Development of the Motor Activity of the Rat Gastrointestinal Tract by In Vitro Measurement

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Abstract To clarify the postnatal developmental changes of the motor activity of the gastrointestinal tract, the frequency and amplitude of spontaneous intraluminal pressure of the isolated stomach, duodenum, jejunum, and ileum of the 1- to 5-week-old rat and adult (over 12 weeks old) were examined in vitro. The spectral frequencies of the spontaneous motor activity of 1- to 2-week-old rat were significantly lower than those of the adult. They became similar to the values of the adult at 3–4 weeks after birth. The amplitudes of spontaneous motor activity of 1- to 3-week-old rats were significantly smaller than those of adults. They became similar to the values of adults at 4 weeks after birth. Body weight, stomach wet weight and the length of the total intestine increased gradually and they were still below the values of the adult even at 5 weeks after birth. The stomach was filled with just milk until the end of 2 weeks. However, by the end of 3–4 weeks, milk and solid food were found in the stomach. By the end of 5 weeks, just solid food was seen in the stomach. Therefore, the motor activity of the gastrointestinal tract at birth seems immature and gradually develops postnatally. It seems to be mature by the end of 3–4 weeks after birth. Interestingly, the time of the pacemaker or motor maturity of the gastrointestinal tract according to spontaneous frequency or pacemaker activity and amplitude seemed almost consistent with the weaning time.

Key words: pacemaker, BER, ontogenic development, gastrointestinal system.

The motor activity of the gastrointestinal tract seems to develop gradually after birth in dogs and sheep. The frequency of slow waves increases postnatally [1]. Spontaneous motor activity seems to be controlled by slow waves. It is reported that slow waves or BER (basic electric rhythm or ECA, electrical control activity) associates intraluminal pressure changes in the intestine [2]. Therefore,
we compared the frequency of spontaneous intraluminal pressure waves of the gastrointestinal system of normal and diabetic rats in vitro, probably slow wave-associated [3]. Similar spontaneous motor activity may be recorded in the neonatal gastrointestinal system of the rat. Therefore, it seems possible to examine the ontogenic developmental changes of the gastrointestinal system, by recording the BER-associated spontaneous motor activity in vitro. The purpose of the present study is to examine the ontogenic developmental changes in the amplitude and spectral frequency of the in vitro spontaneous intraluminal pressure of the isolated stomach and the intestine of the rat. The frequency and amplitude of the spontaneous motor activity increased gradually and reached the adult level around 4 weeks after birth.

MATERIALS AND METHODS

Pregnant Wistar female rats were purchased commercially. Each dam bore 12–14 newborn rats. They were allowed to suck freely and later they were also fed ad libitum. Their body weight was measured on the experimental day. It was impossible to record intraluminal pressure of the gastrointestinal tract until 4–5 d after birth because of the smallness of the system and tissue fragility. One-week-old rats contained that of 4–7 d old; 2-week-old rats contained that of 8–14 d old; 3 weeks, that of 15–21 d old; 4 weeks, that of 22–28 d old; and 5 weeks, 29–35 d old. The total gastrointestinal tract was dissected out from the offspring 1–5 weeks old and from adult rats (over 12 weeks old) under ether anesthesia. The stomach was easy to identify by its shape. The length of the other alimentary tract was measured. The duodenum was identified as that part from the pylorus to Treiz’s band. The next caudal part was used as the jejunum. The oral part of the large caecum was used as the ileum. The inside of the stomach, when possible, and the divided intestinal segments were flushed and rinsed with Krebs solution. Their wet weight was measured. They were kept in iced Krebs solution until the experimental use. The composition of the Krebs solution was as follows (mM): NaCl, 116; KCl, 4.4; CaCl₂, 2.1; MgSO₄, 1.2; KH₂PO₄, 1.5; NaHCO₃, 29; and glucose, 4.0.

