Role of Oxytocin in the Regulation of Feeding Behavior of Young Mammals during the Lactotrophic Period

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The effect of exogenous oxytocin on the regulation of sucking motions is studied in rat pups of different age (from day 1 to day 16) during the lactotrophic period. It is shown that specificities of behavior (suckling) in the pups over each period are governed by oxytocin and its concentration. Oxytocin regulates the time during which the pups are attached to the nipple during the first 10 days of the postnatal period, and it also suppresses the feeding behavior of the pups.

Key Words: *oxytocin; regulation; feeding behavior; lactotrophic period*

Along with biologically active substances, peptides (prolactin, calcitonin, somatostatin, β-casomorphine, and oxytocin) are delivered with the mother's milk to the organism of young mammals [11]. As is well known, oxytocin (OT), which has long been regarded as a lactation-associated hormone, is able to elicit behavioral effects [6,10], specifically, to affect the feeding behavior, suppressing it in adult animals [4,7,12].

We aimed to study the pattern of feeding behavior of rat pups and the effect of OT on the behavior during the lactotrophic period.

MATERIALS AND METHODS

The study was carried out on 150 noninbred albino rat pups on postnatal days 1 to 16. The sucking motions of the pups were recorded as follows: a nembutal-narcotized (40 mg/kg) lactating rat was fixed in the supine position, the skin on the abdomen was incised along the linea alba, and the mammary duct (most frequently of the first pair of abdominal mammary glands) was moved aside by the blunt method with the forceps inserted under the skin of the nipple. A rubber cap (length 10-15 mm and outer diameter 1.5-2.0 mm [3]), connected to a polyethylene tube filled with water, was implanted under the skin. The opposite end of the tube was placed under a Biolam microscope with an FMEL-1 photoadapter (comprising a UBPV-1 power unit). The aperture of the attachment was some distance from the water meniscus in the polyethylene tube [1]. The oscillations of the water meniscus, resulting from sucking, were recorded on an N 338-IP recorder. Before the experiment, the rat pups, placed in a Medikor-IK-13/A box, where a stable humidity and a temperature of 33°C were maintained, were deprived of food for 3-22 h. OT was intraperitoneally injected to the adult rat (5 and 0.5 μg/kg) and to the pups during sucking (0.5 μg/kg). The volume of injected solution was 0.3 ml. The record of sucking motions before injection of OT served as the control. OT synthesized at the Experimental Plant of the Institute of Organic Synthesis (Academy of Sciences, Latvia) was used in the experiments.

RESULTS

The follow-up of the behavior of rat pups and recording of the sucking motions for 10 min - 1.5

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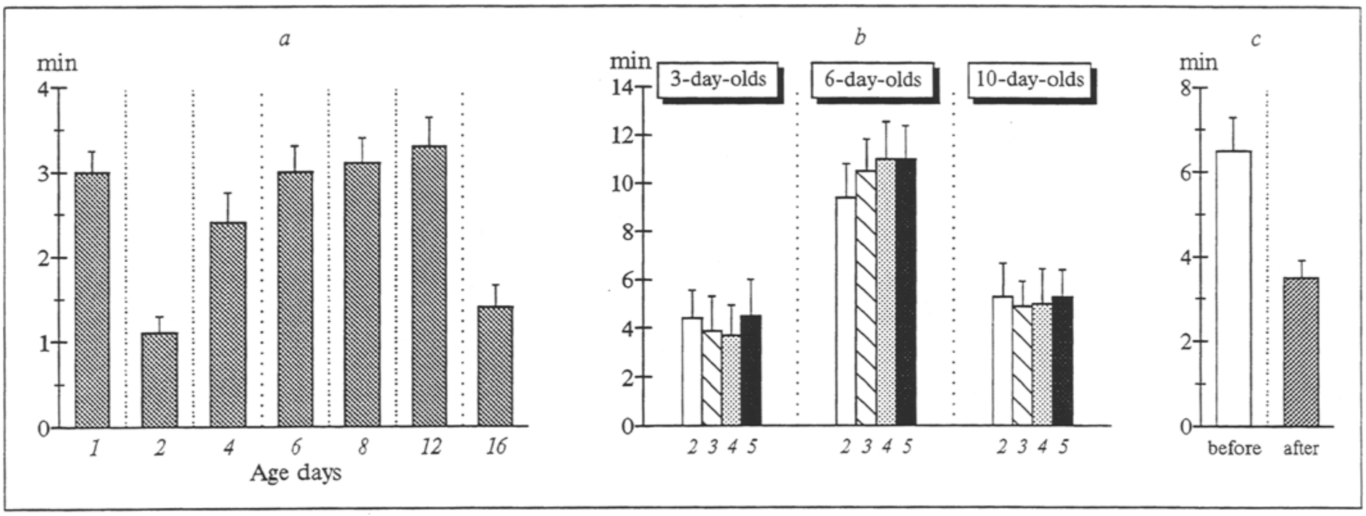

