Light exposure patterns reveal phase and intrinsic period of the human circadian clock

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Supplementary Online Material

Correlation between DLMO and intrinsic period. As DLMO showed a weak but almost significant correlation with estimated intrinsic period (R^2 = 0.144; p = 0.099), we tested whether the significant relationships between (DLMO – sleep onset/offset) and intrinsic period could be solely explained by this weak relationship between DLMO and intrinsic period. To this end, we simulated 20 sets of intrinsic period values that correlated with DLMO with an R^2 of 0.144 and calculated the chance of finding a significant relationship between both (DLMO – sleep onset) and intrinsic period and (DLMO – sleep offset) and intrinsic period. This chance was only 5%, suggesting that there is a very slight chance that our findings were only due to DLMO being slightly related to intrinsic period.

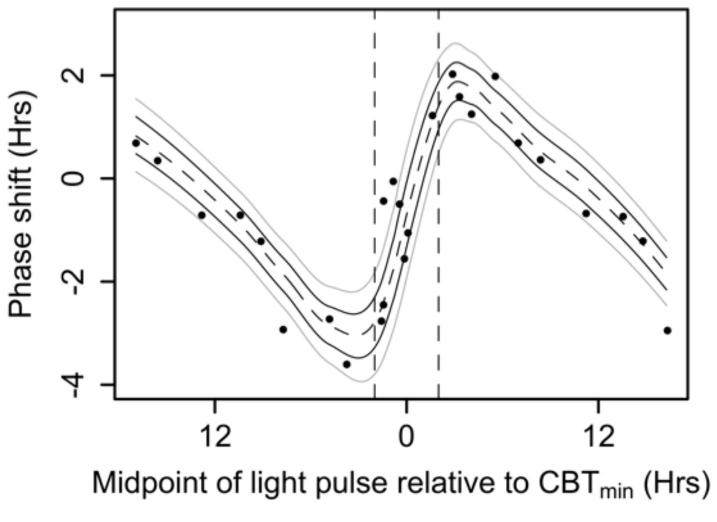

Figure S1. Kronauer's model prediction on PRC data from Khalsa et al. (2003). Kronauer's model showed an accurate fit to the data (dashed black curve), with a mean-square error (MSE) of 0.58h for the entire dataset, and an MSE of 0.2h when the light pulses timed close to CBT_{min} (4-hour window, marked by dashed vertical lines) were omitted. The MSE was calculated as the sum of squared deviations from the data points to the model fit divided by the number of data points. We allowed the model parameter for intrinsic period to deviate from 24.18 with one standard deviation (black solid lines; 68% confidence band) or two standard deviations (grey solid lines;

95% confidence band) based on the distribution reported by Czeisler et al. (1999). This approach showed that 13 out of 20 data points (65%; 58% when data within the critical region was omitted) fell within (or very close to) the 68% confidence band, whereas 3 out of 20 data points (15%; 8.3% when data within the critical region was omitted) fell outside the 95% confidence band. The fact that the data points are distributed around the default model prediction with a distribution similar to what would be expected based on differences in intrinsic period, suggest that the majority of error in predicting Khalsa's PRC data originates from these individual differences in circadian period length. As in uncontrolled conditions, the majority of light exposure occurs outside the critical region of the PRC, the model should be able to predict clock phase with a very high accuracy in our dataset.

Table S1. Equations and parameter valuess of the limit cycle oscillator model

1)	$\alpha = \alpha_0 \left(\frac{I}{I_0}\right)^p \left(\frac{I}{I + 100}\right)$
2)	$\hat{B} = G(1 - n)\alpha$
3)	$\dot{n} = 60[\alpha(1 - n) - \beta n$
4)	$\dot{x} = \left(\frac{\pi}{12}\right) \left[x_c + \left(\frac{1}{3}\mathrm{x} + \frac{4}{3}x^3 + \frac{256}{105}x^7\right) + B\right]$
5)	$\dot{x}_c = \left(\frac{\pi}{12}\right) \left\{qBx_c - x\left[\left(\frac{24}{0.97729\tau_x}\right)^2 + kB\right]\right\}$
6)	$B = \hat{B}(1 - 0.4x)(1 - 0.4x_c)$
7)	$\mathrm{CBT}_{min} = \varphi_{XcX} + \varphi_{ref}$
	$\mu = 0.13$
	$q = \frac{1}{3}$
	$\tau_x = 24.2$
	$k = 0.55$
	$\beta = 0.007\ \mathrm{min}^{-1}$
	$G = 37$
	$\alpha_0 = 0.1\ \mathrm{min}^{-1}$
	$p = 0.5$
	$I_0 = 9500$
	$\varphi_{ref} = 0.97$
	$\varphi_{XcX} = -2.98$ rad

