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# Dynamics and Ultradian Structure of Human Sleep in Real Life

## Highlights

- Limb movement during sleep shows patterns exploitable for large-scale field studies
- Non-linear conversion to inactivity reveals rhythms linked to sleep physiology
- Inactivity oscillates with a 110-min period and gradually declines across the night
- Inactivity amplitude and gradual decline are markedly reduced with age

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## In Brief

Winnebeck et al. present a method that extracts basic patterns of sleep physiology from simple records of wrist movement. This new procedure extends sleep research beyond laboratory studies, for the first time enabling large-scale analyses of sleep characteristics in real life under the most diverse conditions.

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# Dynamics and Ultradian Structure of Human Sleep in Real Life

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## SUMMARY

**The temporal dynamics that characterize sleep are difficult to capture outside the sleep laboratory. Therefore, longitudinal studies and big-data approaches assessing sleep dynamics are lacking. Here, we present the first large-scale analysis of human sleep dynamics in real life by making use of longitudinal wrist movement recordings of >16,000 sleep bouts from 573 subjects. Through non-linear conversion of locomotor activity to "Locomotor Inactivity During Sleep" (LIDS), movement patterns are exposed that directly reflect ultradian sleep cycles and replicate the dynamics of laboratory sleep parameters. Our current analyses indicate no sex differences in LIDS-derived sleep dynamics, whereas especially age but also shift work have pronounced effects, specifically on decline rates and ultradian amplitude. In contrast, ultradian period and phase emerged as remarkably stable across the tested variables. Our approach and results provide the necessary quantitative sleep phenotypes for large field studies and outcome assessments in clinical trials.**

## INTRODUCTION

Possibly one of the most intriguing features of sleep is that it occurs in cycles. First recognized in the 1950s [1, 2], the two fundamental states of sleep in humans and other mammals—rapid eye movement and non-rapid eye movement sleep (REM and NREM sleep)—alternate throughout the sleep bout producing cycles of 90–110 min in duration. These NREM-REM cycles are accompanied by other physiological oscillations such as in cortical electric activity [2–4], respiratory and cardiovascular physiology [1, 5, 6], penile erection [7, 8], hormone secretion [9, 10], and also body movements [1, 2, 11]. Some of the pioneers of sleep research called these ultradian sleep cycles (i.e., cycles with periods <24 hr) "the presumptive physiological unit" [12] of sleep, which they predicted to be central to the function of sleep.

Nonetheless, systematic and comprehensive investigations of the ultradian dynamics of sleep have still not been realized, likely because sleep monitoring and analysis techniques are not amenable to gathering large datasets outside the laboratory. Then and now, the gold standard of sleep monitoring is laboratory polysomnography (PSG), an informative but costly and time-consuming technique that encompasses electroencephalographic (EEG), electrooculographic, and electromyographic recordings followed by manual analysis of the sleep record [13].

In recent years, this technical obstacle to ambulatory and longitudinal sleep research has been partly overcome. Thanks to pioneering work in the 1970s and 1980s (e.g., [14–17]) and the now wide availability of small and relatively cheap accelerometers, researchers have been able to use continuous recordings of locomotor activity (actimetry or actigraphy) via small wrist-worn devices to study sleep outside the laboratory. By identifying the gaps in the activity record, i.e., episodes of relative immobility, one can judge timing and duration of sleep bouts with reasonable accuracy [18, 19] (Figures 1A and 1B). However, the use of actimetry to simply detect sleep bouts does not exploit the method's full potential as the actual movement during sleep and the information contained therein is largely ignored. The disregard of movement patterns during sleep is all the more astonishing as some pioneering studies of this technique already used these patterns successfully to describe effects of sleep medication and depression [20–22]. Furthermore, earlier research (admittedly using more complicated forms of movement detection) suggested a relationship of body movements during sleep with state transitions and sleep stages and also that movement may occur in ultradian cycles [1, 2, 11, 23–28].

Here, we present a simple method that allows assessment of the ultradian sleep structure and other sleep dynamics based on recordings of wrist-locomotor activity. Despite its expectedly lower resolution than standard laboratory recordings, our method enables quantitative investigation of sleep dynamics outside the laboratory in large numbers and diverse conditions without the need for complicated recording equipment. To demonstrate the potential of this method, we applied it to our existing database of over 20,000 days of activity recordings from all of our recent field studies. In this first large-scale analysis of human sleep structure, we identified several internal and external factors influencing human sleep dynamics in real life. This demonstrates the power of such actimetry-based approaches to significantly advance our understanding of sleep by making sleep dynamics quantifiable in everyday contexts and in huge numbers of nights and people [29].

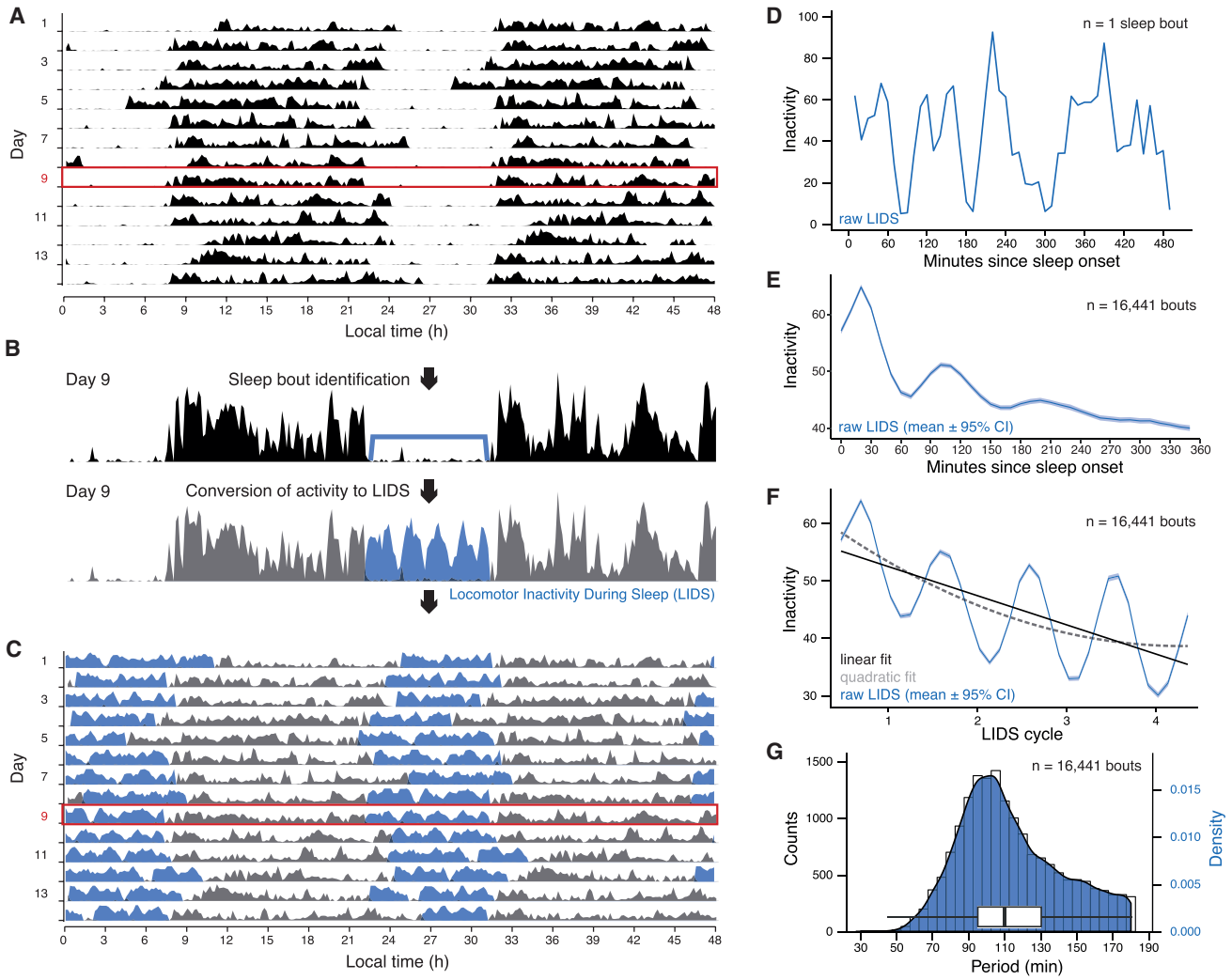



**Figure 1. Ultradian Rhythm of Wrist Movement during Sleep Revealed by Conversion of Locomotor Activity to Inactivity**

(A) Double-plotted actogram displaying 2 weeks of wrist locomotor activity of a single person.

(B) Schematic representation of our sleep analysis from actimetry records (using day 9 from A). Sleep bouts are first identified by relative immobility. Locomotor activity during sleep is subsequently converted to "Locomotor Inactivity During Sleep" (LIDS) by inversion, rescaling, and smoothing.

(C) Actogram from (A) showing activity (gray) and LIDS (blue).

(D) LIDS profile of a single sleep bout.

(E and F) Average LIDS profiles (± 95% CI) based on the raw LIDS values of all sleep bouts from actimetry database. Timelines in (F) were normalized to individual LIDS periods prior to averaging.

(G) Distribution of cosine-estimated ultradian LIDS periods across database sleep bouts.

## RESULTS

### Ultradian Rhythms in Locomotor (In)activity during Sleep

In our circadian analyses of human locomotor activity (wrist actimetry), we routinely identify sleep bouts via relative immobility (Figures 1A and 1B). During this process, we noticed that the low residual activity in some sleep bouts appeared regular; activity and inactivity seemed to wax and wane in an ultradian fashion. This pattern became clearer and appeared in more bouts when we transformed the residual activity during sleep non-linearly to enhance the contrast between movement and non-movement. Namely, we inverted activity to inactivity resulting in values from 0 to 100 and smoothed it via a 30-min centered moving average. In our resulting inactivity index, "100" represents complete inactivity, whereas increasing movements push the index toward zero. We termed the result of this conversion "Locomotor Inactivity During Sleep" (LIDS) (Figures 1B–1F).

For a systematic analysis of activity patterns during sleep, we applied the LIDS conversion to all sleep bouts in our actimetry database. This database holds records from most of our recent studies and comprises >20,000 days of actimetry from 574 subjects from 8 to 92 years (Table 1). Our sleep-detection algorithm [30] identified over 25,000 putative sleep bouts, of which 16,441 fulfilled our analysis criteria of duration and cosine fit quality (median duration: 7.3 hr; 573 subjects). Mostly, bouts were excluded because they were too short in duration for meaningful analyses

**Table 1. Actimetry Database Details**

| | | Database Groups | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | All Combined | *Children* | *Adolescents* | *Adults* | *Adol. psych. pat.* | *Shift workers* | *Quilo.* |
| Subjects | | | | | | | | |
| n | | 574 | 53 | 104 | 141 | 76 | 111 | 89 |
| Sex | females | 53% | 42% | 65% | 63% | 86% | 5% | 63% |
| Age (y) | median | 26 | 10 | 17 | 33 | 15 | 36 | 55 |
| | range | 8–92 | 8–11 | 13–22 | 18–82 | 11–19 | 20–59 | 18–92 |
| Sleep Bouts (Analysis Criteria: 3–12 hr Duration, Significant Cosine Fit) | | | | | | | | |
| n | total | 16,441 | 1,596 | 2,747 | 6,401 | 1,130 | 2,927 | 1,640 |
| | %[a] | 63% | 81% | 68% | 61% | 71% | 65% | 49% |
| Per subject | median | 26 | 30 | 27 | 47 | 13 | 23 | 20 |
| Per subject | range | 1–84 | 9–43 | 4–46 | 13–84 | 2–32 | 7–78 | 1–37 |
| Duration (hr) | total | 119,886 | 14,165 | 19,342 | 46,272 | 8,528 | 19,787 | 11,793 |
| Per subject | median | 7.3 | 9.2 | 7.2 | 7.3 | 7.7 | 6.7 | 7.3 |
| Per subject | range | 3–12 | 3–12 | 3–12 | 3–12 | 3–12 | 3–12 | 3–12 |
| Actimeters | | | | | | | | |
| Models | | Daqto, AW2/7,AWSpec | AW7 | Daqto, AWSpec | Daqto, AWSpec | Daqto | Daqto | AW2 |

The actimetry database used in this study contained human wrist-actimetry records from most of our recent studies conducted between 2006 and 2014. Database groups were the inherent groups occurring in our database. Age ranges partly overlap between groups to accommodate other group characteristics. Abbreviations are as follows: Adol. psych. pat., *Adolescent psychiatric patients*; Quilo., *Quilombola*; Daqto, daqtometer; AW2/7, Actiwatch 2/7; AWSpec, Actiwatch Spectrum. See also Figure S1.

