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# Effect of Behavioural Feedback on Circadian Clocks of the Nocturnal Field Mouse *Mus booduga*

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# Effect of Behavioural Feedback on Circadian Clocks of the Nocturnal Field Mouse *Mus booduga*

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## Abstract

The effect of 'novel running wheels' on circadian clocks of the nocturnal field mouse *Mus booduga* was investigated during free-running and entrained conditions. In order to find out whether daily access to novel running wheels can entrain the locomotor activity rhythms experimental animals ($n = 6$) were provided with 'novel running wheels' at a fixed time of the day. The control animals ($n = 5$) were handled similar to the experimental animals but were not given access to novel running wheels. The results show that daily access to novel running wheels entrained the free-running locomotor activity rhythm of these mice. The post-entrainment free-running period ($\tau$) of the experimental animals was significantly shorter than the pre-entrainment $\tau$, whereas the pre- and post-treatment $\tau$ of the control animals did not differ significantly. In separate set of experiments, the effect of access to novel running wheels on the rate of re-entrainment was studied after a 6 h phase advance/delay in 24 h (12:12 h) light/dark (LD) cycles. Experimental animals were given access to novel running wheels for 3-h, 1 h after the 'lights-off' only on the first day of the 'new LD cycles'. Experimental animals took fewer cycles to re-entrain to 6-h phase advanced LD cycles compared to the control animals. After a phase delay in the LD cycles by 6 h, the experimental animals took more number of cycles to re-entrain compared to the control animals. These results thus suggest that access to novel running wheel can act as a Zeitgeber for the circadian clocks of the nocturnal mouse *M. booduga*, and can also modify the rates of re-entrainment to phase shifted LD cycles, in a time-dependent manner.

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**Keywords:** Circadian, locomotor activity, novel running wheel, entrainment, re-entrainment.



## Introduction

Circadian regulation of behaviour, metabolism, and physiology is a conserved feature across most eukaryotic and some prokaryotic taxa (Aschoff, 1981; Dunlap et al., 2003). In mammals, the pacemakers located in the hypothalamic suprachiasmatic nuclei (SCN) control these circadian rhythms (Klein et al., 1991). Entrainment of these circadian pacemakers (clocks) occurs predominantly by photic time cues (Zeitgeber), conveyed directly to the SCN via the retinohypothalamic tract (Moore & Linn, 1972; Pikard, 1982; Morin, 1994; Johnson et al., 1998). Although light is a predominant Zeitgeber for the circadian clocks of several diurnal, nocturnal and crepuscular animals, various non-photic stimuli can also phase shift and entrain circadian clocks (Reebs et al., 1989; Van Reeth & Turek, 1989; Edger & Dement, 1991; Klerman et al., 1998; Hut et al., 1999).

Phase shifts and entrainment of circadian rhythms by various non-photic stimuli such as scheduled voluntary exercise (Edger & Dement, 1991; Edgar et al., 1997; Marchant & Morin, 1998), forced treadmill running (Mistlberger, 1991; Marchant & Mistlberger, 1996; Marchant et al., 1997), arousal due to saline and triazolam injections (Van Reeth & Turek, 1989; Sumova et al., 1996), daily schedules of cage changes and social interactions (Mrosovsky, 1988), restricted foraging (Rusak et al., 1989), triazolam-induced wheel running (Van Reeth & Turek, 1989), and novelty-induced wheel running (Reebs & Mrosovsky, 1989) are well documented specially for nocturnal mammals. It is also known that non-photic stimuli induce large phase advances in nocturnal mammals during the subjective day, and evoke less or no phase shifts during the subjective night (Mrosovsky, 1988; Mrosovsky et al., 1989; Van Reeth & Turek, 1989; Wickland & Turek, 1991; Hastings et al., 1992; Marchant et al., 1997). In the European ground squirrel (*Spermophilus citellus*), wheel running activity entrained circadian rhythms in a manner similar to that seen in nocturnal animals (Hut et al., 1999). On the other hand, scheduled wheel running did not entrain the locomotor activity rhythm of the crepuscular animal *Octodon degus*, instead, it exerted weak phase control (Kas & Edgar, 2001).

In humans, effect of intense physical activity on circadian clocks has been well-documented (Klerman et al., 1998). Brief exercise, especially during mid-subjective night, phase delayed the circadian rhythms of body temperature and hormone levels (Van Reeth et al., 1994; Buxton et al., 1997). Long duration exercise, phase shifted human circadian clocks in a manner qualitatively similar to that seen in nocturnal rodents (Klerman et al., 1998).

