PHYSIOLOGY

Impact of Exogenous Oxytocin on the Motor Function of the Mammalian Small Intestine in the Lactotrophic Period

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The establishment of the motor function of the small intestine during postnatal ontogeny and the impact of exogenous oxytocin on this function in the lactotrophic period were examined in rats. In the first week of life, only peristaltic movements of the small intestine were detectable, possibly due to the weak development of the longitudinal and circular muscle layers in the small intestine wall. Oxytocin was found to have an inhibitory effect on small intestine motor activity in rat pups.

Key Words: *oxytocin; small intestine motor activity; lactotrophic period; biogenic amines*

The establishment of gastrointestinal tract (gastrointestinal tract) function during postnatal ontogeny remains a poorly researched area. The relevant information in the literature is scanty and contradictory [3,8]. The discovery of various biologically active substances, including peptides [7,11], in the maternal milk raised the question of their participation in the regulation of bodily functions, in particular the motor activity of the digestive tract, in the offspring. One such substance is oxytocin, which enters the gastrointestinal tract with the milk and has also been shown to influence intestinal motor function in adult animals [2,4,6].

The present investigation on rats was undertaken to examine how the motor function of the small intestine (SI) develops during postnatal ontogeny and to measure the effect of oxytocin on this function in the lactotrophic period.

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MATERIALS AND METHODS

For the experiments, a total of 75 random-bred rats were used, including 65 pups aged 1 to 20 days and 10 young adult rats aged 2 months. The development of the muscular coats (longitudinal and circular layers) of the SI wall was examined on histological specimens prepared by staining longitudinal and transverse sections of these layers with hematoxylin and eosin. The thickness of the muscle wall layers was measured using an eyepiece micrometer. Adrenergic nerve supply and enterochromaffin cells were demonstrated by a fluorescence histochemical technique using glyoxylic acid [9] on total SI wall preparations placed between two slides. Motor activity of the SI in the pups was recorded photometrically [1]; for this, the pups were anesthetized with Nembutal (40 mg/kg subcutaneously), an SI loop was isolated through midline incision, and an area suitable for biomicroscopy was found. Thereafter, the movements of the intestinal wall (in pups aged ≤1 week) and mesenteric blood vessels (in older pups) were re-

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corded during intestinal motor activity. Signals from the photometric attachment were amplified and recorded on an automatic N-338-1P recorder. Oxytocin (5.5 pg/ml) was injected from a fine needle through the intestinal wall in a volume of 0.3 ml, which did not cause intestinal distention. The control animals were injected with the same volume of physiological saline.

RESULTS

It was found that during the period from day 1 to days 7-10 after birth the thickness of the longitudinal layer increases from 9.53±0.24 to 14.44±0.40 μ and that of the circular layer from 20.43±0.41 to 24.74±0.40 μ, i.e., to a lesser extent. The unequal development of the circular and longitudinal layers was reflected in different ratios of their thicknesses, which equaled 2.1 in neonates and 1.7 in pups aged 7-10 days. In the young adult rats, the circular and longitudinal layers were much thicker than in the pups - 75.17±6.01 and 37.50±2.94 μ, respectively (Fig. 1, *I*).

The fluorescence histochemical study of SI walls in the pups and adult rats revealed the presence of numerous adrenergic fibers in the muscular layers. Shortly after birth, longitudinal and (more massive) transverse nerve fiber bundles were observed to form a network in the intestinal muscular layer, and small numbers of fibers were found running along blood vessels. The latter fibers were more conspicuous by days 9-10 after birth, at which time the transverse and longitudinal fiber bundles had become thicker, with a considerable increase in the distances between parallel bundles in the network. In adult animals, bundles of fibers running along blood vessels were noted. No other fibers were detected at this age.

Concurrently with the adrenergic fibers, enterochromaffin cells were seen, whose characteristic feature was the increase of the fluorescence with age. In the 2-day-old pups, a weak fluorescence of the cytoplasm adjoining the nucleus was observed. In adult rats, most cells had a process, and the cells were larger than those in the pups (Fig. 2).

