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Disrupted light–dark cycle abolishes circadian expression of peripheral clock genes without inducing behavioral arrhythmicity in mice

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ABSTRACT

The environmental light–dark (LD) cycle entrains the central circadian clock located in the suprachiasmatic nucleus (SCN) of mammals. The present study examined the effects of disrupted LD cycles on peripheral clocks in mice housed under a normal 12 h light-12 h dark cycle (LD 12:12) or an ultradian LD 3:3 cycle. Drinking behavior seemed to be free-running with a long period (26.03 h) under ultradian LD 3:3 cycles, in addition to light-induced direct suppression (masking effect). Core body temperature completely lost robust circadian rhythm and acquired a 6-h rhythm with a low amplitude under LD 3:3. Robust circadian expression of *Per1*, *Per2*, *Clock* and *Bmal1* mRNAs was similarly flattened to intermediate levels in the liver, heart and white adipose tissue under LD 3:3. Robust circadian expression of *Rev-erbα* mRNA was completely damped in these tissues. Circadian expression of *Dbp*, a clock-controlled gene, was also disrupted in these tissues from mice housed under LD 3:3. The aberrant LD cycle seemed to induce the loss of circadian gene expression at the level of transcription, because rhythmic pre-mRNA expression of these genes was also abolished under LD 3:3. In addition to the direct effect of the aberrant LD cycle, abolished systemic time cues such as those of plasma corticosterone and body temperature might be involved in the disrupted expression of these circadian genes under LD 3:3. Our findings suggest that disrupted environmental LD cycles abolish the normal oscillation of peripheral clocks and induce internal desynchrony in mammals.

1. Introduction

Endogenous oscillators control many behavioral and physiological circadian rhythms such as sleep/wake cycles, body temperature, blood pressure, heart rate, hormonal secretion and metabolism. The central circadian clock is located in the suprachiasmatic nucleus (SCN) of the anterior hypothalamus in mammals [1]. The molecular mechanism of the circadian clock is cell-autonomous and it arises from autoregulatory negative feedback loops consisting of the periodic expression of clock genes [2,3]. Basic helix-loop-helix (bHLH)-PAS transcription factors such as CLOCK and BMAL1 are positive regulators of autoregulatory transcription-translation feedback loops of the molecular circadian clock [2,3]. The CLOCK/BMAL1 heterodimer drives the rhythmic transcription of the clock genes, *Period* (*Per1*, *Per2*, and *Per3*), *Cryptochrome* (*Cry1* and *Cry2*), and *Rev-erbα* through E-box (CACGTG/T) elements located in their promoters. As the PER and CRY proteins are translated, they form multimeric complexes that are translocated to the nucleus, where they inhibit their own transcription by directly interacting with the CLOCK/BMAL1 heterodimer. The circadian expression of *Bmal1* is driven by an additional feedback loop comprising the orphan nuclear receptors, RORα and REV-ERBα, which respectively act as positive and negative regulators.

Clock genes are expressed in a circadian manner in most peripheral tissues such as the heart, lung, liver, kidney, and skeletal muscle, as well as circulating white blood cells. Studies *in vitro* and

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ex vivo have shown that cell-autonomous oscillatory mechanisms function in cultured cells and tissue explants from various peripheral organs. Ablation of the SCN abolishes the circadian expression of clock genes in peripheral tissues [4], suggesting that peripheral clocks are normally governed by the central clock in the SCN. The SCN clock coordinates peripheral clocks via multiple pathways including the autonomic nervous system, body temperature and hormonal signals such as those of glucocorticoids and insulin. Most of these time cues are significantly affected by feeding rhythms. Indeed, time-imposed restricted feeding can synchronize peripheral circadian clock gene expression independently of the central clock in the SCN. These facts suggest that peripheral clocks continuously tick circadian rhythms in phase with the SCN clock and/or feeding rhythms in genetically intact mammals.

Environmental light is the critical cue for the daily resetting of the central clock in the SCN, and the phase and period of the pacemaker are entrained to environmental light–dark (LD) cycles [1]. According to the discrete (non-parametric) entrainment model [5], the circadian rhythm becomes synchronized to LD cycles by daily phase-resetting to adjust the endogenous (tau) to the Zeitgeber (T) period. The central circadian clock cannot entrain to environmental LD cycles when phase shifts caused by light pulses are smaller than the difference between tau and T. We previously showed that both wheel-running activity [6] and drinking behavior [7,8] are rhythmic and with a longer period under ultradian LD 3:3 cycles in mice. These observations coincide with the rhythmic expression of circadian clock protein in the SCN under ultradian LD cycles [9]. Several studies have shown that autonomic innervation from the SCN relays photic information to oscillators in peripheral organs such as the adrenal glands and the liver, and then induces the transient expression of circadian clock genes [10,11]. The present study examines the effects of ultradian LD 3:3 cycles on circadian rhythms of drinking and feeding behaviors, core body temperature, plasma corticosterone concentrations and the expression of peripheral clock genes in mice.

