Common scale-invariant patterns of sleep–wake transitions across mammalian species

Chung-Chuan Lo*, Thomas Chou†, Thomas Penzel‡, Thomas E. Scammell§, Robert E. Strecker‖, H. Eugene Stanley*, and Plamen Ch. Ivanov*‡

*Center for Polymer Studies and Department of Physics, Boston University, Boston, MA 02215; †Department of Neurology and Program in Neuroscience, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, MA 02215; ‡Department of Psychiatry, Harvard Medical School, Brockton Veterans Affairs Medical Center, 940 Belmont Street, Brockton, MA 02301

Contributed by H. Eugene Stanley, November 5, 2004

Although mammals of different species have different sleep patterns, brief sleep–wake transitions commonly are observed across species and appear to occur randomly throughout the sleeping period. The dynamical patterns and functions of these brief awakenings from sleep are not well understood, and they often are viewed as disruptions (random or pathologic) of the sleep process. In this article, we hypothesize that brief awakenings from sleep may reflect aspects of the endogenous sleep control mechanism and thus may exhibit certain robust dynamical patterns across species. We analyze sleep recordings from mice, rats, cats, and humans, and we compare the distributions of sleep and wake episode durations. For all four species, we find that durations of brief wake episodes during the sleep period exhibit a scale-free power-law behavior with an exponent α that remains the same for all species (α = 2.2). In contrast, sleep episode durations for all four species follow exponential distributions with characteristic time scales, which change across species in relation to body mass and metabolic rate. Our findings suggest common dynamical features of brief awakenings and sleep durations across species and may provide insights into the dynamics of the neural circuits controlling sleep.

power law | sleep regulation | sleep fragmentation

Sleep and wake are governed by complex interactions between neurons in many brain regions, including the hypothalamus and brainstem. Collectively, these neurons act as a sleep–wake “latch” that may help produce stable sleep and wakefulness (1, 2). Several mathematical and conceptual models have been proposed to account for the stability and control of sleep and wakefulness over time scales of hours and days (1–3). However, in addition to the regular sleep–wake pattern, humans and animals often exhibit brief awakenings from sleep. These brief awakenings seem to occur throughout the entire sleep period and are traditionally viewed as random disruptions of sleep associated with body motion or pathologic conditions such as sleep apnea. Because of that explanation, brief awakenings during sleep rarely are addressed in most current models of sleep regulation (4, 5).

However, recent studies suggest that arousals and brief awakenings may have a more essential role in the process of sleep regulation, posing further questions to the origin and function of brief awakenings (5). A closer look at the temporal structure of the brief sleep–wake transitions reveals a complex picture (Fig. 1). In contrast to the circadian and ultradian cycles, which dominate the regulation of sleep and wakefulness at time scales of hours, brief awakenings from sleep exhibit distinct features: (i) they appear to be random, not periodic, and (ii) the duration of sleep and wake episodes during the sleep period ranges from seconds to several tens of minutes. In this article, we investigate whether a robust structure underlies the complex dynamics of the brief sleep–wake transitions across species.

Some of us recently have reported that for humans the duration t of the wake episodes during sleep follows a scale-free power-law distribution P(t) ∼ t−α with a scaling exponent α, whereas the duration t of the sleep episodes follows an exponential distribution P(t) ∼ exp(−t/τ) with a characteristic time scale τ (6). Here, we ask whether the same type of distributions describe durations of wake and sleep episodes in other mammals and how parameters of these distributions change across species.

Methods

We analyze durations of sleep and wake episodes in mice, rats, cats, and humans during the inactive/sleep periods of each species. The sleep and wake states are scored based on electroencephalography (EEG), electromyography (EMG), and electrooculography (EOG) recordings. We follow traditional experimental conditions and scoring criteria as described in refs 7–10. We map our data onto a two-state format and consider all sleep stages as a single sleep state. Our database consists of the following polysomnographic recordings: (i) Five 24-hour recordings from five adult male C57BL6/J mice (age 3 months), with

Fig. 1. Examples of sleep–wake behavior in different mammals. (a) The human data are recorded during nocturnal sleep. (b) Cat recordings are acquired during the day starting at 9 a.m. (c and d) Rat (c) and mouse (d) recordings are obtained during the daytime period from 7 a.m. to 7 p.m., their normal period of inactivity and sleep. Arrows indicate the consolidated awakenings for the rats and mice. Note the large number of brief awakenings from sleep in all four species.
17546
ponent
episode durations follow a power-law distribution with an ex-
wake and sleep episode durations for mice, rats, and cats are very
four species share similar features, i.e., the distributions of the
consolidated wakenings with periods of 2–4 hours (Fig. 1).