[a]percentage of all available bouts prior to exclusions based on analysis criteria

(79% of total exclusions) (see STAR Methods and Figure S1 for more details). Altogether, this provided close to 120,000 hr of sleep for LIDS analysis.

The analysis across these database sleep bouts clearly demonstrates an ultradian oscillation in LIDS. When LIDS is averaged across all bouts, the signal is initially rhythmic but quickly dampens (Figure 1E). However, if individual bout timelines are normalized to their LIDS period (as determined via cosine model fitting), the progressive desynchronization due to different periodicities is counteracted and the rhythmicity is maintained (Figure 1F). The distribution of the cosine-determined ultradian periods is depicted in Figure 1G and shows enrichment between 95 and 130 min (median: 110 min), durations similar to those of NREM-REM sleep cycles (e.g., [2, 31, 32]).

Just like with sleep cycles [31, 33], LIDS cycle durations appear to vary considerably within single sleep bouts. Therefore, the cosine-estimated period reflects not the durations of individual LIDS cycles but the bout's predominant or mean LIDS period providing an overall gestalt of the bout. Mean bout periods estimated via wavelet analyses, which take account of the non-stationarity of the LIDS oscillations, correlate significantly with the cosine-derived periods as tested in a wavelet-suitable subset of bouts (Pearson $r = 0.40$, $p < 0.001$; 8,049 sleep bouts). Hence, the normalization of bout timelines to the cosine-derived period brings out the substantial ultradian oscillation in the averaged LIDS profile across the 16,441 sleep bouts.

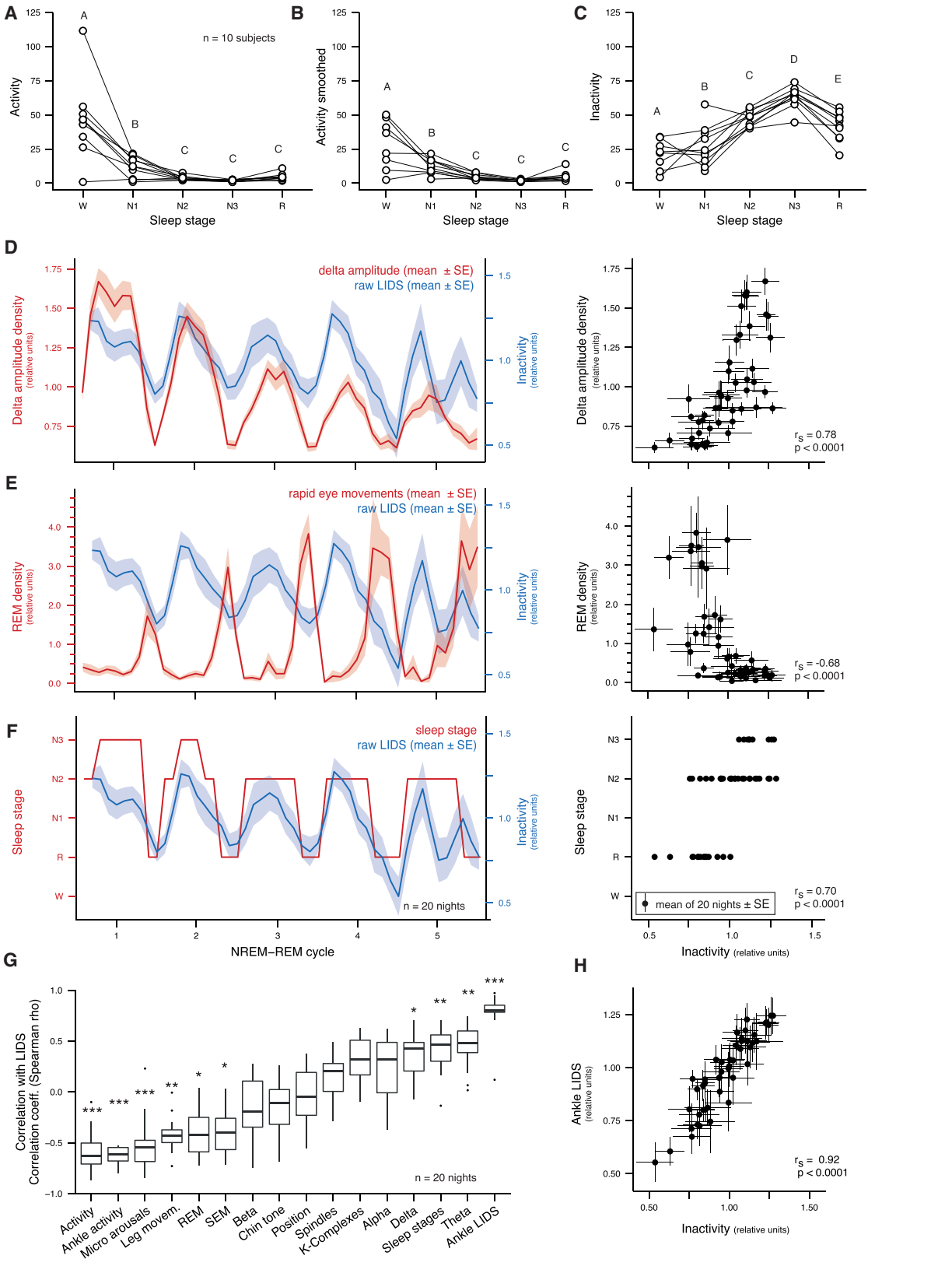
Besides LIDS rhythmicity, the average profile also reveals that LIDS mean levels decline by about 5%–10% per cycle in a quadratic fashion (Figure 1F). This means that movement gradually increases during sleep. Notably, the LIDS decline was rarely apparent in single sleep bouts and revealed only by averaging across bouts (a feature well known in sleep analyses [26, 31, 32, 34]). The LIDS decline is reminiscent of the decline in the sleep EEG's slow wave power, commonly used as a proxy for sleep homeostasis [35–37]. In summary, these initial results from our actimetry database demonstrate that wrist movement during sleep occurs in ultradian cycles reminiscent of sleep cycles and shows dynamics similar to measures of sleep homeostasis.

## LIDS Rhythms Correspond to Rhythms in Sleep Physiology

To probe whether LIDS rhythms indeed correspond to ultradian rhythms in sleep physiology as measured in the sleep laboratory, we collected a dataset of 20 nights of simultaneous actimetry and PSG (10 healthy participants, 2 nights each). Importantly, PSG and actimetry records were merged at the 30-s level of the PSG record but analyzed at our standard 10-min resolution for human locomotor activity.

Our data support previous findings showing that wrist locomotor activity generally varies with sleep stage. Activity levels tend to decrease with increasing sleep depth; however, differences in activity levels are prominent and systematic mostly only between wake and sleep, but not between sleep stages [25, 38–40]. This was also the case for activity in our dataset, and data smoothing (as done for the LIDS conversion) had no influence (Figures 2A and 2B; mixed model analysis in Table S1). In contrast, levels of LIDS—as expected for inverted activity—increased with increasing sleep depth and differed systematically not only between wake and sleep but also between all sleep stages (Figure 2C; Table S1). This result suggests that LIDS is able to mirror relevant information about sleep structure.

If LIDS is indeed representative of sleep structure, the temporal pattern of LIDS should share features with common




*(legend on next page)*

parameters of sleep physiology. We therefore graphically assessed the correspondence of temporal profiles and determined their quantitative associations via correlation analyses. Figures 2D–2F show the time courses (left) and direct associations (right) of LIDS and key PSG parameters averaged over all 20 nights. For graphs of individual nights and all measured parameters, see the additional figures provided via Mendeley Data. Key results are summarized below.

As was the case for the database LIDS profile, the averaged LIDS profile across 20 PSG nights shows clear ultradian oscillations (blue lines in Figures 2D–2F), although timelines were normalized to individual NREM-REM cycles instead of LIDS periods as in Figure 1F. Thus, LIDS oscillations and sleep cycles have comparable periods. In addition, although 20 nights were too few to show a decline in LIDS levels as seen over 16,441 bouts (Figure 1E versus Figure 2D), mixed model analysis indicates a trend toward a decline also in these data (−1.57 LIDS units per cycle; $b_{sleepcycle}$; Table S2).

The synchrony of LIDS and NREM-REM cycles was also reflected in individual PSG measures (of which many are used for NREM-REM cycle determination; Figures 2D–2F). In the average profiles, LIDS oscillated in phase with the amplitude densities of all relevant EEG frequency bands (beta, alpha, theta, and delta), which are highest during "deep" sleep when cortical activity is most synchronized [3]. LIDS oscillated also in phase with densities of K-complexes and sleep spindles, two characteristic EEG waveforms that are hallmarks of stage 2 sleep [13]. In contrast, LIDS oscillated in anti-phase to micro arousal densities and also to eye movement densities. Times of frequent slow eye movements ("light" sleep or sleepy wake) and rapid eye movements (REM sleep and wake) both coincided with LIDS troughs. Consequently, LIDS was found to oscillate in-phase with markers of "deeper" sleep and out-of-phase with markers of "lighter" as well as REM sleep.

This close relationship between LIDS and sleep depth is also illustrated in the sleep stage profile, which shows the predominant sleep stage for each time point (Figure 2F). Deep sleep stages N3 and N2 dominated during LIDS peaks (i.e., times of little movement), whereas REM sleep dominated during LIDS troughs (i.e., times of more movement). Although muscle atonia is one of the hallmarks of REM sleep [13, 41, 42], this sleep stage is also marked by intermittent muscle twitching [13, 41, 43] and specific fine movements [2, 24] while also surrounded with episodes of lighter sleep and increased movement at the state transition [2, 24, 43] (see also discussion in [23]). With our 10-min resolution, LIDS rhythms may therefore well reach minima (i.e., activity maxima) around REM sleep episodes. Overall, the LIDS oscillation seems an excellent representation of the ultradian gestalt of sleep.

That LIDS can also provide insight into sleep of single individuals and single nights is illustrated in Figure 2G, which displays correlation coefficients between LIDS and PSG parameters based on individual nights. Leaving measures of locomotor activity aside, the consistently highest negative correlations with LIDS were found for slow and rapid eye movements (median rho = −0.4), while the consistently highest positive correlations were seen for sleep stages and theta and delta amplitudes (median rho = 0.4–0.5). Although correlation coefficients were (expectedly) lower in the individual analysis, the pattern was very similar to the averaged analysis and did not change systematically from night 1 to 2 in 9 of 10 individuals (Figure S2A). Furthermore, when the temporal order of locomotor activity was randomized within each night prior to the LIDS conversion, all associations between LIDS and PSG parameters disappeared (Figure S2B). These results confirm that the in- and out-of-phase relationships between LIDS and polysomnographic sleep parameters are highly systematic and are detectable features of each night.

In summary, our data strongly indicate that LIDS reflects physiological rhythms during sleep. Notably, measures of ankle movement (ankle activity and its derived LIDS as well as leg movement density from tibial electromyograms) all correlated highly with LIDS derived from wrist actimetry (Figures 2G and 2H). Therefore, not just wrist but limb movement rhythms in general appear to be an integral part of the fundamental ultradian sleep program.

## LIDS Rhythms Are Influenced by Many Parameters

Our sleep lab experiments indicated that LIDS is closely associated with PSG-monitored sleep physiology—at least in healthy subjects. Actimetry and LIDS may thus be useful tools to address fundamental questions about sleep that require large datasets and field settings.

We therefore extended our analysis of the 16,441 sleep bouts from the actimetry database to tease out LIDS features common or specific to certain populations. To this end, we performed mixed model analyses using age and sex as covariates but

**Figure 2. Correspondence between Rhythms in LIDS and in Sleep Physiology**

Data are from simultaneous recordings of wrist actimetry and PSG in 10 subjects for 2 nights each.

