PROCEEDINGS OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE **172**, 232–238 (1983)

Role of Nocturnal Feeding in the Development of the Diurnal Rhythm of Jejunal Sucrase Activity (41551)

SUSAN J. HENNING[1] AND DOLORES M. GUERIN

Department of Biology, University of Houston, Houston, Texas 77004

Abstract. A diurnal rhythm of jejunal sucrase activity has been shown previously to make its developmental appearance in the rat at the time of weaning (Day 22). In this study we found that the rhythm was not present on Day 23 if the onset of feeding was not coordinated with the onset of darkness. Conversely, the sucrase rhythm appeared precociously (Day 19) in pups weaned onto chow on a schedule in which the onset of feeding is coordinated with the onset of the dark period. It is concluded that the normal developmental appearance of the sucrase rhythm is due, at least in part, to the fact that *ad libitum* feeding becomes nocturnal around Day 22.

In adult rats, numerous digestive and absorptive activities of the jejunum exhibit circadian rhythms. Disaccharidases have been the most widely studied of these activities. In rats fed *ad libitum*, maltase and sucrase activities peak during the dark period of the light/dark cycle (1, 2). If feeding is restricted to the light period, the phase of the enzyme rhythms changes such that maximal activities coincide with the time of feeding (1, 2). Likewise, when adult rats are kept in continuous light or continuous darkness, peak values of maltase and sucrase activities occur at the time of feeding (3, 4), even when food is offered at unusual intervals such as every 12 hr (3) or every 32 hr (5). Thus, in the adult, the rhythms of these disaccharidase activities are synchronized more strongly by the feeding rhythm than by the lighting rhythm. Surprisingly, it is the protein component of the diet rather than the carbohydrate which elicits disaccharidase rhythms (3, 6). Furthermore, these enzyme rhythms cannot be a direct consequence of rhythmic availability of nutrients in the lumen because maltase and sucrase activities continue to show a rhythmic pattern in fasted animals in continuous light (5), in bypassed jejunal sacs (6), and in animals receiving intravenous nutrition (7). Thus it is likely that the rhythmic changes in disaccharidase activities in adult rats are generated by an endogenous circadian time-keeping mechanism and the time of feeding merely sets the phase of the enzyme rhythms.

During development, disaccharidase rhythms are not present in fetal rats (8) or in suckling rats (9, 10). When rat pups are allowed *ad libitum* access to both their dam and solid food, the sucrase rhythm is first detected on the 22nd postnatal day (9), coincident with the time that weaning is normally completed. When animals are prevented from weaning, no rhythm of jejunal sucrase activity is present on Day 22 (9). This observation led to the conclusion that the ontogenic appearance of the sucrase rhythm is cued by some aspect of weaning (9). The overall aim of the current study was to further elucidate this role of weaning.

The process of weaning constitutes a complex environmental change for the intestinal tract. The diet changes in composition and there is a significant change in the rhythmic pattern of *ad libitum* ingestion. Suckling rats normally feed predominantly during the light period (11, 12), despite the fact that they seem to be intrinsically nocturnal feeders (13). Diurnal suckling is probably imposed on the pups by the mother as a result of her nocturnal pattern of feeding and activity. Only when the pups begin to nibble chow can they express their own nocturnal feeding rhythms (9, 11). Thus, one potentially critical aspect of normal weaning is that the onset of feeding becomes coincident with the onset of the dark period. In this regard it is important to note that the study in which weaning was prevented (9) utilized a suckling schedule wherein the onset of feeding was not coordinated with the onset of the dark period. The aim of this work was to clarify the role of the timing of

---

[1] To whom all correspondence should be addressed.

0037-9727/83/020232-07$01.50/0

the feeding rhythm with respect to the developmental appearance of the circadian rhythm of jejunal sucrase activity.

Materials and Methods. *Chemicals.* Sucrose used for assay of sucrase was ultra pure grade (Schwarz-Mann, Orangeburg, N.Y.). Glucose was measured using Statzyme Glucose (500 nm) from Worthington Biochemicals (Freehold, N.J.). It was necessary to dissolve this reagent in 500 m*M* Tris, pH 7.4 (instead of water), in order to inhibit residual sucrase activity. Bovine serum albumin (Sigma Chemical Co., St. Louis, Mo.) was used as the protein standard. All other chemicals were reagent grade.

