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ORIGINAL RESEARCH

Weekday-Weekend Shifts of Light/Dark Regimen Extend Sleep and Lifespan of *Drosophila melanogaster*

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Purpose: Daytime workers/learners report reduction of sleep duration on weekdays. However, this reduction can be partially compensated by an advance in circadian sleep timing caused by an advance in the phase of the circadian clock. This advance occurs in response to an advance in the 24-h pattern of exposure to light emitted by natural and artificial light sources. It is difficult to separate health impacts of weekday sleep reduction and weekday-weekend shifts in the circadian phase in human studies. Therefore, an animal model can be used to clarify the impact of these shifts. A limited number of previous studies on insects and rodents have yielded conflicting results. We used a *Drosophila* model to document the effects of weekday-weekend shifts in the dark-light cycle on sleep, development, and survival.

Methods: Locomotor activity and sleep, fecundity, rate of imago emergence, and longevity were assessed under two pairs of control and experimental conditions in two generations of flies from two *melanogaster* strains with faster and slower speeds of the aging process, Harwich and Canton-S, respectively.

Results: At least in one of these two pairs with the 4-h weekday-weekend shifts in the light/dark regimen as experimental condition, significant differences from the control condition were documented for the levels of locomotor activity and sleep, rate of development from eggs to imago, and longevity. In this experimental condition, two generations of Canton-S but not Harwich flies slept longer on weekdays than the control flies. Moreover, flies of both strains developed longer to imago stage and lived longer than the control flies in this experimental condition. Overall, any of such differences between conditions in lifespan and sleep were beneficial for the experimental flies.

Conclusion: It is unlikely that the light-induced 4-h weekday-weekend shifts in circadian timing are detrimental to survival, reproductive health, and sleep in *Drosophila melanogaster*.

Plain Language Summary: Weekday sleep duration is reduced in daytime workers/learners. This reduction can be partially compensated by an advance in circadian sleep timing caused by an advance in the phase of the circadian clock in response to an advance in the 24-h pattern of exposure to light emitted by natural and artificial light sources. Both weekday sleep reduction and weekday-weekend shifts in the circadian phase have been proposed to negatively impact health. However, it is difficult to separate their impacts in human studies. Therefore, an animal model can be used to clarify the impact of weekday-weekend shifts of the circadian sleep phase on sleep, reproductive health, and survival. We examined the effects of weekday-weekend shifts in the 24-h light/dark schedule on locomotor activity and sleep, fecundity, rate of development from eggs to imago, and longevity of fruit flies from two strains with faster and slower speeds of the aging process (Harwich and Canton-S, respectively). The results suggest that the daily levels of locomotor activity and sleep, development from eggs to imago, and longevity can be significantly changed in response to the 4-h weekday-weekend shifts in the light/dark regimen. Paradoxically, such changes are beneficial for weekday sleep duration in one of the strains (Canton-S) and for rate of development and lifespans in both strains. We concluded that, at least in the absence of additional stressors, the light-induced the 4-h weekday-weekend shifts of the circadian phase seem not to be detrimental to fly's sleep, reproductive health, and survival.

Keywords: animal model, fruit fly, life span, fertility, sleep duration, sleep-wake regulating processes

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Introduction

The sleep times of daytime workers/learners can be at odds with the times determined by their endogenous processes of sleep-wake regulation. Wittmann et al[1] coined the term "social jetlag" to highlight the conflict of the biological clocks with the so-called "social clocks". To arrive at their work/study location in the morning, daytime workers/learners can be forced to wake up on weekdays much earlier than after *ad lib* sleep on weekends. If risetimes after *ad lib* sleep are expected to be set by the biological clocks, the preceding and following weekday risetimes appear to be determined by the social clocks, that is, by the typical demands of the work-rest schedule of daytime workers/learners. Since biological clocks prevent such a large advance of weekday bedtimes as an advance of weekday risetimes dictated by social clocks, weekday sleep duration is reduced in daytime workers/learners.[1] We previously showed that such a reduction in weekday sleep duration is partially compensated for by an advance in circadian sleep timing caused by an advance in the phase of biological clocks in response to an advance in the 24-h cycle of exposure to light emitted by natural and artificial light sources.[2,3]

The problem of human studies is the difficulty of separation of the two possible negative health impacts of early weekday wakeups. Both weekday sleep reduction and weekday-weekend shifts of the circadian phase can be hypothesized to compromise the health of daytime workers/learners.[2,3] Therefore, an animal model can be used to clarify whether one of these possible negative effects, weekday-weekend shifts in the circadian phase in response to shifts in the light/dark regimen, can compromise health and lifespan. In a pioneering study published by Aschoff et al in 1971,[4] weekly 6-h shifts in the light/dark cycle significantly decreased the survival time of blowflies. However, only a limited number of recent studies on insects and rodents have provided conflicting results. In particular, contradictory results have been reported in studies using rodent models. Nelson and Halberg[5] subjected mice to weekly 12-h shifts of the daily light-dark schedule beginning at 7, 20, or 52 weeks of age and continued until death. A statistically significant effect of such shifting of the light/dark schedule on survival time was not found in these mice, regardless of when the shifting began.

