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Development of gastric slow waves in preterm infants measured by electrogastrography

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Liang, Jie, Edward Co, Ming Zhang, Josef Pineda, and J. D. Z. Chen. Development of gastric slow waves in preterm infants measured by electrogastrography. *Am. J. Physiol.* 274 (Gastrointest. Liver Physiol. 37): G503–G508, 1998.—The aim of this study was to investigate the developmental process of gastric myoelectrical activity (GMA) in preterm infants. Nineteen healthy preterm infants were studied. GMA was recorded using surface electrogastrography, and six follow-up studies were performed in each subject. Spectral analysis methods were applied to compute the parameters of the electrogastrogram (EGG). The results showed that there was a developmental process of GMA with age during the first 6 mo of life. 1) The percentage of normal slow waves showed a progressive increase after birth (36.7 ± 6.1 , 37.8 ± 6.2 , 47.0 ± 10.0 , 52.2 ± 12.2 , 55.2 ± 9.7 , and $65.8 \pm 13.5\%$ at 1 and 2 wk and 1, 2, 4, and 6 mo, respectively); 2) there was a significant postprandial increase in the percentage of normal slow waves during the first 2 mo after birth; and 3) the percentages of normal slow waves for different gestation ages were not statistically significant. In conclusion, the percentage of normal slow waves is low at birth and there is a developmental process that may be stimulated by enteral feeding.

gastrointestinal motility; gastric emptying; stomach

THE SURFACE ELECTROGASTROGRAM (EGG) is a noninvasive measurement of myoelectrical activity of the stomach (3, 21). Numerous studies (7, 13, 18, 31) have reported normal patterns of the EGG in healthy adult subjects. A higher prevalence of abnormal EGG patterns such as gastric dysrhythmias has been associated with gastrointestinal motor disorders, such as gastroparesis, and symptoms of nausea and vomiting (1, 9, 20, 22, 25, 29, 30, 34). Although the vast majority of studies are being performed in adults, an increasing interest has developed in utilizing the EGG for the study of gastric electrophysiology in infants (14, 28).

Although the structural features of the gastrointestinal tract are well developed by the end of the second trimester of pregnancy, functional maturation continues throughout fetal gestation and into postnatal life. Neither gastric secretory function nor gastric motility is fully developed at birth in humans (37). Production rates for acid are <50% of adult values during the first 3 mo of life and reach mature levels only after 2 years of age (2). By 27–28 wk of gestation, the gastric antrum exhibits 20–25% of the motility level reached by term infants (5). Similar situations can be found in gastric myoelectrical activity (GMA) in neonates. Our previous study (12) in subjects of different age groups revealed that the normal gastric slow waves are almost absent at birth, present at the age of 2–4 mo, and well developed at the age of 4–11 years. It is both physiologi-

cally and clinically significant to know how GMA develops and when it matures in humans. The aim of this study was to investigate the developmental process of GMA in preterm infants from birth to 6 mo.

METHODS

Subjects

The study was performed in 19 preterm infants (12 male, 7 female; gestational age at birth, 33.5 ± 2.6 wk; birth wt, $1,749 \pm 50$ g). None of the infants had systemic disease, feeding intolerance, or esophageal reflux or needed mechanical ventilation or were under intensive care. They were healthy, growing, and under stable conditions before and during the study. All subjects were kept nothing per oral for 1–2 days after birth and then enteral feeding began, gradually increased, and reached full feeding by 1 wk after birth. The study of the EGG was initiated at 1 wk after birth. The study protocol was approved by the Institutional Review Board at the Integris Baptist Medical Center of Oklahoma. Written consent was obtained from the parents of the subjects before the study.

Electrogastrography

GMA in each subject was measured using surface electrogastrography. Before attachment of electrodes, the abdominal skin at the recording sites was cleaned using sandy skin-preparation paste (Omniprep, Weaver, Aurora, CO) to reduce the impedance. Three pediatric disposable silver-silver chloride electrodes (Hewlett-Packard, Andover, MA) were placed on the abdomen. One electrode was placed at the midpoint between the xiphoid and the navel, one was placed at 3 cm to the left and 3 cm above this point, and a reference electrode was placed in the lower quadrant close to the left costal margin. The two epigastric electrodes were connected to yield a bipolar EGG signal, while the other electrode was used as a reference. The EGG signal was recorded using a portable EGG recording device (Digitrapper EGG, Synectics Medical, Irving, TX) with low and high cutoff frequencies of 1 and 18 cycles/min (cpm), respectively.