Animals. Pregnant rats of the Sprague–Dawley strain (Charles River CD) were received from Charles River Breeding Laboratories (Wilmington, Mass.) on the 15th day of gestation. They were housed in air-conditioned quarters (21° + 1°) with a 12-hr light/dark cycle. On the due date, cages were checked every 2 hr for the presence of pups. The birthdate was regarded as Day 0. Approximately 24 hr postpartum, all litters were reduced to nine pups. Each litter was housed with its mother with food (Purina Lab Chow) and water available *ad libitum* until the age when experiments were begun.

Food intake. Preliminary studies showed that for a 4-hr feeding period, the weight of stomach contents accurately reflected the weight of food ingested. In addition, we found that precociously weaned pups were much more likely to thrive if they were housed in groups of four or eight than if they were housed singly. Because measurement of individual food intake would require single housing, we preferred to house pups in groups and to use stomach contents as a measure of ingestive behavior.

Experiment 1A. Three litters of nine pups were used for this experiment. At 20 days of age, mothers were removed during the first 3 hr of the light period. From that time onward, pups were provided with solid food (Purina Lab Chow) during the entire dark period and for the first 4 hr of the light period. Thus, on this schedule the onset of feeding was coordinated with the onset of the dark period. Food was removed during the latter 8 hr of the light period. Water was available at all times. The sacrifice sequence began during the light period on the 22nd day of age. One pup was removed from each litter every 4 hr until all nine pups in each litter had been sacrificed. To avoid disturbances in the animal quarters at the time of the light/dark and dark/light transitions, the time points were arranged to occur 0.5 hr after lights-off and lights-on. At each time point, pups were weighed and then sacrificed by decapitation. Stomach contents were removed and weighed, and the small intestine (from the ligament of Treitz to the ileocecal junction) was removed. The proximal half of the small intestine (defined as the jejunum) was flushed thoroughly with ice-cold 0.9% NaCl, then wrapped in Parafilm (American Can Co., Greenwich, Conn.) and stored at −10°.

Experiment 1B. Three litters of nine pups were used for this experiment. Procedures were exactly as described for Experiment 1A except that from Day 20 onward, the food was made available during the last 4 hr of the dark period and through the entire light period; i.e., pups were without food during the first 8 hr of the dark period. Thus on this schedule the onset of feeding occurred 8 hr after lights-off.

Experiments 2A and 2B. The details of these experiments were basically the same as those of Experiment 1A and 1B, respectively, except that mothers were removed on Day 17, the rhythmic availability of chow was instituted at that time, and the sacrifice sequence began on Day 19. Moreover, because weaning at such an early age is known to have deleterious consequences for the pups (14), each litter was given an "aunt" at the time that the mother was removed. "Aunts" were virgin females who were trained on the appropriate feeding schedule for 1 week prior to use in the experiments. Since weanling rats mimic the feeding behavior of adults placed with them (15), the presence of trained "aunts" could be expected to minimize the time of adaptation to the solid diet and to the appropriate feeding schedule.

Assay procedures. Sucrase was assayed in the mid-jejunum where it has maximal activity (16). For this purpose, the middle 10 cm of the jejunum was slit lengthwise and scraped with a steel spatula to remove the mucosa. Homogenates of mucosa were prepared in 9 vol 0.154 *M* KCl by nine strokes (approximately 45 sec) of a Potter Elvehjem Teflon/glass homogenizer. Enzymic activity in 0.1 ml homogenate was measured by incubating at

37° with 0.4 ml 62.5 mM sodium maleate buffer, pH 6.0, containing 0.3 M sucrose. The reaction was stopped by precipitation of protein with 0.2 ml of 1.8% $Ba(OH)_2 \cdot 8H_2O$, and the mixture was then neutralized with 0.2 ml 2% $ZnSO_4 \cdot 7H_2O$. Glucose produced from sucrose was measured with glucose oxidase reagent. Corrections were made for endogenous glucose in the tissue and in the substrate. This method for assay of sucrase activity is essentially the same as that originally described by Doell and Kretchmer (17). Protein was determined in duplicate by the method of Lowry *et al.* (18). Sucrase activities were first expressed as micromoles of glucose produced per hour per milligram mucosal protein. Values from each litter were then normalized by the method of Stevenson *et al.* (2). This method involved dividing the individual values by the mean value for that litter, thus setting the daily mean for each litter equal to 1.00. Normalization facilitated comparison of the magnitudes of the diurnal fluctuations irrespective of the absolute activity at a given developmental age.