(A–C) Average wrist mobility per subject and sleep stage at a 10-min resolution using different locomotor measures, activity (A), smoothed activity (B), inverted and smoothed activity (LIDS) (C). Letters report results of mixed model analysis (Table S1); sleep stages marked by different letters are systematically different in their wrist mobility. All wake occurred after initial sleep onset.

(D–F) Time courses (left) and direct associations (right) of LIDS and key PSG parameters averaged for all 20 nights. Data are expressed relative to the NREM-REM cycle and as deviations from individual mean; error bars indicate standard error of the mean. Spearman correlations are given on the right.

(G) Correlations of LIDS with polysomnographic parameters for each night. n = 20 except for ankle activity and ankle LIDS (n = 9), leg movements and body position (n = 7). Asterisks indicate statistical significance of at least 70% of r values per parameter (*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$). Correlation coefficients for sleep stage are provided for completeness, although sleep stage is a nominal variable (albeit with an implicit order for NREM stages). Boxplots are Tukey boxplots with whiskers encompassing all data points within 1.5 times the interquartile range.

(H) Direct association between wrist and ankle LIDS. Error bars indicate standard error of the mean.

Abbreviations are as follows: PSG, polysomnography; N1-3, non-REM sleep stage 1–3; R, REM sleep; W, wake; REM, rapid eye movements; SEM, slow eye movements; alpha, beta, theta, and delta refer to amplitude densities in respective frequency bands of the EEG. Please note that indicated sleep stages represent the most prevalent stage within each 10-min or NREM-REM cycle bin. As there was no bin with stage N1 as the most frequent sleep stage across all nights, there are no data points for N1 in (F). See also Figure S2 and Tables S1 and S2.

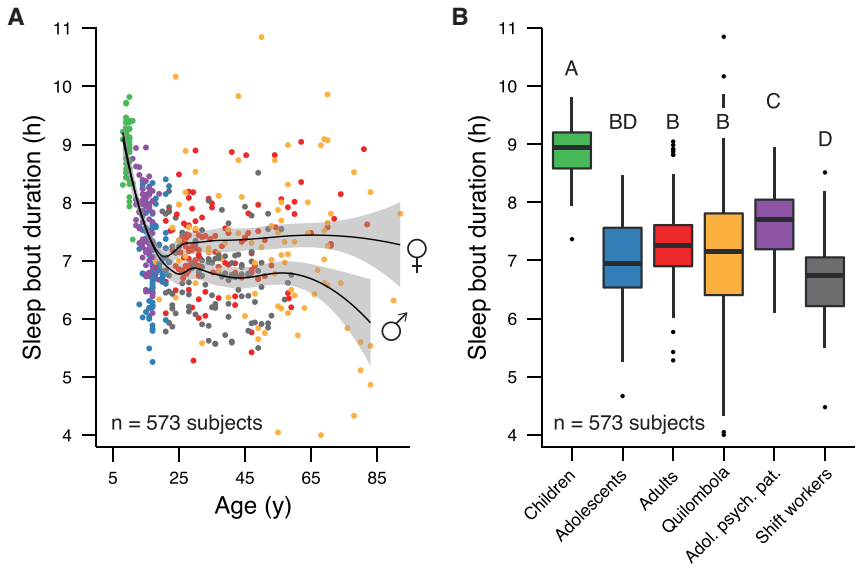



**Figure 3. Durations of Sleep Bouts Extracted from Actimetry Database**

Plotted are average bout durations per subject.

(A) Relationship of bout duration with age, sex, and database group. Colors signify group as used in (B). Loess smoother (±95% CI) is depicted in black.

(B) Sleep bout durations per database group. Letters report results of Dunn's post hoc test after Kruskal-Wallis rank sum test ($H(5) = 182.93$, $p < 0.0001$); database groups marked by different letters were significantly different. Short sleep bout durations in some of the *Quilombola* result from biphasic nocturnal sleep (see also Figure S1). Subject numbers per group are as follows: *Children* n = 53; *Adolescents* n = 104; *Adolescent psychiatric patients* n = 76; *Adults* n = 141; *Shift workers* n = 111; and *Quilombola* n = 89, as per Table 1. Adol. psych. pat., *Adolescent psychiatric patients*. Boxplots are Tukey boxplots with whiskers encompassing all data points within 1.5 times the interquartile range.

See also Figure S1.

also taking into account the naturally occurring groups in our database. Each participant was assigned to one of six groups differing mainly by age, working times, mental health, and ethnicity: *Children*, *Adolescents*, *Adults*, *Shift workers*, *Adolescent psychiatric patients* (all Caucasian), and *Quilombola* (Brazilians of African descent living in communities with varying levels of electrification). All shift workers in the database worked in rotating shifts including night shifts. Psychiatric patients were both in- and out-patients predominantly suffering from depression or eating disorders (for detailed group description, see STAR Methods and Table 1).

Importantly, our database sample of sleep bouts recapitulates previous reports on sleep duration and its modulation by age and sex almost exactly (e.g., from 65,000 self-reports [44]). Children and young adolescents slept much longer than older adolescents and adults, whereas women slept longer than men from late adolescence onward (Figure 3A). The database groups also exemplify this pattern, with *Children* exhibiting the longest median bout duration at 8.9 hr, the day-working *Adults* an intermediate duration of 7.3 hr, and the predominantly male *Shift workers* the shortest at 6.8 hr—with rotating-shift work a known major contributor to the short sleep [45] (Figure 3B). To account for these differences in sleep duration between database groups, we also included sleep bout duration as covariate in all regression analyses.

Both the statistical and graphical analyses revealed complex influences of age, sex, sleep duration, and group on LIDS and LIDS rhythms. When LIDS was averaged across individual sleep bouts (with timelines normalized to the LIDS period of each bout), all groups showed clear LIDS oscillations with declining mean levels over the course of the sleep bout (Figure 4). However, the absolute LIDS levels, the rate of LIDS decline, and LIDS amplitude differed between groups and/or were modulated by age, sex, and/or sleep duration. These results are described in detail below, with effect estimates from mixed model analyses indicated in brackets.

Groups differed in their overall LIDS levels (Figures 4A–4C), with *Children*, *Quilombola*, and *Shift workers* displaying systematically lower levels than the other groups (−7.14, −19.17, and −3.97 LIDS units, respectively; $b_{group}$; Table S3). However, since activity in *Children* and *Quilombola* was recorded with devices different from our standard model used in all other groups, the pronounced level differences of these two groups might be device specific rather than reflecting group differences. Comparing LIDS levels between different devices (worn on the same wrist), we found that those worn by the *Quilombola* underestimate LIDS levels by about one-third compared to our standard device, moving their LIDS level nearer to the other groups. In contrast, the devices used in *Children* overestimated LIDS by about 20%, indicating even more nocturnal movements, i.e., lower LIDS in *Children* than implied in Figure 4A.

The lower LIDS levels of *Shift workers* (Figure 4B; Table S3), however, were recorded with our standard actimeter and may therefore be taken at face value. Mixed model analysis indicates that *Shift workers* have systematically lower LIDS levels (i.e., move more during sleep) than day workers, which is not explained by differences in age, sex, or sleep duration (−3.97 LIDS units; $b_{group}$; Table S3). In addition, men exhibited consistently lower LIDS levels than women (−2.85 LIDS units; $b_{male}$; Table S3) (Figure 4D), and this sex difference remained the same when the predominantly male *Shift workers* were removed from the analyses (−3.08 LIDS units; $b_{male}$ ; full model not shown). This result substantiates the previous finding from a much smaller sample [46] that women move less during sleep than men.

Decline rates in mean LIDS levels over the course of the sleep bout seemed also group specific in visual analysis (Figures 4A–4C), with *Quilombola* displaying the shallowest and *Adolescent psychiatric patients* the steepest decline. Mixed model analysis (modeling linear declines for ease of interpretation) reveals that there are several factors leading to these apparent group differences (Table S3): first, age exerts a marked effect on the rate of LIDS decline. Young people have a much steeper decline than older people (Figure 4E). For every year of age, the rate of decline flattens by 0.06 LIDS units per cycle ($b_{cycle*age}$; Table S3). Therefore, a

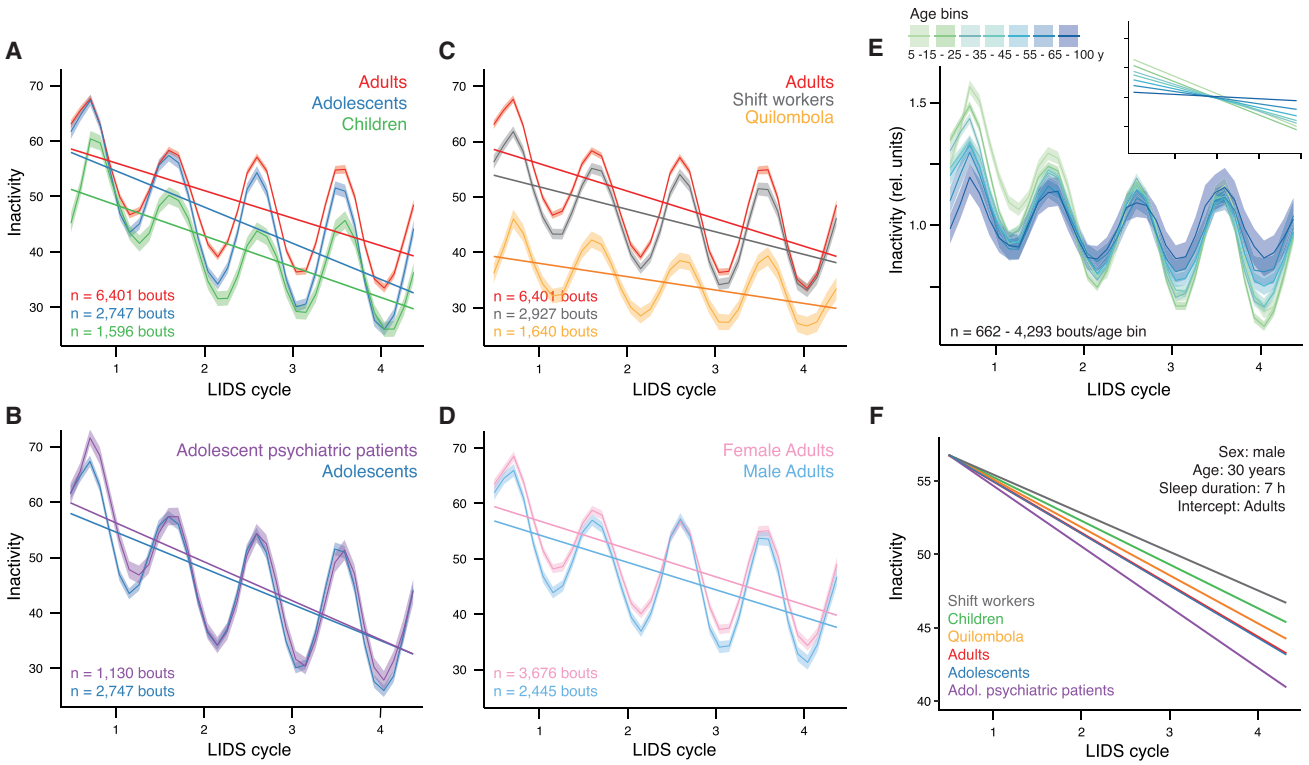



**Figure 4. LIDS Gestalt across Database Groups**

(A–E) Average raw LIDS profiles (±95% CI) and linear fits for indicated groups or ages from the actimetry database. Note that absolute LIDS levels for *Children* and *Quilombola* must not be directly compared to the other groups because recordings were performed with different actimeters. Timelines of sleep bouts underlying these graphs were normalized to individual LIDS periods prior to averaging.

(F) Mixed-model-predicted LIDS decline for a 7-hr-long sleep bout of a 30-year-old male from different database groups. For better comparison of decline rates, intercepts were adjusted to *Adults* for all groups.

See also Table S3.