2. Methods

2.1. Animals and behavioral analysis

Male ICR mice (Japan SLC Inc., Hamamatsu, Japan) were housed with access to food and water *ad libitum* until the age of 7–8 weeks under a 12 h light-12 h dark cycle (LD 12:12; lights on at Zeitgeber time (ZT) 0 and lights off at ZT12), and then the lights for one group were switched to LD 3:3. The light source was a white fluorescent lamp (500 lux at cage level). To determine the circadian phase of the central oscillator in the SCN, the mice were released from the LD conditions into constant darkness (DD). Drinking behavior was continuously recorded every 5 min using the Chronobiology Kit (Stanford Software Systems, Stanford, CA). The circadian period was assessed using χ^2 periodgrams (Chronobiology Kit software). Temporal food intake was recorded every 10 min using the FDM-300 system (Melquest, Toyama, Japan). Data were analyzed using Feedam software (Melquest, Toyama, Japan). Our institutional Animal Care and Use Committee approved all procedures associated with this study (Permission #2013-020).

2.2. Monitoring core body temperature

Mice were surgically implanted intra-abdominally with Temp-Disk TD-LAB data loggers (Labo Support Co. Ltd., Suita, Osaka, Japan) that were programmed to record body temperature (Tb) ± 0.1 °C every 10 min. Recording started one week after the surgical implantation and the data obtained from each logger were analyzed using RhManager Ver. 2.09 (KN Laboratories Inc., Ibaraki, Osaka, Japan).

2.3. Measurement of plasma corticosterone concentrations

Mouse blood collected in EDTA-coated tubes was immediately separated by centrifugation for 15 min at 5800× *g*. Platelet-poor plasma was collected and stored at −80 °C. Plasma corticosterone concentrations were measured using AssayMax Corticosterone ELISA Kits (AssayPro LLC., St. Charles, MO, USA).

2.4. Measurement of peripheral clock gene expression

Mice were housed under either LD 12:12 or LD 3:3 cycles for two weeks, during which drinking activity was monitored in the latter group to determine their circadian phase. The mice were sacrificed at four-hour intervals, whole blood was withdrawn, and then the liver, heart, white adipose tissue (WAT), and brown adipose tissue (BAT) were dissected, rapidly frozen and stored in liquid nitrogen. Mice under the LD 12:12 cycle were sampled at ZT 2, 6, 10, 14, 18 and 22 and those under the LD 3:3 cycle were sampled at circadian time (CT) 2, 6, 10, 14, 18 and 22, which was determined from their behavioral rhythms.

2.5. Quantitative reverse transcription (RT)-PCR

Total RNA was extracted using RNAiso Plus (Takara Bio Inc., Otsu, Japan). Single-stranded cDNA was synthesized using PrimeScript™ RT reagent kits with gDNA Eraser (Takara Bio Inc., Otsu, Japan). Real-time RT-PCR proceeded using SYBR® Premix Ex Taq™ II (Takara Bio Inc., Otsu, Japan) and a LightCycler™ (Roche Diagnostics, Mannheim, Germany). The reaction conditions were 95 °C for 10 s followed by 45 cycles of 95 °C for 5 s, 57 °C for 10 s and 72 °C for 10 s. Supplemental Table 1 shows the sequences of the primer pairs. The amount of target mRNA was normalized relative to that of *β-actin*.

2.6. Statistical analysis

All values are expressed as means ± standard error of the mean (SEM). All data were statistically evaluated by a two-way analysis of variance (ANOVA) and the Tukey multiple comparison test using Excel-Toukei 2010 software (Social Survey Research Information Co. Ltd., Osaka, Japan). Correlations were evaluated using the Pearson's product-moment correlation coefficient (r), which was also calculated using Excel-Toukei 2010 software. $P < 0.05$ indicated a statistically significant difference.

3. Results

The mice were completely entrained to the LD cycle under LD 12:12 (Fig. 1A and B). Under ultradian LD 3:3, the drinking activity rhythm seemed to be free-running with a period of 26.03 ± 0.22 h, in addition to the direct, light-induced suppression of the drinking behavior (masking effect). The free-running period during DD exceeded 24 h (24.76 ± 0.20 h) when the mice were transferred from LD 3:3, although the period was shorter than 24 h (23.85 ± 0.034 h) when the mice were transferred from LD 12:12. The theory of “after-effects” can explain these findings [5]. The time of activity onset on the first day of DD was maintained from LD 3:3, suggesting that the central clock in the SCN was free-running under LD 3:3.

