Correspondences

The human circadian clock entrains to sun time

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The human biological clock, which regulates processes from gene expression to behaviour, like that of most organisms, synchronises to the Earth's 24 hour rotation using signals from the environment (zeitgebers). This synchronisation is an active process called entrainment [1]. Daily rhythms also persist in temporal isolation [2], deviating modestly from 24 hours (hence circadian). Light is the strongest zeitgeber for all circadian systems, yet social cues also entrain human clocks [3], possibly via behaviour, for example changing light exposure by closing eyes during sleep [4,5]. Here, we ask what zeitgebers entrain the human clock in real life by exploiting the common discrepancy between social time and sun time. Our results show that the human clock entrains to sun time.

Within a given time zone, people live according to a common social time - which tells them, for example, when to go to work or watch the evening news. Dawn and dusk, however, progress from East to West, creating a continuum in sun time. This creates discrepancies between, for example, the actual mid-dark phase and midnight according to local clock time. By definitions of the time zones, mid-dark and midnight coincide in London or in any other place that is a multiple of 15° longitude East or West of Greenwich (mid-dark and midnight precisely coincide only twice a year; mid-dark undulates around midnight, deviating by approximately ± 15 minutes, independently of location). Accordingly, midnight

occurs almost one hour before mid-dark in Paris and more than 90 minutes earlier in Santiago de Compostela. In orienting ourselves predominantly according to the social clock, we appear to be oblivious to these discrepancies. This raises the question as to whether the human clock is an exception to the rules determined for other circadian systems, which are predominantly entrained to light. If humans were entrained by social time, average sleep-wake behaviour should not change from East to West, while a gradual change, or at least some systematic deviation from time zone constancy, should be apparent if the human clock is (also) influenced by dawn and dusk.

We determine sleep-wakebehaviour by assessing

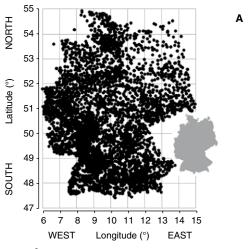
Figure 1. Chronotype and place of residence.

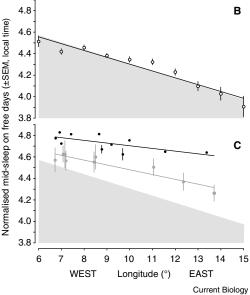
(A) The geographical distri-

bution of the German places of residence of individuals contributing to this study (N = 21,600). A map of Germany is shown by the small grey insert. (B) The dependence on longitude of normalised chronotype of people living in areas with up to 300,000 inhabitants. representing 82% of the German population (for normalisation, see Supplemental data; chronotypes are averaged within longitudinal bins spanning the West-East extension of Germany; regression line: r = 0.962; p < 0.0001; slope -34.2 min per 9°). (C) The dependencies of average chronotype on longitude for 9 towns with populations between 300,001 and 500,000 (grey symbols; r = 0.934; p <0.001: slope -24.2 min per 9°) and 11 cities with more that 500,000 inhabitants (black symbols; r = 0.703; p = 0.010; slope -13.6 min per 9°). All correlations are also highly significant for the respective raw, un-binned datasets. For reference, the slopes of the shaded areas in (B,C) reflect approximate differences in dawn times at the different longitudes on June 21st (the difference between lonaitude 6° and 15° is 36 min). Standard error of the mean is present for all data points but often is smaller than the size

of the dots.

chronotype with a dedicated questionnaire (MCTQ). It asks people for their habitual activity and rest times on work and free days [6-8], and calculates chronotype by using the mid-sleep times on free days, corrected for sleep debt accumulated over the work week (see Supplemental data available on-line with this issue). For genetic and epidemiological studies, such as this one, further normalisations for age and sex are applied. Chronotype reflects how individual circadian clocks are entrained within the 24 hour day - earlier or later. Partly because of genetic variation, chronotypes form a normal distribution in a population ranging from extreme early to extreme late types [7]. The MCTQ database currently comprises more than 40,000





individuals; for this study, we used the 21,600 responses which contained a German postal code and the correct name of the corresponding location to unambiguously allow geographical mapping (Figure 1A). The sample's sex ratio is identical to that in the German population (51% women), and the number of entries for each location highly correlates with its population size (r = 0.96). Entries were grouped according to population size (300,000; 300,001-500,000; >500,000) based on the hypothesis that - in general - exposure to natural light decreases statistically the bigger the city thereby weakening the strength of this zeitgeber. Within the first group, chronotype (averaged in longitudinal bins) is tightly coupled to sun time (Figure 1B), while those in larger and big cities (averaged by city) show a progressively weaker coupling (Figure 1C).

Our results strongly suggest that the human circadian clock is predominantly entrained by sun time rather than by social time. We have deliberately selected only German residents for this study to prevent possible confounding influences of cultural differences. It could be argued that post-war Germany was separated into two states of different cultural influence until 1989. However, the same slope (determined as for Figure 1B) is also found for locations in Southern Germany alone, which were not part of the former German Democratic Republic (correlation between the results for all of Germany and Southern Germany alone: r = 0.99). These results exclude potential sociocultural influences on the gradual changes of sleep-wake behaviour from East to West. They also indicate that the observed phenomenon, entrainment to sun time, is independent of latitude.

The question remains why inhabitants of large cities show, on average, a later chronotype and a less stringent correlation with the East–West progression of the sun. It has to be noted that 82% of Germans live outside of the 20 cities with

more than 300,000 inhabitants. On a European scale, this includes cities such as Bordeaux, Innsbruck, Leicester, Pamplona, Porto or Venice. That inhabitants of even larger cities are less coupled to sun time could be due to less exposure to outdoor light, resulting in a weaker zeitgeber strength of the natural light–dark cycle. Light and darkness even play a role when humans are entirely entrained by social cues: when we sleep, we close our eyes and in most cases, avoid light.

That social cues alone cannot entrain the human circadian clock - without concurrent (behavioural) light changes - is evident in blind people without any residual vision: their clocks run free with their own non-24 hour periodicity in spite of regular work schedules [9]. Normally, the darkness caused by behaviour coincides more or less with the environmental night. In shift workers who have to sleep during the day but who cannot completely escape the natural light-dark cycle (for example, on their way to and/or from work and in their free time), two light-dark-cycles compete in the entraining process. As a result. these workers have difficulties entraining to their work schedules while, for example, shift workers on oil rigs who only alternate between their night-work and their enclosed cabins have no difficulties [10]. The gradual uncoupling of the circadian clock from sun time of people living in large cities may reflect the gaining strength of the behavioural light-dark cycle as the strength of the environmental light-dark cycle decreases. Whenever the latter becomes more dominant, the overall zeitgeber strength will be weaker as predicted for people in metropolitan hubs. Weaker zeitgebers also predictably lead to later chronotypes [1,7], and our data show that chronotype is progressively delayed with increasing population size.

Our findings emphasise the importance of individual, circadian time rather than social, external time in scientific studies, in school and work schedules or in medical considerations. They also demand careful re-examination of how changing to and from daylight saving time affects individuals [11,12].

Acknowledgments

We thank Myriam Juda and Domien Beersma for helpful comments on the manuscript. Our work is supported by EUCLOCK, a 6th Framework Programme of the European Union, and by ClockWORK, a Daimler-Benz-Stiftung network.

Supplemental data

Supplemental data are available at http://www.current-biology.com/cgi/content/full/17/2/R44/DC1

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