Experimental Protocol

The study consisted of six follow-up recordings of the EGG at the postnatal ages of 1 and 2 wk and 1, 2, 4, and 6 mo. An overnight EGG recording of up to 12 h was made in each session. Although there were a lot of motion artifacts, clean periods of >30 min were available for both preprandial and postprandial data because of the long period of recordings. Most of the recordings were made at the subjects' homes, except a few that were made at the Neonatal Intensive Care Unit for some of the newborn infants at 1–2 wk. Regular milk was given, based on the choice of the parents. The meal intervals were equal to or longer than 3 h. Feeding time was recorded on the data sheets during all six follow-up recording sessions.

To examine the physical development of the infants, parents were requested to complete infant monitoring question-

naires at the end of the study (6 mo after birth). The content of the questionnaire was derived from the developmental literature and included communication, gross motor, fine motor, adaptive, personal-social, and overall scales. The score for each question was in the range of 0–6 with 0 for yet undeveloped and 6 for well developed.

Data Analysis

The EGG signal was digitized with a sampling frequency of 1 Hz and stored on the portable recording device. At the end of each study, the device was connected to a 486 personal computer and the EGG data were uploaded to the computer. Before quantitative and statistical analyses, the EGG recording was first displayed on the computer and the portions contaminated by motion artifacts were deleted. The deletion was performed visually by a laboratory staff member who did not know the study design. The staff was trained using EGG data in 20 healthy adult subjects who mimicked various motions during the recording of the EGG. Motion artifacts were characterized by an abrupt increase in amplitude and usually reached maximum values of the digitization. All data within one-half hour before the meal (they must be at least 2.5 h after the previous meal) were considered as preprandial data, and all data within 1 h after the meal were considered as postprandial data. The pattern of the EGG was characterized by several quantitative parameters, including the percentage of regular 2- to 4-cpm slow waves, EGG dominant frequency, and power, which are described below.

Percentage of regular 2- to 4-cpm slow waves. The percentage of 2- to 4-cpm slow waves is a quantitative assessment of the regularity of the gastric slow waves measured from the EGG. It was defined as the percentage of time during which normal 2- to 4-cpm gastric slow waves were observed in the preprandial or postprandial EGG recording. The percentage of normal 2- to 4-cpm slow waves was computed from the running power spectra of the EGG using an adaptive spectral analysis method (11). One power spectrum was generated for every 2 min of EGG data, and the spectral peaks in each spectrum were examined visually. A spectrum was defined as normal if it had a clear peak in the 2- to 4-cpm range. The percentage of regular 2- to 4-cpm slow waves was determined by computing the ratio between the numbers of normal and total spectra.

EGG dominant frequency. The frequency at which the EGG power spectrum had a peak power in the range of 0.5–9.0 cpm was defined as the EGG dominant frequency. The EGG dominant frequency has been shown to be equal to the frequency of the gastric slow wave measured from the implanted serosal electrodes (13, 18, 31). It was computed using the smoothed power spectral analysis method (6), which produced average power spectra for the EGG during the 30-min fasting state (preprandial) and the 30-min fed state (postprandial).

EGG dominant power. The power at the dominant frequency in the power spectrum of the EGG was defined as the EGG dominant power. Previous studies (10, 31) have shown that the relative change of the EGG dominant power reflects gastric contractility. Decibels (dB) were used to represent the power of the EGG. It is expressed as

$$P(\text{dB}) = 10 \times \log_{10} A^2$$

where P is power and A is the amplitude of the spectra.

Relative postprandial increase of percentage of 2- to 4-cpm slow waves. The relative postprandial increase of the percentage of 2- to 4-cpm slow waves was defined as the ratio of the

difference between the postprandial and preprandial values and the preprandial value.