In nocturnal mammals, some of the strongest non-photic effects involve manipulations that induced initiation of locomotor activity, at times when the animal would normally be resting, i.e., the subjective day (Smith et al., 1992; Mrosovsky, 1996; Hastings et al., 1998). When mice were provided with ‘novel running wheels’ during the subjective day, they usually become active, started digging and scratching their

body, started scent marking, and pushing grains (Mrosovsky, 1988). These actions serve to establish a home territory for the animals and therefore might have social implications. Previous studies in hamsters showed that access to novel running wheels for 3 h phase shifted the circadian clocks, and the magnitude of the phase shift was a function of the wheel rotations per unit time (Reebs & Mrosovsky, 1989; Reebs et al., 1989; Janik & Mrosovsky, 1993; Mrosovsky, 1996). Similarly in *tau* mutant hamsters phase shifts and period changes were obtained following a single exposure to novel running wheel (Mrosovsky, 1993). In rats, entrainment due to periodic access to novel running wheels produced sizable changes in post- entrainment $\tau$ (Kuroda et al., 1997). Under constant dim light, mean $\tau$ of Syrian hamsters housed in spring-suspended cages without running wheel was shorter than those housed in cages with running wheel (Aschoff et al., 1973). In DD, slightly shorter values of $\tau$ have been reported for hamsters with access to running wheels compared to the hamsters housed in a simulated burrow system (Pratt & Goldman, 1986). A single 3 h access to novel running wheels was found to lengthen the $\tau$ of the locomotor activity rhythm in hamsters (Mrosovsky, 1993; Weisgerber et al., 1997). Shortening of $\tau$ due to running wheel access has also been reported in blinded rats (Yamada et al., 1986; Yamada et al., 1990; Kuroda et al., 1997), and mice (Edgar et al., 1991). Such differences in responses to novel running wheel access have also been reported in rats (Edgar et al., 1993), mice (Edgar et al., 1991), and hamsters (Pratt & Goldman, 1986). The activity of an animal could modify the $\tau$ of the circadian clocks in possibly two different modes (reviewed in Mrosovsky, 1996). The activity could directly effect circadian clocks and thereby lengthen $\tau$. Alternatively, access to novel running wheels could induce high level of activity during the phase advancing portion of the non-photic phase response curve (PRC), resulting in daily phase advances or apparent $\tau$ shortening. The intra- and inter-species differences in the response to non-photic cues lead to the notion that non-photic Zeitgebers are week in nature (Mrosovsky, 1996). Given the variability in the response of circadian timing systems to non-photic cues, more studies should be carried out in several species of rodents from different ecological background to understand the action of non-photic cues on circadian clocks.

In addition to phase shifts and period changes behavioural activity is also known to accelerate re-entrainment of circadian clocks to phase shifted LD cycles (Joy et al., 1989). Evidence such as effects of activity on the $\tau$ of the free-running locomotor activity rhythm in rats (Aschoff et al., 1973; Edgar et al., 1991; Edgar et al., 1993), and acceleration of rate of re-entrainment to phase shifted LD cycles in hamsters (Joy et al., 1989), suggests that behavioural feedback influence the phase of circadian clocks. Notwithstanding the importance of non-photic cues such as behavioural feedback in re-entrainment process of circadian clocks, evidence for the role of non-photic cues on rate of re-entrainment has been scanty.

We have extensively studied the role of light and melatonin on the circadian clocks of the nocturnal field mouse *Mus booduga* (Singaravel et al., 1996; Sharma et al., 1999; Sharma & Chidambaram, 2003; Sharma, 2003; Sharma et al., 2003). The circadian clocks of this animal are sensitive to light and external melatonin injections in a time dependent manner, quite different compared to other species of rodents

(Sharma et al., 2003). In addition, these animals are caught directly from paddy fields of a tropi-cal climate (9°58′N lat., 78°10′E long.), where the seasonal variations in photope-riod and temperature are minimal. The LD cycles at this latitude could serve as the most reliable Zeitgeber and therefore in principle these animals should depend the least on behavioural feedbacks for fine tuning their circadian clocks. It would therefore be interesting to investigate the effects of access to novel running wheels on the circadian clocks of this Murid species and to evaluate properties of behavioral feedback as a potential Zeitgeber. In this paper, we report the effects of access to novel running wheels on the free-running locomotor activity rhythm in DD and on the rates of resynchronization after phase advance and delay in LD cycles by 6 h, in the nocturnal field mouse *M. booduga*.

## Materials and Methods

Adult male field mice ($n = 42$) *M. booduga* weighing about 8–13 g were captured from paddy fields near Madurai Kamaraj University campus (9°58′N lat., 78°10′E long.), and were maintained under laboratory LD cycles for about 15 days before being used in the experiments. After acclimatization to laboratory conditions the animals were placed in individual running wheels in constant dark (DD) experimental rooms. The 'novel running wheels' used in the experiments rotated at a speed of 80 ± 10 (mean ± SD) cycles per minute on a scale where the speed of the 'normal running wheels' was 30 ± 15 (mean ± SD) revolution per minute (henceforth will be referred as novel and normal running wheel). The speed of the running wheels was estimated by introducing animals ($n = 5$) into the wheels during subjective night when they are generally most active and counting the number of rotations made per minute. The running wheels were of about 20 cm in diameter, attached to a transparent plexiglass cage that was 7 × 11 × 9 cm, with a small opening of 2 cm diameter. Reed-relays attached to the wheels activated the writing stylets of an Esterline Angus A620X Event Recorder when the mice ran the wheel. Illumination in the cages during the light period was ~100 lux incandescent light (Lumia, India), as measured with UDT-optometer.

