of RNA synthesis. After all, the chemistry of the transcription reaction in prokaryotic and eukaryotic organisms is, in essence, identical. Yet bacterial transcription is catalyzed by a five subunit core complex — $\alpha_2\beta\beta'\omega$, comparable to eukaryotic Rpb1,2,3,6,11 — with promoter recognition conferred by one of only a handful of different σ subunits that associate with the core enzyme. Instead, the complexity of the eukaryotic Pol II machinery is a consequence of both the organization of the eukaryotic genome, including the packaging of DNA into chromatin, and the myriad regulatory parameters that control gene expression.

The challenge that lies ahead is to unravel the physical interactions that occur among and within the different transcription complexes and how these interactions occur in response to different stimuli. High-resolution three-dimensional images have provided remarkable insight into the structural basis of Pol II function. However, the size, complexity and dynamic nature of the TFIID, TFIIH and MED complexes make it unlikely that high-resolution images of these intact complexes will be forthcoming. Instead, new technologies, including novel methods for crosslinking protein–protein and protein–DNA interactions, are likely to illuminate the structural basis of transcription in small, but highly informative increments.

Further reading

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Dim nighttime illumination accelerates adjustment to timezone travel in an animal model

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Jetlag reflects a mismatch between local and circadian time following rapid timezone travel [1]. Appropriately timed bright light can shift human circadian rhythms but recovery is slow (e.g., 1–2 days per timezone). Most symptoms subside after resynchronization, but chronic jetlag may have enduring negative effects [2], including even accelerated mortality in mice [3]. Melatonin, prescription drugs, and/or exercise may help shift the clock but, like bright light, require complex schedules of application [1]. Thus, there is a need for more efficient and practical treatments for addressing jetlag. In contrast to bright daytime lighting, nighttime conditions have received scant attention. By incorporating more naturalistic nighttime lighting comparable in intensity to dim moonlight, we demonstrate that recovery after simulated jetlag is accelerated when nights are dimly lit rather than completely dark.

In the present studies of male Siberian and Syrian hamsters, the sole difference between experimental groups was whether nights were either completely dark or dimly lit (< 0.2 lux) by a low power, green-light-emitting diode (see Supplemental Data, available online with this issue). After recording wheel-running activity rhythms for one week, an eastward trip across four time zones was simulated, with a return trip two or three weeks later (Figure 1A and Figure S1 in Supplemental Data).

Dim nighttime illumination accelerated readjustment of the activity rhythms following simulated travel in both eastward and westward directions for each hamster species (Figure 1B and Table S1). Resynchronization of young adult Siberian hamsters occurred at least 49% faster when nights were dimly lit rather than completely dark, and adult Syrian hamsters realigned at least 38% faster.

Because resynchronization can be influenced by age, we investigated whether dim nighttime illumination would accelerate recovery from simulated jetlag in Siberian hamsters 82–100 weeks of age (Figure S1). Old Siberian hamsters took longer to resynchronize than younger animals, yet dimly lit nights still increased the rate of resynchronization (Figure 1B and Table S1). Notably, resynchronization for old animals with dimly lit nights was not different from that of young animals with dark nights even though these groups differed in age by more than a year (Figures 1B and S2).

We also examined whether dim nighttime illumination facilitates resynchronization after longer simulated journeys. Syrian hamsters were provided simulated journeys across eight time zones (Figure S1). Again, dimly lit nights accelerated recovery (Figure 1B and Table S1). To determine whether previous exposure to dimly lit nights is sufficient to facilitate recovery, nighttime illumination was extinguished for Syrian hamsters immediately before a final 8-hour eastward journey (Figure S1). To accelerate full resynchronization, dim nighttime light was required during simulated travel (Table S1).

In summary, dim nighttime illumination sped adjustment of activity rhythms after simulated travel in two hamster species, in both eastward and westward directions, after 4-hour and 8-hour shifts, and in young and aged animals. The present results demonstrate a latent circadian plasticity that emerges under conditions incorporating dimly lit nights. This contrasts with the conventional wisdom that the circadian clock is largely blind to light the intensity of dim moonlight, a view based on studies of photic thresholds for phase resetting and melatonin suppression [4] mediated by melanopsin-containing retinal ganglion cells [5]. Confirming previous results [4], our dim illumination had only modest effects on classic circadian measures of photic resetting and melatonin secretion in