We also evaluated the circadian rhythm of food intake that is usually accompanied by drinking behavior, since daily feeding cycles are dominant time cues for molecular clocks in the periphery

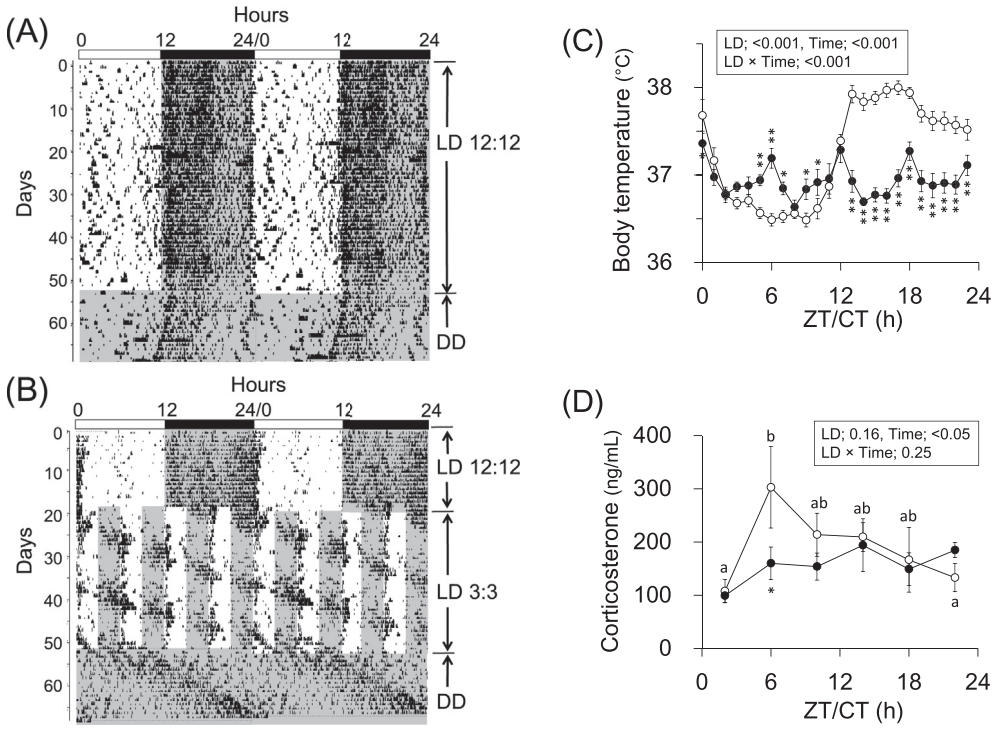

Fig. 1. Representative double-plot actograms of drinking behavior and temporal profiles of core body temperature and blood corticosterone concentrations in LD 12:12 and LD 3:3. Mice fed with normal chow *ad libitum* were acclimated under LD 12:12 (lights on at 0 h) and then maintained on LD 12:12 (A) or transferred to ultradian LD 3:3 (B) cycles for 32 days before transfer to constant darkness (DD). Dark-phase duration is shaded in gray. Horizontal unfilled and filled bars indicate light and dark periods, respectively. Dots represent drinking behavior at 5-min intervals. (C) Core body temperature was measured during week 4 under LD 12:12 (unfilled circles) or LD 3:3 (filled circles). Data are shown as means ± SEM ($n = 7$). (D) Plasma corticosterone concentrations at indicated times in mice housed under LD 12:12 or LD 3:3. Data are shown as means ± SEM ($n = 5$). Superscript letters indicate statistical significance ($p < 0.05$) for LD 12:12. Statistical significance determined by ANOVA is shown in boxes. Significant differences between LD 12:12 and LD3:3 are indicated as $^{*}p < 0.05$ and $^{**}p < 0.01$ at corresponding ZT/CTs. CT, circadian time; ZT, Zeitgeber time.

[12]. Feeding rhythms were also free-running with longer periods like those of drinking behavior under LD 3:3 (Supplemental Fig. 1).

Core body temperature fluctuated in an ultradian manner that peaked at the dark-to-light transition under LD 3:3, while body temperature fluctuated in a robust circadian manner and increased at the light-to-dark transition under LD 12:12 (Fig. 1C). The peak-trough amplitude of body temperature in LD 3:3 was significantly reduced at the intermediate levels of normal fluctuation. Daily average body temperature was significantly decreased under LD 3:3 (37.3 °C ± 0.1 °C and 36.9 °C ± 0.1 °C in LD 12:12 and LD 3:3, respectively).

Plasma corticosterone levels fluctuated in a circadian manner that peaked at midday in LD 12:12, but remained essentially constant at the normal intermediate level throughout the day in LD 3:3 (Fig. 1D). Comparisons of values at all time-points indicated a significant decrease in the plasma corticosterone concentration at ZT/CT6.

Circadian mRNA expression of the core clock genes, *Per1*, *Per2*, *Clock*, and *Bmal1* were obviously disrupted, and the mRNA abundance of these genes was flattened at intermediate levels throughout the day in the liver (Fig. 2), heart (Supplemental Fig. 2), and WAT (Supplemental Fig. 3) of mice under LD 3:3. The robust circadian expression of *Rev-erbα* mRNA was completely damped in these tissues. The circadian expression of the clock-controlled gene *Dbp* was also disrupted in these tissues from mice housed under LD 3:3. Robust circadian expression of *Dbp* mRNA in the heart was flattened to intermediate levels under LD 3:3, while that in the liver and WAT was completely damped.