Results of several studies suggested that, although the negative health effects were found, these were either older or unhealthy rodents. Penev et al[6] reported that, in cardiomyopathic hamsters, chronic reversal of the external light-dark cycle at weekly intervals resulted in a significant decrease in survival time. Davidson and co-workers[7] exposed young and old mice to a 6-h advance or delay of the light/dark cycle once a week and found that phase-advancing the light/dark cycle hastens the death of old but not young mice. In a study by Castanon-Cervantes et al[8] a magnified response to endotoxins was observed after four consecutive weekly 6-h phase advances in the light/dark schedule. In addition, Takasu and other[9] showed that fertility decreased in middle-aged female mice when they were phase-shifted back and forth once a week for several weeks. However, this loss was reversed by rearing them for a few weeks in light/dark regimes adjusted to their endogenous periods.

Drosophila models have also provided limited evidence of an association between circadian phase shifts and mortality. Johnson and co-workers[10] reported that a weekly 6 h phase advance and delay had no influence on *Drosophila* lifespan. In contrast, Boomgarden et al[11] found a reduced lifespan in flies subjected to daily 4-h phase delays in the light/dark schedule. However, the light/dark schedule in this study was changed daily, whereas in the aforementioned studies, it was changed weekly. In fact, flies permanently lived under a 28-h (non-circadian) light/dark cycle in this study rather than under the mostly 24-h cycle tested in other studies.

Negative effects of weekly shifts of light regimen on cognitive, physiological and circadian network functioning were also reported. Roach and other[12] found that a 3-h delay in the timing of lights on Friday night and then 3-h advance back 3 h on Sunday night did not disrupt *Drosophila* sleep but impaired short-term memory and shifted temperature preference to a higher level. Moreover, weekend light shifts in the study of Nave and co-workers[13] evoked persistent circadian neural network desynchrony in *Drosophila*. However, the effects of desynchronization on mortality and health have not been tested in their study.

Consequently, we examined whether weekday-weekend shifts of the 24-h light/dark schedule compromise sleep, reproductive health, and longevity of flies from two strains of *Drosophila melanogaster* that differ in the speed of the aging process (Harwich and Canton-S). In the first experimental condition, only time of morning light exposure was shifted ahead on weekdays that is resulted in a longer photoperiod on weekdays. In the second experimental condition, the photoperiod was not changed in the result of the 4-h shift of the 24-h cycle of light exposure. Considering the

conflicting literature reviewed above, we hypothesized that the health impact of these weekly shifts in lighting conditions could be either non-significant, as reported in some of reviewed studies,[4,10] or negative, as reported in some of other reviewed studies.[5–9] In particular, we hypothesized to find the following effects compromising health and survival of flies in the experimental conditions: a reduction of amount of sleep on weekdays, a reduction of fecundity, a faster development from eggs to imago, and a shorter lifespan.

Several previously reported studies suggested that negative health effects of weekly shifts of light regimens were significant in older or unhealthy animals[6,7,9] rather than in younger or healthy animals. Therefore, we used an opportunity provided by *Drosophila melanogaster* model to test these effects in younger and older flies from two strains of *Drosophila melanogaster*. Flies from one of these strains (Canton-S) are healthier than flies from another strain (Harwich), and these two strains can serve as an animal model of faster and slower aging processes (see[14] for previously reported results on the differences between flies from these two strains in levels locomotor activity and sleep, fecundity, rate of development from egg to imago, and longevity).

Materials and Methods

Flies From Two Strains

Flies of old laboratory strains of *Drosophila melanogaster*, Harwich, and Canton-S, were obtained in 1990 from the Obninsk Drosophila collection and in 1996 from L. Z. Kaidanov. Starting from these dates, flies were cultivated at the Institute of Cytology and Genetics at room temperature (22–25°C) and under a natural indoor photoperiod of Novosibirsk (light between 7:30 and 19:30 during equinoxes in the absence of any additional artificial illumination in the room).

In a previous publication,[14] we demonstrated that these two strains could be used as multicellular eukaryote models to study the effects of individual differences in the speed of aging processes on the physiological responses to various environmental factors under different light/dark regimens. The particular differences between Harwich and Canton-S include a reduced level of locomotor activity, larger amount of sleep, faster rate of development, smaller body weight, lower concentration of each of the two main sugars, lower fecundity, and shorter lifespan.[14]

Light-Dark Regimens

Flies were tested for fecundity, locomotor activity, and longevity under either control or experimental conditions. Two pairs of control and experimental lighting conditions were chosen for such a testing. Light was scheduled either on 2 or 4 h earlier at the end of Sunday night, and light delayed on either 2 or 4 either only in the morning or in the morning and evening, respectively, at the end of Friday night in either the first or the second experimental condition, respectively. The light regimen was always the same for the control and experimental conditions during weekends (Saturday and Sunday), but it was always different for five weekdays (from Monday to Friday).