20-year-old would be predicted to have a rate of decline of 5.0 and an 80-year-old of 1.4 LIDS units per cycle ($b_{cycle}$ + age × $b_{cycle*age}$; Table S3). Second, mixed model analysis also indicates an association between LIDS decline and sleep bout duration: longer bouts have a shallower decline. For every hour of sleep, rate of decline per cycle flattens by 0.15 LIDS units ($b_{cycle*duration}$; Table S3). We favor the interpretation that the dynamics in LIDS decline (analogous to the dissipation in sleep pressure) influence the duration of the sleep bout rather than vice versa. The likelihood of waking will increase with decreasing LIDS levels and at certain phases of the cycle corresponding to lighter sleep stages (see also below). Statistical adjustment for the influence of age and sleep duration (Figure 4F) annihilates the apparent differences in decline for *Children*, *Adolescents*, *Adolescent psychiatric patients*, and *Quilombola* compared with *Adults* (−6.22 LIDS units per cycle for all groups; $b_{cycle}$; Table S3), whereas those of *Shift workers* still persist. *Shift workers* show a shallower decline than the non-shift-working *Adults* (−5.33 LIDS units per cycle; $b_{cycle}$ + $b_{cycle*group}$; Table S3). This remaining difference suggests that LIDS dynamics may be influenced by frequently shifting working and sleeping times as is done in rotating shift work.

Besides differences in LIDS levels and their decline, groups also showed differences in LIDS amplitude. Amplitude is a fundamental measure reflecting the strength of a rhythm, with larger-amplitude oscillations usually more stable or less flexible than lower-amplitude oscillations (if all other system parameters are identical). For our analyses, we used the range of oscillation per cycle calculated directly from the raw LIDS values of each cycle (rather than the range of oscillation per bout taken from the cosine model), since raw amplitude demonstrates how amplitude evolves throughout the sleep bout, potentially indicating qualitative changes in sleep (Table S4).

The most prominent effect on LIDS amplitude is exerted by age (Figure 5A). With every year of age, amplitude decreases by 0.29 LIDS units ($b_{age}$; Table S4), predicting that a 25-year-old has an oscillatory range ~12 LIDS units higher than a 65-year-old. Notably, after adjustment for this age effect, both *Children* and *Quilombola* have larger amplitudes than the other groups (by 3.92 and 7.62 LIDS units, respectively; $b_{group}$; Table S4), implying that their ultradian rhythmicity is especially stable. Importantly, these results are unlikely to result from the use of different devices in these two groups. First, initial device comparisons suggest that LIDS amplitudes are similar (*Quilombola* devices) or possibly even underestimated (*Children* devices) compared to those from our standard device. Second, in a sensitivity analysis, when mixed models are calculated without the data from *Quilombola* and *Children*, the age effect on

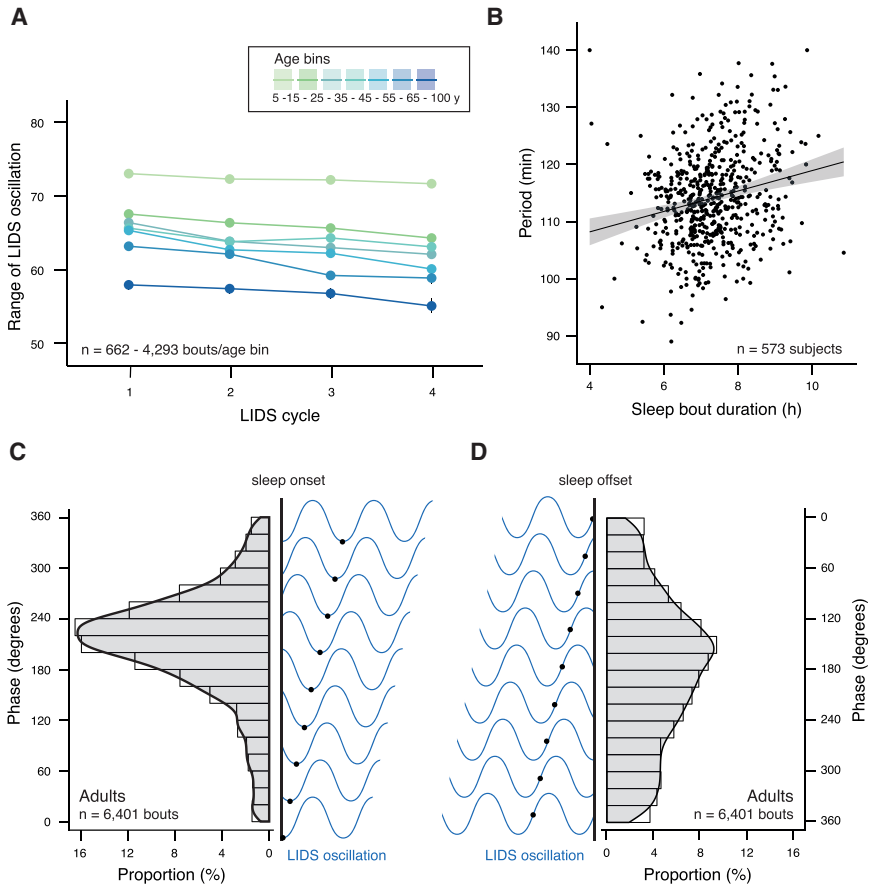



**Figure 5. LIDS Amplitude, Period, and Phase across Database Sleep Bouts**

(A) Range of LIDS oscillation (±95% CI) per LIDS cycle for indicated age groups.

(B) Association between LIDS period and sleep bout duration. Plotted is the average per subject and the linear regression line (±95% CI) as an illustration of the effect detected on a single bout level via mixed model analysis. One data point is outside the y axis limit.

(C and D) Distribution of LIDS phases at sleep onset (C) and offset (D) in the group of *Adults* representative of other database groups (gray: histogram, blue: schematic illustrating LIDS phase for every second histogram bar). Phase was determined from cosine models as difference in degrees between sleep onset and LIDS trough (C) or sleep offset and LIDS point of inflection (D), indicated by the black dot in the schematic.

See also Tables S4–S6.

LIDS amplitude remains essentially the same (total sample: $b_{age} = -0.29$ [Table S4]; reduced sample: $b_{age} = -0.35$).

Similar to LIDS levels, LIDS amplitude shows a systematic decline over the course of the sleep bout (although the decline in amplitude is much smaller than the decline in levels) (Table S4). This amplitude decline is also attenuated with age (0.02 LIDS units flatter per year; $b_{cycle*age}$; Table S4) (Figure 5A). Adjusted for this age effect, the rate of amplitude decline in *Children*, *Adolescents*, *Adolescent psychiatric patients*, and *Adults* is 1.85 LIDS units per cycle ($b_{cycle}$; Table S4). *Quilombola* have a steeper decline (−2.94 LIDS units per cycle; $b_{cycle} + b_{cycle*group}$; Table S4) and *Shift workers* a shallower decline (−1.10 LIDS units per cycle; Table S4). This again distinguishes *Shift workers* from the other solely day-working groups.

In contrast to the above-mentioned LIDS parameters, the period of the LIDS rhythm (as determined per bout from cosine fits) proofed unexpectedly constant at a median of 105–110 min. Our analyses (Table S5) uncovered no influence of group or sex and also no substantial influence of age given the analysis resolution of 5 min (0.09 min per year; $b_{age}$; Table S5). However, the one parameter markedly associated with LIDS period was sleep duration (Figure 5B): longer bouts had longer periods. For every hour of sleep, period lengthened by 1.8 min ($b_{duration}$; Table S5). With bout durations ranging from 3 to 12 hr, this results in a difference of 16.2 min over the entire range. This result implies that the duration of sleep may be inherently linked with ultradian cycle length (see [47] for a similar suggestion in mice).

An oscillation is not only characterized by its amplitude and period but also by its phase. Theoretically, the LIDS oscillation could adopt any phase in relation to sleep onset and offset, i.e., start or end on a trough, peak, or any other phase. Yet, LIDS phases as determined from cosine fits are clearly systematic, especially at sleep onset ($rho_{onset} = 0.52$; $rho_{offset} = 0.20$; $p < 0.001$; Rayleigh test). Almost 50% of *Adult* sleep bouts experience a LIDS peak within the first 80° (0.2 cycles) of their LIDS oscillation or within the first 24 min of sleep if assuming a 110-min ultradian period (Figure 5C). This means that the first deep sleep in terms of limb movement occurs mostly soon after sleep onset. This is in direct concordance with PSG-determined deep sleep (stage N3), which has its highest likelihood of occurrence after 0.2 NREM-REM cycles [32]. Sleep offset, in contrast, more likely occurs after a LIDS peak on the declining phase of the oscillation, i.e., shortly after deep sleep in terms of limb movement (Figure 5D). 25% of *Adult* bouts end between 40° and 100° (0.1–0.3 cycles) after the last LIDS peak or 12–30 min in a 110-min rhythm. Mixed model analysis (assuming linearity of the inherently circular measure of phase analogous to Figures 5C and 5D) uncovered no substantial group differences in phase distribution in either sleep onset or offset (Table S6). Differences between groups, even if non-random, had low effect sizes (maximally 6° in either direction from the *Adults*; Table S6). Furthermore, neither age nor sex appears to exert any influence on LIDS phase. Whether the association between long bout durations and earlier LIDS phase at sleep onset (−3.39° per hour; $b_{duration}$; Table S6) is biologically meaningful remains to be seen. Furthermore, whether phase at sleep offset differs between spontaneous and externally induced wake-up remains to be investigated. In conclusion, LIDS phase as determined from cosine fits is systematic but not sensitive to any of the analyzed parameters.

In summary, the mixed model analyses of LIDS rhythms across the 16,441 sleep bouts identified LIDS phase and period

as remarkably stable parameters, which are potentially only modulated by sleep duration (or vice versa). In contrast, LIDS levels and their decline as well as LIDS amplitudes and their decline were markedly influenced by age, sex, and/or rotating shift work.

## DISCUSSION

We hereby confirm in a large dataset what was already noted several decades ago [1, 2, 11]: that human body and limb movements during sleep are rhythmic and that their rhythms correspond directly to ultradian sleep cycles measured by PSG. Our non-linear conversion of locomotor activity to LIDS enhances the rhythmicity of the movement plus its capacity to distinguish between sleep stages and reveals also a gradual decline in inactivity during sleep. We postulate that all these features harbor information about sleep structure and dynamics since limb and body movement are part of, or linked directly, with sleep physiology. These LIDS features may thus be used to extract quantitative and objective information about sleep dynamics from simple movement records without the need for other physiological measurements, which can then be related to a multitude of other internal and external parameters in large datasets. Using our existing actimetry database, we presented an example of such an analysis. This first LIDS analysis in a large human dataset provides new insights into human locomotor activity during sleep, insights into parameters altering the locomotor activity, and ultimately insights into sleep itself, its rhythmicity, and dynamics.

One of the notable findings from our dataset is that age strongly influences sleep structure dynamics: the LIDS decline as well as LIDS amplitude were all progressively reduced with age. This may partly reflect maturation and aging of the motor system; for instance, some studies find reduced movement during sleep in older age groups [48, 49]. In our study, however, LIDS levels did not change systematically with age, which may well be a feature of LIDS itself (notably, LIDS levels were, however, significantly reduced in men and shift workers). Therefore, rather than being a consequence of movement reduction, the age-dependent changes of LIDS likely reflect substantial changes in sleep itself that occur with age. Prominent and well known among these are changes in EEG slow waves, which are—like LIDS—reduced both in their amplitude and in their rate of decline with increasing age [50–52]. Do these strikingly parallel age developments in LIDS and slow waves indicate that both are parallel outputs of the same sleep process that is altered by age? Or could LIDS be subject to alterations in slow waves? In any case, LIDS may be a marker for the dynamics of slow waves and therefore ultimately also for sleep homeostasis [35–37].

The ease with which we detected these well-known age changes in sleep dynamics based on LIDS illustrates the great potential of using movement during sleep for sleep analyses. Since locomotor activity can be recorded continuously for long periods of time in many different individuals and conditions without great costs or burden to subjects, the LIDS approach enables quantitative and objective sleep research (1) in large numbers, (2) outside the laboratory, and (3) in context of prior and subsequent wake and sleep episodes. In essence, LIDS should finally allow sleep research access to big-data studies with phenotypes beyond those from questionnaires. We predict that such studies will become fruitful complements to laboratory studies through testing laboratory findings in real life and in large numbers as well as providing new hypotheses to be tested in more detail in the laboratory. Examples for such possible cross-pollinations are plentiful, ranging from the study of people with extreme habitual sleep durations to the study of psychiatric patients with and without sleep pathologies during treatment, recovery, or relapse.