Fig. 1. HMA after first attachment to the nipple (*a*), normal latency (*b*), and latency before and after injecting OT to the mother (*c*). *b*): *1, 2, 3, 4,* and *5* denote the number of successive detachment responses.

h, starting from the moment of attachment to the nipple, enabled us to identify several phases in the pattern of feeding behavior of rat pups: high motor activity (HMA) following the first seizure of the nipple; low motor activity (LMA); rigidity; and subsequent HMA, alternating periodically throughout the period of suckling.

HMA of rat pups was characterized by intensive movements of the body, paws, and head. In 1-, 2-, 4-, 6-, 8-, 12-, and 16-day-old pups HMA lasted 2.98±0.12, 1.14±0.08, 2.33±0.16, 2.88±0.15, 3.07±0.21, 3.34±0.16, and 1.42±0.08 min, respectively. The duration of HMA reliably differed among 2-, 4-, and 16-day old pups (Fig. 1, *a*). A weak motor activity during suckling was characteristic of LMA.

During the following phase - that of rigidity - tension, body arching, extending the fore and hind limbs, and opening the mouth were observed in the pups. This phase lasted for 5-15 sec.

The HMA periodically occurring in the pups throughout the period of suckling was characterized by forelimb pulling movements directed toward the gland, shifting from one paw to another, and pressing with the fore paws on the areola.

A synchronous response of detachment from the nipple was also observed in the rat pups, which was usually preceded by rigidity followed by HMA. The detachment response was noted in 80% of cases. The latency of the first detachment response was longer than that of later responses. In 3-, 6-, and 10-day-old pups the latencies constituted 6.9±1.63 and 24.83±5.09, 6.23±2.01 and 23.78±3.26 (in one litter of this age the latency was as long as 42 min), and 7.57±1.36 and 19.00±1.41 min, respectively. The latency of subsequent detachment responses decreased, becoming relatively constant, and was 4.12±0.24, 9.9±0.74, and 5.15±0.14 min, on average, in 3-, 6-, and 10-day-old pups, respectively (Fig. 1, *b*). In the pups older than 10 days the detachment response was rarely observed or was entirely absent. Starting from days 11-12, the synchronicity of the suckling phases was disturbed in the pups, i.e., each pup exhibited individual behavior at the nipple: the pups would abandon one nipple, go to another one, and spend some time without attaching to the nipple. The time between the first attachment to the nipple and detachment from it was 1.85±0.28 min in 16-day-old pups; later, the pups left the nipple at intervals from 3.35±0.51 to 8.97±1.18 min.