The sleep patterns of cats and rodents differ substantially from
inactive period.

years; from the SIESTA project in ref. 11). For mice and rats, we
nocturnal sleep recordings from 52 human subjects (age 25
from nine adult male cats (age 9–16 months) starting at 9 a.m.
periods of light starting at 7 a.m.; (iii) nine 8-hour recordings
from nine adult male cats (age 9–16 months) starting at 9 a.m.
with 12-hour periods of light starting at 7 a.m.; and (iv) 52
nocturnal sleep recordings from 52 human subjects (age 25 ± 5
years; from the SIESTA project in ref. 11). For mice and rats, we
analyze the data between 7 a.m. and 7 p.m., corresponding to the
inactive period.

Results
The sleep patterns of cats and rodents differ substantially from
those of humans. An adult cat spends two-thirds of its time
sleeping, mainly in short periods scattered throughout 24 hours.
Mice and rats are nocturnal and exhibit a significant rhythm of
consolidated wakkenings with periods of 2–4 hours (Fig. 1).

Despite these different sleep–wake patterns, we find that all
four species share similar features, i.e., the distributions of the
wake and sleep episode durations for mice, rats, and cats are very
similar to those of humans. Specifically, we find that wake
episode durations follow a power-law distribution with an ex-
ponent $\alpha = 2.2 \pm 0.3$ (group average $\pm$ SD) for mice, $\alpha = 2.3 \pm
0.2$ for rats, and $\alpha = 2.0 \pm 0.3$ for cats (Fig. 2a). Further, our
analysis shows that these exponent values are almost identical to
the exponent value of $\alpha = 2.3 \pm 0.3$ for the human subjects in
our database. To verify that the distribution of durations of the
wake state is better fit by a power law than by any other
functional form, we use the Levenberg–Marquardt method.

Specifically, we find that both the exponential and the stretched
exponential forms lead to worse fits. In sharp contrast, we find
that sleep episode durations follow exponential distributions
with characteristic time scales $\tau = 5.9 \pm 0.8$ min (group
average $\pm$ SD) for mice, $\tau = 6.2 \pm 1.0$ min for rats, and $\tau =
11.3 \pm 2.0$ min for cats (Fig. 2b). These values are significantly
different from the time scale $\tau = 22.0 \pm 3.0$ min that we observe
for human subjects. We further observe a hump-like tail for the distribution of wake episode durations of mice and rats at large time scales ($t > 2$ min for mice and $t > 10$ min for rats; see Fig. 2a). This structural feature may be caused by the pronounced rhythm of consolidated wakefulness associated with physical activity in mice and rats (Fig. 1c and d).