Statistics. All data were assessed by the use of a two-tailed Mann–Whitney U test. For jejunal sucrase activity, two hypotheses were tested. Hypothesis I was that there is a rhythm synchronized by the light/dark cycle. To test this hypothesis, the first two time points of the light period were compared with all other points. If these two points were found to be significantly lower than all others, a rhythm synchronized by the light/dark cycle was considered to be present. Hypothesis II was that there is a rhythm synchronized by the feeding cycle. To test this hypothesis, the last point of the feeding period and the first point of the fasting period were compared with all other points. If these two points were significantly lower than all others, a rhythm synchronized by the feeding cycle was considered to be present. For stomach contents the presence of a rhythm was assessed by comparing the time point in the middle of the fasting period with all other time points. The results of these statistical analyses are shown in Table I.

For comparison of individual means for either sucrase activity or stomach weights, Student's two-tailed t test for unpaired values was used.

Results. *Experiment 1A.* When pups were raised from Day 20 on a schedule in which the onset of feeding was coordinated with the onset of the dark period, a distinct rhythm of jejunal sucrase activity was present at 22–23 days of age (Fig. 1). Sucrase activities were highest in the 8-hr period spanning the onset of darkness. They declined during the latter part of the dark period and were minimal 4 hr after lights-on. The first two points in the light period were significantly lower than all other points ($P < 0.001$, both hypotheses, Table I) and the ratio of highest to lowest sucrase activity was 3.3. The weight of stomach contents also displayed a distinct rhythm ($P < 0.001$, Table I). However, this rhythm was out of phase with the sucrase rhythm in the sense that the stomach contents were minimal 4 hr before lights-off whereas sucrase activities were maximal at that time.

Sucrase activities in Fig. 1 have been normalized (see Methods) to facilitate comparison with younger animals (Fig. 2). When the data from Experiment 1A were plotted as absolute values (μmole/min/mg protein), a rhythm superimposable on that shown in Fig. 1A was obtained. The mean activity at the lowest point of the curve was 2.87 ± 0.13 and that at the highest point was 9.53 ± 0.46 μmole/hr/mg protein, respectively.

Experiment 1B. When pups were raised from Day 20 on a schedule in which the onset of feeding did not coincide with the onset of darkness, there was no detectable rhythm of jejunal sucrase activity by 23 days of age (Fig. 1). P values given in Table I show that there were no significant variations of sucrase synchronized by either the light cycle (Hypothesis I) or the feeding cycle (Hypothesis II). The absolute activities of sucrase in this experiment ranged from 6.30 ± 0.87 to 10.58 ± 1.45 μmole/hr/mg protein, respectively. The lack of diurnal rhythm of sucrase activity could not have been due to lack of rhythmic feeding or inadequacy of food intake since the weights of stomach contents displayed a significant rhythm ($P < 0.001$, Table I) similar to that of Experiment 1A. In both experiments these weights were minimal 4 hr after food was removed from the cages. In Experiment 1B the ratio of highest to lowest mean weight was 8.1 as compared with 5.1 for Experiment 1A. Moreover, the absolute magnitudes of the stomach weights were just as great as in the previous experiment.