For use of the movement or LIDS phenotypes in big-data studies, we need to understand how different recording technologies and devices influence the outcome. Although the absolute activity output can vary greatly between device types depending on hardware and software (recording axes, sensitivities, filters, data conversion, etc.), the overall activity patterns are usually very similar. Accordingly, in our dataset and LIDS analysis method, different actimeter models influenced absolute LIDS levels, but not periods or rates of decline. Thus, our results indicate that the LIDS gestalt is essentially the same across devices. Further research is also needed to extend the usefulness of the LIDS concept to patients with sleep or movement disorders or those who are bedridden. So far, actimetry-based sleep bout detection depends on marked differences in locomotor activity between wake and sleep and can have shortcomings in certain patient cohorts [18, 19]. We have to investigate whether the LIDS conversion by itself—with wake and sleep being distinguished by some other method—is applicable and useful in such cohorts. These investigations will greatly profit from the large-scale possibilities of actimetry and our sleep analysis method.

One of the guiding principles in our design of this sleep analysis method was simplicity in order to enable its wide use. Depending on the research question, however, one needs to adapt the method accordingly. For example, by analyzing the ultradian rhythmicity via cosine fits, we wanted to describe the ultradian gestalt of a sleep bout as a single quantitative trait. Since individual bouts can be very noisy, the gestalt captures an overall feature that is otherwise only revealed via averaging across relevant sets of bouts. However, if interested in intra-bout changes in period for instance, more detailed analyses (e.g., wavelets) may be warranted. Furthermore, the number of sleep bouts required per individual or across individuals for an optimal signal-to-noise ratio may differ between specific settings (e.g., age, disease, variance in sleep timing, etc.) and research questions, just as appropriate inclusion and exclusion criteria may have to be adapted. As the LIDS method is applied to more and more datasets, experience will help to provide general guidelines on best practices.

In conclusion, we propose that locomotor (in)activity during sleep is a valuable resource for the study of sleep. Given its link with basic sleep physiology, (in)activity provides a wealth of information on sleep dynamics and structure, without the need for complicated recording equipment. Thus, sleep dynamics can be recorded easily and cheaply in a large number of subjects and large number of sleep episodes per subject in virtually any setting—something that has not been possible before. Our simple algorithms can be applied to thousands of activity measurements that already exist throughout the world and on many more yet to come. Such large and diverse datasets will

pave the way for important new insights into sleep physiology and medicine that one may not be able to gain with traditional methods and sample sizes. The use of (in)activity will allow to investigate much more widely which features of sleep are physiologically and clinically meaningful and how they are influenced by internal and external factors such as age, genetics, lifestyle, and disease. Ultimately, we hope, this approach will help us to understand sleep itself, and why its temporal dynamics are so pronouncedly ultradian.

## STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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### SUPPLEMENTAL INFORMATION

Supplemental Information includes two figures and six tables and can be found with this article online at https://doi.org/10.1016/j.cub.2017.11.063.

### AUTHOR CONTRIBUTIONS

E.C.W. analyzed the data, designed and performed the PSG experiments, contributed records to the database, and wrote the manuscript with input and contributions from T.R. and D.F. D.F. performed statistical analyses (mixed models), contributed records to the database, and assisted with manuscript writing. T.L. performed wavelet analyses and other verifications of rhythmicity measures. T.R. developed the LIDS conversion, conceived the project, analyzed data, and edited the manuscript.

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# STAR★METHODS

## KEY RESOURCES TABLE

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---|---|---|
| Deposited Data | | |
| LIDS data (database and PSG dataset) | this paper; Mendeley Data | Mendeley Data: https://doi.org/10.17632/f8szy2bghb.1 |
| Figure: correspondence between LIDS and PSG parameters – averaged data | Mendeley Data | Mendeley Data: https://doi.org/10.17632/f8szy2bghb.1 |
| Figure: correspondence between LIDS and PSG parameters – individual nights | Mendeley Data | Mendeley Data: https://doi.org/10.17632/f8szy2bghb.1 |
| Software and Algorithms | | |
| ChronoSapiens | [30] | N/A |
| R 3.0.2 "Frisbee Sailing" (2013-09-25) and 3.4.0 (2017-04-21) "You Stupid Darkness" | [53] | http://www.r-project.org/ |
| R package "ggplot2" | [54] | http://cran.r-project.org/package=ggplot2 |
| R package "dunn.test" | [55] | http://cran.r-project.org/package=dunn.test |
| R package "lme4" | [56, 57] | http://cran.r-project.org/package=lme4 |
| R package "LmerTest" | [58] | https://cran.r-project.org/package=lmerTest |
| R package "circular" | [59] | https://CRAN.R-project.org/package=circular |
| Excel | Microsoft | N/A |
| MATLAB, release 2017a | MathWorks | N/A |
| MATLAB toolbox "Jlab" | [60, 61] | https://de.mathworks.com/matlabcentral/fileexchange/52885-jlab–a-matlab-toolbox-for-data-analysis |

## CONTACT FOR REAGENT AND RESOURCE SHARING

Further information and requests for resources and reagents should be directed to and will be fulfilled by the Lead Contact, Till Roenneberg (till.roenneberg@med.uni-muenchen.de).

## EXPERIMENTAL MODEL AND SUBJECT DETAILS

### Actimetry Database

At the time of study, our actimetry database contained activity records collected between 2006 and 2014 as part of several individual studies led by the Institute of Medical Psychology or collaborators (see Acknowledgments). Individual study protocols adhered to the Declaration of Helsinki and had been approved through the ethics committee of the LMU medical faculty and/or the industry works councils at the study sites for workplace studies, the ethics committee of the Hospital de Clinicas de Porto Alegre or the local education authority of Salzburg. All participants (and, if applicable, their parents/guardians) had provided informed consent. Specifically, the database comprised over 20,000 days and nights of wrist-actimetry from a total of 574 subjects (8-92 years, 53% female; 573 of which were included in the analysis). See Table 1 for details on database composition. Subjects were grouped into one of the following six categories: *Children* (n = 53, 42%F, 8-11 y), *Adolescents* (n = 104, 65%F, 13-22 y), *Adolescent psychiatric patients* (n = 76, 86% F, 11-19 y), *Adults* (n = 141, 63%F, 18-82y), *Shift workers* (n = 111, 5%F, 20-59y) and *Quilombola* (n = 89, 63%F, 18-92y). Except for the *Quilombola*, who are an ethnic minority of African descent living in Brazil, subjects lived in Germany or Austria and were mainly Caucasian. *Adolescents* were generally defined as the age group 13-22 y, *Children* below and any adults above. However, these age boundaries could not be absolutely adhered to for the sake of other categorization variables (e.g., shift work or mental disorder), and thus, groups may contain a few individuals just outside these age boundaries (Table 1). *Shift workers* comprised only workers on rotating shift schedules encompassing night shifts; 75 subjects were on 8-hr forward-rotating schedules including morning, evening and night shifts with standard transition times at 0600, 1400 and 2200 [62, 63], the other 36 subjects were on a 12-hr rotational schedule including a day shift (0600-1800) and a night shift (1800–0600). *Adolescent psychiatric patients* comprised a diverse group of psychiatric in- and out-patients with acute or remitted disease. Specifically, 43 subjects suffered from depression (20 remitted), 24 from eating disorders and 9 from various other psychiatric disorders.

### Comparison Actimetry-Polysomnography

A dedicated dataset was recorded for a direct comparison between actimetry and polysomnography (PSG). To this end, we recruited 10 healthy volunteers (5 females) without known sleep disorders, no history of shift work and no recent time zone crossings. As this

was an exploratory study without known effect sizes, sample size was based on practical and theoretical considerations and not determined using *a priori* power calculations. Subjects' mean age was 29.0 years (range: 22-41y). The study was approved by the Ethics Committee of the Medical Faculty of the LMU (#071-13), and all subjects gave written informed consent.

## METHOD DETAILS

### Locomotor Activity Recording

Locomotor activity was recorded using activity-monitoring devices (actimeters) that were continuously worn around the wrist by volunteer subjects over multiple weeks (median: 32 d). Subjects were free to choose on which wrist to wear the device but had to keep this constant over the recording period.

In most instances, the actimeters used were Daqtometers (Versions 2.3 and 2.4, Daqtix, Germany), dual-axis accelerometers detecting both static and dynamic acceleration, i.e., motion and changes of position. Acceleration is internally converted to activity counts by summing the linear differences of subsequent readings for each axis. Devices were set to sample acceleration every second and to store activity counts every 30-60 s as the mean of all samples within the storage interval. A few *Adults* (n = 3) and *Adolescents* (n = 4) were monitored using the Actiwatch Spectrum (Philips Respironics; 32 Hz sampling rate, 30 s storage interval); all *Children* using the Actiwatch 7 (Camntech, UK; 32 Hz sampling rate, 15 s storage interval); all *Quilombola* using the Actiwatch 2 (Philips Respironics; 32 Hz sampling rate, 60-120 s storage interval).

### Activity Data Processing

Activity data were processed using our in-house analysis program ChronoSapiens [30], MS Excel and R [53]. All activity records were analyzed in bins of 10 min; activity counts were aggregated into these bins via summation. Episodes when actimeters had not been worn were identified as stretches of at least 6-10 consecutive bins (60-100 min) of zero activity as well as from subjects' self-reports (actimetry logs) and excluded from the analysis.

#### *Identification of Sleep Bouts*

Identification of sleep bouts in the activity records relied on the identification of stretches of relative immobility as detailed in Roenneberg et al. [30]. In this approach, bins with activity counts below 15% of the 24-hr centered moving average were classified as potential sleep. This raw readout was then filtered for sleep bouts with durations of at least 30 min (3 consecutive bins) to increase specificity and consolidated into longer bouts based on correlations with generated test series of different lengths as illustrated in Roenneberg et al. [30]. Our preliminary analyses indicate good correspondence of our activity-derived sleep bouts with those from sleep logs and polysomnography. Our use of the term ''sleep bout'' is equivalent to a ''sleep sequence'' as defined in [64]. All bout-level information such as bout duration and timing were derived from this analysis step.

#### *Analysis Criteria for Bout Inclusion*

For all analyses, we only considered sleep bouts with durations of 3-12 hr. Durations < 3 hr preclude reliable analysis of rhythm parameters with expected cycle lengths of 0.5-3 hr; bouts > 12 hr we deemed exceptional cases of sleep, which we chose not to include in our analyses. This reduced the number of bouts available for analysis from > 25,000 to 18,135 (97% of exclusions for < 3hr; 3% for > 12hr). Furthermore, we required a statistically significant cosine fit to LIDS ($p < 0.05$ for r; see below) for bouts to be included in the analysis, further reducing the number to 16,441. Notably, database groups differed in their exclusion proportions for all three criteria (Kruskal-Wallis rank sum test with Dunn's post hoc test; Figure S1). Differences in exclusions based on the duration criteria indicate differences in sleep organization/fragmentation between the groups but not directly in LIDS (which may nonetheless result from this differential sleep organization). Differences in exclusions based on the cosine fit quality, however, are suggestive of differences in LIDS rhythmicity.

#### *LIDS Conversion*

Locomotor Inactivity During Sleep (LIDS) was calculated from locomotor activity during identified sleep bouts according to the non-linear transformation $\mathrm{LIDS} = 100/(\mathrm{activity\ count} + 1)$ and then smoothed using a centered moving average with a 30-min window (i.e., across 3 bins in a 10-min resolution).

#### *Period and Phase Determination via Cosine Fit*

The best-fit cosine model was determined by iterative fitting of a 1-harmonic cosine model [30] to LIDS with periods from 30 to 180 min in steps of 5 min; best-fit criterion was the maximal Munich Rhythmicity Index (MRI = range of oscillation × r) that represented a peak. The bivariate correlation coefficient r for the best-fit was > 0.4 for 75% of all bouts of 3-12 hr; the cosine fit was statistically significant at $p < 0.05$ for 91% of bouts of 3-12 hr. All bouts with non-significant fits were excluded from the analysis (see above and Figure S1). The predominant or mean LIDS period per bout was directly extracted from the best-fit cosine model. For LIDS phase at sleep onset and offset, the absolute difference (in minutes) between sleep onset and first LIDS maximum/sleep offset and last LIDS maximum was determined and then converted to relative difference or phase angle (in degrees) by division through the best-fit period. For linearization of the inherently circular measure of phase, we cut at the point of lowest occurrence and rescaled this to 0°, which was the LIDS trough for sleep onset and the LIDS point of inflection for sleep offset.