We note that estimates of the values of $\alpha$ and $\tau$ may change
because of the difference between the length of epochs used in
the sleep stage scoring for different species. We therefore
perform additional procedures to validate our results based on
identical epoch lengths. Sleep stages usually are scored by
partitioning a sleep recording into nonoverlapping epochs of
equal length. A single sleep stage is assigned for each epoch. If
more than one sleep stage occurs within an epoch, the sleep stage
that takes up the greatest portion of the epoch is scored as the
stage for the whole epoch. Because of differences in the exper-
imental designs, the length $\ell$ of the scoring epochs is often
different for different species (in our database we have for
humans: $\ell = 30$ s; cats: $\ell = 10$ s; rats: $\ell = 12$ s; and mice: $\ell =
1$ s). To assess the influence of varying epoch lengths on the
outcome of our analysis, we score mouse data by using different
epoch lengths ranging from $\ell = 1$ s to $\ell = 30$ s, and we plot the
power-law exponent $\alpha$ and the exponential time scale $\tau$ as a
function of $\ell$. We find that the exponent $\alpha$ for the wake episode
durations is independent of the $\ell$. However, the time scale $\tau$ for
the sleep episode durations varies with $\ell$, i.e., $\tau = a + b\ell^c$, where
$a$, $b$, and $c$ are parameters depending on the species (Fig. 3).
This relation between $\tau$ and the epoch length $\ell$ allows us to estimate
values of $\tau$ for different $\ell$, enabling a comparison of $\tau$ for
different species based on the same epoch length. We find the
same functional form for the relationship between $\tau$ and $\ell$ for rat
and cat data as well. Because our human data are scored by using
epochs of $\ell = 30$ s, following the well established Rechtschaffen
and Kales’ criteria (10), the values of $\tau$ for mice, rats, and cats
shown in Fig. 2a are obtained after rescaling the $x$ axis of the
different species to account for an identical scoring epoch of $\ell =
30$ s.

Discussion
The presence of power-law behavior at small time scales fol-
lowed by a hump-like tail at large time scales in mice and rats
(Fig. 2a) suggests that short and long awakenings in these species
most likely are governed by two different dynamics: (i) long
periodic awakenings governed by the homeostatic sleep drive
(3, 12), and (ii) the power-law behavior of short awakenings driven
by short-term nonperiodic fluctuations in the interactions of
sleep- and wake-promoting neurons (1, 2). Finding a power-law
behavior for the distributions of wake durations suggests a
scale-invariant dynamic that is typical for fractal-like phenomena
observed in systems undergoing phase transitions or self-
organized criticality, where fluctuations over a broad range of
scales play an important role (13, 14).

The exponential behavior for the distribution of sleep episode
durations suggests a dynamical process with a characteristic time
scale $\tau$, which varies for different species. Because $\tau$ represents

Fig. 2. Distributions of wake and sleep episode durations for mice, rats, cats,
and humans. (a) Double-logarithmic plot for the distributions of the duration
of wake episodes. Curves are vertically offset for clarity. All distributions form
parallel straight lines, indicating that wake episode durations for all species
closely follow a power-law behavior characterized by almost identical expo-

nents $\alpha$. (b) Semilogarithmic plot for distributions of sleep durations. Curves
are vertically scaled so that they all start from $P = 1$. All distributions form
straight lines with different slopes, indicating that all species follow an exponen-
tial distribution with a different value of characteristic time constants $\tau$.  

Lo et al.  
www.pnas.org/cgi/doi/10.1073/pnas.0408242101  
17546
Fig. 3. Dependence of the value of the characteristic time scale $\tau$ of sleep episodes and the power-law exponent $\alpha$ of wake episodes on the length of the scoring epoch. (a) Distributions of wake episode durations of mice obtained for different epoch lengths $\ell$. Curves from top to bottom correspond to $\ell = 10$ s ($\triangle$), $\ell = 5$ s ($\triangledown$), $\ell = 3$ s ($\square$), and $\ell = 1$ s ($\circ$) and are vertically offset for clarity. Dashed lines indicate power-law curves with an exponent $\alpha = 2.2$. The power-law exponent $\alpha$ of the distribution of wake durations remains unchanged when the data are rescored by using different epoch lengths $\ell$, thus confirming the validity of our results in Fig. 2a, where data from different species are scored by using different $\ell$. (b) Distributions of sleep episode durations of mice obtained for different epoch lengths $\ell$. Curves from top to bottom correspond to $\ell = 30$ s ($\triangle$), $\ell = 20$ s ($\triangledown$), $\ell = 10$ s ($\square$), $\ell = 5$ s ($\circ$), $\ell = 3$ s ($\triangledown$), and $\ell = 1$ s ($\circ$) and are vertically scaled so that they all start from $P = 1$. We find that the exponential characteristic time $\tau$ in the distribution of sleep episode durations increases with the epoch length $\ell$. (c) Dependence of $\tau$ on $\ell$ for mouse data. We perform the same analysis for rats and cats and find the same functional form. We use this functional form to estimate the time scale of $\tau$ corresponding to the same epoch length $\ell$ for different species. The curves shown in Fig. 2b are rescaled in the $x$ axis to match values of $\tau$ based on $\ell = 30$ s.