Experiment 2A. At 19 days of age, pups

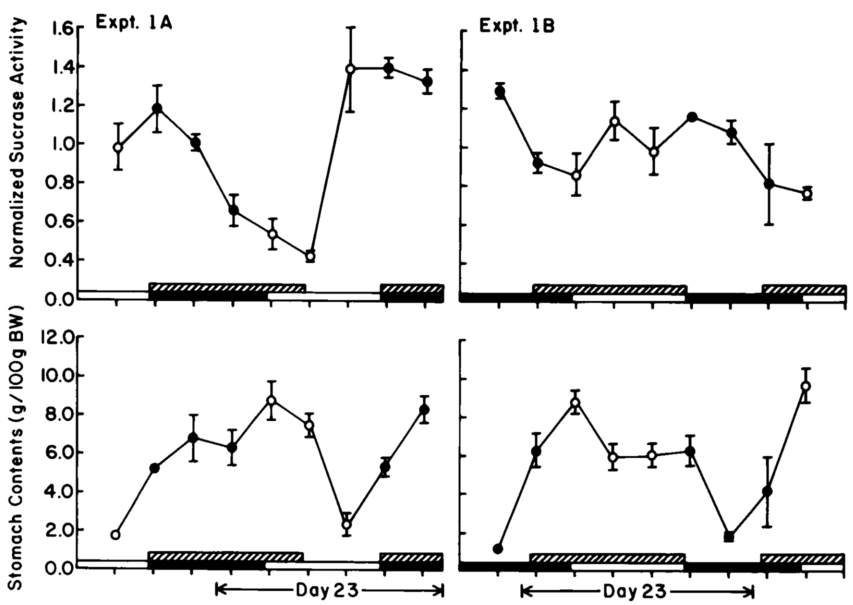

FIG. 1. Jejunal sucrase activity and weight of stomach contents for rat pups aged 22–23 days on either a coordinate feeding schedule (Experiment 1A) or a discoordinate feeding schedule (Experiment 1B). Values are given as mean ± SE ($n = 3$). Lack of error bars indicates that the SE is smaller than the symbol. Time is shown on the axis by marks every 4 hr and by the age of the pups. Black bars indicate hours of darkness and solid symbols show values for animals sacrificed in the dark whereas open symbols show values for animals sacrificed in the light. Hatched bars indicate the feeding period.

raised with both mother and chow available *ad libitum* do not display a diurnal rhythm of jejunal sucrase activity (9). However, when pups were precociously weaned using a schedule in which the onset of feeding was coordinated with the onset of the dark period (Fig. 2A), a distinct sucrase rhythm was present. The phase of the rhythm was the same as that previously observed with the older pups (Fig. 1A), with minimal sucrase activities occurring during the first 4 hr of the light period and peak activities at the onset of darkness ($P < 0.02$, Table I). However, the ratio of the highest to lowest mean sucrase value in the younger pups (Fig. 2A) was only 1.7, showing that the amplitude of the rhythm was approximately half that found in the older pups (Fig. 1A). This smaller amplitude may be related to the fact that, although there was a feeding rhythm ($P < 0.002$, Table I), the ratio of highest to lowest stomach weights of the younger pups (Fig. 2A) was only 3.5 (as compared with 5.2 for the older pups). In this experiment the absolute values for sucrase activity were 4.60 ± 0.62 μmole/hr/mg protein at the lowest point of the cycle and 7.50 ± 0.68 μmole/hr/mg protein at the highest point of the cycle. The relationship between the phases of the rhythms of stomach contents and jejunal sucrase activity (Fig. 2A) was the same as previously noted for Experiment 1A, i.e., the greatest rise of sucrase activity occurred during the middle 4 hr of the light period while the weights of stomach contents were showing their greatest decline.

Because sucrase values in Figs. 1A and 2A are expressed on the basis of the mucosal protein content, it is possible that the observed sucrase rhythm is due to a converse rhythm

TABLE I. STATISTICAL ANALYSES FOR ALL EXPERIMENTS

Experiments	Sucrase activities: Hypothesis I[a]	Sucrase activities: Hypothesis II[b]	Stomach contents
1A	$P < 0.001$	$P < 0.001$	$P < 0.001$
1B	$P > 0.18$	$P > 0.46$	$P < 0.001$
2A	$P < 0.02$	$P < 0.02$	$P < 0.002$
2B	$P > 0.34$	$P > 0.36$	$P < 0.015$

[a] Hypothesis I is that there is a rhythm synchronized with the light/dark cycle.

[b] Hypothesis II is that there is a rhythm synchronized with the feeding cycle.