In more details, the first pair of control and experimental regimens were as follows: for two weekends, the 14-h photoperiod with light between 7:00 and 21:00, and for five weekdays, either the same or 16-h photoperiod, respectively, with light starting at 5:00 for the experimental flies and at 7:00 for the control flies. In other words, the experimental flies were additionally subjected to the 2-h earlier "risetimes" on weekdays. The second pair of control and experimental regimens was as follows: for two weekends, the 12-h photoperiod with light between 7:00 and 19:00, and for five weekdays, the same 12-h photoperiod, but with light started at 3:00 for the experimental flies and at 7:00 for the control flies. In other words, the experimental flies were subjected to 4-h shifts of "rise- and bedtimes" on weekdays.

The offspring of flies kept under the second pair of regimens during the testing period were maintained under the same control and experimental regimens, ie, without and with shifting light exposure back and forth, once a week.

Thus, the flies of the first generation were or were not subjected to either the 2-h shift of morning light on weekdays (7:00–7:00 and 5:00–7:00, respectively) or the 4-h shift of the light/dark cycle on weekdays (7:00–7:00 and 3:00–7:00, respectively). Similar to their parents subjected to the second pair of control and experimental light regimens, the flies of the second generation were or were not subjected to this 4-h shift of the light/dark cycle on weekdays (7:00–7:00 and 3:00–7:00, respectively).

All methods applied in the present study for the collection and analysis of data have been described in detail in several publications.[14–18]

Prior to testing flies of the first generation from each of the two strains, parent flies were kept in standard vials at room temperature (22–25°C) and under a near-natural photoperiod that was established from the windows of a laboratory room in the absence of additional artificial illumination (light between 7:30 and 19:30 during equinoxes). Flies were moved to either control or experimental lighting condition at age 4 days. The experiments were conducted in a ТСО-1.80 СПУ thermostat (the chamber volume is 80 L) at temperature 22°-23° C. The experimental and control light regimens were established by using a timer FinePower ST-A0120 to switch a lamp (LED lamp Wolta 25Y75R7GX53 7W) on and off. This lamp has spectrum 3000K and intensity 150–200 lux, as measured with a lux meter ТКА-ПКМ 08.

Recording of Locomotor Activity and Calculation of Daily Amount of Sleep

To measure locomotor activity, male flies were collected from a tube with five pairs of one-week-old parents after laying eggs with females for one day. Flies of the second generation obtained from flies kept under the second pair of control and experimental regimens were kept under the same control and experimental regimens, respectively. DAMS (Drosophila Activity Monitoring System; "Trikinetics", Waltham, MA, USA) and its software package (www.trikinetics.com, accessed on August 12, 2025) were used to monitor locomotor activity.[19,20] Locomotor activity was initially expressed as the number of beam breaks in one-min bins, and the initial counts of locomotor activity were then used to quantify sleep events in accordance with the Donelson et al.[21] In total, the analysis of locomotor activity and sleep included data on almost 300 individual flies, 155 and 144 male flies were recorded under the first (Table S2 and Figures S3 and S4) and second pair of experimental regimens (Table 1 and Figures 1A and B, S1A–1D–S9A–9D, S10A, S10B, S11A, and S11B). The parent flies were kept under a natural regimen and then transferred under either a control or experimental regimen after testing their fecundity. Offspring of these flies were born under either control or experimental regimen and maintained thereafter under the same control or experimental regimen, before and during testing of their fecundity and locomotor activity.

Table 1 Daily Levels of Locomotor Activity and Sleep on Weekdays: Effect of the 4-h Shift of Light/Dark Cycle

rANOVA	Regimen	Control: 7:00–7:00			Experimental: 3:00–7:00			Main effect		
#, N, Measure	Strain	Mean	−95%	+95%	Mean	−95%	+95%	*F*	*df*	η^2
Age 4 days (Parents)										
#1, 32, Activity	Harwich	10.8	7.7	13.9	12.1	9.0	15.2	0.4	1/30	0.012
#2, 32, Activity	Canton-S	29.5	25.6	33.3	19.3	15.4	23.1	14.9***	1/30	0.332
#3, 32, Sleep	Harwich	21.8	20.1	23.6	22.8	21.1	24.6	0.7	1/30	0.022
#4, 32, Sleep	Canton-S	14.4	13.3	15.6	18.6	17.4	19.8	26.7***	1/30	0.471
Age 4 or 5 weeks (Parents)										
#5, 52, Activity	Harwich	14.6	12.2	17.3	20.7	18.1	23.3	11.1**	1/50	0.181
#6, 52, Activity	Canton-S	26.3	23.1	29.5	13.7	10.5	16.9	31.6***	1/50	0.387
#7, 52, Sleep	Harwich	20.0	18.7	21.3	19.1	17.7	20.4	1.3	1/50	0.020
#8, 52, Sleep	Canton-S	20.2	19.2	21.1	23.2	22.2	24.2	20.0***	1/50	0.286
Age 7 days (Offspring)										
#9, 28, Activity	Harwich	8.8	5.8	11.6	8.8	6.3	11.3	0.0	1/26	0.000
#10, 28, Activity	Canton-S	28.5	23.7	33.3	15.2	10.8	19.7	17.1***	1/26	0.397
#11, 28, Sleep	Harwich	23.7	21.9	25.5	23.5	21.9	25.0	0.0	1/26	0.001
#12, 28, Sleep	Canton-S	15.1	13.0	17.1	20.3	18.3	22.2	14.4***	1/26	0.357

