

Development of the 24-h rest-activity pattern in human infants

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Abstract

The development of the 24-h rest-activity pattern was investigated in human infants under naturalistic conditions as assessed by continuous actigraphy. Seven infants and their mothers were recorded for 4 ($n = 1$), 6 ($n = 5$) and 12 months ($n = 1$) after birth. Periodogram analysis of rest-activity data was performed over consecutive 10-day intervals. A weak 24-h rest-activity pattern was already present in some infants during the newborn period. The magnitude of the 24-h component in individual periodograms increased across the first months following a saturating function. The time constants of fitted saturating exponential functions – reflecting the rate of development of the 24-h pattern – ranged from 49 to 110 days ($n = 6$) indicating a large interindividual variability. Furthermore, intraindividual variation was observed; the magnitude of the 24-h rest-activity component showed fluctuations around the trend. Miniaturized actigraphs are ideal tools for long-term longitudinal monitoring of rest-activity behavior in infants.

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1. Introduction

The emergence of the 24-h sleep–wake cycle is an important developmental milestone during infancy and a central topic in practical infant care. By the end of the third month most infants have established a consolidated sleep period at night and show a 24-h periodicity of sleep and wakefulness (for comprehensive reviews see [Allen, 2000](#); [Löhr, & Siegmund, 1999](#)).

A number of studies have addressed the development of the 24-h sleep–wake rhythm in early human life. The first continuous long-term observations of infant sleep–wake behavior were carried out by [Kleitman and Engelmann in 1953](#). They collected sleep–wake data of 19 infants by reports of the mothers from the 3rd to the 26th week after birth and found that “the day–night asymmetry (i.e., more sleep at night than during the day) already present in the first 4-week period (weeks 3–6) becomes more pronounced in the following period (weeks 7–26; [Kleitman & Engelmann, 1953, pp. 272](#))”. This finding was confirmed by [Parmelee in 1961](#) who described the sleep–wake behavior of a boy from birth to 35 weeks of age on the basis of maternal diaries. A 24-h sleep–wake pattern emerged in the 6th week and was present “very definite” after the 12th week (pp. 169). No attempts, however, were made in these early pioneering studies to examine the development of the 24-h rhythm by quantitative methods. Only later, scientists have started to use techniques such as maximal entropy ([Tomioka, & Tomioka, 1991](#)) or power spectral analysis ([Hellbrügge, 1974](#);

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Table 1
Infant and recording characteristics ($n = 7$).

Infant	Gender	GA (weeks)	Birth order	BW (g)	BL (cm)	Breastfeeding duration (months)	Birth month	Start (day)	Duration (days)
# 01	F	40	3	3740	53	5	October	6	366
# 02	F	38	1	3070	52	6	February	2	195
# 03	M	40	2	3800	54	6	April	4	163
# 04	F	40	1	3110	49	6	April	3	176
# 05	F	38	2	3150	50	5	July	3	172
# 06	M	40	2	3900	56	2.5	November	1	122
# 07	M	38	2	3480	49	6	March	6	189
Mean		39.1	1.9	3464	51.9	5.2		3.6	198
S.D.		1.1	0.7	356	2.7	1.3		1.9	78

GA, gestational age; BW, birth weight; BL, birth length; Start: start of recording in days after birth.

Löhr & Siegmund, 1999; Meier-Koll, Hall, Hellwig, Kott, & Meier-Koll, 1978), autocorrelation (Nishihara, Horiuchi, Eto, & Uchida, 2002) or χ^2 periodogram analysis (Gnidovec, Neubauer, & Zidar, 2002; Tomioka & Tomioka, 1991) to detect rhythmic components in sleep–wake behavior. Two features of the 24-h sleep–wake pattern during ontogeny, however, are still a matter of debate: the age of emergence and the age of full expression of the 24-h sleep–wake pattern. While some investigations have shown that the 24-h component appears at the end of the first month of life (Hellbrügge, 1960; Kleitman & Engelmann, 1953; McGraw, Hoffmann, Harker, & Herman, 1999; Meier-Koll et al., 1978; Parmelee, 1961; Shimada, Takahashi, Segawa, Higurashi, Samejim, & Horiuchi, 1999), others have reported expression of a weak 24-h pattern even after the first days of life (Freudigman, & Thoman, 1994; Tomioka & Tomioka, 1991; Wulff, Dedek, & Siegmund, 2001).