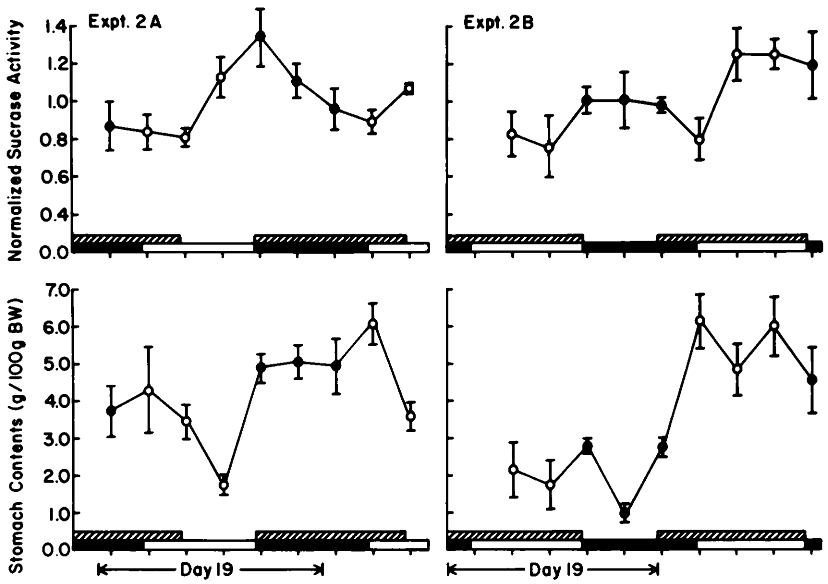

FIG. 2. Jejunal sucrase activity and weight of stomach contents for rat pups aged 19–20 days on either a coordinate feeding schedule (Experiment 2A) or a discoordinate feeding schedule (Experiment 2B). All schematic details of this figure are exactly as described for Fig. 1.

of mucosal protein. However, examination of the protein values (data not shown) indicated that this was not the case. There was, if anything, a tendency toward higher protein values at the time of peak sucrase values, although statistical analysis revealed no significant rhythm ($P > 0.8$) in the mucosal protein content.

Experiment 2B. In accordance with the findings in older pups (Fig. 1B), precociously weaned pups maintained on a schedule in which the onset of feeding was not coordinated with the onset of darkness (Fig. 2B) had no detectable rhythm of jejunal sucrase activity ($P > 0.34$ for both hypotheses, Table I). Absolute values for sucrase activity in this experiment ranged from 4.91 ± 1.07 to 8.09 ± 0.72 μmole/hr/mg protein, respectively. Comparison of the sucrase data with those for stomach contents, indicates that there was no change of sucrase at the time when stomach weights showed their maximal decline. If a sucrase rhythm was cued solely by the feeding rhythm, then the results of Experiments 1A and 2A would predict that a maximal rise of sucrase activity would be temporally coincident with the maximal decline of stomach weights. Although a feeding rhythm did occur in the pups of Experiment 2B ($P < 0.015$, Table I) the absolute weights of stomach contents during the feeding period of Day 19 were significantly lower than those during the feeding period of Day 20 ($P < 0.005$). Moreover, body weights of the pups in Experiment 2B at the time of sacrifice (39.1 ± 0.9 g) were significantly lower ($P < 0.001$) than those of pups in Experiment 2A (46.7 ± 1.1 g). Thus, it is possible that low food intake on Day 19 (and earlier) accounted for the lack of a sucrase rhythm in this experiment. However, it is important to note that even at a later age when the discoordinate feeding schedule was robustly established (Fig. 1B) there was still no sucrase rhythm.

Discussion. The findings from our experiments indicate that the coordination of the onset of feeding with the onset of the dark period is a critical factor in the ontogenic appearance of the diurnal rhythm of jejunal sucrase activity. At 22 days of age a sucrase rhythm is present in rat pups raised in the standard fashion (i.e., allowed *ad libitum* access to both mother and chow until Day 21 and then *ad libitum* access to chow alone) (9). In the current study a more pronounced rhythm was found in 22-day-old pups that were weaned onto chow at Day 20 on a feeding schedule wherein the onset of feeding and darkness were coordinated. However, when these events were not coordinated there was no sucrase rhythm at 22 days. The efficacy of the coordinated feeding schedule in eliciting rhythmic sucrase activity is illustrated by the fact that the sucrase rhythm appeared early (Day 19) in precociously weaned pups. Thus, during normal development, it seems a key reason for the appearance of the sucrase rhythm between Day 19 and Day 22 is that *ad libitum* feeding of chow becomes nocturnal during this period (9).

In view of the fact that the development of jejunal sucrase activity is powerfully affected by glucocorticoids (17) and that endogenous corticosterone displays a diurnal rhythm beginning around Day 19 (19), it is logical to consider the possibility that corticosterone is responsible for the rhythms reported in this study. We believe this is highly unlikely for three reasons. First, in adult rats the sucrase rhythm is just as robust in adrenalectomized animals as in sham-operated controls (9). Second, the developing intestine has been shown to lose its glucocorticoid responsiveness around days 17–18 (20, 21). Third, Miyabo *et al.* (22) examined the effects of suckling schedule on the development of the corticosterone rhythm in rats and found that the hormone rhythm appeared at 20 days of age, regardless of whether pups were suckled in the light period or in the dark period.