We examined the temporal abundance of pre-mRNAs in the liver to evaluate the effects of an ultradian photoperiod on peripheral clocks at the transcriptional level (Fig. 3). The amounts of pre-mRNA and of mature mRNA for all circadian genes examined robustly fluctuated under LD 12:12. The acrophase of *Per2* pre-mRNA expression was obviously phase-advanced by several hours compared with that of mature mRNAs under LD 12:12, although the phase of rhythmic expression of pre-mRNA for other genes such as *Per1*, *Clock*, *Bmal1*, and *Rev-erbα* was almost identical to that of mature mRNA. As with mature mRNA, the robust circadian expression of pre-mRNAs was abolished under LD3:3. The abundance of pre-mRNA for *Rev-erbα* was continuously low, whereas that for other genes was intermediate, at the levels of normal oscillation.

To evaluate the effects of an ultradian photoperiod on the post-transcriptional regulation of circadian genes, we analyzed correlations between levels of pre-mRNA and mature mRNA for each gene (Fig. 4). The expression levels of pre- and mature mRNAs for the *Per1*, *Clock*, *Bmal1*, *Rev-erbα*, and *Dbp* genes positively correlated under both LD 12:12 and LD 3:3. Correlations were very close ($r > 0.9$) for *Per1*, *Rev-erbα*, and *Dbp* under both photoperiods. On the other hand, the correlation coefficient for the *Per2* gene was low under both photoperiods, and the correlation was not significant under LD 3:3.

4. Discussion

The present study showed that an ultradian photoperiod abolished the circadian expression of peripheral clock genes in mice while the circadian rhythm of behavior was maintained. The robust circadian rhythm of core body temperature was completely lost and a small-amplitude 6-h rhythm appeared under LD 3:3. These findings suggest that a disrupted photic environment caused internal desynchrony between the central circadian oscillator and

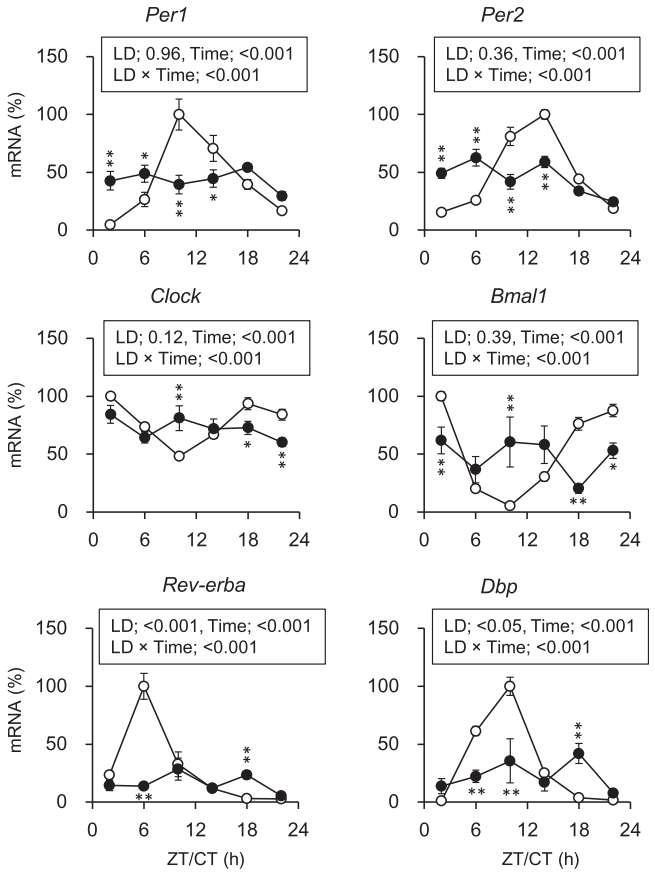

Fig. 2. Temporal mRNA expression profiles of circadian clock-related genes in peripheral tissues of mice under LD 12:12 and LD 3:3. Messenger RNA expression of clock and clock-controlled genes in livers from mice housed under LD 12:12 (unfilled circles) or LD 3:3 (filled circles). Maximal value under LD 12:12 is expressed as 100%. Data are shown as means ± SEM ($n = 5$). Statistical significance determined by ANOVA is shown in boxes. Significant differences between LD 12:12 and LD3:3 are indicated as $^{*}p < 0.05$ and $^{**}p < 0.01$ at corresponding ZT/CTs. CT, circadian time; ZT, Zeitgeber time.