High-amplitude (HA) and low-amplitude (LA) components of suckling, corresponding to certain phases of the feeding behavior of rat pups, were revealed in the records of sucking motions (Fig. 2, *a*, *b*). Sucking with HA is characteristic of HMA, and with LA of LMA. The overall duration of the LA component was slightly longer than that of the HA component. Although there is no consensus on the role of the HA and LA components [8], presumably, the HA component of suckling reflects the motor activity providing for stimulation of the responsive zones of the areola and nipple. The LA component of suckling is due to the actual sucking motions, which was demonstrated in experiments on a nonlactating dam. For instance, a recording of pups' suckling in the case of a nonlactating rat showed that the HA component of suckling manifested itself only in the case of the first attachment to the nipple, provided that the pup received tactile stimulation. The LA component of sucking motions was mainly observed. Along with this, the entire complex of the above-

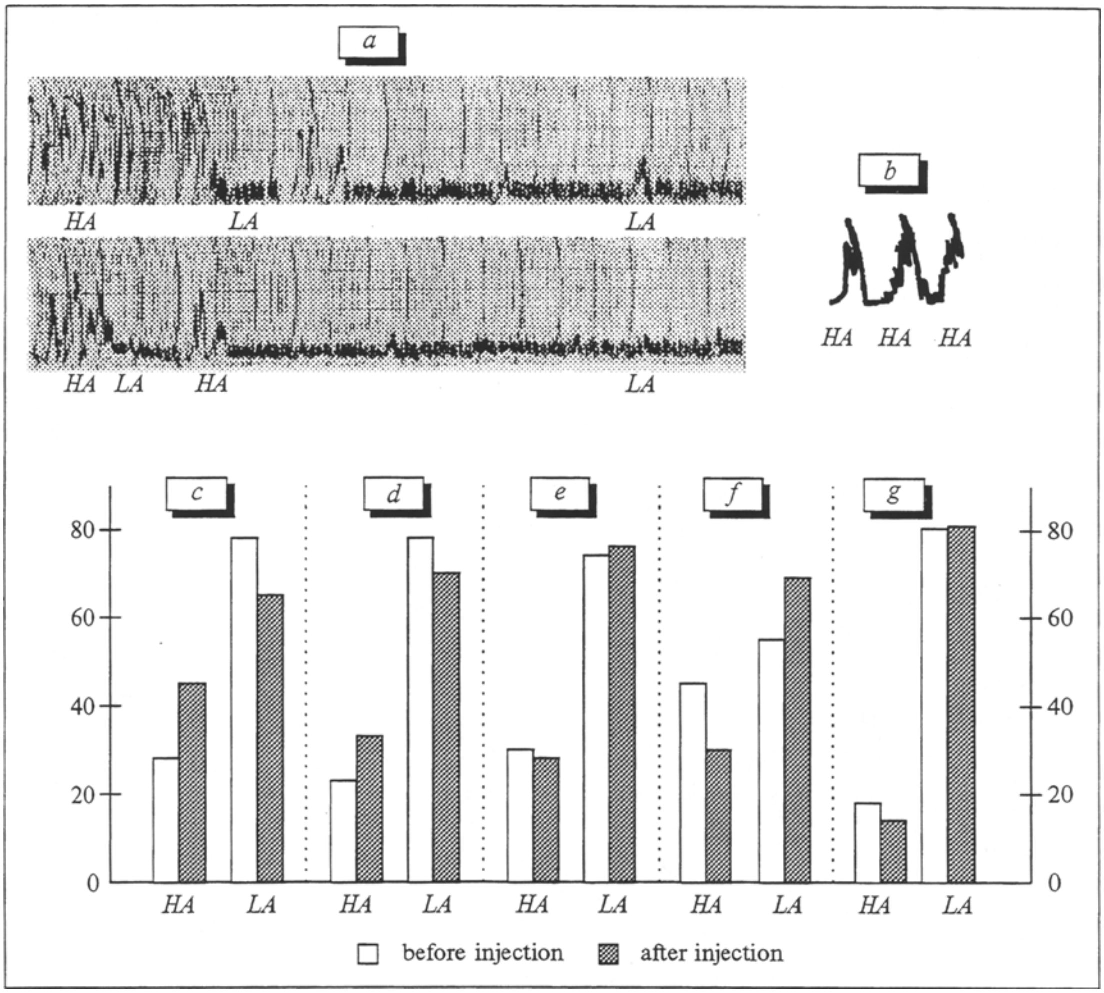

Fig. 2. Normal sucking motions of 1- (*a*) and 16- (*b*) day-old rat pups. Duration of HA and LA components of suckling after OT (*c* and *d*) and physiological saline (*e*) were injected to the mother, and after OT (*f*) and physiological saline (*g*) were injected to the pups.

mentioned phases was not revealed in the feeding behavior of these pups.