The experimental rooms, with dimensions 3.05 × 2.44 × 4.01 m, did not have windows but were gently ventilated. Temperature remained constant at 25° ± 1°C and relative humidity was 75 ± 5%. Food and water were available *ad libitum*. Since cage cleaning, replenishing food and water, wheel changing etc are likely to disturb the animals, enough care was taken to keep the disturbance level at a minimum. These activities were carried out only thrice a week at irregular intervals, each lasting about 15 min. Red light of $\lambda > 640$ nm obtained with a combination of red and orange filter fitted to a battery operated torch light was used inside the cubicles for feeding the animals, cleaning cages and for handling animals. Actograms were obtained by pasting 24 h activity-rest strips chronologically, one below the other in a standard manner.

The onset of locomotor activity was taken as the phase reference point for all calculations. After about 15 days in DD, steady-state free-run was attained and $\tau$ was

calculated using linear regression lines through the onsets of activity. Eleven animals were maintained in total darkness (DD) for entrainment by access to novel running wheels. Similarly, thirty-one animals were maintained in a 12:12 LD cycle to estimate the rate of re-entrainment after 6 h phase advance/delays in LD cycles. In order to investigate how access to novel running wheels influence the circadian clocks of the nocturnal field mouse *M. booduga*, the following experimental protocols were followed.

**Experiment-I**

The locomotor activity rhythm of the animals ($n = 11$) was first monitored in DD for about 15 days in their home cage, attached with normal running wheels. On the 16th day, six out of eleven mice were given access to novel running wheel (henceforth these animals will be referred as experimental animals) whereas the remaining five were provided with normal running wheel (henceforth will be referred as control animals). The experimental animals were provided access to fresh novel running wheels daily for 3 h from 07:00 till 11:00 h, after which they were shifted back to their home cages. The timing of replacement of fresh novel running wheels marks the mid-subjective day (based on first day of pulse at around 07:00–11:00 h of local time). The control animals were handled similar to the experimental animals, i.e., these animals were also introduced daily into normal running wheels for 3 h from 07:00 and 11:00 h in an isolated room. After a 3-h pulse, these animals were shifted back to their home cages. Experimental as well as control animals had free access to their resting cages even during the treatments. The only difference between the experimental and control animals was that the experimental animals were given access to novel running wheels whereas the control animals were provided with normal running wheels. After a 24 day long treatment both the experimental and the control animals were maintained in DD for about 15 days and the $\tau$ of locomotor activity rhythm was estimated.

**Experiments-II**

In these experiments the animals ($n = 31$) were first entrained to LD cycles (12:12 h; 'lights-off' at 12:00 h and 'lights-on' 24:00 h). After stable entrainment was achieved, these animals were divided into two groups; the first group was subjected to a 6-h of phase advance in the LD cycles, and the second group was subjected to a 6 h of phase delay in the LD cycles.

In the phase advance group, the experimental animals ($n = 9$) were removed from their home cages, 1 h after the 'new dark onset', on the first day of LD shift and provided access to fresh novel running wheels for 3 h in an isolated room. The control animals ($n = 7$) were handled similar to the experimental animals, i.e., they were also taken out from their home cages 1 h after the new dark onset on the first day of LD shift and were introduced into normal running wheels for 3 h. After a 3 h treatment the experimental and the control animals were returned back to their respective home cages. Similarly, in the 6-h phase delay group, the experimental animals ($n = 9$) were

removed from their home cages 1 h after the new dark onset, on the first day of LD shift, and were provide access to fresh novel running wheel for 3 h in an isolated room. The remaining animals ($n = 6$) were treated as controls.

Linear regression analysis was used to assess free-running and entrained steady states. Regression lines were drawn through the onsets of locomotor activity, and the lines with slopes different from 0 at 0.05 level of significance were taken to represent a free-run while regression lines with slopes that did not differ significantly from 0 were considered to represent entrainment. Stable entrainment was assumed to occur only when the locomotor activity rhythm free-ran from a phase determined by the cyclic novel wheel access and not by the rhythm prior to entrainment. A strict visual criterion was used to estimate the number of transients and to assess the patterns. To specify when resynchronization had occurred, we used number of days required for an animal to begin wheel running within 10 min of the onset of darkness in the new LD cycles. Comparison of the number of transient cycles taken for re-entrainment and the pre- and post- entrainment τ was carried out using Student's *t*-test.

## Results

### Experiment-I

The τ of the locomotor activity rhythm of the experimental and the control animals were 23.39 ± 0.07 h (mean ± SD) and 23.65 ± 0.19 h (mean ± SD), respectively. The τ of the locomotor activity rhythm in control animals did not show any change due to handling and daily restriction to home cage access. All the experimental animals entrained to a daily access to novel running wheels. The post-entrainment τ of the experimental animals was significantly shorter than the pre-entrainment τ (+0.14 ± 0.04 h, $t = 2.57$, $df = 5$, $P < 0.05$) (Fig. 1). The post-treatment τ of the control animals did not differ significantly from the pre-treatment τ (+0.06 ± 0.009 h, $t = 2.77$, $df = 4$, $P > 0.05$). The pre- and post-treatment τ of the control animals were 23.39 ± 0.07 h (mean ± SD) and 23.33 ± 0.06 h (mean ± SD), respectively (Fig. 2).