(*Continued*)

Table 1 (Continued).

rANOVA	Regimen	Control: 7:00–7:00			Experimental: 3:00–7:00			Main effect		
#, N, Measure	Strain	Mean	−95%	+95%	Mean	−95%	+95%	*F*	*df*	η^2
Age 9 days (Offspring)										
#13, 32, Activity	Harwich	8.5	6.8	10.3	10.3	8.6	12.1	2.5	1/30	0.071
#14, 32, Activity	Canton-S	33.1	27.3	38.8	20.1	14.4	25.8	10.7**	1/30	0.263
#15, 32, Sleep	Harwich	23.6	22.3	24.8	22.1	20.8	23.4	3.0	1/30	0.090
#16, 32, Sleep	Canton-S	15.5	13.6	17.4	19.4	17.5	21.3	9.0**	1/30	0.231

Notes: Results of 16 three-way rANOVAs of locomotor activity and sleep (##1-16) of flies of different ages from two generations (Parents and Offspring) and two strains (Harwich and Canton-S) on 30-min intervals of two weekdays under either control or experimental regimen, either 7:00–7:00 or 3:00–7:00 (ie, either without or with the 4-h shift of the light-dark cycle on weekdays, respectively). Mean and SEM: Regimen-averaged estimate of daily locomotor activity and sleep and its Standard Error. Level of significance $^{**}p < 0.01$ and $^{***}p < 0.001$ for F-ratio; *df*: Degree of freedom for main effect of independent factor Regimen; η^2: Partial Eta Squared.

One-min values were averaged within 30-min intervals for each individual record and further averaged over individual flies to calculate the regimen-averaged curves shown in Figures S1–S9. Since the first full-day interval mainly reflects the habituation process, it was excluded. The following 30-min estimates of locomotor activity and sleep were used for statistical