Influence of Gestation Age, Weight, and Feeding Method

To investigate the effect of gestation age at birth on the gastric slow wave, the infants were divided into two groups based on their gestation ages at birth. The dividing gestational age was 31 wk. The mean gestational age at birth was 29.7 ± 0.8 wk for one group (6 infants) and 33.2 ± 0.8 wk for the other group (10 infants). The percentages of 2- to 4-cpm slow waves between these two groups were compared in infants at the ages of 2 wk and 4 mo. To study the influence of feeding methods (breast feeding or formula feeding) on the gastric slow wave, the infants were classified into two groups according to the feeding method during the first 2 wk. There were eight infants in the breast-feeding group and seven infants in the formula-feeding group. Infants with mixed feeding during this 2-wk period were excluded. The percentages of 2- to 4-cpm slow waves between these two groups were compared at the age of 2 wk. The correlation between the percentage of 2- to 4-cpm slow waves and the weight was assessed at the ages of 1 wk and 4 mo to see if the development of the gastric slow wave was associated with weight.

Statistical Analysis

Analysis of variance was used to assess the difference among the six different ages. The Student's t -test was applied to study the difference between the preprandial and postprandial EGG and the effects of gestation age, weight, and feeding method. Statistical significance was assigned for $P < 0.05$. All data were presented as means \pm SD.

RESULTS

GMA demonstrated developmental changes as a function of advancing postnatal age in the preterm infants studied. The percentage of 2- to 4-cpm slow waves was

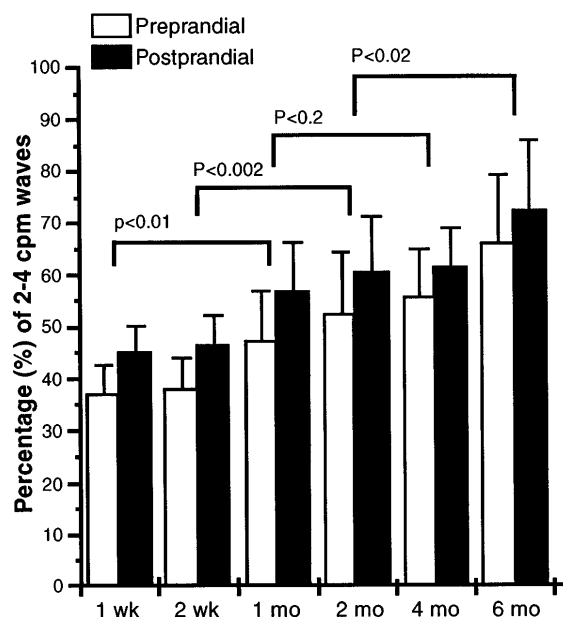


Fig. 1. Preprandial and postprandial percentages of the normal 2- to 4-cycles/min (cpm) slow waves in preterm infants at the ages of 1 and 2 wk and 1, 2, 4, and 6 mo. P values resulted from comparison between paired fasting data or paired fed data.