Current knowledge about the 24-h sleep–wake behavior of infants is primarily based on sleep diary information from parents. We should note, however, that parental reports may be unreliable, because they generally underestimate nocturnal waking (Sadeh, Raviv, & Gruber, 2000). Polysomnography is the gold standard for the study of sleep physiology in infants and children (Coons, & Guilleminault, 1984; Jenni, Borbély, & Achermann, 2004; Louis, Cannard, Bastuji, & Challamel, 1997), although long-term recordings under naturalistic conditions are not feasible. In recent years, actigraph monitors – capable of collecting activity data non-invasively over extended time periods – were introduced for recording children's rest-activity patterns (for a review see Sadeh, & Acebo, 2002). Actigraphy provides a valid tool for long-term assessment of periods of rest and activity in infants and may, thus, reflect temporal and qualitative aspects of sleep behavior (Sadeh, Acebo, Seifer, Aytur, & Carskadon, 1995). Activity monitoring has been repetitively used to describe the 24-h rest-activity pattern in human infants (Nishihara et al., 2002; Wulff et al., 2001). To date, however, no longitudinal study has been performed in the first few months of life using continuous actigraphic recordings.

We recorded rest-activity behavior in human infants and their mothers continuously across the first months after birth. The aim of the study was to describe the development of the 24-h rest-activity pattern under naturalistic conditions and to estimate the emergence, the full expression and the rate of development of the 24-h component using periodogram analysis (Dörsscheidt, & Beck, 1975). We present a methodological approach to quantify the strength of the 24-h component in individual periodograms of rest-activity data.

2. Methods

2.1. Subjects

Twelve infants and their mothers were recruited for this longitudinal study. Due to withdrawal of consent ($n = 2$) and failure of actigraphs ($n = 3$), only seven infant-mother recordings could be analyzed (Table 1). We recruited the subjects from participants of a longitudinal infant sleep EEG study (Jenni et al., 2004) and by private sources. We aimed to collect data over a period of 6 months. One infant dropped out of the study earlier (at age 4 months, # 06). Another mother-infant pair wore the actigraphs for a period of 12 months (# 01, data from months 6 to 12 were not used for periodogram analysis). The parents were contacted prior to birth to provide a detailed explanation of the study aim and to obtain informed written consent. All infants were delivered without peri- and postnatal complications. At

birth, physical and neurological status was normal. All families had middle to upper-class educational levels and the mother was primarily responsible for the daily care of the infant. Infant–parent bed sharing did not occur. The infants remained healthy throughout the study period. The Ethics Committee of the University Children's Hospital of Zurich approved the study protocol. The study was performed according to the Declaration of Helsinki.

2.2. Data acquisition

Rest-activity behavior of the infant and the mother was recorded continuously using actigraphy. The actigraph (Actiwatch Plus®, Cambridge Neurotechnology, Cambridge, UK, 16 g, 27 mm × 26 mm × 9 mm) is a miniaturized, wristwatch-like activity monitor based on an omnidirectional acceleration sensor (piezoelectric element) that records physical activity. The activity counts were accumulated in 1-min epochs and stored in the internal memory (32 kByte, continuous monitoring for 44 days). It was not possible to reliably exclude artifacts caused by intense passive movements (e.g., movements caused by a car, by a stroller on rough pavement, or by the mother carrying the sleeping infant) because simultaneous rest-activity diaries during the study period could not be obtained.

The actigraph was attached to the infant's left ankle and the mothers wore monitors on their non-dominant wrist. Recordings started 4 ± 2 days (mean \pm S.D., range 1–6 days) after birth and lasted on average for 198 ± 78 days (range 122–366 days; Table 1). The data were transferred to a computer at regular intervals.

