrin, changed to relative percentages of dorsal hippocampal neurons activated and inhibited during feeding behavior. Application of oxytocin increased the percentage of neurons activated during feeding behavior whereas application of pentagastrin led to restoration of the original relative percentages of neurons responding in different ways (Table 1). Changes in unit activity during conflict-inducing feeding behavior are illustrated by the data in Table 2.

Infliction of ES on the hungry rabbit when it attempted to eat carrot led to cessation of feeding behavior. Under these conditions 25 (64%) of the 39 neurons changed their activity characteristic of feeding behavior. In response to the second combination of offering of carrot with ES, these changes were even more marked and were observed in 72% of neurons tested. Microiontophoretic application of oxytocin increased the changes in "feeding" activity even more. No changes in activity characteristic of feeding behavior were observed in only 5 of the 39 neurons during combination of the offering of carrot with either the first or the second ES (Fig. 1).

On microiontophoretic application of pentagastrin together with oxytocin to the dorsal hippocampal neurons, they began to exhibit activity characteristic of feeding behavior even when the rabbits did not eat carrot because they received ES when they attempted to do so.

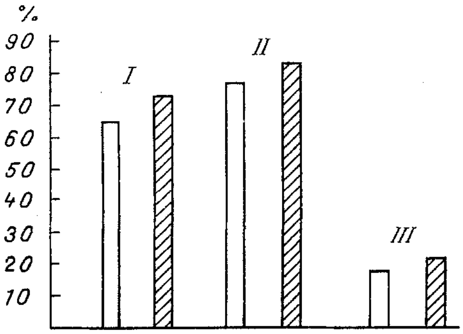

Fig. 1

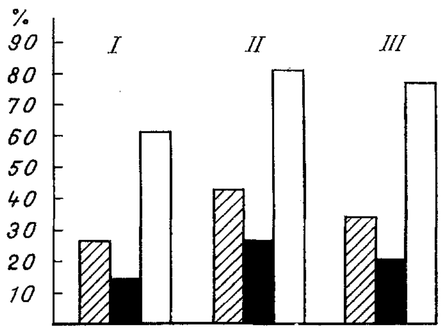

Fig. 2

Fig. 1. Number of neurons changing their electrical activity characteristic of feeding behavior during first (unshaded columns) and second (shaded columns) infliction of ES while rabbit attempted to eat carrot. I) Background; II) oxytocin; III) oxytocin + pentagastrin.

Fig. 2. Relative percentages of responses of the same kind during resultative and conflict-inducing feeding behavior, in response to first ES (I), to repeated stimulation (II), and in all combinations of the offering of carrot with ES (III). Obliquely shaded columns, background; black columns, oxytocin; unshaded columns, oxytocin + pentagastrin.

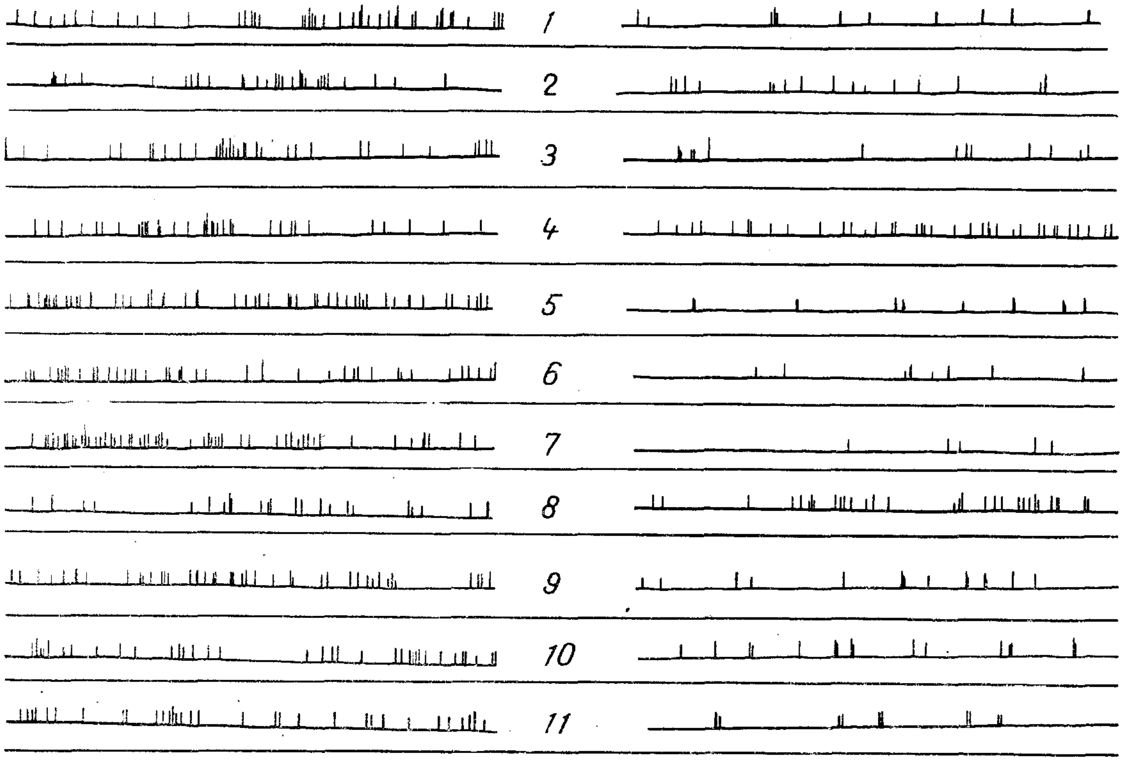

Fig. 3. Changes in firing pattern of hippocampal neuron in area CA3: 1) eating carrot; 2, 3) offering carrot and infliction of ES; 4) microiontophoretic application of oxytocin; 5) eating carrot; 6, 7) combination of offering of carrot with ES during application of oxytocin; 8) application of pentagastrin together with oxytocin; 9) eating carrot against the background of application of pentagastrin and oxytocin; 10, 11) combination of offering of carrot with ES against the same background.

In 23 neurons, similar changes in unit activity were recorded during application of pentagastrin, whether the feeding behavior was resultful or induced conflict (Figs. 2 and 3).

Infliction of ES on a hungry rabbit while attempting to eat food thus causes the cessation of feeding behavior. The dominant feeding motivation of the animals was replaced by defensive while the metabolic demand for food was maintained. Most hippocampal neurons in area CA3 thus changed their firing pattern characteristic of feeding behavior.

On the basis of our hypothesis that dominant feeding-motivated excitation induces the formation of a peptide factor similar in structure to gastrin in neurons [3], it can be tentatively suggested that dominance of the defensive motivation in a hungry rabbit evidently leads to inhibition of formation of the gastrin-like factor in the majority of neurons of the dorsal hippocampus, despite the need for food. The presence of oxytocin in the neuronal space of the hippocampus accelerates this process. Meanwhile application of pentagastrin to the neurons causes the appearance of activity characteristic of feeding behavior, even when, instead of feeding behavior, the rabbit exhibits defensive behavior. This is evidence that the presence of pentagrastrin in the perineuronal space evidently leads to involvement of the majority of dorsal hippocampal neurons in the organization of feeding behavior.

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