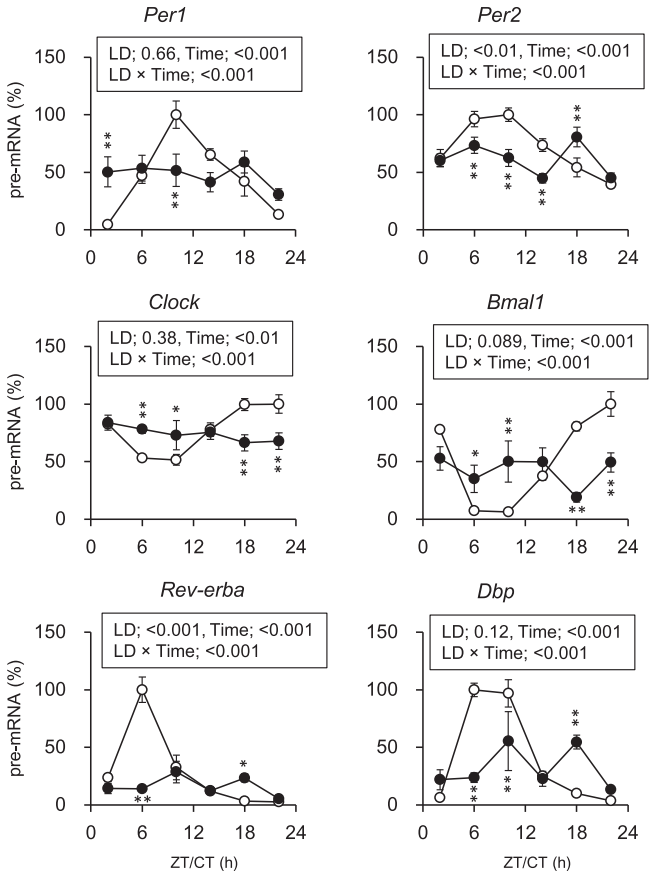

Fig. 3. Temporal pre-mRNA expression profiles of circadian clock-related genes in livers from mice housed under LD 12:12 and LD 3:3. Maximal value under LD 12:12 is expressed as 100%. Data are shown as means ± SEM ($n = 5$). Statistical significance determined by ANOVA is shown in boxes. Significant differences between LD 12:12 (unfilled circles) and LD3:3 (filled circles) are indicated as $^{*}p < 0.05$ and $^{**}p < 0.01$ at corresponding ZT/CTs. CT, circadian time; ZT, Zeitgeber time.

other physiological and molecular circadian rhythms such as those of core body temperature, hormonal secretion and peripheral clock gene expression in mammals.

The aberrant LD cycle-induced loss of rhythmic gene expression seemed to be caused at the transcriptional level, because the rhythmic pre-mRNA expression of these genes was also abolished under LD 3:3 (Fig. 3). Correlations between pre-mRNA and mature mRNA levels for *Per1*, *Rev-erbα*, and *Dbp* were very high ($r > 0.9$) under LD 12:12 (Fig. 4A) and maintained under LD 3:3 (Fig. 4B), suggesting that the ultradian photoperiod little affected the post-transcriptional regulation of these genes. In addition to the transcriptional regulation of clock genes, post-transcriptional mechanisms such as pre-mRNA processing and mature mRNA degradation also play important roles in producing appropriate rhythmic gene expression in mammals [13,14]. On the other hand, levels of pre-mRNA and mature mRNA for the *Per2* gene only weakly correlated under both LD 12:12 and LD 3:3, but closely correlated for those of the *Per1*, *Rev-erbα*, and *Dbp* genes (Fig. 4). Expression of the *Per2* gene appears to be largely dependent on post-transcriptional regulation [14] compared with other clock genes. Antiphase circadian expression between *Per2* and *Bmal1* mRNAs [15] was also maintained under LD 3:3 (Supplemental Fig. 4), suggesting that the ultradian photoperiod-induced reduced amplitude of circadian gene expression was not the result of a disrupted, cell-autonomous autoregulatory transcription-translation feedback loop. The standard deviations of each gene under LD 12:12 and LD 3:3 were calculated to determine intra-animal variability under LD 3:3 (Supplemental Fig. 5). The standard deviation of most circadian genes was identical between LD 12:12 and LD 3:3 except for that of *Bmal1*, suggesting that the reduced amplitude of circadian gene expression induced by the ultradian photoperiod was not the result of desynchrony between animals at each time point. These findings suggest that the ultradian photoperiod flattened the circadian transcription of clock genes by desynchronizing the cellular clocks in each tissue without disrupting the intercellular molecular clock. On the other hand, the circadian expression of *Rev-erbα*, a circadian transcriptional repressor of which the rhythmic expression is transcriptionally regulated by the bHLH-PAS transcription factors CLOCK and BMAL1 [2,3], was completely damped in all tissues examined under LD 3:3. Exposure to dim light at nighttime reduces the amplitude of *Rev-erb* mRNA expression in peripheral tissues of mice such as the liver and WAT but not in the hypothalamus or hippocampus [16]. Thus, these findings indicate that the circadian expression of peripheral *Rev-erbα* is sensitive to environmental photic conditions, although the underlying mechanism remains unknown.