2.3. Data analysis

To visualize the data in a compact form (visual pattern description), individual rest-activity plots were computed (Fig. 1). An arbitrary threshold of five activity counts per 1-min epoch was applied to discriminate rest from activity. The threshold was selected after visual inspection of different threshold levels and scaling methods (grey and color scaling). The selected threshold corresponded to approximately 5% of the mean activity per day in infants. The raw data were subdivided into consecutive 10-day intervals, displayed on the computer screen (Fig. 2, upper panels) and visually analyzed for artifacts. Periods with zero activity for longer than 60 min were excluded (selected cut-off to separate physiological inactivity from not wearing the monitor). The rationale for analyzing 10-day intervals was based on Sokolove and Bushell (1978) demonstrating that a reliable estimate of 24-h periodicity is possible with intervals of 10 days, even with noisy data. Because our focus was the development of the strength of the 24-h pattern, it was important to obtain complete 10 days for all calculations. Therefore, incomplete 10-day intervals were excluded for further analysis. In general zero activity over prolonged periods was rare (# 01, Fig. 1, white lines due to downloading data in the lab during the day; # 02, missing data resulting from increasing non-compliance with increasing age).

The aim of this study was to examine the occurrence and the development of the 24-h component in infant rest-activity behavior. We used an approach based on periodogram analysis, a method designed to detect rhythmic components in rest-activity data (see Enright, 1965; Enright, 1990). Periodic patterns of activity are detected in the presence of random fluctuations. This implies a statistical approach to assess the significance of periodic components. Our analysis was based on the periodogram method of Dörrscheidt and Beck (1975). A standardized root mean square amplitude $q(p)$ was estimated as a function of the period p and a confidence limit $q_S(p)$ was determined based on the F -distribution (for details see Dörrscheidt & Beck, 1975, p. 112). The function $q(p)$ is illustrated in Fig. 2 (lower panels) for two 10-day intervals in the same infant (during the first few days of life and at age 4 months). In addition, the 99% confidence limit $q_S(p)$ is indicated as a function of period p . Peaks above the confidence limit were considered significant (Dörrscheidt & Beck, 1975). We defined the strength of the 24-h component as the difference between the peak and the 99% confidence limit ($s_2 - s_1$, Fig. 2). Period p was varied in steps of 15 min. The 12-h peak at 4 month represented a higher harmonic component (Fig. 2, lower right panel). Simulations revealed that the height of the peak in the periodogram was related to the amplitude of the rhythm but did not depend on its period or phase.

3. Results

3.1. Rest-activity patterns across age

Fig. 1 visualizes long-term patterns of rest-activity behavior in individual infants and their mothers in a compact form. While an ultradian pattern of rest-activity was predominate in the newborn period (see also Fig. 2, upper left