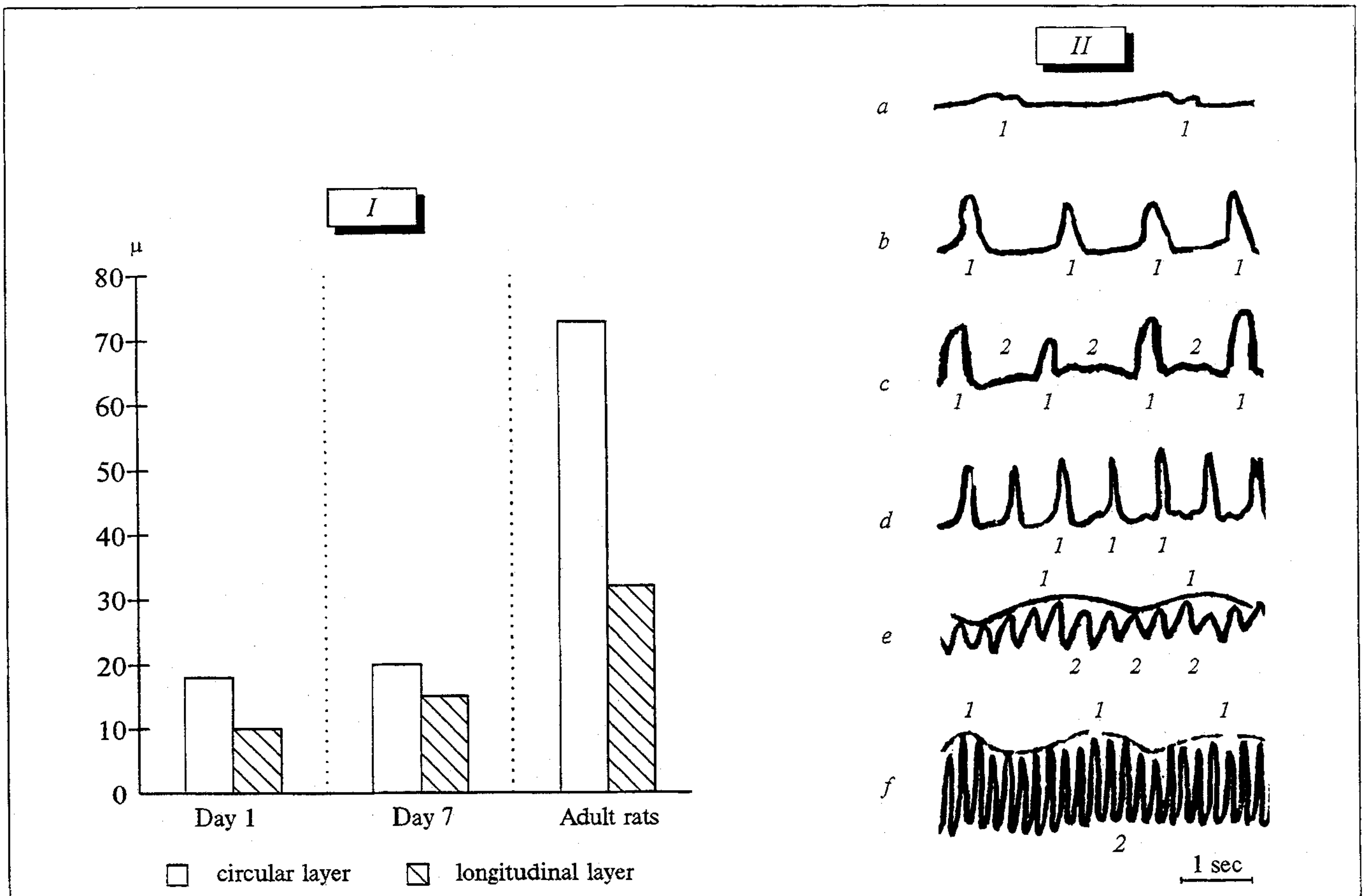

Fig. 1. Ratio between two muscular layers of the SI in rats of different ages (*I*) and motor activity of the SI during postnatal ontogeny in rats at the age of 2 (*a*), 5 (*b*), 7 (*c* and *e*), 14 (*d*), and 20 (*f*) days (*II*). *1)* peristaltic movements; *2)* penduliform movements.