Fig. 4. Dependence of the power-law exponent $\alpha$ for wake durations and the exponential time scale $\tau$ for sleep durations on the size of species. We compare $\alpha$ and $\tau$ with average body mass (a) and average brain mass (b) of species. The exponent $\alpha$ remains the same across species, whereas the time scale $\tau$ increases with the size of the species. Average brain mass data are taken from ref. 18. The inherent time scale of the neural network controlling the sleep–wake transitions, and the scale of this network may vary across species, we next investigate how $\tau$ correlates with the body or brain mass of the species. We find that $\tau$ increases with both brain and body mass for all four species studied (Fig. 4). This finding suggests that the time scale of the neural network regulating the sleep process is smaller in the smaller species. Perhaps smaller species switch from sleep to wake more quickly because they need to monitor their environment more frequently. Furthermore, previous studies have shown that (i) the total sleep time of a species correlates with its basal metabolic rate (15), and that (ii) the basal metabolic rate $R$ follows a power-law behavior with the body mass $M$ of the species $R \approx M^{\alpha}$ (16, 17), giving the basal metabolic rate per unit body mass $r = R/M \approx M^{-\alpha}$. Our empirical estimate for the sleep characteristic time $\tau$ suggests the possibility that $\tau \approx M^{0.2}$ (Fig. 4a). Substituting $M$ with $r$, we obtain $\tau \propto r^{-0.8}$ or $1/\tau \propto r^{0.8}$, indicating that the rate (1/\tau) of transitions from sleep to wake is positively correlated with the metabolic rate per unit body mass $r$. We note that more data sets and more species are needed to reliably determine the functional form of the relation between $\tau$ and the body or brain mass of the species.

In contrast, we find that the exponent $\alpha$ characterizing the power-law behavior of the wake episode durations does not change with the body or brain mass of the species (Fig. 4). This finding indicates that brief awakenings from sleep are controlled by species-independent mechanisms in the sleep–wake neural
networks. These mechanisms might be related to the species-independent structural characteristics of the neural networks, the nature of the fluctuations around the sleep–wake transitional threshold, or other neurophysiologic features independent of species size.

We note that our findings of that scale-invariant behavior for the wake episode durations and exponential behavior for the sleep episode durations resemble the dynamics of certain physical systems exhibiting self-organized criticality. Such systems are characterized by recurring avalanches (excitations from a “quiet” state) triggered by the accumulation of incoming energy (13, 14). The durations of avalanches follow a scale-invariant power-law distribution with an exponent independent of the specific system parameters, whereas the quiet (intervavalanche) periods are exponentially distributed (19), with a characteristic time scale depending on the system size and the rate of energy inputs. In the context of sleep–wake transitions, internal and external inputs may excite wake-promoting neurons, leading to brief awakenings with power-law characteristics remaining the same across species. Recent empirical studies also have reported power-law behavior in the size and duration of neural excitations in cortical networks (20). In contrast, the sleep (quiet) episodes exhibit a characteristic time scale that depends on the species size or on the energy consumption of the neurons (metabolic rate per unit mass) in the network responsible for sleep–wake transitions.

Our observations reveal an unexpected richness in the dynamics of sleep and wake control; they suggest that brief awakenings from sleep are not simply random disruptions of the sleep process but rather are related to the underlying mechanisms of sleep control and exhibit robust scale-invariant features across different mammalian species. Further, our findings provide a dynamical concept for these mechanisms and can facilitate the development of neural circuit models that can predict and interpret data obtained in studies of the neuronal regulation of sleep and wakefulness.

We thank T. Mochizuki for providing mouse data (National Institutes of Health Grants MH62589 and HL079046) and the SIESTA project (funded by the European Commission DG XII, as Biomed-2 project BMH4-CT97-2040) for providing human sleep recordings. We thank L. Dauphin for the cat data and R. McCarley for advice on the manuscript. This work was supported by National Institutes of Health/National Center for Research Resource Grants P41 RR 13622, HL071972, and HL079046.