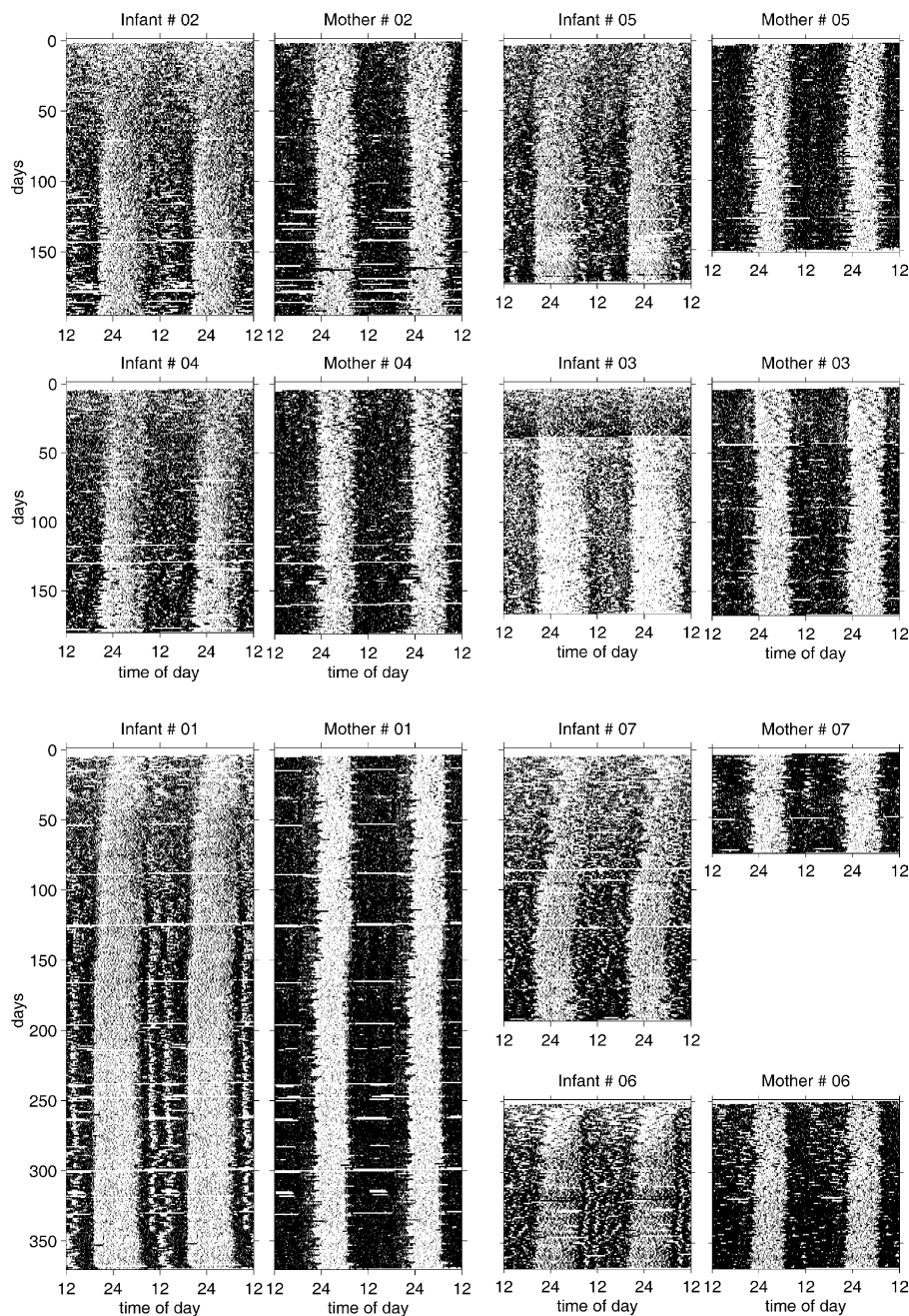


Fig. 1. Individual rest-activity plots of infants and their mothers in compact form. The horizontal axis represents 48 h; each 24-h period was double plotted. Black and white areas and dots represent activity or rest periods, respectively. An arbitrary threshold of five activity counts based on 1-min epochs was applied to discriminate rest from activity. White horizontal lines over multiple hours indicate periods when the actigraph was taken off (missing data). # 03: the mother's and infant's actigraph were unintentionally exchanged at day 35. The clear-cut differences in black–white scaling levels demonstrate substantial inter-device variability in sensitivity.

panel, # 05), the infants gradually developed a 24-h pattern with night preference for rest and day preference for activity. A large variability among infants was seen in daytime rest behavior (naps). Some infants (# 01, 05, and 06) developed daily regular nap schedules in the course of their first 6 months, others (# 02, 03, 04, and 07), however, showed irregular length and frequency of daytime rest periods. Within the first weeks after birth, the mothers showed