### Experiment-II

Animals with access to novel running wheels re-entrained to phase advanced LD cycles significantly faster than the control animals, following a 6-h phase advance in LD cycles ($t = 4.79$, df = 14, $P < 0.001$) (Fig. 3a, b). Control animals took 11.29 ± 1.80 (mean ± SD) days for re-entrainment, whereas experimental animals took 7.66 ± 1.23 (mean ± SD) days (Fig. 5).

Following a 6-h phase delay in LD cycles, the experimental animals took significantly more number of cycles to re-entrain compared to the control animals ($t = -9.12$, $df = 13$, $P < 0.0001$) (Fig.4 a, b). The number of cycles taken for re-entrainment by the experimental and the control animals were 7.33 ± 1.41 (mean ± SD) and 2.33 ± 1.25 (mean ± SD), respectively (Fig. 5). Therefore, in this case access to novel running wheels slowed down the rate of re-entrainment.

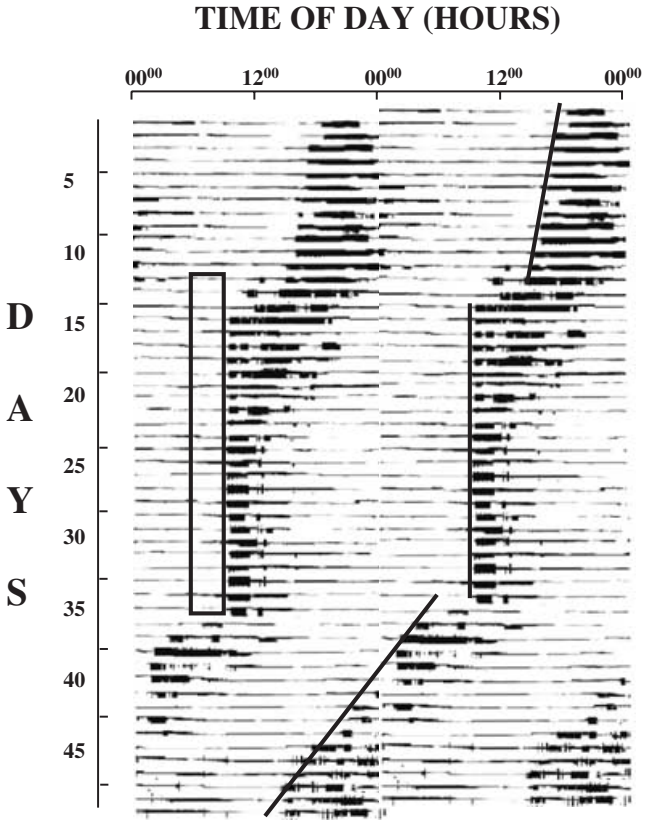


*Figure 1.* Representative double-plotted actogram of a mouse from the experimental group maintained in constant darkness and provided daily access to fresh novel running wheels for 3 h between 07:00 to 11:00 h for 24 days, indicated by an empty box. The pre- and post-entrainment τ of this animal was 23.67 and 22.56 h, respectively. Lines through the onsets of activity are drawn to give a visual impression of the approximate trend of locomotor activity rhythm during the pre-entrainment, entrainment and post-entrainment steady states.

## Discussion

The results of our experiments suggest that daily 3 h access to fresh novel running wheels entrains the clocks of the nocturnal field mouse *M. booduga* in DD regime. After the treatment schedule was terminated, the locomotor activity rhythm of the experimental animals free-ran from the apparent phase of entrainment. Further, the τ of the locomotor activity rhythm following entrainment was significantly shorter compared to the pre-entrainment τ, which suggests that greater level of activity induced by novel running wheel shortens τ of the locomotor activity rhythm. This is in concordance with the results of similar studies in mice (Edgar et al., 1991), rats (Yamada et al., 1990; Kuroda et al., 1997) and Syrian hamsters (Weisgerber et al., 1997). In

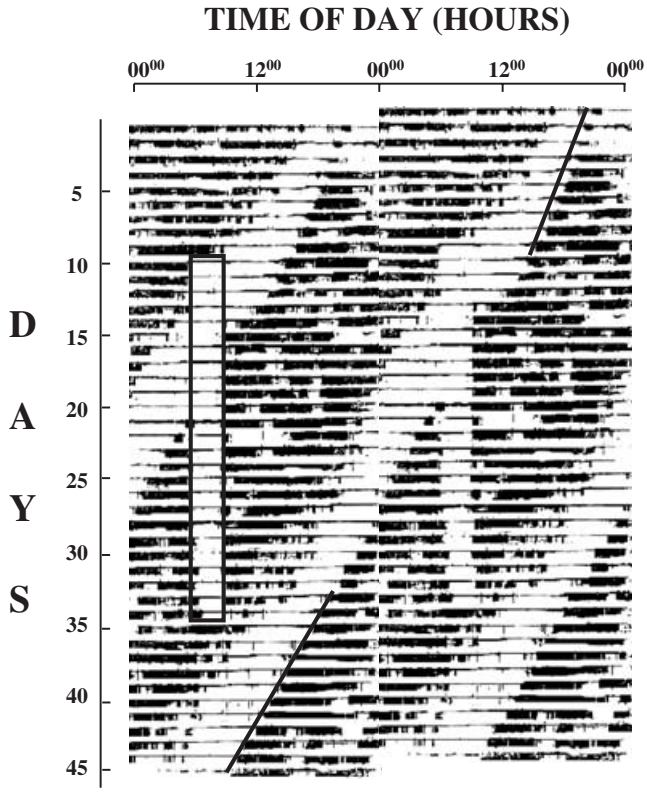


*Figure 2.* Representative double-plotted actogram of a mouse from the control group of animals that was maintained in constant darkness and handled similar to the experimental animals for 3 h between 07:00 to 11:00 h (indicated by an empty box) for 24 days but did not get access to novel running wheels. The pre- and post-entrainment τ of this animal was 23.36 and 23.35 h, respectively. Other details as in Figure 1.