It is apparent that in the adult rat the rhythmic pattern of jejunal sucrase activity is generated by an endogenous circadian oscillator. The strongest evidence for this is the finding that with continuous light and with food offered for 8 hr once every 32 hr the sucrase rhythm has a period of 32 hr, but when these same animals are fasted, the period of the rhythm reverts to approximately 24 hr (5). Assuming that the oscillator is located in the rat brain (23), there must be a neural or hormonal signal which interacts with the intestinal epithelial cells. In the suckling rat the central oscillator seems to be active, as there is an adult-like circadian rhythm of *N*-acetyltransferase activity in the pineal gland as early as the first postnatal week (24–27). Moreover, suckling rats display an intrinsic preference for nocturnal feeding (13). Thus, the lack of disaccharidase rhythms during the suckling period (9, 10) is probably due to lack of the signal mechanism or absence of a coupling between the signal and the oscillator. When feeding becomes coordinated with the natural (nocturnal) phase of the oscillator, the signal mechanism becomes operative. Once the sucrase rhythm is established there is apparently no longer a requirement for coordinated feeding because in adult rats the sucrase rhythm is not abolished when feeding is restricted to the light period (1, 2).

Given the evidence for the significance of coordinate feeding in the ontogenic appearance of the sucrase rhythm, we would have liked to determine whether the nature of the food is important. We were particularly interested in the question of whether nonweaned pups would display a sucrase rhythm if they were forced to suckle on a schedule in which the onset of suckling was coordinated with the onset of the dark period. In the earlier study from this laboratory (9), weaning prevention was achieved by the "16 + 8" suckling schedule originally described by Walker *et al.* (28). On this schedule the dam is removed to a separate feeding cage for the first 8 hr of the dark period and then is returned to the pups for the next 16 hr. The schedule has the advantage of allowing the dam to feed nocturnally as is her preference. In a preliminary experiment in the current series we attempted to modify the "16 + 8" schedule so that each day from Day 11 onward, the dams were removed to a feeding cage during the last 8 hr of the light period. They were then returned to the home cage so that suckling could begin at the onset of the dark period. Starting on Day 19, pups were removed and sacrificed every 4 hr for a 32-hr period. Inspection of stomachs indicated that the pups obtained negligible milk during the first 8 hr of the dark period. This may have been a result of the dams' continuing to be nocturnally active. In this species, milk ejection occurs only when the dam is sleeping (29). In any event, the lack of milk intake by the pups during the early hours of the dark period meant that we were unable to investigate directly the question posed.

In summary, we conclude that the developmental appearance of the diurnal rhythm of jejunal sucrase activity is due primarily to the emergence of a nocturnal feeding pattern in the pups at the time of weaning. Both phasing and periodicity of the sucrase rhythm in the adult rat appear quite labile (5, 6), suggesting a weak coupling between the central pacemaker and the driven oscillators (the sucrase system). From the adaptive standpoint, such a coupling may represent distinct advantage since availability of specific foods at defined times is unlikely in nature. In light of the relatively weak coupling system in the adult rat, it seems even more probable that appearance of a sucrase rhythm during development depends upon congruent input, i.e., phasing of food and light/dark signals.

The authors wish to thank Mark Woodward for technical assistance and Drs. M. Messer, S. Roberts, and V. Rao for their helpful comments on the manuscript. This work was supported by Grant HD 14094 from the National Institutes of Health.