#### *Wavelet Analysis*

To assess the validity of our cosine model-derived parameters given the substantial LIDS rhythm variability within bouts (i.e., violation of the stationarity assumption), we performed wavelet analyses of a subset of sleep bouts to which the wavelet analyses could be validly applied (7-12 hr; 10,895 bouts) and compared the results. The analytic wavelet transform (AWT) was computed using the

jlab package [60, 61] in MATLAB (MathWorks, Natick, MA, release 2017a). The AWT for a Morse wavelet function with $\beta = 10$, $\gamma = 3$ was applied to LIDS from bouts at least 7 hours in length, using a segment beginning 1 hour after start (to avoid initial steep decreasing segment) to the end of the 7$^{th}$ hour, for consistency across the set of bouts. Rhythmicity index (RI) equals the height of the largest peak in the autocorrelation of this 6-hr-segment corresponding to a lag between 30 and 180 minutes. Wavelet-estimated periods were only considered for the 75% of bouts that had an RI above a threshold of 1/6 (1 divided by the square root of the number of time points; n = 8,049). The AWT ridges of maximal wavelet coefficients were also computed using jlab [60, 61], retaining only the coefficients corresponding to amplitudes of at least 8 and periods between 30 and 180 min; the first and last 30 min of each bout's AWT were discarded to avoid edge effects. The AWT mean period equals the mean taken across the AWT ridge coefficients for that bout.

#### *Average LIDS Profiles*

For averaging of LIDS across sleep bouts, timelines of bouts – normally represented by external time (10-min bins of local time; $t_{ext}$) – were converted to internal time ($t_{int}$) relative to the LIDS period of the particular bout (*optPer*). To this end, $t_{ext}$ was divided by *optPer* and then normalized to 90 min/cycle ($t_{int} = t_{ext}/optPer \times 90\ min$). Data were subsequently re-assigned to 10-min bins via interpolation before averaging each bin across bouts. Since sleep bouts differed in duration and number of LIDS cycles, the number of bouts contributing data to each cycle decreased with cycle number. We therefore restricted our figures to 4 LIDS cycles, since the 4$^{th}$ cycle generally incorporated still around 50% of bouts that contributed to cycle 1. Beyond cycle 4, this was markedly less. The statistical analysis (mixed models, see below), however, incorporated all cycles of all bouts.

#### *Range of LIDS Oscillations*

As range of oscillation per cycle, we determined the difference between the maximum and minimum LIDS value per LIDS cycle. LIDS cycle boundaries were determined from the LIDS period – for normalized timelines this was 90 min, i.e., LIDS cycles were nine 10-min bins long. For non-normalized timelines, individual bout periods were used for cycle boundary determination. If the period was not a multiple of 10 min and cycle boundaries thus fell in the middle of the 10-min bins, cycles were allowed to alternate in length around the period to avoid progressive phase shifts within bouts due to rounding (e.g., for a period of 135 min, cycle durations alternated between 13 and 14 bins or 130 and 140 min instead of being rounded to either 13 or 14 bins).

### Actimeter Comparisons

To probe for systematic differences in LIDS results between actimeter models used, we performed a small pilot study in which 2 volunteers wore all 4 actimeter models on the same wrist for 2 weeks. We found very good correspondence in both subjects between our main actimeter, the Daqtometer, and the other 3 devices, in detected sleep bouts (> 97.0% of bins; Fleiss' kappa > 0.92) as well as in LIDS (Spearman rho > 0.84, $p < 0.001$). However, the pronounced differences in activity count levels among devices (up to 30-60-fold) resulted in systematic differences in median LIDS levels ($p < 0.001$, Kruskal-Wallis, Dunn's post hoc), with the AW2 (used for *Quilombola*) producing around 31%–35% lower and the AW7 (used for *Children*) 10%–39% higher median LIDS levels than the Daqtometers. Accordingly, LIDS median amplitude (range of oscillation per LIDS cycle) differed also between devices ($p < 0.05$, Kruskal-Wallis, Dunn's post hoc), albeit only the AW7 (used for *Children*) in 1 of the 2 volunteers produced statistically different amplitudes from the Daqtometer (28% lower). LIDS median period was the same between devices ($p > 0.63$, Kruskal-Wallis, Dunn's post hoc). Hence, although LIDS levels and potentially also amplitude should be compared with caution across devices, LIDS Gestalt should be directly comparable.

### Comparison Actimetry-Polysomnography

#### *Polysomnography*

Each subject spent 2 nights in our sleep laboratory at the Institute of Medical Psychology. Here, overnight PSG was performed with a Neurofax system (Nihon Kohden) according to American Academy of Sleep Medicine (AASM) criteria [13] and encompassed at least the following recordings: electroencephalogram (F3, F4, C3, C4, O1, O2 - referenced to the contralateral mastoid electrode; sampling rate of 512 Hz), electrooculogram, submental electromyogram, electrocardiogram as well as digital video and audio recording. Most recordings also involved a position monitor. To ensure that subjects did not present with common sleep disorders, additional parameters (respiratory effort, arterial oxygen saturation, nasal airflow, tibial electromyogram) were monitored during each subject's first night. Subjects were allowed to choose their own bed times (including use of alarm clocks).

#### *Actimetry*

During the PSG nights, locomotor activity was recorded with 2 Daqtometer actimeters (Version 2.4, Daqtix, Germany) per subject, one worn around the wrist and one around the ankle. Acceleration was sampled at 1 Hz (as for the other Daqtometer activity records) but stored at an increased rate of 5 s to allow for good matching with the 30 s epochs of the PSG. For synchronization between activity and PSG records, system times were aligned at equipment setup, and dedicated movement and light pulses were recorded on both systems at the end of a PSG night if more than 1 day had passed between setup and PSG night. The latter was then used for manual synchronization of the records afterward.

#### *Data Processing*

PSG records were filtered and visually scored in 30 s epochs according to AASM criteria [13] by an experienced, external scorer blinded to the aim of the study. NREM-REM cycles were determined in R following criteria by Feinberg and Floyd [31] as used by Aeschbach and Borbély [3], requiring the direct succession of a NREM episode ($\geq$15 min) by a REM episode ($\geq$5 min except for cycle 1). NREM episodes were delineated between the first instance of stage N2 and the first instance of stage R for each cycle,

REM episodes were defined between consecutive NREM episodes. Since brief awakenings have been found not to interrupt sleep cycles [32, 65], intermittent stage W or N1 within a NREM or REM episode were included in either episode unless stage W occurred in more than 20 consecutive epochs (> 10 min). In this case, the wake-interruption was marked as a WAKE episode, which either left a cycle incomplete if following a NREM episode (direct succession of NREM and REM episode was required for a complete cycle) or terminated a cycle if following a REM episode. Spectral analysis of the scalp EEG signal was performed using windowed Fast-Fourier-Transform (5.12 s square window, 2.5 s stagger; Neurofax Review Program, Version 01-93). Results were summed into standard EEG frequency bands (alpha = [8.0, 13.0 Hz); beta = [13.0, 30.0 Hz); theta = [4.0, 8.0 Hz); delta = [0.2, 4.0Hz)), expressed as amplitude density (uV/Hz) through multiplication by the window size, i.e., division by the frequency resolution, aggregated into the respective 30 s PSG epochs via averaging and averaged over all 6 main scalp electrodes (F3, F4, C3, C4, O1, O2) to obtain a global signal. Automated PSG waveform detection of the Polysmith software (Version 9.0, Neurotronics Inc.) was used to identify and obtain the number of occurrences of K-complexes, sleep spindles, rapid eye movements (REMs), slow eye movements (SEMs), microarousals and leg movements per epoch and to obtain categorized chin muscle tone levels (low, medium, high) per epoch.

PSG results and activity records were combined at the 30 s PSG epoch level after manual matching of timelines (using the dedicated movement and light pulses if required; see above) and summation of activity counts into corresponding bins. Subsequently, combined data were further aggregated using mean for numeric variables and mode for categorical variables a) into 10-min bins for standard analysis or b) into NREM-REM cycle deciles for a combined analysis of all nights following the principle used by Aeschbach and Borbély [3]. For this combined analysis, each night's data was aggregated into cycle deciles, rescaled by division through each subject's mean (only numeric variables) and then collapsed across all nights (again via mean for numeric variables and via mode for categorical variables). Since nights differed in duration and thus number of NREM-REM cycles, the number of nights contributing data to each cycle decreased with cycle number, i.e., cycles 1, 2, 3, 4 and 5 contained data from 20, 20, 18, 15 and 10 nights respectively (cycle 6 with data from only 2 nights was excluded from the analysis). Notably, aggregation via mode for categorical variables means that the sleep stage listed for any single 10-min bin represents the most prevalent stage during that bin.

All data analysis focused on the nightly stretches between initial sleep onset (defined as first epoch of N1 unless succeeded by > 10 consecutive 30 s-epochs of W) and final wake up (determined by PSG). On average, these records were 7.6 hr long (range: 4.8-9.2 hr). The stage composition of the combined 151 hr of recordings was: 8% stage W (range in single nights: 1%–30%), 11% stage N1 (6%–18%), 42% stage N2 (22%–54%), 21% stage N3 (5%–28%) and 19% stage R (9%–26%).

## QUANTIFICATION AND STATISTICAL ANALYSIS

Statistical analyses were performed in R [53] and graphs plotted with the R package "ggplot2" [54]. All presented boxplots are Tukey boxplots with whiskers encompassing all data within 1.5 times the interquartile range. Sample sizes can be found in the STAR Methods under "Subject details," in each figure and/or legend as well as in Table 1 for the actimetry database.

### Correlation Analyses

Associations between variables in the PSG dataset were assessed via Spearman rank order correlations including all pairwise-complete observations. Rank order correlations were chosen rather than Pearson to accommodate variables not normally distributed or at ordinal scale. Since oscillations in PSG parameters were either in direct phase or anti-phase to LIDS, phase shifting of parameters did not systematically improve results (data not shown). When correlations included sleep stage, sleep stage was treated as an ordinal variable with the order W < R < N1 < N2 < N3. Note, however, that stage R has no inherent place in this order. To analyze if associations between LIDS and other parameters in the PSG dataset are systematic, correlation analyses were also performed for LIDS from scrambled activity where the order of activity values was randomized within each night by sampling without replacement via the sample-function in R.

### Kruskal-Wallis Test

We tested for database group differences in sleep duration (Figure 3) or in exclusion proportion (Figure S1) using the Kruskal-Wallis rank sum test on a per subject basis after Shapiro-Wilk normality test had indicated that these variables were not normally distributed at an alpha-level of 0.05. Post hoc testing was conducted with Dunn's test of multiple comparisons with Dunn's Bonferroni adjustments at a family-wise error rate of 0.05. Dunn's test was performed with the R package "dunn.test" [55].

### Mixed Model Analyses

Where indicated in the results, we computed linear mixed effects regression models with a nested structure of up to three levels (depending on the analyzed variable) assuming an autoregressive variance-covariance matrix. LIDS or NREM-REM cycles (lowest level) were nested within sleep bouts (intermediate level), which were nested within subjects (highest level). As fixed effects, we always included age and sex, and dependent on the analyzed variable, additionally also database group, sleep stage, sleep duration and/or a measure of sleep progression such as hours asleep, LIDS cycle or NREM-REM cycle. To model variable-specific declines across LIDS cycles, we also included interactions between LIDS cycle and group, LIDS cycle and sleep duration and LIDS cycle and age in the respective models. We specified random intercepts for each nested effect as well as random slopes within each individual, thereby accounting for unsystematic variation in LIDS levels and decline. The exact model structures including random and fixed effects for each individual model are presented in Tables S1–S6. Although the calculation of p values for mixed model analysis is

not without controversy [56], we provide p values (applying the Satterthwaite approximation to estimate the degrees of freedom) in addition to t-values in the model tables (Tables S1–S6). In the Results text, we only report statistically significant effects ($\alpha < 0.05$) and indicate the table number of the respective model (e.g., Table S3). To help the non-specialist reader, we also provide the specific model estimate in brackets with letter b and the respective variable in subscript (e.g., "$b_{age}$"), and, where the combination of two estimates is reported (interaction effects), we provide the underlying calculation (e.g., "$b_{cycle}$+age × $b_{cycle*age}$"). Although we only report models for data with cycle-normalized timelines, we also calculated models for data with fixed 10-min timelines, and results were equivalent. We computed linear models for ease of interpretation; model fit will likely increase with a non-linear fit yet not affect estimate directions, which were our main focus. Mixed model analyses were conducted using the R package "lme4" [56, 57] and p values determined using the R package "LmerTest" [58].