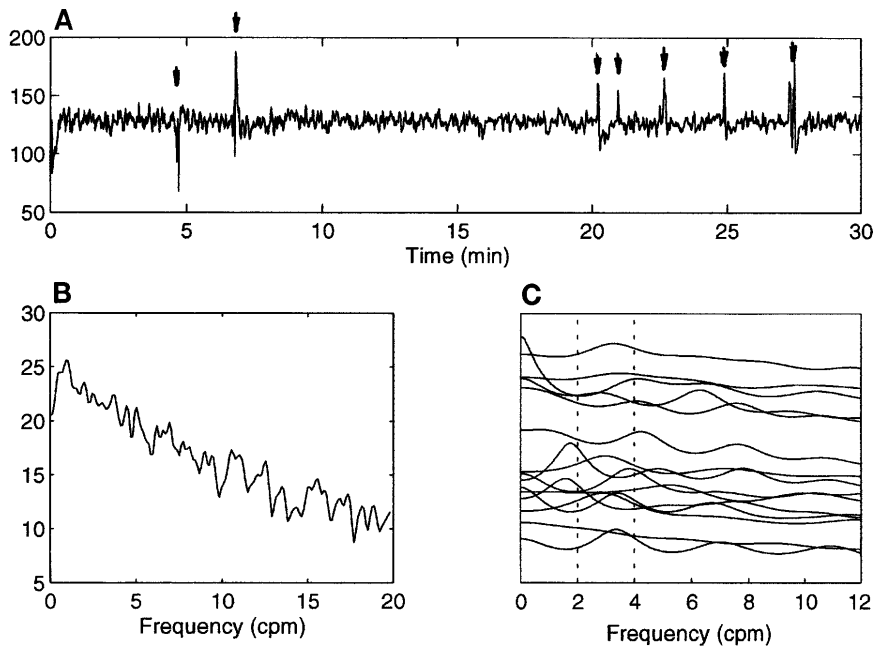


Fig. 2. Typical electrogastrogram (EGG) recording and its spectral analyses for a preterm infant at 1 wk. *A*: EGG recording. For clarification, some motion artifacts (indicated by arrows), which were deleted for spectral analysis, are shown here. *B*: power spectrum of EGG shown in *A*. There is no dominant peak in the 2- to 4-cpm range in the spectrum. *C*: running power spectra of EGG shown in *A*. The % of 2- to 4-cpm slow waves is low (few spectra have spectral peaks in the 2- to 4-cpm range).

low at birth and steadily increased during the first 6 mo after birth. As can be seen in Fig. 1, the preprandial and postprandial percentages of the slow waves increased from $36.7 \pm 6.1\%$ and $44.9 \pm 5.3\%$ at 1 wk to $65.8 \pm 13.5\%$ and $72.2 \pm 13.8\%$ at 6 mo, respectively. Between these two ages P was <0.001 for both preprandial and postprandial EGG. Figures 2 and 3 show typical EGG recordings in an infant and their spectral analyses. It was noted that the development of the gastric slow wave was two times faster during the first 2 mo than during 3–6 mo. As can be seen from Fig. 4, the rate of increase per month of the percentage of 2- to 4-cpm slow waves was 9.2% during the first 2 mo and 3.4% during 3–6 mo.

Postprandial increases of the percentages of 2- to 4-cpm slow waves were observed at all six ages. The average relative postprandial increases of the percentages of 2- to 4-cpm slow waves were 22.3, 21.6, 20.2, 15.1, 10.7, and 9.7% at the ages of 1 and 2 wk and 1, 2, 4, and 6 mo, respectively (see Fig. 5*A*). That is, the postprandial increase steadily decreased with age. In addition, the increase became statistically less significant as the infants grew up. P increased from 0.005 at the age of 1 wk up to 0.25 at the age of 6 mo (see Fig. 5*B*).

Obvious dominant peaks in the EGG power spectra were not observed until 2 mo (see typical examples in Figs. 2*B* and 3*B*). None of the infants had dominant