several species of mammal, the τ of the locomotor activity rhythm depends upon the amount of wheel running activity. A nonlinear relationship between activity levels and τ has been reported in mice (Weinert & Weiß, 1997). Weinert and Weiß (1997) have reported that the activity levels and the τ were negatively correlated in less active mice, whereas a positive correlation was found in more active mice. A similar inverse relationship between activity levels and τ was reported in mice (Edgar et al., 1991; Weinert and Weiß, 1997), rats (Yamada et al., 1988) and hamsters (Mrosovsky, 1996). These results suggest that there is a causal link between level of locomotor activity and the τ, because manipulating the level of activity seems to changes τ (Kas & Edgar, 2001).

Non-photic cues such as benzodiazepine injections (Van Reeth & Turek, 1987), access to novel running wheels (Mrosovsky & Salmon, 1987), socio-sexual cues in hamsters (Honrado & Mrosovsky, 1989) and olfactory cues in females of *Octodon*

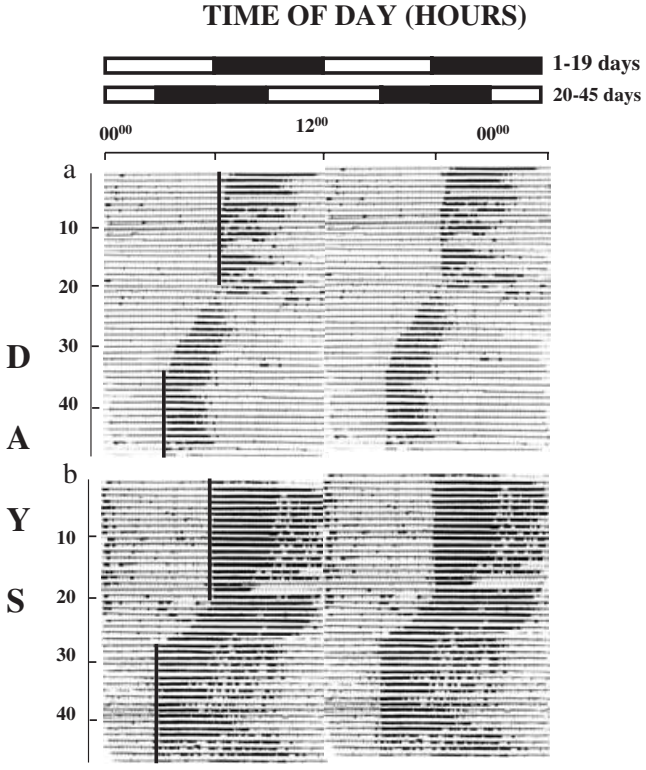


*Figure 3a–b.* Representative double plotted actograms of control (a) and experimental (b) mice that were first maintained in LD conditions for 19 days. After a baseline recording of the rhythm for first 19 days, the LD cycle (12:12 h) was phase advanced by 6 h. The experimental animals were given a single access to fresh novel running wheels, 1 h after the 'lights-off' of the new LD cycle, which lasted for 3 h. The control animals were handled similar to the experimental animals, but did not have access to novel running wheels. Open and solid horizontal bars on the top of the figure depict the LD cycles prevailing before and after the 6 h phase advance.

*degus* (Governale & Lee, 2001) reportedly speeded up re-entrainment process after phase advancement in LD cycles. Short-acting drugs accelerated resynchronization, bringing about acute instantaneous phase resetting of the locomotor activity rhythm (Mrosovsky, 1991; Mead et al., 1992; Golombik & Cardinali, 1993). Some short acting drugs such as benzodiazepine (BZP), triazolam (Turek & Losse-Olson, 1986; Turek & Van Reeth, 1988), and melatonin (Golombik & Cardinali, 1993; Singarvel et al., 1996; Sharma et al., 2003), differs significantly in their effects on circadian timing systems.