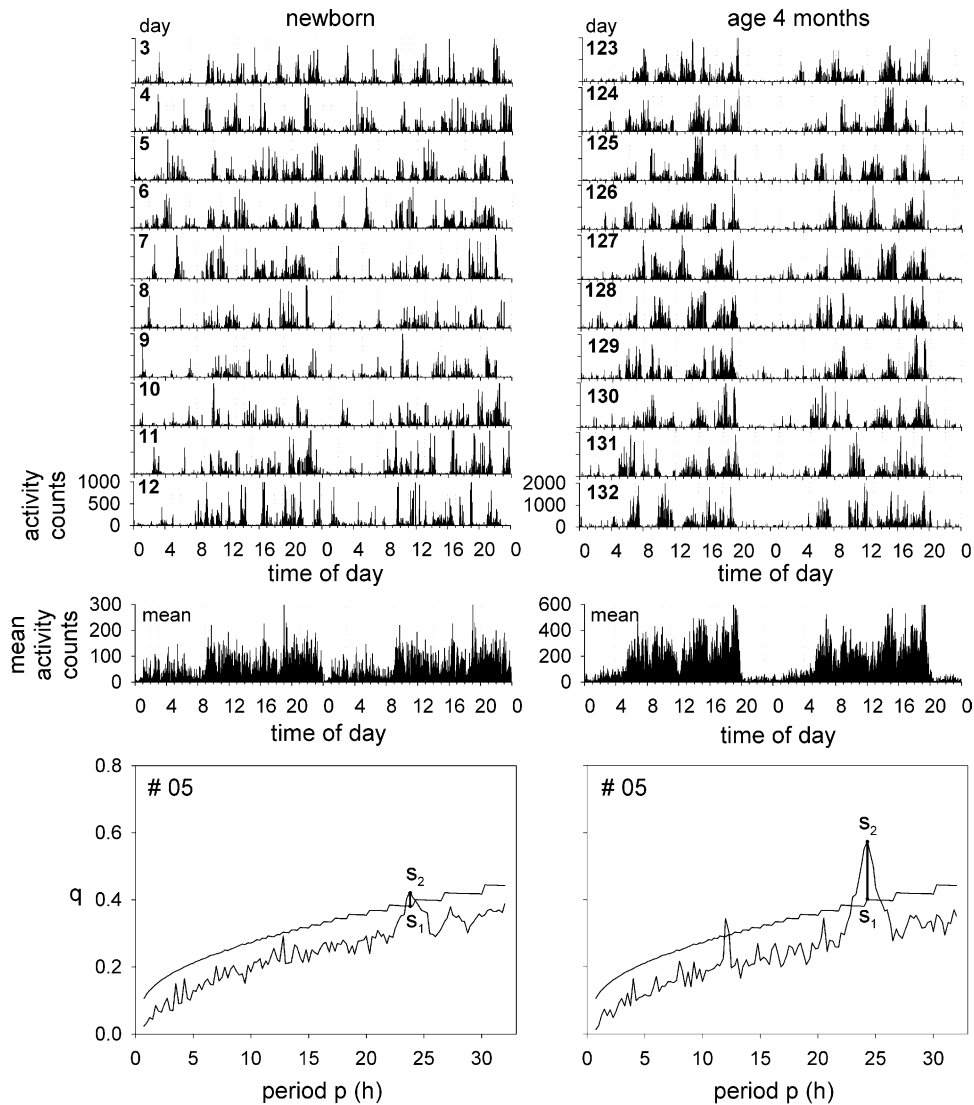


Fig. 2. *Upper panels*: Double plots of raw activity data over 10 consecutive days (infant # 05). Days 3–12 (newborn, left) and days 123–132 (age 4 months, right) are illustrated. Black vertical lines represent activity counts of 1-min epochs. *Middle panels*: Mean 24-h activity profile (double plotted). Average 10-day activity was calculated for 1-min epochs. *Bottom panels*: Periodograms according to Dörrscheidt and Beck (1975) of the corresponding 10-day intervals. Standardized root mean square amplitude q and the 99% confidence limit q_s are plotted as a function of period p . Period p was varied in steps of 0.25 h. The strength of the 24-h component was determined as the difference ($s_2 - s_1$) between the peak (s_2) and the corresponding 99% confidence limit (s_1).

increased nighttime activity (feeding of the infant) and naps during the day. In some infants shifts in their rest-activity pattern were observed (e.g., # 07, because of travels across time zones).