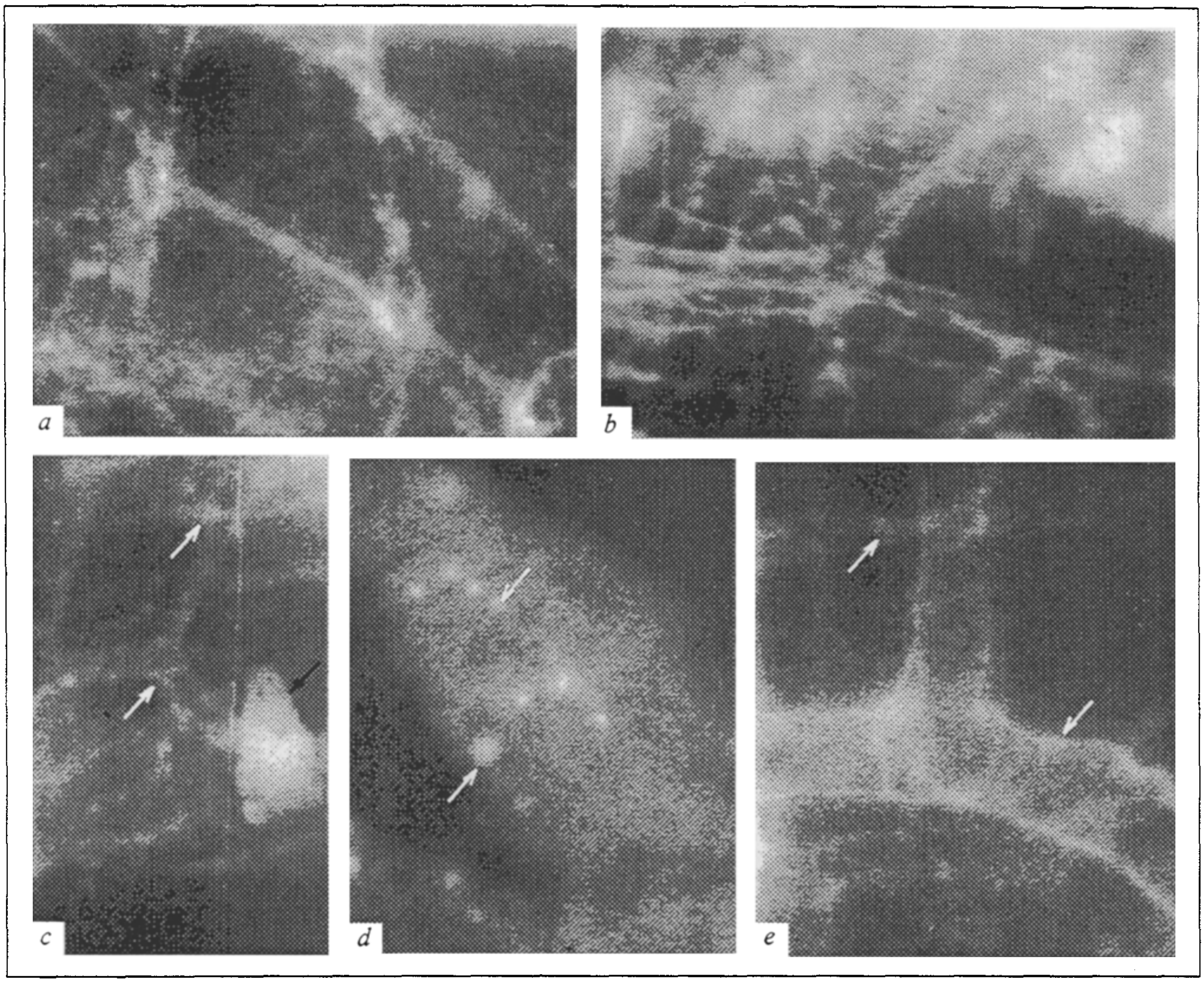

Fig. 2. Distribution of biogenic amines in the SI wall of rat pups at different ages. Network of adrenergic fibers in a blood vessel at the age of 1 (*a*), 2 (*b*), and 10 (*c* and *e*) days (black arrow: villus; white arrow: fibers); *d*) villus (arrows indicate chromaffin cells). *a*, *d*, and *e*) ×400; *b* and *c*) ×100.

Motor activity of the SI also changed with age (Fig. 1, *II*). The SI of most pups aged ≤1 week performed peristaltic movements almost exclusively. In pups aged 7-14 days, penduliform as well as peristaltic movements were recorded. The frequency of penduliform movements ranged from 6-12 per minute in some pups (Fig. 1, *II*, *c*) to 18-27 per minute in others (Fig. 1, *II*, *e*). Penduliform movements were more frequent in older pups (27-33 per minute) (Fig. 1, *f*).

It should be noted that the frequency of peristaltic movements increased by the middle of the lactotrophic period (Fig. 1, *II*, *d*) and then decreased with age (Fig. 1, *II*, *e* and *f*).

Thus, as this study has shown, peristaltic movements of the SI occur in rats during the first week of life, while penduliform movements are also recorded later. The increasing complexity of intestinal motor activity is probably linked with the development of muscular layers in the intestinal wall. Since the longitudinal muscular layer is better developed by day 7 after birth than the circular, the appearance of penduliform movements may be associated with the increasingly complex organization of this layer. The further development of nerve supply to the muscle wall is reflected not only in its increasing thickness, but also in the stepped-up rate and force of muscle contractions.