Following a 6 h phase advance in the LD cycles, the experimental animals provided with novel running wheels, took fewer cycles to resynchronize compared to the control animals. However, after a 6 h phase delay in the LD cycle, the experimental

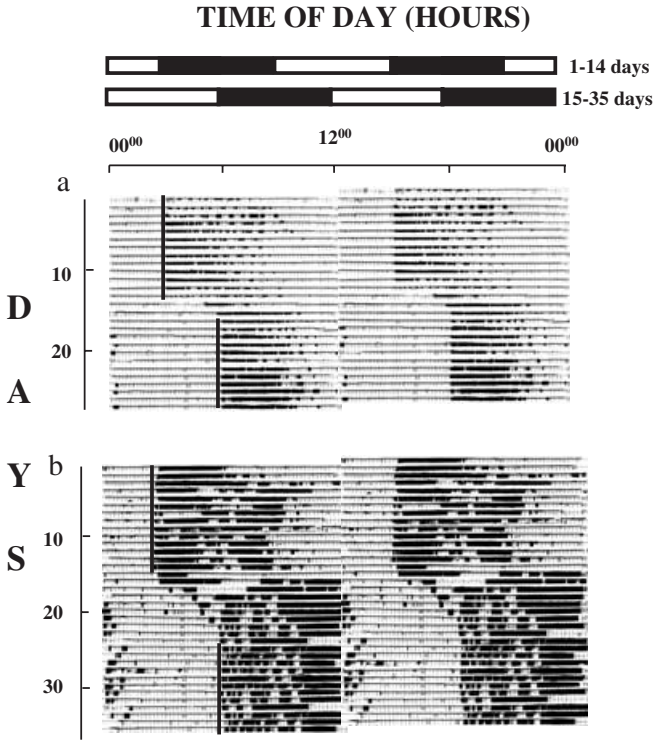


*Figure 4a–b.* Representative double plotted actograms of control (a) and experimental (b) mice that were first maintained in LD conditions for 14 days. After a baseline recording of the rhythm for first 14 days, the LD cycles were phase delayed by 6 h. The experimental animals were given a single access to fresh novel running wheels for 3 h, 1 h after the 'lights-off' of the new LD cycle. The control animals were handled similar to the experimental animals, but did not have access to novel running wheels. Open and solid horizontal bars, on the top of the figure depict the LD cycles prevailing before and after the 6-h phase delay.

animals took more number of days to resynchronize compared to the control animals. Although novel running wheels have been reported earlier to accelerate re-entrainment (Mrosovsky & Salmon, 1987), the results of our experiments provide additional insight into the effects of novel running wheels on the entrainment mechanisms of circadian clocks. It suggests that novel running wheels modify the rates of re-entrainment in a time-dependent manner, i.e., novel running wheels do not always accelerate re-entrainment, the rates of re-entrainment appear to be conditional upon the phase of access to novel running wheels. Perhaps re-entrainment to phase shifted LD cycles in our experiments would have been faster if animals were given access to novel running wheels at an appropriate phase of their circadian clocks.

Interestingly the results of our experiments, though contrary to our expectations, suggest that the nocturnal field mouse *M. booduga* have retained the capacity to fine-

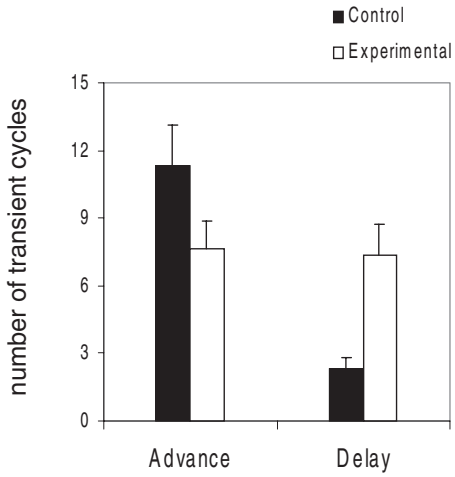


*Figure 5.* Number of days (mean ± SD) required for the locomotor activity rhythm to resynchronize to the phase shifted LD cycles, i.e., after 6 h of phase advance and 6 h of phase delay in the LD cycles, in the nocturnal field mouse *Mus booduga*.

tune their circadian clocks due to behavioural feedbacks, even living in stable LD cycles. It appears that even organisms living in a tightly regulated photoperiod do have the capacity to use non-photic time cues such as behavioural feedbacks to fine-tune their circadian clocks. This suggests that most organisms possess redundant mechanisms for timekeeping in the fluctuating environment. In a previous study on *M. booduga* to asses the rate of re-entrainment due to melatonin, melatonin injections were given for three consecutive days immediately close to new dark onset of the LD cycles, following a 6 h phase delay in the LD cycles (Singarvel et al., 1996). Melatonin injections slowed down rate of re-entrainment to phase shifted LD cycles. However, a similar dose of melatonin, given during the early subjective day, i.e., close to old dark onset of the LD cycles, speeded up re-entrainment (Sharma et al., 1999). The results of the present experiments also suggest that the accelerating or decelerating effects of any stimuli depends upon the phase at which access to novel running wheel is made. This suggests the circadian clocks of these mice are sensitive to non-photic Zeitgeber such as melatonin and novel running wheels in a time-dependent manner and it may be possible to use behavioural feedbacks to alleviate 'jet-lag'.

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## References

Aschoff J, Figala J, Poppel E (1973): Circadian rhythms of locomotor activity in the golden hamster (*Mesocricetus auratus*) measured with two different techniques. *J Comp Physiol Psychol 85*: 20–28.

Aschoff J (1981): A survey on biological rhythms. In: Aschoff J., ed., *Handbook of Behavioural Neurobiology IV Biological rhythms*. New York, London, Plenum press, pp. 81–93.

Buxton OM, Frank SA, L'Hermite-Baleriaux M, Leproult R, Turek FW, Van Cauter E (1997): Role of intensity and duration of nocturnal exercise in causing phase delay of human circadian rhythms. *Am J Physiol 273*: E536–E542.