A weak day–night asymmetry (i.e., sleep predominantly during nighttime than during daytime) was observed in most infants as early as in the first month of life. This asymmetry became more robust with increasing age. In two infants (# 01, # 05), the asymmetry between day and night could even be seen in the first 2 weeks after birth (see Fig. 2, upper left panel, # 05) which was confirmed by a significant peak at the 24-h period ($p < 0.01$). Between 2 and 6 months, the transitions from rest to activity in the mornings often occurred at irregular times (Fig. 2, right upper panel), whereas evening activity decreased switch-like to low levels at the onset of the nocturnal rest (Fig. 1).

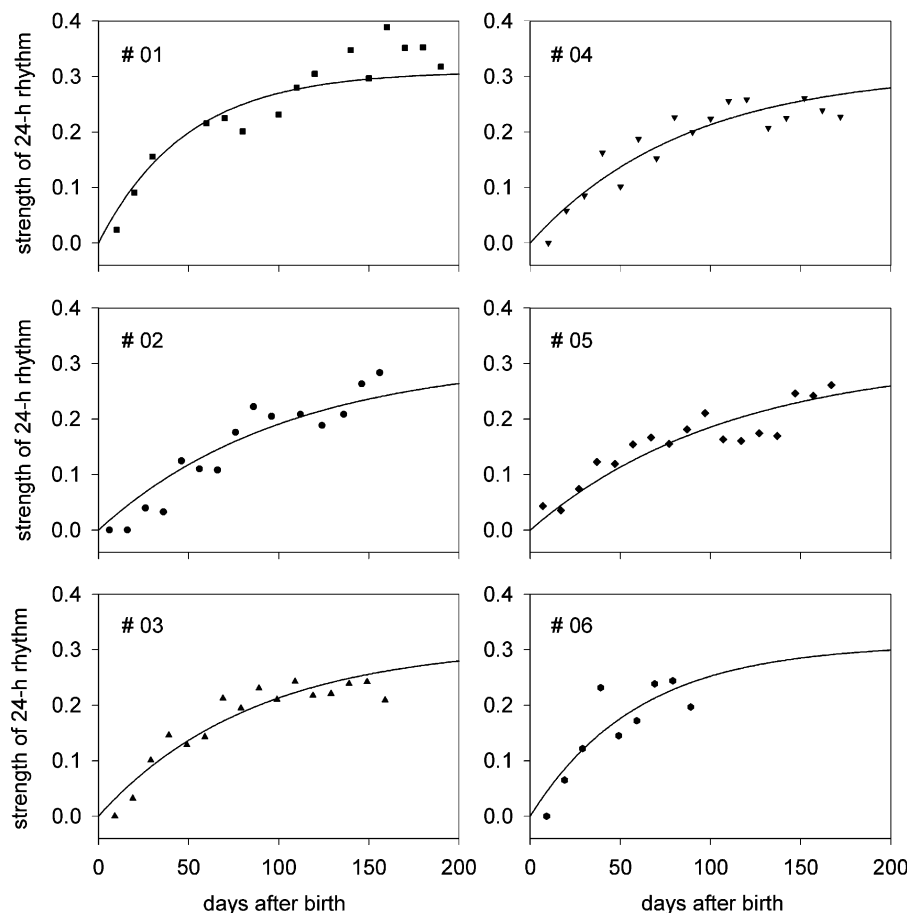


Fig. 3. Developmental time course of the 24-h rest-activity component in individual infants. Data points of 10-day periodogram intervals are plotted at mid intervals (for methodological details see text and Fig. 2). Intervals with missing data (>60 min, cut-off separated physiological inactivity from monitor not worn) or with artifacts were excluded from the analysis. The time course of the 24-h component was estimated by fitting saturating exponential functions to the data (solid lines): $S(t) = 0.3097 - (0.3097 \times e^{-t/\tau})$. The asymptote was set at 0.3097 (average mother's strength of the 24-h component in the last 20 days of recording). τ is the time constant. Only data points until age 190 days were used for the fitting procedure.