Daily feeding–fasting cycles are dominant time cues for peripheral clocks and time-imposed daily restricted feeding can entrain the peripheral circadian expression of clock genes independently of the master clock in the SCN [12], suggesting that the aberrant feeding rhythms induced by an ultradian photoperiod

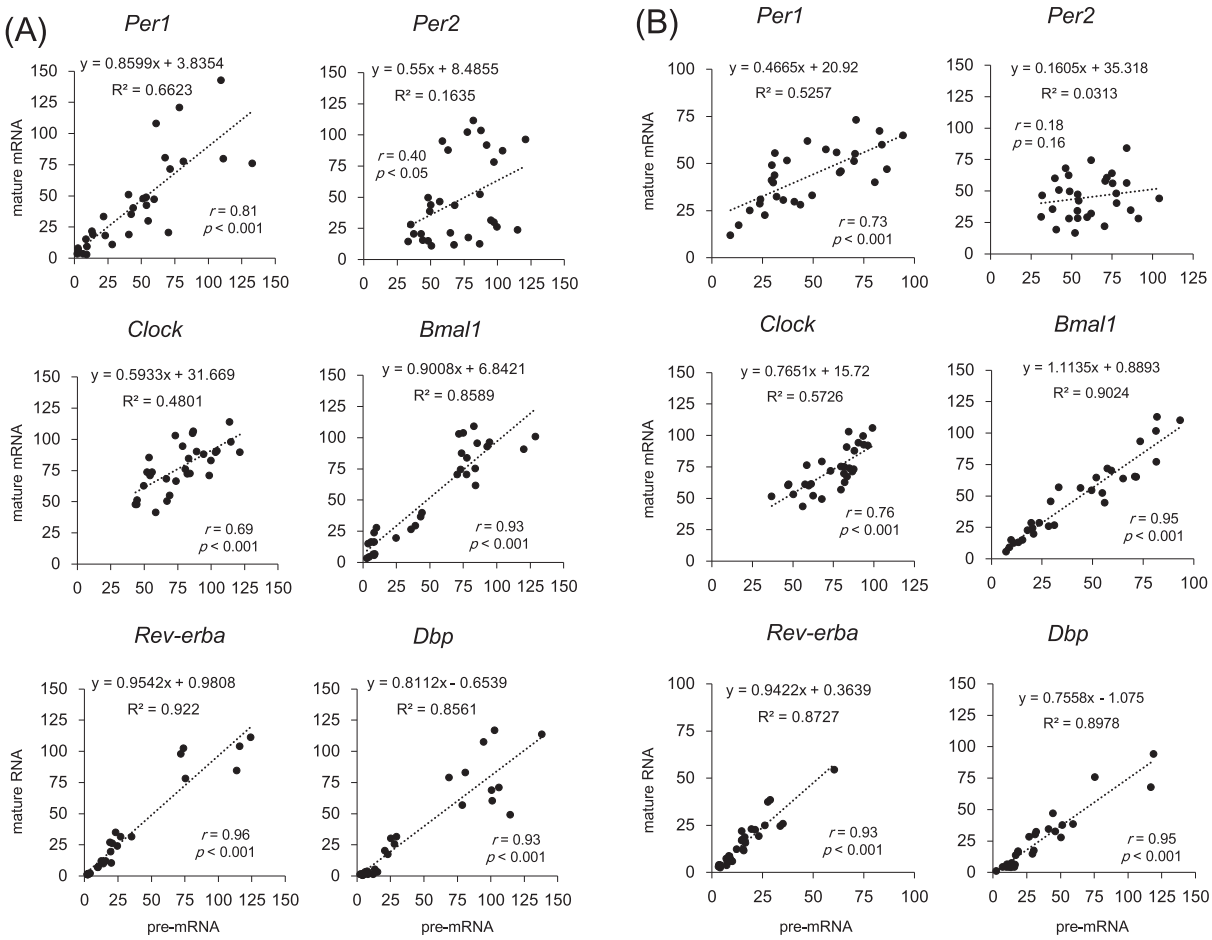

Fig. 4. Scatter plots of pre-mRNA and mature mRNA expression in livers from mice housed under LD 12:12 (A) and LD 3:3 (B). Relative expression levels of pre-mRNA (See Fig. 3) and mature mRNA (See Fig. 2) in livers from mice housed under LD 12:12 (A; $n = 30$) or LD 3:3 (B; $n = 30$). Regression lines, coefficient of determinations (R^2), Pearson's product–moment correlation coefficients (r), and p-values are described in corresponding plots.

might disrupt peripheral circadian gene expression. However, the circadian rhythms of food intake (Supplemental Fig. 1) and drinking behavior (Fig. 1) were maintained under LD 3:3. Furthermore, a completely ultradian feeding schedule (diet delivered every six hours) does not significantly affect the circadian expression of clock-related genes such as *Per1*, *Per2*, and *Dbp* in rats under LD 12:12 [17]. Therefore, the peripheral clock disruption probably did not result from a loss of the circadian feeding rhythm under LD 3:3.