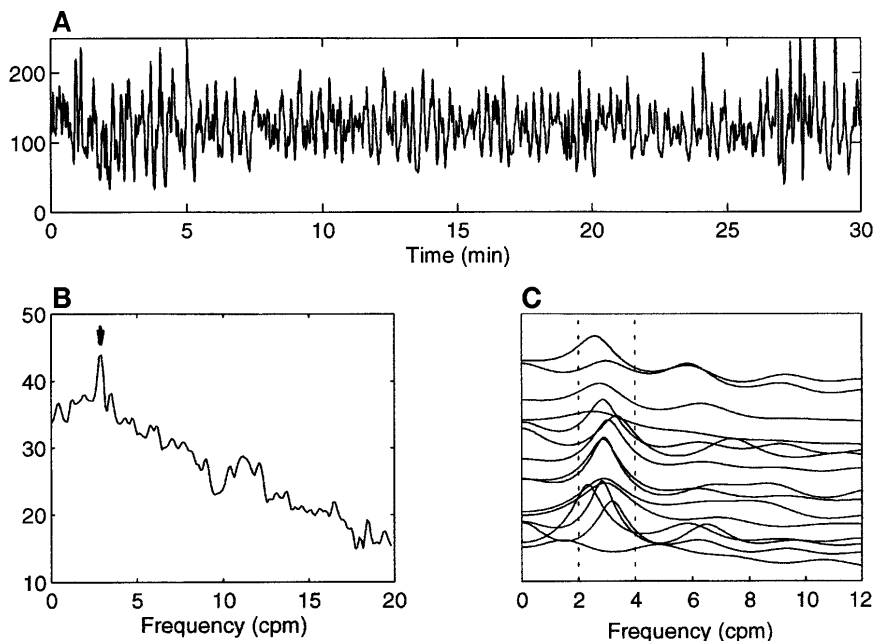


Fig. 3. Typical EGG recording and its spectral analyses for the same infant that data were collected from for Fig. 2, but at 6 mo. *A*: EGG recording. *B*: power spectrum of EGG shown in *A*. There is an obvious dominant peak (indicated by an arrow) at ~ 3 cpm in the spectrum. *C*: running power spectra of EGG in *A*. The % of 2- to 4-cpm slow waves is much higher at 6 mo (a majority of the spectra have spectral peaks in the 2- to 4-cpm range) than at 1 wk.

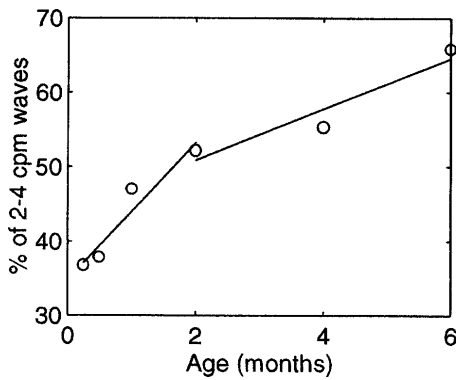


Fig. 4. Linear curve fitting for % of 2- to 4-cpm normal slow waves in preterm infants. Fitting was performed in 2 time periods. One was from 1 wk to 2 mo and the other was from 2 to 6 mo. The slopes of the 2 lines were 9.2 and 3.4, respectively, indicating that there was an increase of 9.2 in the % of 2- to 4-cpm waves per month during the first 2 mo and of 3.4% per month during 3–6 mo.

peaks at 1 wk, 47% of them had dominant peaks at 2 mo, and 69% had dominant peaks at 6 mo. The change of dominant power after the meal, if any, was inconsistent. The mean dominant frequency at 6 mo was 3.13 cpm in the fasting state, and the meal did not induce any significant changes.

The percentages of 2- to 4-cpm slow waves between the two groups of infants of different gestation ages at birth were compared at 2 wk and 4 mo of age. Figure 6 shows both preprandial and postprandial percentages at the two ages. The difference between the two groups was small and statistically insignificant, i.e., gestation age at birth did not affect the development of the gastric slow waves.

The difference in the percentage of 2- to 4-cpm slow waves between the breast-feeding and formula-feeding groups was assessed at the age of 2 wk. The preprandial and postprandial percentages of 2- to 4-cpm slow waves were $37.7 \pm 6.1\%$ and $44.3 \pm 6.7\%$ for the breast-feeding group and $39.2 \pm 6.1\%$ and $49.2 \pm 4.2\%$ for the formula-feeding group. No significant difference was observed.

No effects of weight on the development of the gastric slow wave were observed. Figure 7 presents the correlation between the percentage of 2- to 4-cpm slow waves

and weight at the ages of 1 wk ($r = 0.5$, $P = 0.2$) and 4 mo ($r = -0.2$, $P = 0.6$).

The infants were found to be physically well developed at the end of the study (6 mo after birth). The average total scores were 5.8, 5.8, 5.5, 5.7, and 5.7 for communication, gross motor, fine motor, adaptive, and personal-social, respectively. No correlation was noted between the percentage of 2- to 4-cpm slow waves and any of these developmental parameters.

DISCUSSION

This study has shown that GMA demonstrated developmental changes as a function of advancing postnatal age in the preterm infants studied. The percentage of 2- to 4-cpm slow waves steadily increased from birth to 6 mo, and there was a postprandial increase in the percentage of 2- to 4-cpm slow waves during the first 6 mo after birth. Also, the relative postprandial increase of the percentage became smaller and statistically less significant with age.