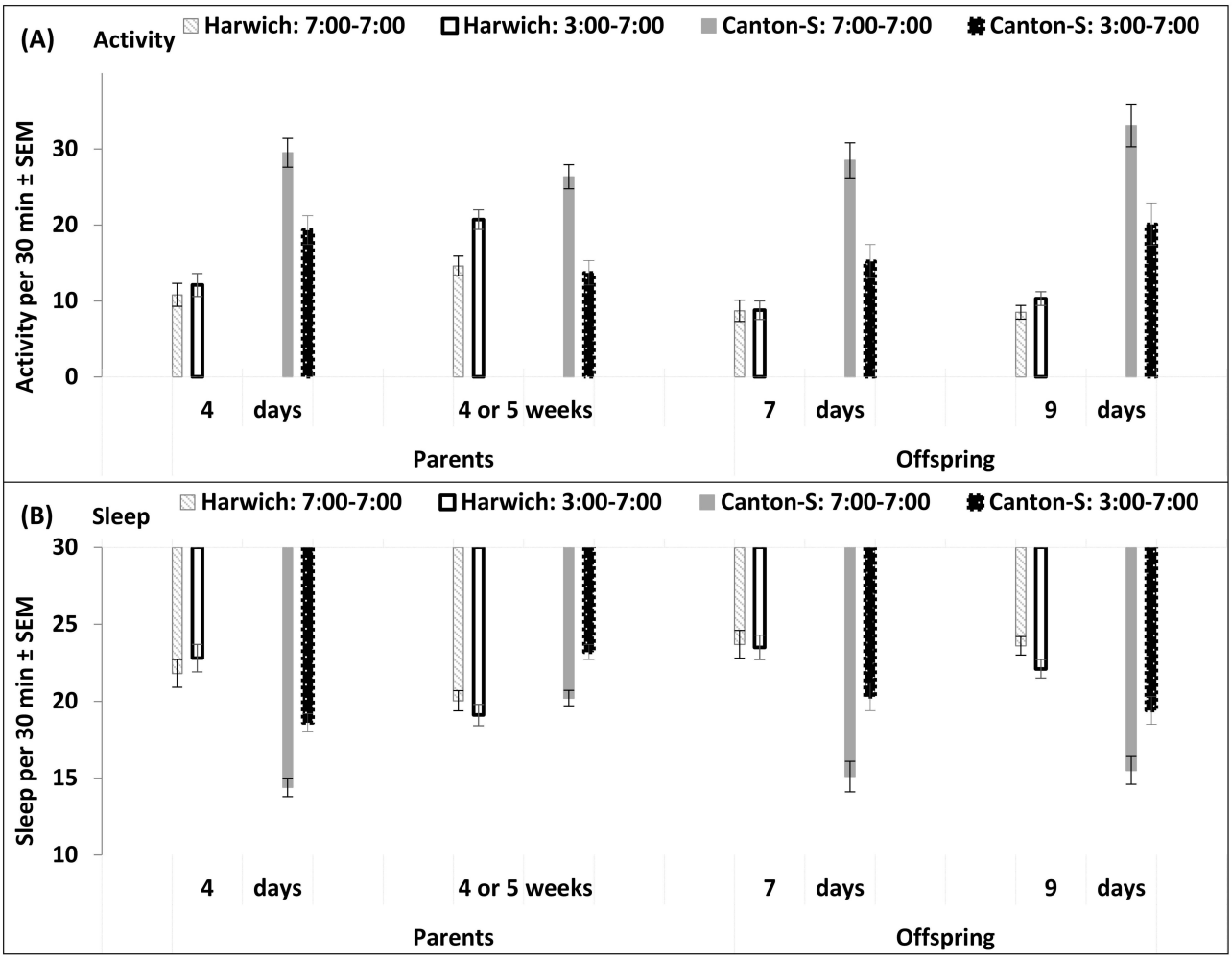

Figure 1 Daily levels of locomotor activity and sleep on weekdays under either control or experimental light/dark regimens. Locomotor activity was measured under either control or experimental regimen, either 7:00–7:00 or 3:00–7:00, that is, either without or with the 4-h shift of the light/dark cycle on weekdays, respectively. Parents and Offspring: Flies under either control or experimental regimen in the first and second generation, respectively. (**A**) Levels of locomotor activity is expressed as the number of beam breaks on 30-min time interval. (**B**). Levels of sleep was conventionally defined as five consecutive minutes in the absence of any locomotor activity. Sleep is expressed as min of sleep within 30-min time interval.

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analyses reported in Tables 1 and S1 and to illustrate the difference between flies under control and experimental conditions (Figures S3–S9, and Tables 1 and S2) and the differences between the ages of old flies (Figures S1 and S2, and Table S1).

Further averaging provided day- and nighttime estimates (Figure S10 and Tables S3 and S4) and daily mean estimates of locomotor activity and sleep (Tables 1, S1 and S2 and Figures S1 and S11).

Testing Fecundity and Delay of Emergence From Eggs to Imago

To test fecundity and to estimate the rate of development of offspring from egg to imago under the control and experimental conditions for each of the two strains, five male and five female flies were kept together in each of the 10 tubes for one day of egg laying. The emerging flies were counted for three consecutive days (Table 2 and Figures 2A–C, S12A–S12C, and S13A–S13C). In total, fecundity was tested in 800 males and 800 females (Table 2). Flies of the first generation were kept under a natural regimen and then transferred under either a control or experimental regimen to test fecundity. Offspring (flies of the second generation) were born under either control or experimental regimen and maintained thereafter under the same control or experimental regimen, before and during testing of fecundity (Table 2).

The following formula was used to calculate delay of emergence named "Delay" in Table 2 and Figures 2C, S12C, and S13C:

$$\text{Delay} = (\text{N} * 1 + \text{N} * 2 + \text{N} * 3)/3 - 1,$$

where N is a number of emerging flies collected in the first, second, and third days of imago collection (1, 2, and 3, respectively; Figures 2A and B, S12A, S12B, S13A, and S12B).

Table 2 Number of Emerging Flies and Delay of Adult Emergence: Effect of the Shifts of Light Exposure

rANOVA	Regimen	Control			Experimental			Main effect		
#, N, Measure	Strain	Mean	−95%	+95%	Mean	−95%	+95%	*F*	*df*	η^2
		Regimen: 7:00–7:00			5:00–7:00			Parents		
#1, 40, Number	Harwich	13.1	11.9	14.3	14.0	12.8	15.2	1.3	1/36	0.033
#2, 40, Number	Canton-S	14.9	13.5	16.3	14.6	13.2	16.0	0.1	1/36	0.003
#3, 40, Delay	Harwich	0.74	0.68	0.80	0.69	0.63	0.75	1.2	1/36	0.031
#4, 40, Delay	Canton-S	1.18	1.10	1.25	1.10	1.02	1.17	2.5	1/36	0.066
		Regimen: 7:00–7:00			3:00–7:00			Parents		
#5, 40, Number	Harwich	7.9	7.1	8.6	8.2	7.4	8.9	0.3	1/36	0.009
#6, 40, Number	Canton-S	11.0	9.9	12.2	9.3	8.1	10.5	4.4*	1/36	0.109
#7, 40, Delay	Harwich	0.30	0.21	0.38	0.73	0.65	0.82	52.8***	1/36	0.594
#8, 40, Delay	Canton-S	0.77	0.66	0.89	1.35	1.23	1.47	49.3***	1/36	0.578
		Regimen: 7:00–7:00			3:00–7:00			Offspring		
#9, 80, Number	Harwich	7.2	6.4	7.9	9.9	9.2	10.6	29.2***	1/76	0.277
#10, 80, Number	Canton-S	12.3	11.2	13.5	10.9	9.8	12.1	2.8	1/76	0.036
#11, 80, Delay	Harwich	0.91	0.77	1.05	0.72	0.58	0.86	3.6	1/76	0.045
#12, 80, Delay	Canton-S	1.12	1.00	1.24	1.27	1.15	1.40	3.1	1/76	0.039

Notes: Results of 6 four-way and 6 three-way rANOVAs (##1-12) of the number of offspring (emerging flies) and delay of adult emergence for each of the two strains (Harwich and Canton-S). Two factors in addition to either Regimen and Day (three emerging days) or only Regimen, respectively, were younger and older ages of reproducing flies and sex of their offspring. N: Number of tubes with five pairs of parent flies in each tube; 7:00–7:00: Control regimen; 5:00–7:00 or 3:00–7:00: Experimental regimen (either with the 2-h shift of morning light exposure on weekdays or with a 4-h shift of the light/dark cycle on weekdays, respectively). Parents and Offspring: Flies under either control or experimental regimen in the first and second generation, respectively. Mean and −95%, +95%: Regimen-and day-averaged estimate of Mean number of emerging flies or regimen-averaged estimate of Delay and 95% confident intervals of the Mean; *df*: Degree of freedom for main effect of independent factor Regimen. Level of significance for F-ratio: *$p < 0.05$ and ***$p < 0.001$ for F-ratio for main effect of factor Regimen and its interaction with Day, η^2: Partial Eta.