Dunlap JC, Loros JJ, DeCoursey PJ (2003): *Chronobiology*. Sunderland, MA, Sinauer Associates, Inc. Publishers.

Edgar DM, Dement WC (1991): Regularly scheduled voluntary exercise synchronizes the mouse circadian clock. *Am J Physiol 261*: R928–R933.

Edgar DM, Martin CE, Dement WC (1991): Activity feedback to the mammalian circadian pacemaker: influences on observed measures of rhythm period length. *J Biol Rhythms 6*: 185–199.

Edgar DM, Miller JD, Prosser RA, Daan RR, Dement WC (1993): Serotonin and the mammalian circadian system: II. Phase shifting rat behavioural rhythms with serotonergic agonists. *J Biol Rhythms 8*: 11–31.

Edgar DM, Reid MS, Dement WC (1997): Serotonergic afferents mediate activity-dependent entrainment of the mouse circadian clock. *Am J Physiol 273*: R265–R269.

Golombik DA, Cardinali DP (1993): Melatonin accelerates re-entrainment after phase advance of the light/dark cycle in Syrian hamsters: Antagonism by flumazenil. *Chronobiol Int 10*: 435–441.

Governale MM, Lee TM (2001): Olfactory cues accelerate reentrainment following phase shifts and entrain free-running rhythms in female *Octodon degus* (Rodentia). *J Biol Rhythms 16*: 489–501.

Hastings MH, Mead SM, Vindlacheruvu RR, Ebling FJP, Maywood ES, Grosse J (1992): Non-photic phase shifting of the circadian activity rhythm of Syrian hamsters: The relative potency of arousal and melatonin. *Brain Res 591*: 20–26.

Hastings MH, Duffield GE, Smith EJD, Maywood ES, Ebling FJP (1998): Entrainment of the circadian system of mammals by nonphotic cues. *Chronobiol Int 15*: 25–445.

Honrado GI, Mrosovsky N (1989): Arousal by sexual stimuli accelerates the re-entrainment of hamsters to phase advanced light-dark cycles. *Behav Ecol Socibiol 25*: 57–63.

Hut RA, Mrosovsky N, Daan S (1999): Nonphotic entrainment in a diurnal mammal, the European ground squirrel *Spermophilus citellus*. *J Biol Rhythms 14*: 409–419.

Janik D, Mrosovsky N (1993): Nonphotically induced phase shift of circadian rhythms in the golden hamster: activity response curves at different ambient temperature. *Physiol Behav 53*: 431–436.

Johnson RF, Moore RY, Morin LP (1988): Loss of entrainment and anatomical plasticity after lesions of the hamster retinohypothalamic tract. *Brain Res 460*: 297–313.

Joy JE, Losee-Olsen S, Turek FW (1989): Single injections of triazolam, a short acting benzodiazepine, lengthen the period of the circadian activity rhythm in golden hamster. *Experientia 45*: 152–154.

Kas MJ, Edgar DM (2001): Scheduled voluntary wheel running activity modulates free-running circadian body temperature rhythms in *Octodon degus*. *J Biol Rhythms 16*: 66–75.

Klein DC, Moore RY, Reppert SM (1991): *Suprachiasmatic nucleus: the mind's clock*. New York, Oxford University Press.

Klerman EB, Rimmer DW, Dijk DJ, Kronauer RE, Rizzo IIIJF, Czeisler CA (1998): Nonphotic entrainment of the human circadian pacemaker. *Am J Physiol 274*: R991–R996.

Kuroda H, Fukushima M, Nakai M, Katayama T, Murukami N (1997): Daily wheel running activity modifies the period of free-running rhythm in rats via intergeniculate leaflet. *Physiol Behav 61*: 633–637.

Marchant EG, Mistlberger RE (1996): Entrainment and phase shifting of circadian rhythms in mice by forced treadmill running. *Physiol Behav 60*: 657–663.

Marchant EG, Watson NV, Mistlberger RE (1997): Both neuropeptide Y and serotonin are necessary for entrainment of circadian rhythms in mice by daily treadmill running schedules. *J Neurosci 17*: 7974–7987.

Marchant EG, Morin LP (1998): The entraining effects of timed wheel access in hamsters. *Soc Res Biol Rhythms Abstract 6*: 130.

Mead S, Ebling FJP, Maywood ES, Humby T, Herbert J, Hastings MH (1992): A nonphotic stimulus causes instantaneous phase advance of the light-entrainable circadian oscillator of the Syrian hamster but does not induces the expression of c-fos in the suprachiasmatic nuclei. *J Neurosci 12*: 2516–2522.

Mistlberger RE (1991): Effects of daily schedules of forced activity on free-running rhythms in the rat. *J Biol Rhythms 6*: 71–80.

Moore RY, Lenn NJ (1972): A retinohypothalamic projection in the rat. *J Comp Neurol 146*: 1–14.

Morin LP (1994): The circadian visual system. *Brain Res 647*: 102–127.

Mrosovsky N, Salmon PA (1987): A behavioural method for accelerating re-entrainment of rhythms to new light-dark cycles. *Nature 330*: 372–373.