Although the structure of the stomach is well developed even before birth, both gastric motility and myoelectrical activity are immature at birth (23). For example, by about the seventh month of gestation, the stomach musculature appears mature, both morphologically and histologically (15), but gastric wall compliance in newborns under 30 h old was less than that in adults and receptive relaxation seems negligible in newborn infants (17). This study shows that GMA is immature at birth, there is a developmental process during the first 6 mo, and the maturation rate is highest during the first 2 mo of life. The percentage of 2- to 4-cpm slow waves at 6 mo is still lower than that in healthy adults (12). These results are in agreement with motor patterns in neonates, which differ from those in adults. Previous neonatal motility studies (4, 36) showed that during the fasting state, few infants (both preterm and term) displayed the migrating motor complex. Instead, they demonstrated episodes of motor quiescence that alternated with episodes of nonmigrating phasic activity, which occupied 60% of manometric recordings of preterm and term infants. This is because many aspects of the forward propulsion of enteral nutrients are not fully mature in the neonates.

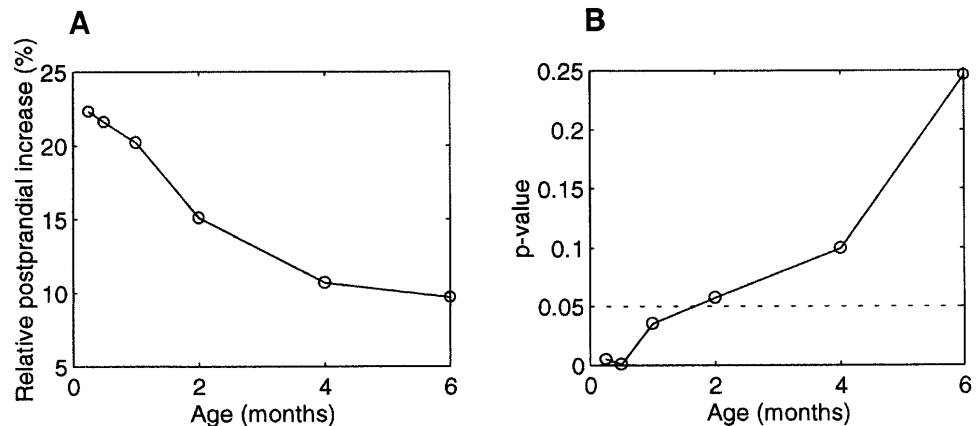


Fig. 5. A: average relative postprandial increases of the % of 2- to 4-cpm slow waves. B: P values of the relative postprandial increase at different ages.

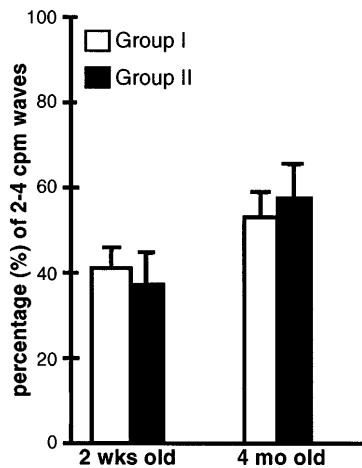


Fig. 6. Percentages of normal 2- to 4-cpm slow waves in preterm infants with different gestation ages. Average gestation age at birth of group 1 was 29.7 ± 0.8 wk, and the average gestation age at birth of group 2 was 33.2 ± 0.8 wk. No significant difference was observed in the % of 2- to 4-cpm waves between the 2 groups.

One of the interesting findings in this study is that there existed significant postprandial increases of the percentage of 2- to 4-cpm slow waves. This has never been reported before in either healthy adults or infants. This postprandial increase was very significant at 1 wk old and became gradually smaller and statistically less significant as the infants grew up. This suggests that feeding stimulates the development of the gastric slow wave in infants. The stimulation became less significant when the gastric slow wave of the infants was closer to maturation. This phenomenon should eventually disappear when the gastric slow wave is fully mature as in healthy adults for whom the preprandial

and postprandial percentages remain statistically unchanged.

The other important EGG parameters are the dominant frequency and power. For a healthy adult, there should exist an obvious peak between 2 and 4 cpm in the EGG power spectra (7). This current study showed that there was no dominant peak in the EGG power spectra at birth, in agreement with our previous findings (12). Similar to the percentage of slow waves, a developmental process of the dominant peaks in the EGG power spectra was observed in this study. A postprandial increase in the EGG dominant power in healthy adults has been consistently reported in numerous studies (16, 19, 26, 32, 33, 35). However, this increase was not observed in this current study. This might be attributed to the following: 1) the test meal was uncontrolled; 2) milk had an inhibitory effect, as it did on postprandial GMA in a study by Chen and McCallum (8); and 3) the dominant power was not identifiable in about one-third of the subjects even at 6 mo.