Thus, two stages of the feeding behavior of rat pups can be identified: the first (till day 10) is characterized by a longer time spent by the pups at the nipple and by the synchronous development of the phases of behavior (LMA, rigidity, HMA, and abandonment of the nipple) in all pups of the same mother. The second stage (from postnatal day 11) is characterized by the establishment of self-regulation of the behavior specific for each pup, which goes hand in hand with regulatory processes provided by the mother. This stage may also be governed by biologically active substances in the mother's milk.

Injection of OT to a lactating dam resulted in the rapid development of synchronous responses (rigidity, HMA, and detachment from the nipple) in the early postnatal rat pups during the LMA phase. When OT was injected in a concentration of 5 μg/kg, these responses were observed after 0.52±0.05 min in 90% of cases. OT in a concentration of 0.5 μg/kg caused rigidity, HMA, and the detachment responses after 2.14±0.56 min in 66.67% of cases, while the mean latency of later detachment responses dropped to 3.06±0.37 min (the normal latency was 6.39±0.34 min) (Fig. 1, *c*). The duration of the HA component of suckling after injection of OT (5 and 0.5 μg/kg) to the lactating rat increased, this being attended by a shortened duration of the LA component (Fig. 2, *c*, *d*).

Intraperitoneal injection of OT (0.5 μg/kg) to rat pups suppressed their motor activity, which manifested itself in the absence of the above-mentioned typical responses: rigidity, HMA, and detachment from the nipple (Fig. 2, *f*). Changes of the HA and LA components of suckling were opposite to those observed after injection of OT to the dam, i.e., the duration of the HA component of suckling decreased and the duration of the LA component increased. Control injection of physi-