3.2. Quantification of the 24-h component: periodogram analysis

We quantified the 24-h component in individual 10-day rest-activity intervals by periodogram analysis (for methodological details see methods and Fig. 2, infant # 07 excluded from the analysis because of travels across time zones, $n = 6$). The magnitude of the 24-h component monotonically increased in the course of the first 6 months of life following a saturating rise (Fig. 3). The temporal trend of the 24-h component was quantified by fitting a saturating exponential function to the individual data using a non-linear regression procedure (SAS Institute, Inc., NC, USA). The asymptote of the function was set at the average level of the mothers' 24-h component (0.3097) determined for the last 20 days of their recording. Results of the fitting procedure are summarized in Table 2. The high r^2 in individual infants indicated a good quality of the fit. The time constants of the exponential functions ranged from 48.6 to 109.6 days. We note that the 24-h pattern showed a monotonic increase in the magnitude of the 24-h component, but fluctuations around the trend also occurred (Fig. 3). No correlation was found between the time constants or the mean square error of individual fitted functions and infant characteristics such as gestational age, birth order, birth month (season), breastfeeding duration and birth weight or birth length.

Table 2

Parameters describing the time course of the magnitude of the 24-h rest-activity component in six individual infants

Infant	<i>n</i>	r^2	τ , days
# 01	15	0.80	48.6 (7.4)
# 02	15	0.88	104.4 (9.2)
# 03	16	0.88	85.9 (5.7)
# 04	17	0.86	85.7 (6.3)
# 05	17	0.82	109.6 (7.5)
# 06	9	0.76	59.4 (8.2)
Mean			82.3 (7.4)

n, number of 10-day intervals included in the analysis. τ , time constant and in brackets asymptotic SEM of the fitted saturating exponential function (see Fig. 3).

4. Discussion

Our study describes the development of the 24-h rest-activity pattern in human infants on the basis of continuous actigraphic recordings over extended periods of time. We present an approach to quantify the magnitude of the 24-h component. In recent years, the emergence of the 24-h pattern in infant rest-activity behavior was found to occur earlier than previously reported (Freudigman & Thoman, 1994; Gnidovec et al., 2002; Nishihara et al., 2002; Tomioka & Tomioka, 1991; Wulff et al., 2001). Our observations corroborate the findings that day–night differences in rest-activity behavior can be detected as early as in the first weeks of life. In two infants, a significant day–night asymmetry was even present within the first 10 days of life.

Most reports about the development of the 24-h rest-activity pattern during infancy were associated with the entrainment of the circadian clock or the maturation of the circadian timing system (Nishihara et al., 2002; Shimada et al., 1999; Tomioka & Tomioka, 1991). The study of endogenous circadian rhythms (near 24-h rhythms), however, requires constant conditions (of light and environment) and the inclusion of additional physiological measures (e.g., body temperature). Like in other studies, we did not control for social cues and light conditions, but examined rest-activity behavior of infants under naturalistic conditions. Thus, developmental aspects of the circadian timing system cannot be sufficiently addressed by our approach and the term ‘24-h rest-activity pattern’ is used throughout this report rather than ‘circadian rest-activity pattern’. We note that parental care strongly affects the activity pattern of the infant and may mask the endogenous circadian rhythm.

4.1. Interindividual variability

We observed large interindividual variation in the rate of development of 24-h rest-activity behavior quantified by the time constant of individually fitted functions. This finding is in line with a number of studies demonstrating a large interindividual variation in biobehavioral characteristics of infants (de Weerth, van Geert, & Hoijtink, 1999). Several authors have proposed that interindividual variation in the emergence of the 24-h rhythm is endogenous in nature and reflects differences in brain maturation (Coons & Guilleminault, 1984; Mirmiran, Baldwin, & Ariagno, 2003; Mirmiran, & Kok, 1991; Shimada, Segawa, Higurashi, & Akamatsu, 1993). However, differences in parental care and environmental conditions may also play an important role (Mann, Haddow, Stokes, Goodley, & Rutter, 1986; McMillen, Kok, Adamson, Deayton, & Nowak, 1991). This view is supported by the behavior of infant # 01 showing an early emergence of the 24-h pattern and additional ultradian components (naps) that were strongly influenced by the care of the mother (personal communication, Tom Deboer). Further, the month of birth may have an impact on the development of the 24-h rhythm (seasonal effects), although no correlation of the time constants with birth month was found in our study. The extent to which differences in the developmental rate of 24-h patterns are the result of biological/maturational or environmental conditions is a matter of debate that requires further exploration.