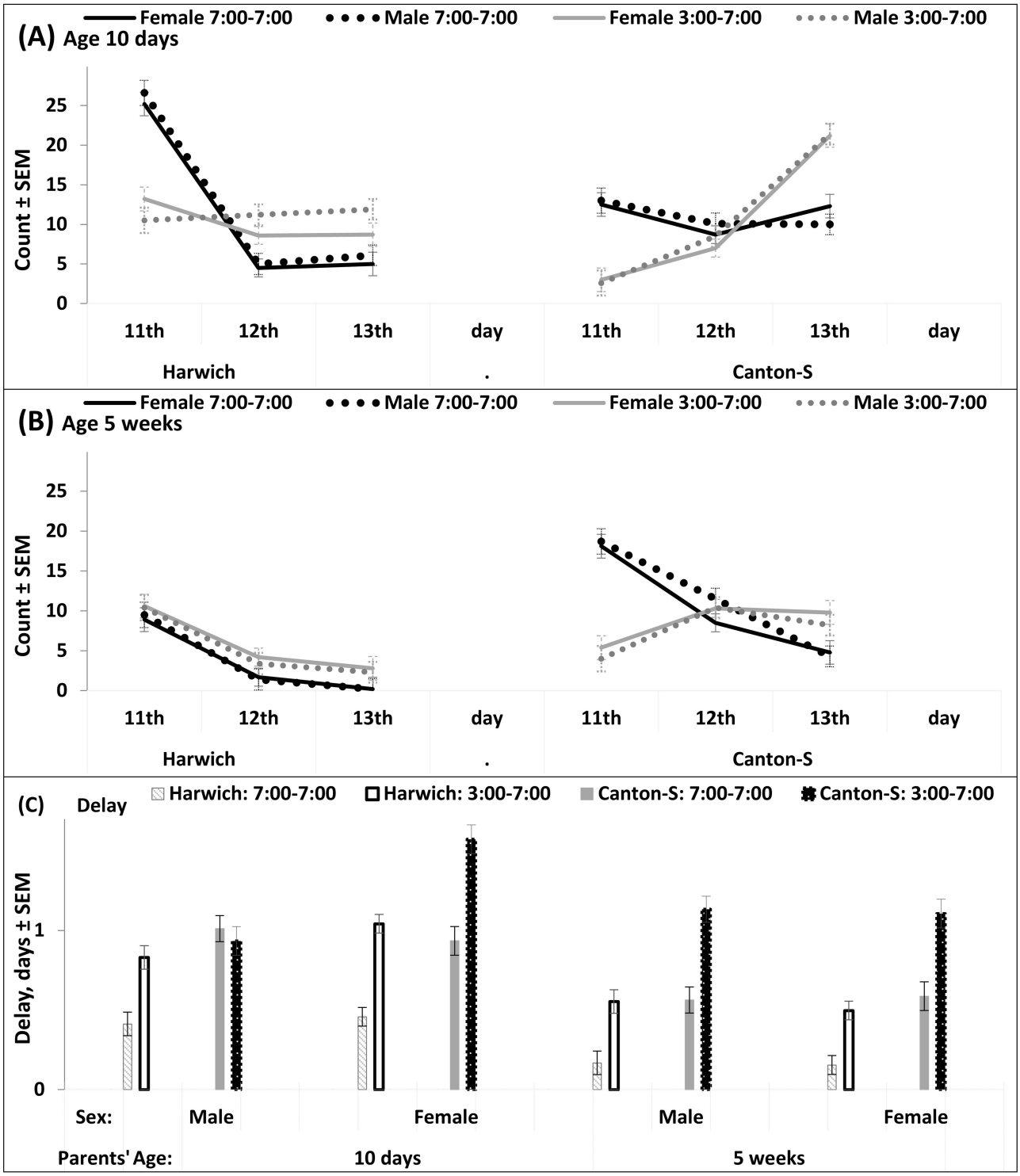

Figure 2 Number of offspring from parents subjected to either control or experimental light/dark regimens. Number of offspring (emerging flies) born in 40 tubes, with 5 pairs of parent flies in each tube. (**A** and **B**): Age of the parent flies was 10 days and 5 weeks, respectively. Flies (100 flies of each age from each of two strains, Harwich or Canton-S) were kept under a natural regimen and then transferred under either control or experimental regimen, either 7:00–7:00 or 3:00–7:00, that is, either without or with a 4-h shift of the light/dark cycle on weekdays, respectively. (**C**) Delay of adult emergence (see Methods).