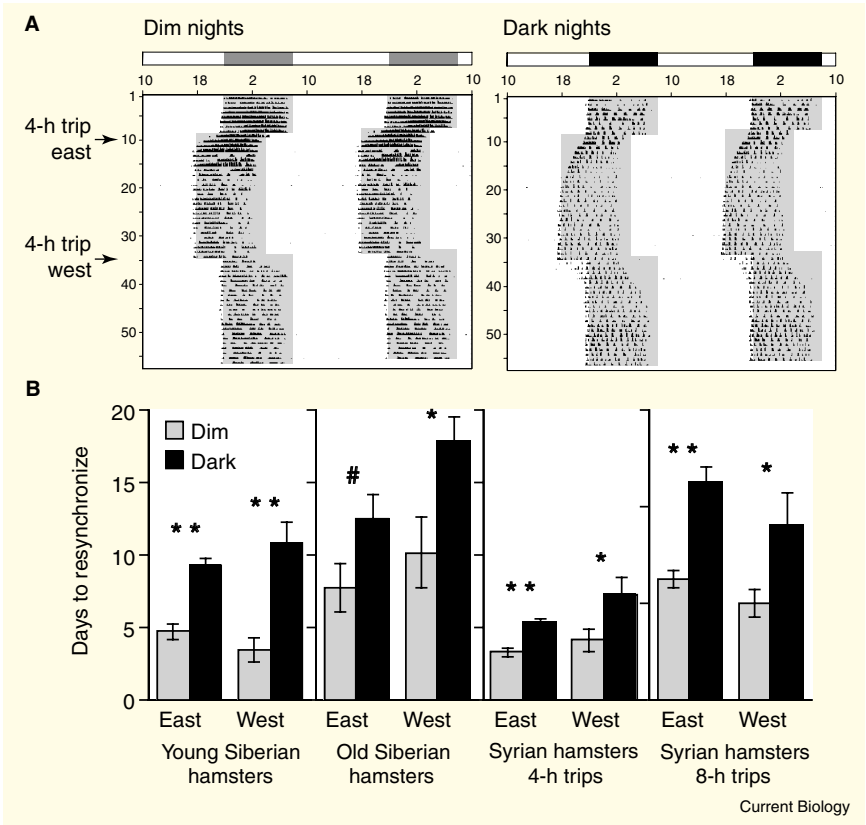

Figure 1. Dimly lit nights accelerate recovery from simulated timezone travel.

(A) Representative double-plotted actograms illustrating the simulated jetlag protocol and wheel-running rhythms of young Siberian hamsters provided dimly lit (left) or completely dark nights (right). White and shaded bars above each actogram illustrate the lighting conditions in place during the first week of the experiment, and the shading within each actogram depicts changes in the phase of relative darkness. (B) Days required for resynchronization (Mean ± SEM) after simulated journeys in the eastward and westward directions, calculated for individual animals using the number of days that elapsed before the midpoint of the active phase shifted from its baseline phase by an amount equal to the shift of the light:dark cycle. ** $p < 0.0001$, * $p < 0.05$, # $p < 0.1$.

Syrian hamsters [6]. Nevertheless, this stimulus acts as an all-purpose facilitator of circadian re-entrainment in this and other paradigms [7].

By what mechanism does dim illumination alter circadian plasticity? Does it merely enhance wheel running and thereby potentiate non-photic feedback on the clock [8]? In young Siberian hamsters, dim nighttime illumination did increase baseline activity levels prior to simulated travel (Figure S1, $p < 0.025$). However, no difference in wheel-running levels was evident between older Siberian hamsters (Figure S1, $p > 0.1$) or Syrian hamsters (Figure S1, $p > 0.2$), showing robust effects of dim light during simulated jetlag (see also [6]). Likewise, no baseline measure of entrainment consistently predicted an effect of dim light during jetlag (Figure S1). Does dim light potentiate the circadian response to bright light pulses? Phase resetting by 5-minute bright light pulses in Syrian hamsters is not differentially affected by nighttime lighting conditions [6]. Instead, the effect of dim light must derive from interactions with processes engaged during repeated or longer bright light exposure. Neurobiological studies show that jetlag induces a transient dissociation among molecular and anatomical components in the circadian pacemaker [9,10]. Dim light may attenuate this desynchrony.

Extension of the present findings may lead to a practical alternative to current jetlag treatments since this procedure may be relatively simple to implement and may be attractive to people unable to take advantage of pharmaceutical treatments (e.g., pilots and athletes). Moreover, while other agents mainly facilitate resynchronization after eastward travel only, dim nighttime illumination accelerated recovery in both directions. Further research is required to assess whether these results generalize to diurnal mammals, such as humans. Clarification of the mechanism of dim light's action in rodents through physiological, cellular and molecular analysis may yield novel targets for enhancing circadian plasticity and, in turn, therapeutic protocols to treat jetlag in humans.

Supplemental Data

Supplemental data are available at http://www.current-biology.com/supplemental/S0960-9822(09)00562-4.

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