### Rayleigh Uniformity Test

To test for unimodal departure from uniformity of LIDS phase, we performed Rayleigh uniformity tests using the R package "circular" [59].

## DATA AND SOFTWARE AVAILABILITY

The data for all analyses and figures reported in this paper can be downloaded from Mendeley Data: https://doi.org/10.17632/f8szy2bghb.1. Figures displaying all individual nights and parameters from the PSG dataset are also provided via Mendeley Data: https://doi.org/10.17632/f8szy2bghb.1.

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## Supplemental Information

# Dynamics and Ultradian Structure of Human Sleep in Real Life

**Eva Charlotte Winnebeck, Dorothee Fischer, Tanya Leise, and Till Roenneberg**

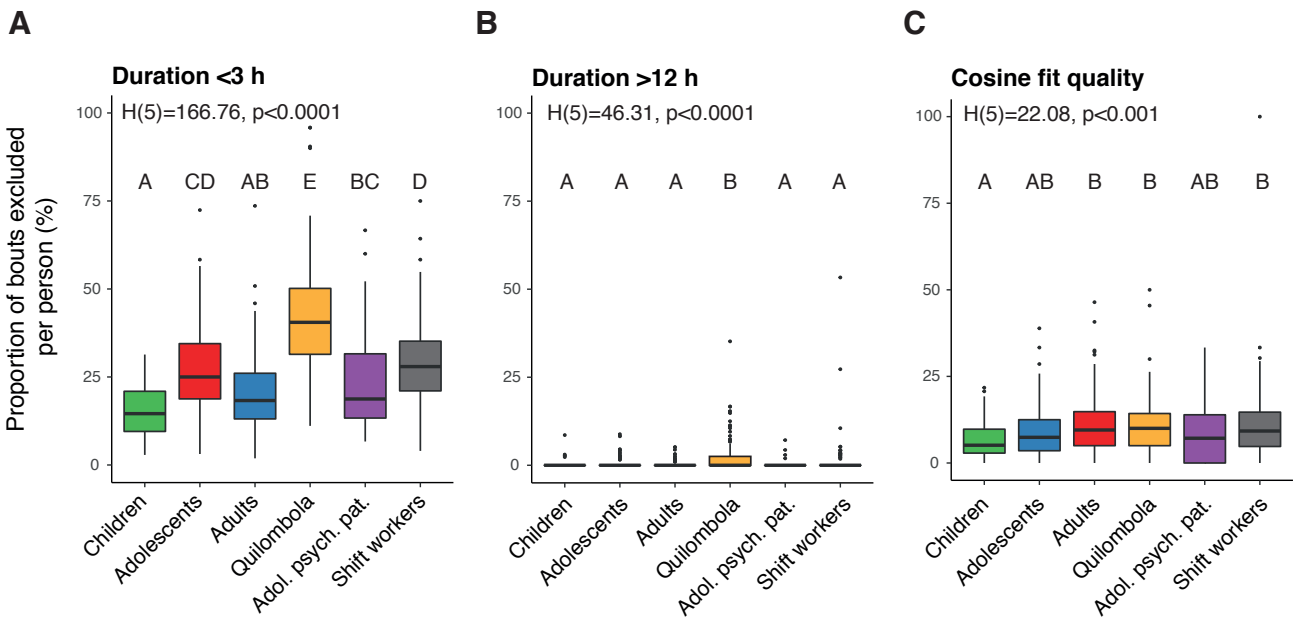
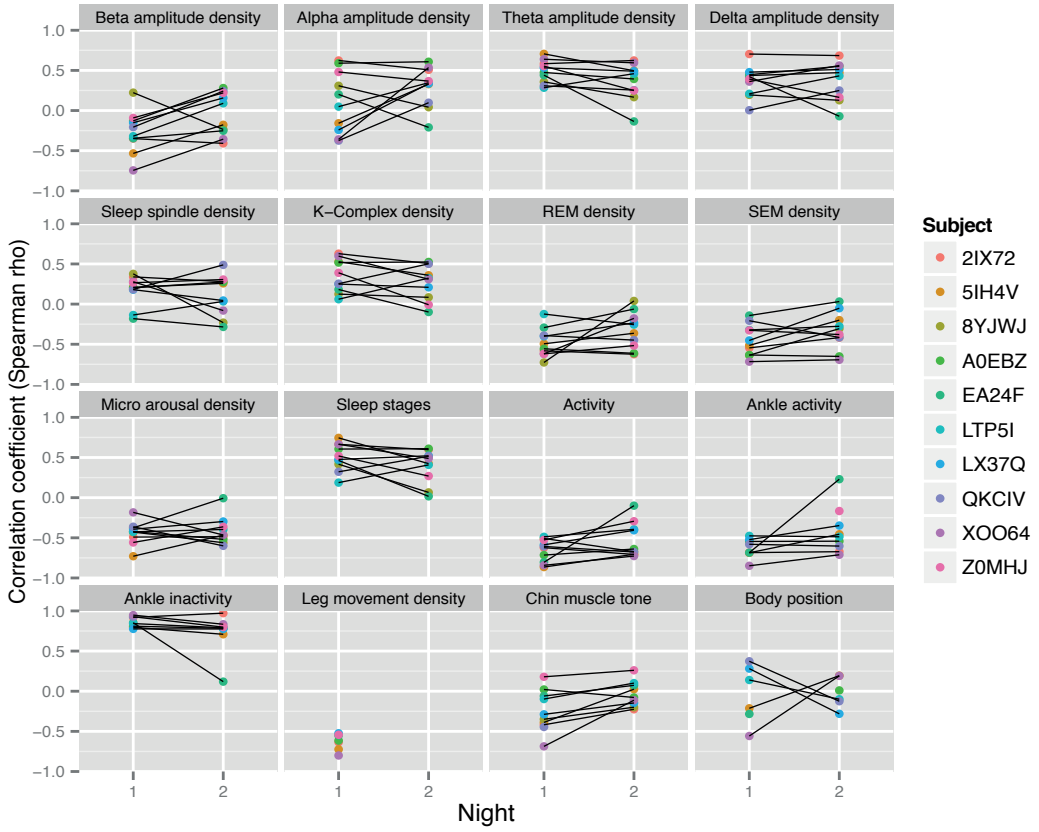



**Figure S1**
**Exclusions of sleep bouts from LIDS analysis based on pre-defined exclusion criteria**
**Related to Table 1 and Figure 3**
Plotted are the proportions of bouts excluded per person for each group and exclusion criterion. A) Exclusions due to bout duration under 3 hours. B) Exclusions due to bout duration over 12 hours. C) Exclusions due to low cosine fit quality ($p>0.05$ of bivariate correlation coefficient r). Results of Kruskal-Wallis rank sum test are provided in each panel, letters report results of Dunn's post hoc test: database groups marked by different letters are significantly different.

**A**




**B**

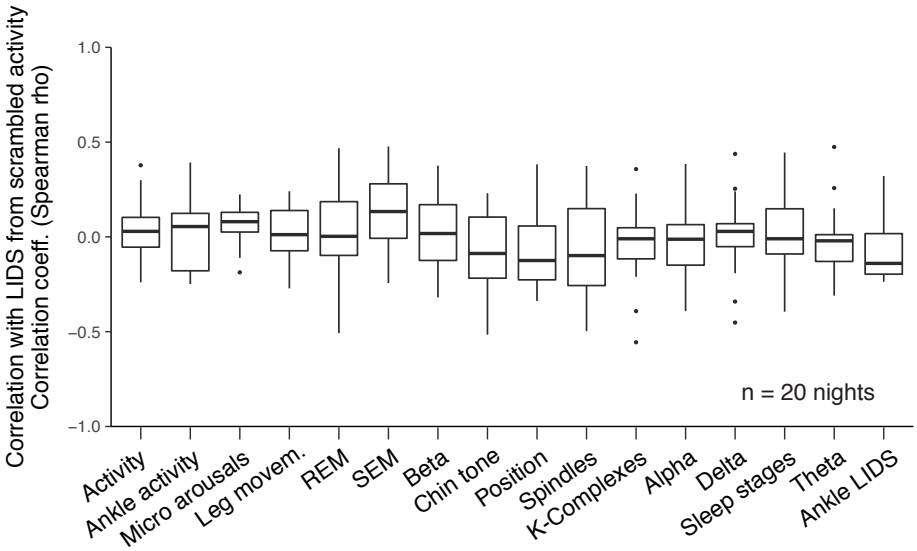



**Figure S2**
**Correlations of LIDS and polysomnographic parameters - individual nights**
**Related to Figure 2**

A) Comparison of correlation coefficients between Night 1 and Night 2 for each subject.
B) Correlation coefficients for LIDS calculated from randomly ordered (scrambled) activity.
N=20 nights except for ankle activity and ankle LIDS (n=9), leg movements and body position (n=7).
Correlation coefficients for sleep stage are provided for completeness although sleep stage is not an ordinal variable (albeit with an implicit order for NREM stages).

**Table S1. Mixed model analysis for activity, activity smoothed and LIDS per sleep stage (PSG dataset). Related to Figure 2**

Data were analysed in 10-min bins from PSG-determined sleep onset to final wake up. To obtain t-values for all sleep stage comparisons, each model was calculated multiple times using each a different stage as reference. The results of the reference iterations are depicted in Figure 2A-C. N = 20 nights (10 subjects). Number of observations: 928 for activity, 888 for activity smoothed and LIDS (loss of 2 data points per night through moving-average smoothing). Abbreviations: R, REM-sleep; N1-3, non-REM 1-3; W, wake; SD, standard deviation; SE, standard error.

**Activity – Timeline: 10 min**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject(Night(Hours asleep)) | (Intercept) | 4.14 | 2.03 | |
| Subject(Night) | (Intercept) | 1.77 | 1.33 | |
| Subject | (Intercept) | 0.00 | 0.00 | |
| | Hours asleep | 0.17 | 0.42 | |
| Residual | | 160.05 | 12.65 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 40.28 | 4.05 | 9.94 | <0.001*** |
| Age (y) | 0.04 | 0.12 | 0.36 | 0.726 |
| Sex[a]: male | 0.30 | 1.45 | 0.21 | 0.839 |
| Hours asleep | 0.67 | 0.25 | 2.70 | 0.011* |
| Sleep Stage[b]: R | -40.58 | 2.04 | -19.87 | <0.001*** |
| Sleep Stage[b]: N1 | -31.57 | 2.37 | -13.30 | <0.001*** |
| Sleep Stage[b]: N2 | -41.19 | 1.92 | -21.46 | <0.001*** |
| Sleep Stage[b]: N3 | -41.65 | 2.06 | -20.19 | <0.001*** |

**Activity smoothed – Timeline: 10 min**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject(Night(Hours asleep)) | (Intercept) | 10.57 | 3.25 | |
| Subject(Night) | (Intercept) | 1.99 | 1.41 | |
| Subject | (Intercept) | 0.07 | 0.27 | |
| | Hours asleep | 0.14 | 0.37 | |
| Residual | | 39.78 | 6.31 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 29.52 | 3.34 | 8.83 | <0.001*** |
| Age (y) | -0.07 | 0.10 | -0.66 | 0.531 |
| Sex[a]: male | -0.21 | 1.25 | -0.17 | 0.873 |
| Hours asleep | 0.22 | 0.19 | 1.11 | 0.280 |
| Sleep Stage[b]: R | -23.16 | 1.37 | -16.95 | <0.001*** |
| Sleep Stage[b]: N1 | -16.16 | 1.52 | -10.65 | <0.001*** |
| Sleep Stage[b]: N2 | -23.74 | 1.30 | -18.27 | <0.001*** |
| Sleep Stage[b]: N3 | -25.87 | 1.36 | -19.01 | <0.001*** |

**LIDS – Timeline: 10 min**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject(Night(Hours asleep)) | (Intercept) | 90.83 | 9.53 | |
| Subject(Night) | (Intercept) | 0.00 | 0.00 | |
| Subject | (Intercept) | 35.72 | 5.98 | |
| | Hours asleep | 0.00 | 0.00 | |
| Residual | | 228.66 | 15.12 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 32.84 | 11.05 | 2.97 | 0.017* |
| Age (y) | -0.33 | 0.35 | -0.93 | 0.382 |
| Sex[a]: male | -0.21 | 4.22 | -0.05 | 0.961 |

| | | | | |
|---|---|---|---|---|
| Hours asleep | -1.12 | 0.41 | -2.74 | 0.007** |
| Sleep Stage[b]: R | 23.28 | 3.35 | 6.96 | <0.001*** |
| Sleep Stage[b]: N1 | 11.06 | 3.69 | 3.00 | 0.003** |
| Sleep Stage[b]: N2 | 29.39 | 3.18 | 9.23 | <0.001*** |
| Sleep Stage[b]: N3 | 41.41 | 3.34 | 12.41 | <0.001*** |

[a]Reference: Female sex; [b]Reference: Sleep stage: W

Significance codes: '***' < 0.001, '**' < 0.01, '*' < 0.05

**Table S2. Mixed model analysis for LIDS levels (PSG dataset)**
**Related to Figure 2**

Data were analysed relative to NREM-REM cycles as depicted in Figure 2D-F. The variable 'Cycle' therefore refers to 'NREM-REM cycle'. N = 20 nights (10 subjects). Number of observations: 810. Abbreviations: SD, standard deviation; SE, standard error.