The circadian rhythm of core body temperature was abolished and synchronized to an ultradian photoperiod in mice with free-running behavior under LD 3:3, although rhythmic body temperature represents a robust output of the master clock in the SCN [18,19]. The six-hour rhythm of core body temperature in LD 3:3 might be a masking effect of the aberrant LD cycles since it immediately disappeared when the mice were transferred from LD 3:3 to DD (data not shown). Several clock molecules are thought to be involved in the circadian and homeostatic regulation of core body temperature [20–23]. *Rev-erbα* is involved in circadian heat production by regulating UCP1 expression in BAT [23]. We found here that levels of *Rev-erbα* expression were significantly damped in BAT under LD 3:3 (Supplemental Fig. 6). The unusually low level of *Rev-erbα* expression might be a cause of the disrupted body temperature rhythm under LD 3:3. On the other hand, others have suggested that the circadian rhythm of core body temperature is an entraining cue for peripheral clocks [24,25]. Heat shock transcription factor (HSF) [26,27] and cold-inducible RNA-binding protein (CIRBP) [28,29] might be involved in temperature-induced clock gene expression in mammals. An unusual body temperature rhythm might disrupt the peripheral clocks by affecting the expression of temperature-dependent transcriptional regulators such as HSF and CIRBP under LD 3:3.

Light can directly induce clock gene expression in peripheral tissues via the autonomic nervous system [11,30] and the central clock is dispensable for the synchronization of peripheral clocks to an environmental LD cycle in mice with a genetically ablated SCN clock [31]. The present findings suggest that disrupted environmental LD cycles abolish the normal oscillation of peripheral clocks and induce internal desynchrony in mammals. Internal desynchronization among peripheral clocks, behavioral, endocrine and body temperature rhythms and a lower average daily body temperature might be involved in metabolic disorders induced by a disrupted photoperiod [6–8]. Further investigation is required to comprehend the underlying mechanisms of the present findings.

Conflict of interest

None.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.bbrc.2015.01.095.

Transparency document

Transparency document related to this article can be found online at http://dx.doi.org/10.1016/j.bbrc.2015.01.095.