Testing Longevity

To compare the survival curves of flies from each of the two strains (Table 3 and Figure 3A–C), 10 flies were kept under control and experimental conditions in each of the 10 tubes. Food vials were replaced at least twice per week and, after the replacement of food vials, dead flies were removed and counted. In total, 1200 flies of both sexes were tested for the

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Table 3 Mean Survival Time: Effect of the Shifts of Light Exposure

Regimen	Control				Experimental				χ^2			Exp(*B*)
Test#, N, strain	Mean	SEM	−95%	+95%	Mean	SEM	−95%	+95%	LR	GW	T-W	HR
	7:00–7:00				5:00–7:00				Parents			
#1, 200, Harwich	46.33	1.23	43.92	48.75	44.24	1.98	40.36	48.12	0.7	1.1	0.1	0.898
#2, 200, Canton-S	47.29	1.52	44.31	50.28	55.58	1.53	52.58	58.58	22.0***	19.1***	21.1***	0.543***
	7:00–7:00				3:00–7:00				Parents			
#3, 200, Harwich	51.83	1.52	48.85	54.81	58.25	1.53	55.26	61.24	10.9**	9.2**	10.2**	0.499**
#4, 200, Canton-S	61.55	1.54	58.54	64.56	65.26	1.44	62.44	68.09	6.1*	3.5	4.4*	0.738*
	7:00–7:00				3:00–7:00				Offspring			
#5, 200, Harwich	39.78	1.10	37.63	41.93	41.86	1.23	39.44	44.28	3.5	2.9	3.2	0.601
#6, 200, Canton-S	48.81	1.44	45.99	51.63	47.30	1.46	44.43	50.17	0.0	0.8	0.4	1.025

Notes: Mean survival time and results of 6 tests of equality of survival distributions (##1-6) of flies from the two strains (Harwich and Canton-S) under control and experimental regimens. 7:00–7:00: Control regimen. Either 5:00–7:00 or 3:00–7:00: Experimental regimen, either with the 2-h shift of morning light exposure on weekdays or with a 4-h shift of the light/dark cycle on weekdays, respectively. Parents and Offspring: Flies under either control or experimental regimen in the first and second generation, respectively. Mean, SEM and −95%, +95%: Regimen-averaged estimate of Mean time of survival, Standard Error of this Mean, and 95% confident intervals. The Kaplan-Meier method was applied to test equality of survival distributions for the experimental and control conditions. Results of three statistical tests examining whether the survival functions are equal: Log Rank (Mantel-Cox), Breslow (Generalized Wilcoxon), and Tarone-Ware (LR, GW and T-W, respectively), Additional analysis: Cox regression, output labeled as Exp(B) for hazard ratio (HR). Level of significance for chi-square (χ^2) of the Kaplan-Meier test and *B* of the Cox regression: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

survival rate under either the control or experimental light/dark regimen (Table 3). Parent flies were kept under a natural regimen before testing survival time of 100 flies of certain age from each of the two strains under either control or experimental regimen. Offspring of parents were always kept under the same either control or experimental regimens before and during testing survival time (Table 3).

Statistical Analysis

The Statistical Package for the Social Sciences ($SPSS_{23}$, IBM, Armonk, NY, USA) was used for the statistical analyses aimed on testing the effect of experimental regimen in each of the two strains, Harwich and Canton-S (Tables 1–3, and S1–S4). We applied repeated measure ANOVAs (rANOVAs) to test significance of the effect of experimental regimen on locomotor activity, sleep, fecundity, and delay of emergence.

Particularly, rANOVAs were run to calculate daily levels of locomotor activity and sleep (Tables 1 and S1) and to test significance of interaction of independent factor "Regimen" with a repeated measure, eg, with "30 min interval" (Tables S1, and Figure S1, S2 and S9). Additionally, daytime and nighttime levels on weekdays were analyzed with rANOVAs (Figure S10 and Tables S3 and S4). Degrees of freedom were corrected using the Greenhouse–Geisser correction, controlling for type 1 errors associated with the violation of the sphericity assumption, but the original degrees of freedom are reported in Table S4.

Moreover, we applied rANOVAs to calculate regimen-averaged number of offspring per emergence day and delay of emergence (Table 2 and Figures 2, S12 and S13).

The Kaplan–Meier estimator and Cox regression were applied for comparison of experimental and control conditions on the survival rate (Table 3). Kaplan–Meier curves (Figure 3) were compared using the log-rank (Mantel–Cox) test (LR) and two additional tests, Breslow (Generalized Wilcoxon), and Tarone-Ware (GW and T-W, respectively). Additionally, the Cox regression analysis was performed to report hazard rate (HR) for an experimental condition (HR; Table 3).