**LIDS – Timeline: NREM-REM cycles**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject(Night(Cycle)) | (Intercept) | 87.39 | 9.35 | |
| Subject(Night) | (Intercept) | 0.00 | 0.00 | |
| Subject | (Intercept) | 0.00 | 0.00 | |
| | Cycle | 3.14 | 1.77 | |
| Residual | | 311.57 | 17.65 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 65.74 | 9.05 | 7.26 | <0.001*** |
| Age (y) | -0.40 | 0.29 | -1.37 | 0.182 |
| Sex[a]: male | 1.51 | 3.53 | 0.43 | 0.671 |
| Cycle | -1.57 | 1.05 | -1.48 | 0.147 |

[a]Reference: Female sex

Significance codes: '***' < 0.001, '**' < 0.01, '*' < 0.05

**Table S3. Mixed model analysis for LIDS levels (database)**
**Related to Figure 4**

Data were analysed relative to LIDS cycles as depicted in Figure 3A-E. The variable 'Cycle' therefore refers to 'LIDS cycle'. Note that absolute LIDS levels for *Children* and *Quilombola* must not be directly compared to the other groups because recordings were performed with different actimeters. N = 16,022 sleep bouts (553 subjects). Number of observations: 593,057. Note that because age and sex was not available for 20 individuals from the database, the number of sleep bouts for mixed model analyses was reduced from a total of 16,441 (573 subjects). Abbreviations: SD, standard deviation; SE, standard error.

**LIDS – Timeline: LIDS cycles**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject(Bout(Cycle)) | (Intercept) | 106.50 | 10.32 | |
| Subject(Bout) | (Intercept) | 19.77 | 4.45 | |
| Subject | (Intercept) | 89.37 | 9.45 | |
| | Cycle | 2.75 | 1.66 | |
| Residual | | 603.76 | 24.57 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 64.10 | 1.81 | 35.32 | <0.001*** |
| Age (y) | -0.02 | 0.04 | -0.63 | 0.527 |
| Sex[a]: male | -2.85 | 0.97 | -2.95 | 0.003** |
| Sleep duration (h) | -0.53 | 0.07 | -7.18 | <0.001*** |
| Cycle | -6.22 | 0.38 | -16.52 | <0.001*** |
| Group[b]: Adolescents | -2.72 | 1.55 | -1.76 | 0.079 |
| Group[b]: Children | -7.13 | 1.95 | -3.66 | <0.001*** |
| Group[b]: Adolescent psychiatric patients | 0.89 | 1.71 | 0.52 | 0.601 |
| Group[b]: Quilombola | -19.17 | 1.51 | -12.73 | <0.001*** |
| Group[b]: Shift workers | -3.97 | 1.40 | -2.84 | 0.005** |
| **Interaction effects** | | | | |
| Cycle*Group[b]: Adolescents | -0.01 | 0.29 | -0.05 | 0.962 |
| Cycle*Group[b]: Children | 0.55 | 0.36 | 1.52 | 0.129 |
| Cycle*Group[b]: Adol. psychiatric patients | -0.62 | 0.32 | -1.90 | 0.058 |
| Cycle*Group[b]: Quilombola | 0.26 | 0.30 | 0.88 | 0.378 |
| Cycle*Group[b]: Shift workers | 0.89 | 0.24 | 3.66 | <0.001*** |
| Cycle*Sleep duration | 0.15 | 0.02 | 6.31 | <0.001*** |
| Cycle*Age | 0.06 | 0.01 | 7.30 | <0.001*** |

[a]Reference: Female sex
[b]Reference: Group Adults
Significance codes: '***' < 0.001, '**' < 0.01, '*' < 0.05

**Table S4. Mixed model analysis for LIDS range of oscillation (database)**
**Related to Figure 5**

Data were analysed relative to LIDS cycles as depicted in Figure 3F. Note that different devices were used for *Children* and *Quilombola* and their results should be interpreted with caution. For more details, please refer to Methods. N = 16,022 sleep bouts (553 subjects). Number of observations: 530,550. Note that because age and sex was not available for 20 individuals from the database, the number of sleep bouts for mixed model analyses was reduced from a total of 16,441 (573 subjects). Abbreviations: SD, standard deviation; SE, standard error.

**LIDS range of oscillation – Timeline: LIDS cycles**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject(Bout) | (Intercept) | 115.68 | 10.76 | |
| Subject | (Intercept) | 82.01 | 9.06 | |
| | Cycle | 7.03 | 2.65 | |
| Residual | | 293.41 | 17.13 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 71.60 | 1.72 | 41.66 | <0.001*** |
| Age (y) | -0.29 | 0.94 | -7.82 | <0.001*** |
| Sex[a]: male | 0.90 | 0.94 | 0.96 | 0.337 |
| Sleep duration (h) | 0.35 | 0.07 | 5.44 | <0.001*** |
| Cycle | -1.85 | 0.48 | -3.88 | <0.001*** |
| Group[b]: Adolescents | -0.17 | 1.47 | -0.12 | 0.907 |
| Group[b]: Children | 3.92 | 1.86 | 2.10 | 0.036* |
| Group[b]: Adolescent psychiatric patients | 0.78 | 1.63 | 0.48 | 0.632 |
| Group[b]: Quilombola | 7.62 | 1.43 | 5.32 | <0.001*** |
| Group[b]: Shift workers | 1.82 | 1.33 | 1.37 | 0.172 |
| **Interaction effects** | | | | |
| Cycle*Group[b]: Adolescents | 0.26 | 0.42 | 0.62 | 0.537 |
| Cycle*Group[b]: Children | 0.42 | 0.43 | 0.79 | 0.428 |
| Cycle*Group[b]: Adol. psychiatric patients | 0.76 | 0.46 | 1.66 | 0.097 |
| Cycle*Group[b]: Quilombola | -1.09 | 0.41 | -2.65 | 0.008** |
| Cycle*Group[b]: Shift workers | 0.75 | 0.35 | 2.14 | 0.033* |
| Cycle*Sleep duration | 0.002 | 0.01 | 0.14 | 0.889 |
| Cycle*Age | 0.02 | 0.01 | 1.99 | 0.047* |

[a]Reference: Female sex

[b]Reference: Group Adults

Significance codes: '***' < 0.001, '**' < 0.01, '*' < 0.05

**Table S5. Mixed model analysis for LIDS period (database)**
**Related to Figure 5**

N = 16,022 sleep bouts (553 subjects). Note that because age and sex was not available for 20 individuals from the database, the number sleep bouts for mixed model analyses was reduced from a total of 16,441 (573 subjects). Abbreviations: SD, standard deviation; SE, standard error.

**LIDS period (min)**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject | (Intercept) | 21.95 | 4.69 | |
| Bout | (Intercept) | 0.54 | 0.73 | |
| Residual | | 780.98 | 27.95 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 97.73 | 1.60 | 61.14 | <0.001*** |
| Age (y) | 0.09 | 0.03 | 3.01 | 0.003** |
| Sex[a]: male | 1.02 | 0.72 | 1.42 | 0.156 |
| Sleep duration (h) | 1.79 | 0.14 | 13.06 | <0.001*** |
| Group[b]: Adolescents | -0.40 | 1.09 | -0.37 | 0.713 |
| Group[b]: Children | -0.11 | 1.40 | -0.08 | 0.937 |
| Group[b]: Adolescent psychiatric patients | 0.12 | 1.33 | 0.09 | 0.928 |
| Group[b]: Quilombola | 0.80 | 1.16 | 0.69 | 0.491 |
| Group[b]: Shift workers | -1.10 | 0.99 | -1.10 | 0.271 |

[a]Reference: Female sex
[b]Reference: Group Adults
Significance codes: '***' < 0.001, '**' < 0.01, '*' < 0.05

**Table S6. Mixed model analysis for LIDS phase at sleep onset and offset (database)**
**Related to Figure 5**

For model calculation, the inherently circular measure of phase was linearized as depicted in Figure 5B-C at its lowest occurrence, which was set to 0° (for sleep onset: LIDS trough; for sleep offset: LIDS inflection point). N = 16,022 sleep bouts (553 subjects). Note that because age and sex was not available for 20 individuals from the database, the number of sleep bouts for mixed model analyses was reduced from a total of 16,441 (573 subjects). Abbreviations: SD, standard deviation; SE, standard error.

**LIDS phase at sleep onset (degrees)**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject | (Intercept) | 77.99 | 8.83 | |
| Bout | (Intercept) | 1.08 | 1.04 | |
| Residual | | 4758.74 | 68.98 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 234.93 | 3.67 | 63.97 | <0.001*** |
| Age (y) | -0.04 | 0.07 | -0.68 | 0.498 |
| Sex[a]: male | -2.47 | 1.59 | -1.55 | 0.121 |
| Sleep duration (h) | -3.39 | 0.33 | -10.14 | <0.001*** |
| Group[b]: Adolescents | -0.63 | 2.40 | -0.26 | 0.795 |
| Group[b]: Children | 5.64 | 3.09 | 1.82 | 0.069 |
| Group[b]: Adolescent psychiatric patients | 6.15 | 3.00 | 2.05 | 0.041* |
| Group[b]: Quilombola | -5.81 | 2.60 | -2.23 | 0.026* |
| Group[b]: Shift workers | 0.48 | 2.18 | 0.22 | 0.826 |

**LIDS phase at sleep offset (degrees)**

| **Random effects** | | Variance | SD | |
|---|---|---|---|---|
| Subject | (Intercept) | 11.04 | 3.32 | |
| Bout | (Intercept) | 0.00 | 0.00 | |
| Residual | | 4758.74 | 68.98 | |
| **Fixed effects** | Estimate | SE | t-value | p-value |
| (Intercept) | 189.76 | 4.29 | 44.25 | <0.001*** |
| Age (y) | -0.03 | 0.07 | -0.41 | 0.684 |
| Sex[a]: male | 0.03 | 1.70 | 0.02 | 0.986 |
| Sleep duration (h) | -0.89 | 0.43 | -2.06 | 0.040* |
| Group[b]: Adolescents | -3.89 | 2.58 | -1.51 | 0.132 |
| Group[b]: Children | -1.34 | 3.35 | -0.40 | 0.690 |
| Group[b]: Adolescent psychiatric patients | -2.82 | 3.38 | -0.84 | 0.403 |
| Group[b]: Quilombola | 0.97 | 2.91 | 0.33 | 0.740 |
| Group[b]: Shift workers | -0.51 | 2.31 | -0.22 | 0.825 |

[a]Reference: Female sex
[b]Reference: Group Adults
Significance codes: '***' < 0.001, '**' < 0.01, '*' < 0.05