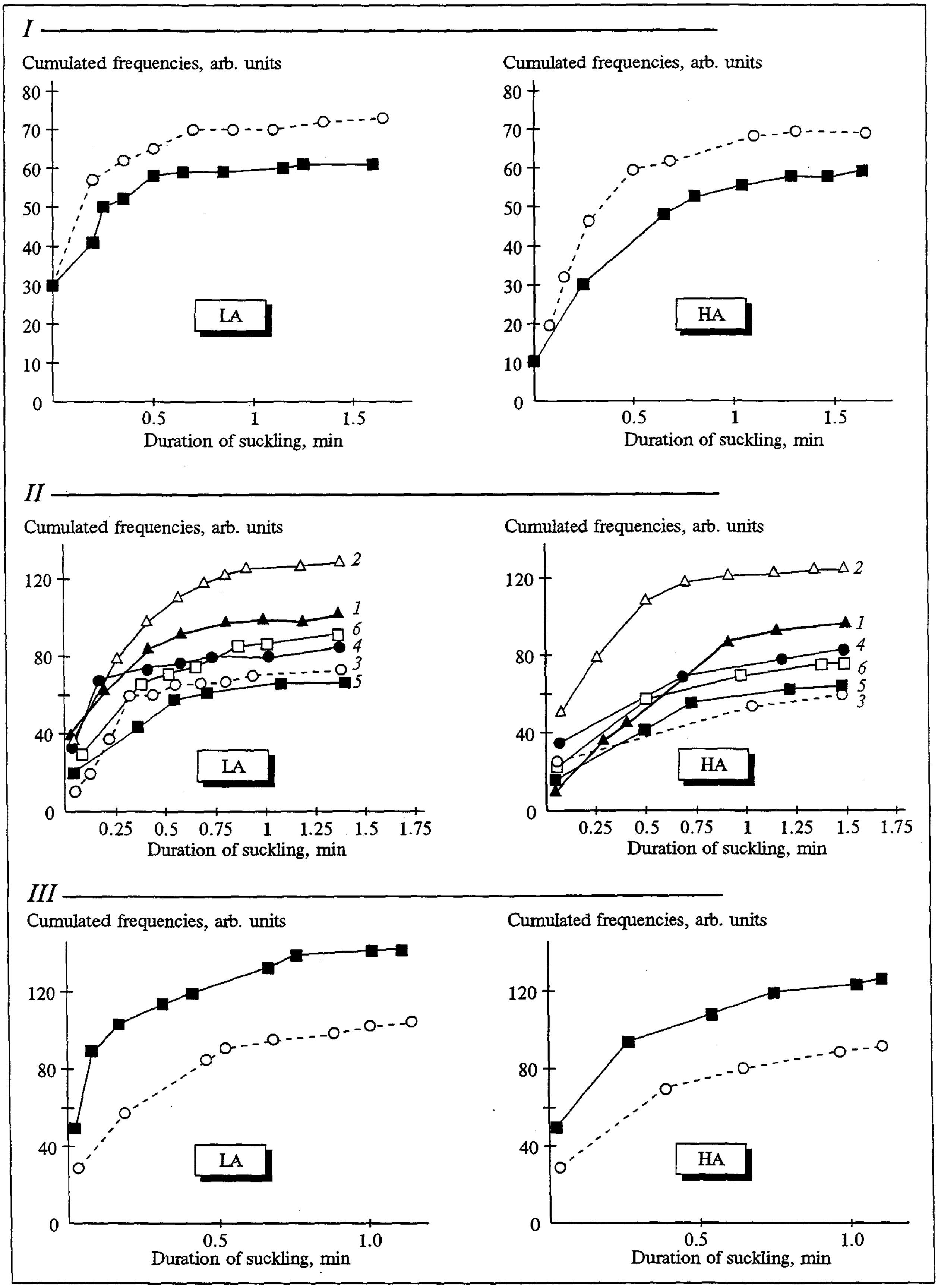

Fig. 3. Duration of suckling after injection of OT to the mother (*I* and *II*) and to the pups (*III*). *II*: *1* and *2*) 3-day-old rat pups; *3* and *4*) 5-day-old rat pups; *5* and *6*) 7-day-old rat pups.

ological saline to either the dam or the pups did not alter the tempo of onset of rigidity, HMA, and detachment from the nipple. The duration of the HA and LA components of suckling did not change reliably after injection of physiological saline to the dam and pups (Fig. 2, *e*, *g*).

The method of variation series, which makes it possible to assess the significance of the HA and LA components of suckling more precisely, demonstrated that their changes were unidirectional. For example, when OT (5 and 0.5 μg/kg) was injected to the dam, the duration of the HA and LA components of suckling increased (Fig. 3, *I*, *II*), and when it was injected to the pups, the duration of the HA, as well as of the LA, component decreased (Fig. 3, *III*).

Thus, the regulation of behavior at the first stage is mediated by biologically active substances in the mother's milk; OT, according to our findings, seems likely to be one of these substances.

Synchronous detachment of the pups from the nipple may be an important factor of adaptation for the mother rat, which needs to leave the nest. Under natural conditions simultaneous discontinuation of suckling is underpinned by the discrete release of OT in the rat, evidence of which is a longer latency of the first detachment response, closely correlating with the time of reflex release of OT. This has also been shown in studies of other researchers [9,13,14].

Analysis of the synchronicity of LMA, rigidity, HMA, and detachment from the nipple suggests that the effects observed are due to changes in the size and shape of the nipple, which are caused by biologically active substances in the mother. Reportedly, both intraperitoneal injection and a short-term (5-50 sec) application of OT to the surface of the gland of the lactating female cause constriction of the vessels, myoepithelial structures, and muscles of the nipple and areola. A change in the shape of the nipple may weaken the hermetic sealing of the space around the nipple [5]. This in turn underlies the synchronous detachment of the pups from the nipple. On the other hand, injection of exogenous OT to pups reduced the HA and LA components of suckling, which testifies to the suppression of feeding behavior and to the regulation of the time spent by the pups at the nipple.

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