Each segment was set in warmed (37°C) and aerated Krebs solution (95% O₂ and 5% CO₂) in a Magnus-type chamber and the polyethylene tube was inserted between the transducer and the preparations. A Mariotte bottle was also connected to that system via a three-way valve. The reference point of the Mariotte bottle was settled at the level of Krebs solution inside the Magnus-type chamber as in the previous works to keep the inside and outside of the preparations isobaric [3, 4]. The spontaneous changes in the intraluminal pressure were recorded on the chart recorder and on floppy computer disks after analog-digital conversion. Spectral analysis was performed using a personal computer by the maximal entropy method (PC 9801 RA, NEC, Japan) [4]. Statistical significance was estimated by Student’s t-test.

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RESULTS

Developmental changes of spontaneous motor frequency

The spontaneous motor frequency of the gastrointestinal tract by spectral analysis increased gradually to the adult level as the rats grew older. The spectral frequency of the stomach at the end of 1 and 2 weeks were $1.42 \pm 0.080$ cycle per minute (cpm) ($n=5$) and $2.26 \pm 0.35$ cpm ($n=5$), respectively. They were significantly slower than those of adults ($4.86 \pm 0.21$ cpm, $n=5$) ($p < 0.001$). The spectral frequency increased to $4.20 \pm 0.73$ cpm ($n=5$) at the end of 3 weeks, to $4.36 \pm 0.19$ cpm ($n=5$) at the end of 4 weeks and to $4.78 \pm 0.23$ cpm ($n=5$) at the end of 5 weeks (Fig. 1).

The spectral frequency of spontaneous duodenal, jejunal, and ileal motor activity increased in a similar manner. The spectral frequency at the end of 1 week was $26.8 \pm 0.70$, $21.6 \pm 0.40$, and $22.5 \pm 0.63$ cpm ($n=5$), respectively, and $31.3 \pm 0.45$, $27.4 \pm 0.52$, and $22.5 \pm 0.63$ cpm ($n=5$), respectively, at the end of 3 weeks. These values were significantly slower (except the ileum) than those of adults ($33.9 \pm 0.25$, $30.4 \pm 0.55$, $24.6 \pm 0.87$, respectively) ($p < 0.001$–0.05). However, at the end of 3 weeks, the values ($34.8 \pm 0.72$, $29.3 \pm 0.93$, $28.8 \pm 1.01$ cpm) were not significantly different from the adult values (Fig. 2).

It is interesting that the frequency gradient along the small intestine [5] is recognizable even in 1-week-old rats, as seen in Fig. 2.

![Fig. 1](image.png)

Fig. 1. Developmental changes in peak spectral frequency of spontaneous motor activity of the stomach according to age in weeks (1–5 weeks and the adult). Adult was defined as over 12 weeks old. Each point and the vertical bar represents the mean and standard error (SE) of 5 preparations ($n=5$). The mean spectral frequency at 1 and 2 weeks old was significantly lower than that of adults ($p<0.001$). It was similar to the adult value at 3 weeks. Ordinate, spectral frequency in cycle per minute (cpm). Abscissa, age in weeks.
Fig. 2. Developmental changes in peak spectral frequency of spontaneous motor activity of the duodenum, jejunum, and ileum from 1 to 5 weeks and to adult \( (n=5) \). The frequency of the duodenum and jejunum at 1–2 weeks old was significantly slower than that of adults \( (p < 0.001 - 0.05) \) and it became similar to the adult value at 3 weeks. Ordinate and abscissa, same as Fig. 1.

**Developmental changes in amplitude of spontaneous motor activity**

The amplitude of intraluminal pressure of the stomach increased gradually. The values were \( 0.023 \pm 0.0012 \) mmHg at the end of 1 week, \( 0.025 \pm 0.0093 \) at the end of 2 weeks, \( 0.035 \pm 0.0057 \) at the end of 3 weeks, \( 0.071 \pm 0.037 \) at the end of 4 weeks, \( 0.070 \pm 0.0090 \) at the end of 5 weeks and \( 0.075 \pm 0.0068 \) for the adults. The amplitude from 1–3 weeks old was significantly smaller (except jejunum) than that of the adults \( (p < 0.001 - 0.05) \) (Fig. 3). The motor amplitude of the duodenum, jejunum and ileum increased in a similar manner as the stomach (Fig. 3).