The influence of gestation age on the gastric slow wave in infants was investigated in this study. The results for two groups with different gestation age have shown that there was no significant difference between them. This is in agreement with a previous study performed by Koch et al. (27), which showed that postprandial GMA in all frequency bands was similar among groups of premature and term infants. Ittmann et al. (24) also reported that there were no differences in the occurrence or amplitude of antral activity between preterm and term infants. As we know, the structure of the stomach is well developed before birth, while GMA is not mature until at least months after birth. Accord-

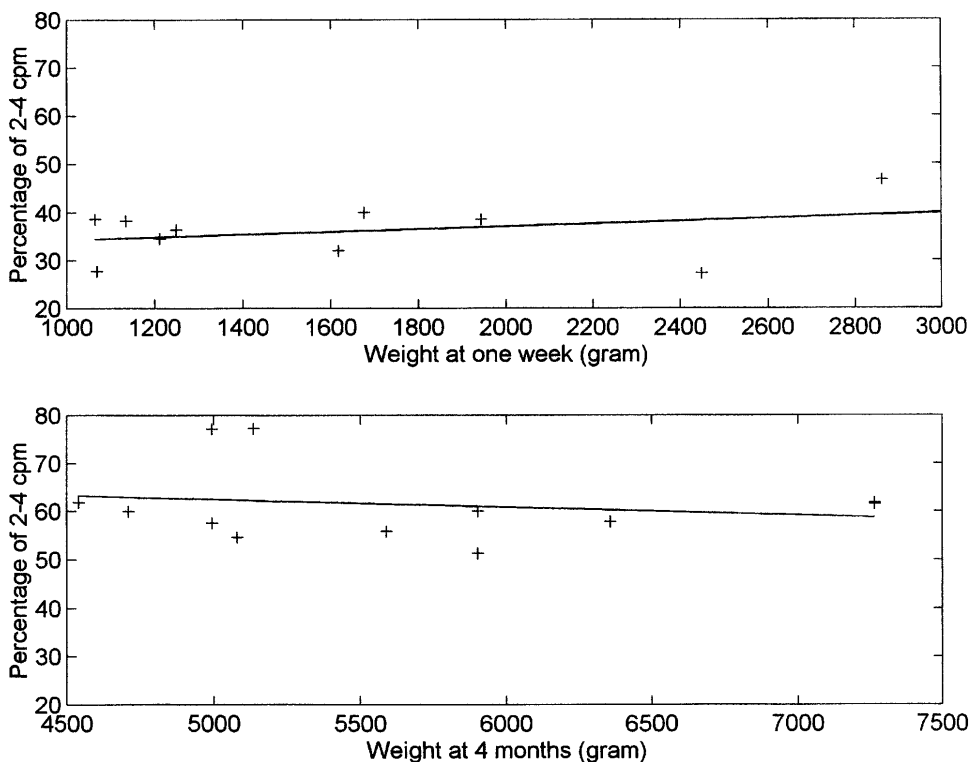


Fig. 7. Correlation of % of 2- to 4-cpm slow waves with weight at ages of 1 wk (top; $r = 0.5$, $P = 0.2$) and 4 mo (bottom; $r = -0.2$, $P = 0.6$).

ing to our study, it seems that the development of GMA may mainly be attributed to the stimulation of feeding. Only after some period of time, for instance, several months of feeding, can GMA become mature. It should also be noted that although GMA is not mature during the first month after birth, infants are able to tolerate milk due to the fact that emptying of liquids is attributed to fundic tones instead of propagated antral contractions. Although this study was performed in preterm infants, it is speculated that the development of the gastric slow wave is not consequent to preterm birth but a common phenomenon for both term and preterm infants. Further studies are required to prove this.

In conclusion, the percentage of normal gastric slow waves is low at birth and progressively increases during the first months of life. The maturation of the gastric slow wave after birth may be attributed to enteral feeding.

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