4.2. Intraindividual variation

In addition to interindividual variability, we also observed intraindividual variation. The magnitude of the 24-h pattern of rest-activity behavior exhibited a monotonic increase, but fluctuations around the trend occurred (Fig. 3).

Several explanations may account for such variability within subjects: (1) measurement errors, (2) changes of maternal behavior in infant care, (3) changes and variation in infant behavior or (4) variation in the patterns of interaction between mother and infant. A number of studies have reported that infant behavior is highly variable across time (see de Weerth et al., 1999). For example, the 24-h crying pattern in the first months of life shows large day-to-day and week-to-week variation (reviewed in Barr, 1990). A tentative explanation is that variable infant 24-h behavior has an adaptive function to retain parent's attention (Soltis, 2004). Variability would ensure continuous parental efforts to take care of the infant's needs and to reach a stable parent–infant relationship (Konner, 1972; Soltis, 2004). The observed intraindividual variation in infant behavior indicates that longitudinal approaches with sufficient amount of data points are needed in infant studies.

When is the full expression of the 24-h rest-activity pattern established? Davis (1981) has proposed that circadian sleep–wake processes have an extended period of maturation and even continue to mature into adolescence, while others have determined the third month as the time of robust expression of 24-h rest-activity behavior (Hellbrügge, Lange, Rutenfranz, & Stehr, 1964; Parmelee, 1961). We report that the asymptote in the magnitude of the 24-h pattern is reached between 5 and 10 months (three times the time constant of individually fitted function). This finding supports the notion that a robust consolidation of sleep at the nighttime does not occur in the first 3 months of life, but rather in the second half of the first year (Iglowstein, Jenni, Molinari, & Largo, 2003).

It is important to note that the evolution of a 24-h rest-activity pattern not only depends on the development of the circadian timing system, but also on the maturation of sleep homeostatic processes. The concept of sleep homeostasis posits a sleep–wake dependent process reflecting sleep need by its accumulation during wakefulness and its dissipation during sleep (Borbély, & Achermann, 2005). Some have proposed that sleep homeostatic mechanisms develop early in life enabling infants to stay awake during the day and to sleep consolidated periods through the night (Jenni et al., 2004; Peirano, Algarin, & Uauy, 2003). To which degree circadian or homeostatic sleep regulatory processes play a role in the development of a 24-h pattern remains to be examined.

Important limitations should be considered when interpreting or generalizing our results. Actigraphy was applied without accompanying sleep–wake diaries because parents were unwilling to complete a diary over several months. Thus, periods with more intense passive movements or with the mother carrying the sleeping infant could not be reliably excluded. In addition, our sample was relatively small and highly selective (participants of a longitudinal infant sleep EEG study (Jenni et al., 2004) and from private sources). Some might suggest to focus our analysis more on the comparison between infant and mother rest-activity patterns, since we also acquired data of the mothers (which were used to determine the upper asymptote of the saturating exponential function, see methods). We learned, however, that rest-activity data are not suitable to investigate interactions between mother and infant behavior, because devices focus primarily on physical activity which may be unspecific. In addition, substantial inter-device variability in sensitivity (see also Fig. 1, # 03) complicates the comparison between mother and infant.

In summary, we found an early emergence of the 24-h rest-activity pattern in human infants that increased in strength across the first months of life. Interindividual variability and intraindividual variation were typical features of rest-activity behavior in developing infants. To what extent environmental conditions, parental care and gestational age (maturation) contribute to this variability needs further examination. Understanding the basic processes responsible for the development of a 24-h pattern in infant behavior would have important implications for parental counseling in clinical practice.

Miniaturized actigraphs are ideal tools for long-term longitudinal monitoring of rest-activity behavior in infants. The approach used in this study to quantify the strength of the 24-h component in individual periodograms of rest-activity data may provide a methodological basis for future studies.

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