**Other general characteristics**

The time course of the increase in body weight and wet weight of the stomach is shown in Fig. 4A. The length of the duodenum and the other small intestine was similar to the adult by the end of 4 weeks (Fig. 4B).

The color of the content of the stomach was purely white at the end of 1–2 weeks, indicating that the content was purely milk. At the end of 3 weeks, the content of the gastric fundus was brown, indicating that the content was solid rat food (commercially obtained), while the contents aboral to the solid food in the gastric body was milk. Thus, white content occupied about 80% of the gastric content at the end of 3 weeks. At the end of 4 weeks, the white content decreased to about 50% and at the end of 5 weeks, brown contents occupied the whole stomach. Therefore, weaning was suggested to begin at 3 weeks and to finish about the end of 5 weeks (Fig. 5).
DEVELOPMENT OF GASTROINTESTINAL PACEMAKER

Fig. 3. Developmental changes in amplitude of spontaneous intraluminal pressure of the stomach, duodenum, jejunum, and ileum. Their amplitude from 1 to 3 weeks (except the jejunum) was significantly smaller than that of the adult ($p < 0.001–0.05$) and it became similar to the adult value at 4 weeks. Ordinate, pressure in mmHg. Abscissa, age in weeks.

DISCUSSION

The motor activity of the gastrointestinal tract seems to be immature at birth and gradually develops postnataally. The frequency of slow waves of the small intestine increases postnataally in the dog, gradually from 10 to 18/min for 40 d [1]. In the case of sheep, the frequency is much higher at birth and increases much more rapidly [1]. The contractility of the smooth muscle of the stomach of neonate is reported to be weaker than that of the adult in some animals [6–10]. The frequency of the spontaneous motor activity of the gastrointestinal tract is reported to be regulated by the presumable pacemaker, the interstitial cells of Cajal [11–14]. Slower spontaneous motor activity at 1–2 weeks than in adults suggest that the pacemaker cells and their network are immature at birth and develop gradually, postnataally.

The amplitude of intraluminal pressure also increased gradually in the stomach and other small intestine. The wet weight of the stomach and the length of small intestine increased gradually. Probably, as the wall thickness increases, the tension
Fig. 4. A: Increase in body weight and the stomach wet weight (ordinate, g) according to age in weeks (abscissa). B: Increase in length of the duodenum and the other small intestine (ordinate, mm) according to age in weeks (abscissa).

produced an increase concomitantly. The contractility of the antral smooth muscles of the newborn is weaker than that of the adult when stimulated with acetylcholine, potassium and calcium [10]. Furthermore, it is reported that the
gastric emptying time is delayed in the newborn, especially in the premature newborn [15, 16]. Similarly, the smooth muscle of the gastric fundus of neonates and adults is reported to contract by utilizing both intracellular and extracellular calcium for contraction. However, in neonates, intracellular calcium stores are not used or are not available for contraction [7]. The number of calcium channels is reported to be fewer in neonates than in adults [17]. These reports suggest that the contractility in neonate smooth muscle is not solely the same as that of adult. It is conceivable that the increase in the amplitude of spontaneous motor activity depends upon the increase in the number of calcium channels and the availability of calcium ions for contraction. It is interesting that the interstitial cells of Cajal generate cyclic potential changes depending upon the concentration of external calcium ions [12].

Most interestingly, the time of maturation of the spontaneous motor activity both in frequency and amplitude of the gastrointestinal tract was consistent with the weaning time in our study.

In summary, the motor activity of the gastrointestinal tract was immature at birth and postnatally developed gradually in preparation for taking solid food.

This paper has already appeared in abstract form [18].
REFERENCES