---

1. Saito M, Murakami E, Nishida T, Fujisawa Y, Suda M. Circadian rhythms in digestive enzymes in the small intestine of rats. I Patterns of the rhythms in various regions of the small intestine. J Biochem **78**:475–480, 1975.
2. Stevenson NR, Ferrigni F, Parnicky K, Day S, Fierstein JS. Effect of changes in feeding schedule on the diurnal rhythms and daily activity levels of intestinal brush border enzymes and transport systems. Biochim Biophys Acta **406**:131–145, 1975.
3. Furuya S, Sitren HS, Zeigen S, Offord CE, Stevenson NR. Alterations in the circadian rhythmicity of rat small intestinal functions. J Nutr **109**:1962–1973, 1979.
4. Nishida T, Saito M, Suda M. Parallel between circadian rhythms of intestinal disaccharidases and food intake of rats under constant lighting conditions. Gastroenterology **74**:224–227, 1978.
5. Saito M, Kato H, Suda M. Circadian rhythm of intestinal disaccharidases of rats fed with adiurnal periodicity. Amer J Physiol **238**:G97–101, 1980.
6. Saito M, Sato Y, Suda M. Circadian rhythm and dietary response of disaccharidase activities in isolated rat jejunum. Gastroenterology **75**:828–831, 1978.
7. Stevenson NR, Sitren HS, Furuya S. Circadian rhythmicity in several small intestinal functions is independent of use of the intestine. Amer J Physiol **238**:G203–207, 1980.
8. Stevenson NR, Byra WM, Day SE. Lack of circadian rhythmicity of rat fetal intestinal enzymes as compared to the dams. Dev Biol **60**:487–492, 1977.
9. Beam HE, Henning SJ. Development of the circadian rhythm of jejunal sucrase activity in the weanling rat. Amer J Physiol **235**:E437–442, 1978.
10. Saito M, Suda M, Matzuda H. Postnatal development of circadian rhythms in disaccharidase activities in rat small intestine. Amer J Physiol **234**:E500–503, 1978.
11. Redman RS, Sweney LR. Changes in diet and patterns of feeding activity of developing rats. J Nutr **106**:615–626, 1976.
12. Stern JM, Levin R. Food availability as a determinant of the rats' circadian rhythm in maternal behavior. Dev Psychobiol **9**:137–148, 1976.
13. Henning SJ, Gisel EG. Nocturnal feeding behavior in the neonatal rat. Physiol Behav **25**:603–605, 1980.
14. Lerman R, Koldovsky O. Growth and food intake of prematurely weaned rats: Effect of cortisone and thyroxine injection during the suckling period. J Nutr **109**:916–923, 1979.
15. Galef BG Jr. Social transmission of food preferences: An adaptation for weaning in rats. J Comp Physiol Psychol **91**:1136–1140, 1977.
16. Rubino A, Zimbalatti F, Auricchio S. Intestinal disaccharidase activities in adult and suckling rats. Biochim Biophys Acta **92**:305–311, 1964.
17. Doell RG, Kretchmer N. Intestinal invertase: Precocious development of activity after injection of hydrocortisone. Science **143**:1–2, 1964.
18. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. J Biol Chem **193**:265–275, 1951.
19. Ramaley JA. The development of daily changes in serum corticosterone in pre-weanling rats. Steroids **21**:433–442, 1973.
20. Henning SJ, Sims JM. Delineation of the glucocorticoid-sensitive period of intestinal development in the rat. Endocrinology **104**:1158–1163, 1979.
21. Henning SJ, Leeper LL. Coordinate loss of glucocorticoid responsiveness by intestinal enzymes during postnatal development. Amer J Physiol **242**:G89–G94, 1982.
22. Miyabo S, Yanagisawa K-I, Ooya E, Hisada T, Kishida S. Ontogeny of circadian corticosterone rhythm in female rats: Effects of periodic maternal deprivation and food restriction. Endocrinology **106**:636–642, 1980.
23. Stetson MH, Watson-Whitmyre M. Nucleus Suprachiasmaticus: The biological clock in the hamster? Science **191**:197–199, 1976.
24. Ellison N, Weller JL, Klein DC. Development of a circadian rhythm in the activity of pineal serotonin N-acetyltransferase. J Neurochem **19**:1335–1341, 1972.
25. Vanecek J, Illnerova H. The regulation of pineal serotonin N-acetyltransferase activity in newborn rats. Dev Biol **68**:287–291, 1979.
26. Yuwiler A, Klein DC, Buda M, Weller JL. Adrenergic control of pineal N-acetyltransferase activity: Developmental aspects. Amer J Physiol **233**:E141–146, 1977.
27. Brammer M, Binkley S, Enrico J, Duffy M. The rise and fall of pineal N-acetyltransferase *in vitro*: The influence of age. Dev Biol **86**:256–258, 1981.
28. Walker PR, Bonney RJ, Potter VR. Diurnal rhythms of hepatic carbohydrate metabolism during development of the rat. Biochem J **140**:523–529, 1974.
29. Voloschin LM, Tramezzani JH. Milk ejection reflex linked to slow wave sleep in nursing rats. Endocrinology **105**:1202–1207, 1979.

Received July 19, 1982. P.S.E.B.M. 1983, Vol. 172.