Oxytocin injected into the SI during the lactotrophic period was found to inhibit its motor activity in pups of all ages. The inhibition lasted 10-15 min, after which intestinal motor activity was restored (Fig. 3, *a-e*). The inhibitory action of oxytocin was manifested in significantly lower amplitudes ($p<0.001$) of penduliform movements performed by the SI in pups aged 7-20 days, followed by a return of the amplitudes to their initial values (Fig. 3, *g*). The frequency of pendu-

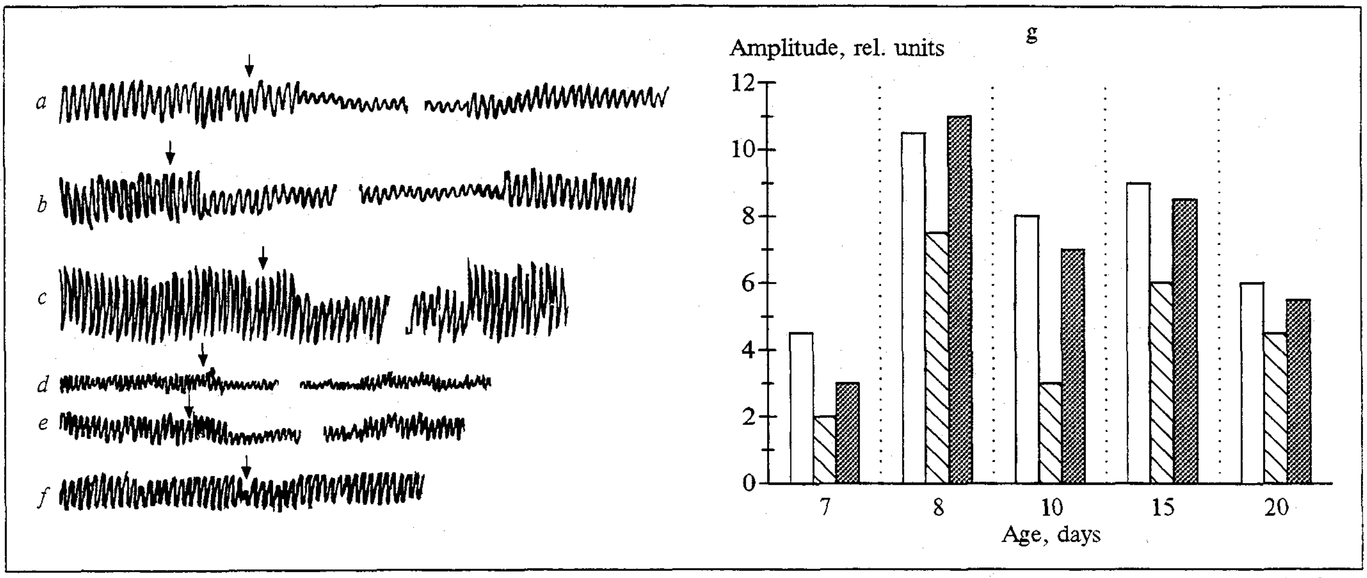

Fig. 3. Effect of oxytocin on motor activity of the small intestine in rats during ontogeny. Age in days: *a)* 7; *b)* 10; *c)* 15; *d)* 18; *e)* 20. The times of oxytocin (5.5 pg/ml, 0.3 ml) and saline (*f*) injection are shown by an arrow. *g*: white bars, before oxytocin or saline injection; black bars, after injection; hatched bars, activity is regained.

liform movements in this age range was not affected by oxytocin and varied from 18 to 36 per minute.

Physiological saline did not significantly change either the amplitude or frequency of penduliform movements in the pups (Fig. 3, *f*).

In conclusion, the present experiments revealed an inhibitory effect of oxytocin on the motor activity of the SI in rat pups of all ages. On the other hand, it is well known that oxytocin exerts an activating effect on the smooth musculature of other organs (uterus, glandular ducts, etc.). Biogenic amines, whose inhibitory influence on the motor function of the gastrointestinal tract is also well known, have been detected at very early stages of postnatal ontogeny [5]. This suggests that biogenic amines may be involved in directing the effect of oxytocin on the motor activity of the SI. Sources of biogenic amines may be enterochromaffin cells and adrenergic fibers which are identifiable from birth on. However, the question of whether receptors for oxytocin are present on enterochromaffin cells during early postnatal ontogeny remains open. Nevertheless, our findings and those of other investigators [2, 10] provide indirect evidence that biogenic amines do mediate the inhibitory effect of oxytocin on SI motility.

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