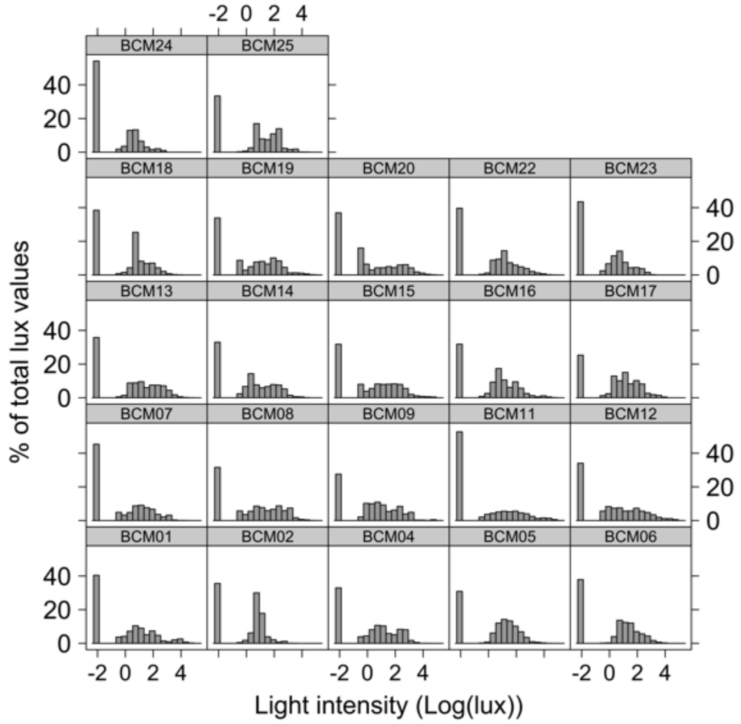

Figure S2. Distribution of light intensities measured during the total 9-days protocol. For each intensity bin (bin-size: 0.4 log(lux)), the number of lux values in that bin is plotted as a percentage of the total amount of lux values measured for each participant separately.

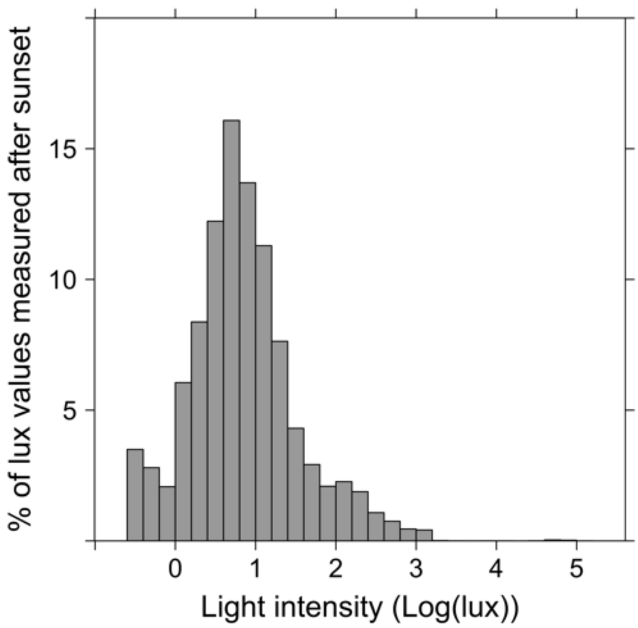

Figure S3. Distribution of light intensities measured during solar darkness. For this distribution, a subset of data was analyzed where only lux-values measured during solar darkness (solar angle relative to horizon: < -6°) were included. For each intensity bin (bin-size: 0.2 log(lux)), the number of lux values in that bin is plotted as a percentage of the total amount of lux values measured during solar darkness for all participants combined. During solar darkness, 99% of the data fell below 615 lux (2.79 log(lux)).