Mrosovsky N (1988): Phase response curves for social entrainment. *J Comp Physiol 59*: 1005–1010.

Mrosovsky N, Reebs SG, Honrado GI, Salmon PA (1989): Behavioural entrainment of circadian rhythms. *Experientia 45*: 696–702.

Mrosovsky N (1991): Double pulse experiments with nonphotic and photic phase shifting stimuli. *J Biol Rhythms 6*: 167–179.

Mrosovsky N (1993): $\tau$ changes after single nonphotic events. *Chronobiol Int 10*: 271–276.

Mrosovsky N (1996): Locomotor activity and non-photic influences on circadian clocks. *Biol Rev 71*: 343–372.

Pickard GE (1982): The afferent connections of the suprachiasmatic nucleus of the golden hamster with emphasis on the retinohypothalamic projection. *J Comp Neurol 211*: 65–83.

Pratt BL, Goldman BD (1986): Environmental influences upon circadian periodicity of Syrian hamsters. *Physiol Behav 36*: 91–95.

Reebs SG, Mrosovsky N (1989): Effects of induced wheel running on the circadian activity rhythms of Syrian hamsters: entrainment and phase response curve. *J Biol Rhythms 4*: 39–48.

Reebs SG, Lavery RJ, Mrosovsky N (1989): Running activity mediates the phase advancing effects of dark pulse on hamster circadian rhythms. *J Comp Physiol 165*: 11–818.

Rusak B, Mistleberger RE, Losier B, Jones CH (1989): Daily hoarding opportunity entrains the pacemaker for hamster activity rhythms. *J Comp Physiol A 164*: 165–171.

Sharma VK, Singaravel M, Subbaraj R, Chandrashekaran MK (1999): Timely administration of melatonin accelerates re-entrainment to phase shifted light dark cycles in the field mouse *Mus booduga*. *Chronobiol Int 16*: 163–170.

Sharma VK (2003): Period responses to zeitgeber signals stabilize circadian clocks during entrainment. *Chronobiol Int 20*: 389–404.

Sharma VK, Chidambaram R (2003): Entrainment of locomotor activity rhythm to periodic injections of melatonin in the nocturnal field mouse *Mus booduga*. *J Exp Zool 296A*: 30–37.

Sharma VK, Chidambaram R, Yadunandam AK (2003): Melatonin enhances the phase shifting effects of light in the nocturnal field mouse *Mus booduga*. *J Exp Zool 297A*: 160–68.

Singarvel M, Sharma VK, Subbaraj R, Nair NG (1996): Chronobiotic effect of melatonin following phase shift of light/dark cycles on the locomotor activity rhythm of the field mouse *Mus booduga*. *J Biosci 21*: 789–795.

Smith RD, Turek FW, Takahashi JS (1992): Two families of phase response curves characterizes the resetting of the hamster circadian clock. *Am J Physiol 262*: R1149–R1153.

Sumova A, Maywood ES, Selvage D, Ebling FJP, Hastings MH (1996): Serotonergic antagonists impair arousal-induced phase shifts of the circadian system of the Syrian hamster. *Brain Res 709*: 88–96.

Turek FW, Losse-Olson S (1986): A Benzodiazepine used in the treatment of insomnia phase-shifts the mammalian circadian clock. *Nature 321*: 167–168.

Turek FW, Van Reeth O (1988): Altering the mammalian circadian *clock with the short-acting benzodiazepine triazolam. Trends Neurosci 11*: 535–541.

Van Reeth O, Turek FW (1987): Adaptation of circadian rhythmicity to shift in light-dark cycle accelerated by a benzodiazepine. *Am J Physiol 253*: R204–R207.

Van Reeth O, Turek FW (1989): Administering triazolam on a circadian basis entrains the activity rhythm of hamsters. *Am J Physiol 256*: R639–R645.

Van Reeth O, Sturis J, Byrne MM, Blackman JD, L'Hermite-Baleriaux M, Leproult R, Oliner C, Refetoff S, Turek FW, Van Cauter E (1994): Nocturnal exercise phase delays circadian rhythms of melatonin and thyrotropin secretion in normal men. *Am J Physiol 266*: E964–E974.

Weinert D, Weiß T (1997): A nonlinear interrelationship between period length and the amount of activity-age dependent changes. *Biol Rhythm Res 28*: 105–120.

Weisgerber D, Redlin U, Mrosovsky N (1997): Lengthening of circadian period in hamster by novelty-induced wheel running. *Physiol Behav 62*: 759–765.

Wickland C, Turek FW (1991): Phase shifting effects of acute increase in activity on circadian locomotor rhythms in hamsters. *Am J Physiol 261*: R1109–R1117.

Yamada N, Shimoda K, Ohi K, Takahashi K, Takahashi S (1986): Changes in period of free-running rhythms determined by two different tools in blinded rats. *Physiol Behav 36*: 357–362.

Yamada N, Shimoda K, Ohi K, Takahashi S, Takahashi K (1988): Free-access to a running wheel shortens the period of free-running rhythm in blinded rats. *Physiol Behav 42*: 87–91.

Yamada N, Shimoda K, Ohi K, Takahashi K, Takahashi S (1990): Relationship between free-running period and motor activity in blinded rats. *Brain Res Bull 25*: 115–119.