References

[1] H.G. Richter, C. Torres-Farfan, P.P. Rojas-Garcia, C. Campino, F. Torrealba, M. Seron-Ferre, The circadian timing system: making sense of day/night gene expression, Biol. Res. 37 (2004) 11–28.
[2] S.M. Reppert, D.R. Weaver, Coordination of circadian timing in mammals, Nature 418 (2002) 935–941.
[3] J.S. Takahashi, H.K. Hong, C.H. Ko, E.L. McDearmon, The genetics of mammalian circadian order and disorder: implications for physiology and disease, Nat. Rev. Genet. 9 (2008) 764–775.
[4] K. Sakamoto, T. Nagase, H. Fukui, K. Horikawa, T. Okada, H. Tanaka, K. Sato, Y. Miyake, O. Ohara, K. Kako, N. Ishida, Multitissue circadian expression of rat period homolog (rPer2) mRNA is governed by the mammalian circadian clock, the suprachiasmatic nucleus in the brain, J. Biol. Chem. 273 (1998) 27039–27042.
[5] C.S. Pittendrigh, S. Daan, A functional analysis of circadian pacemakers in nocturnal rodents: IV. Entrainment: pacemaker as clock, J. Comp. Physiol A 106 (1976) 291–331.
[6] K. Oishi, S. Higo-Yamamoto, Disrupted daily light-dark cycles induce physical inactivity and enhance weight gain in mice depending on dietary fat intake, Neuroreport 25 (2014) 865–869.
[7] K. Oishi, Disrupted light-dark cycle induces obesity with hyperglycemia in genetically intact animals, Neuro Endocrinol. Lett. 30 (2009) 458–461.
[8] K. Oishi, N. Itoh, Disrupted daily light-dark cycle induces the expression of hepatic gluconeogenic regulatory genes and hyperglycemia with glucose intolerance in mice, Biochem. Biophys. Res. Commun. 432 (2013) 111–115.
[9] T.A. LeGates, C.M. Altimus, H. Wang, H.K. Lee, S. Yang, H. Zhao, A. Kirkwood, E.T. Weber, S. Hattar, Aberrant light directly impairs mood and learning through melanopsin-expressing neurons, Nature 491 (2012) 594–598.
[10] C. Cailotto, J. Lei, J. van der Vliet, C. van Heijningen, C.G. van Eden, A. Kalsbeek, P. Pevet, R.M. Buijs, Effects of nocturnal light on (clock) gene expression in peripheral organs: a role for the autonomic innervation of the liver, PLoS One 4 (2009) e5650.
[11] A. Ishida, T. Mutoh, T. Ueyama, H. Bando, S. Masubuchi, D. Nakahara, G. Tsujimoto, H. Okamura, Light activates the adrenal gland: timing of gene expression and glucocorticoid release, Cell. Metab. 2 (2005) 297–307.
[12] S. Shibata, Y. Tahara, A. Hirao, The adjustment and manipulation of biological rhythms by light, nutrition, and abused drugs, Adv. Drug Deliv. Rev. 62 (2010) 918–927.
[13] E. Garbarino-Pico, C.B. Green, Posttranscriptional regulation of mammalian circadian clock output, Cold Spring Harb. Symp. Quant. Biol. 72 (2007) 145–156.
[14] K.C. Woo, T.D. Kim, K.H. Lee, D.Y. Kim, W. Kim, K.Y. Lee, K.T. Kim, Mouse period 2 mRNA circadian oscillation is modulated by PTB-mediated rhythmic mRNA degradation, Nucleic Acids Res. 37 (2009) 26–37.
[15] K. Oishi, K. Sakamoto, T. Okada, T. Nagase, N. Ishida, Antiphase circadian expression between BMAL1 and period homologue mRNA in the suprachiasmatic nucleus and peripheral tissues of rats, Biochem. Biophys. Res. Commun. 253 (1998) 199–203.
[16] L.K. Fonken, T.G. Aubrecht, O.H. Melendez-Fernandez, Z.M. Weil, R.J. Nelson, Dim light at night disrupts molecular circadian rhythms and increases body weight, J. Biol. Rhythms 28 (2013) 262–271.
[17] D. Yamajuku, S. Okubo, T. Haruma, T. Inagaki, Y. Okuda, T. Kojima, K. Noutomi, S. Hashimoto, H. Oda, Regular feeding plays an important role in cholesterol homeostasis through the liver circadian clock, Circ. Res. 105 (2009) 545–548.
[18] K. Abe, J. Kroning, M.A. Greer, V. Critchlow, Effects of destruction of the suprachiasmatic nuclei on the circadian rhythms in plasma corticosterone, body temperature, feeding and plasma thyrotropin, Neuroendocrinology 29 (1979) 119–131.
[19] R.Y. Moore, V.B. Eichler, Loss of a circadian adrenal corticosterone rhythm following suprachiasmatic lesions in the rat, Brain Res. 42 (1972) 201–206.
[20] K. Nagashima, K. Matsue, M. Konishi, C. Iidaka, K. Miyazaki, N. Ishida, K. Kanosue, The involvement of Cry1 and Cry2 genes in the regulation of the circadian body temperature rhythm in mice, Am. J. Physiol. Regul. Integr. Comp. Physiol. 288 (2005) R329–R335.
[21] H. Sei, K. Oishi, Y. Morita, N. Ishida, Mouse model for morningness/eveningness, Neuroreport 12 (2001) 1461–1464.
[22] K. Tokizawa, Y. Uchida, K. Nagashima, Thermoregulation in the cold changes depending on the time of day and feeding condition: physiological and anatomical analyses of involved circadian mechanisms, Neuroscience 164 (2009) 1377–1386.
[23] Z. Gerhart-Hines, D. Feng, M.J. Emmett, L.J. Everett, E. Loro, E.R. Briggs, A. Bugge, C. Hou, C. Ferrara, P. Seale, D.A. Pryma, T.S. Khurana, M.A. Lazar, The nuclear receptor Rev-erbα controls circadian thermogenic plasticity, Nature 503 (2013) 410–413.
[24] S.A. Brown, G. Zumbrunn, F. Fleury-Olela, N. Preitner, U. Schibler, Rhythms of mammalian body temperature can sustain peripheral circadian clocks, Curr. Biol. 12 (2002) 1574–1583.
[25] C. Saini, J. Morf, M. Stratmann, P. Gos, U. Schibler, Simulated body temperature rhythms reveal the phase-shifting behavior and plasticity of mammalian circadian oscillators, Genes. Dev. 26 (2012) 567–580.
[26] E.D. Buhr, S.H. Yoo, J.S. Takahashi, Temperature as a universal resetting cue for mammalian circadian oscillators, Science 330 (2010) 379–385.
[27] T. Tamaru, M. Hattori, K. Honda, I. Benjamin, T. Ozawa, K. Takamatsu, Synchronization of circadian Per2 rhythms and HSF1-BMAL1:CLOCK interaction in mouse fibroblasts after short-term heat shock pulse, PLoS One 6 (2011) e24521.
[28] J. Morf, G. Rey, K. Schneider, M. Stratmann, J. Fujita, F. Naef, U. Schibler, Cold-inducible RNA-binding protein modulates circadian gene expression posttranscriptionally, Science 338 (2012) 379–383.
[29] K. Oishi, S. Yamamoto, D. Uchida, R. Doi, Ketogenic diet and fasting induce the expression of cold-inducible RNA-binding protein with time-dependent hypothermia in the mouse liver, FEBS Open Bio 3 (2013) 192–195.
[30] H. Terazono, T. Mutoh, S. Yamaguchi, M. Kobayashi, M. Akiyama, R. Udo, S. Ohdo, H. Okamura, S. Shibata, Adrenergic regulation of clock gene expression in mouse liver, Proc. Natl. Acad. Sci. U. S. A. 100 (2003) 6795–6800.
[31] J. Husse, A. Leliavski, A.H. Tsang, H. Oster, G. Eichele, The light-dark cycle controls peripheral rhythmicity in mice with a genetically ablated suprachiasmatic nucleus clock, FASEB J. 28 (2014) 4950–4960.