Results

Replicability of the Pattern of Locomotor Activity and Sleep

Figures S1 and S2 illustrate the time courses of locomotor activity and sleep, respectively, in old flies with one-week difference in age (4 and 5 weeks). The results of the analysis of activity and sleep given in Table S1 suggest that the

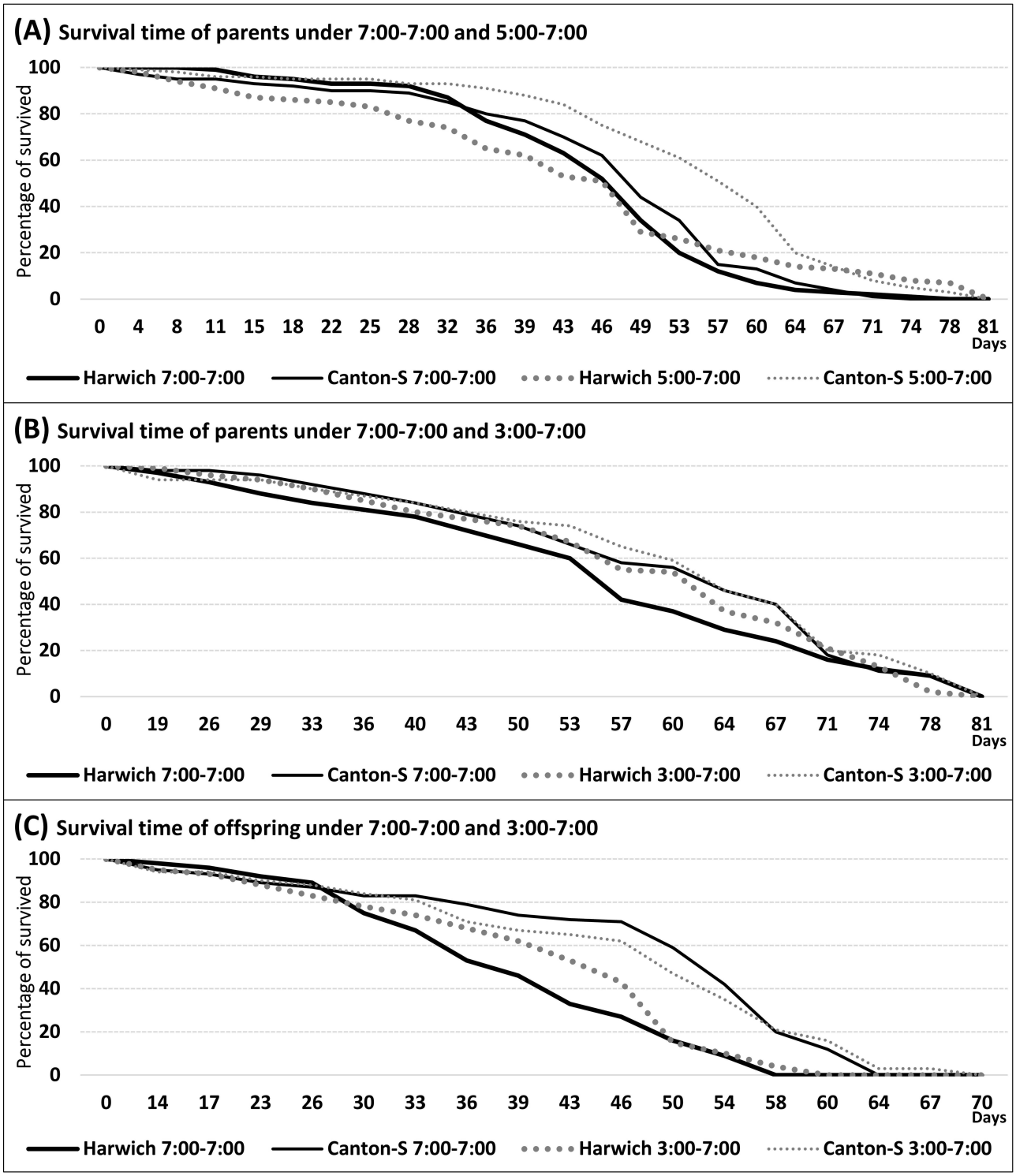

Figure 3 Survival of flies subjected to either control or experimental light/dark regimens. (**A** and **B**) Survival of 100 flies of each of two strains (Harwich and Canton-S) was tested under control vs experimental regimen, that is, without vs with a 2-h shift of morning light exposure on weekdays (A: 7:00–7:00 vs 5:00–7:00) or without vs with a 4-h shift of the light/dark cycle on weekdays (**B** and **C**) 7:00–7:00 vs 3:00–7:00). Parents (**A** and **B**) and Offspring (**C**) Flies were kept under either control or experimental regimen in the first and second generation, respectively. Median time ± SEM in control vs experimental condition was 49.00±0.95 vs 49.00±1.32 and 49.00±0.83 vs 60.00 ±1.63 for Harwich and Canton-S, respectively in (**A**), 57.00±1.37 vs 64.00±1.75 and 67.00±1.44 vs 71.00±1.25 for Harwich and Canton-S, respectively in (**B**), and 39.00±1.47 vs 46.00±1.82 and 54.00±1.16 vs 50.00±1.48 for Harwich and Canton-S, respectively in (**C**).

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circadian patterns of locomotor activity and sleep are replicable in flies of similar age (ie, when flies from each of the two strains are studied at one-week interval in identical control and experimental conditions). Therefore, data from flies of similar age were merged (eg, Figures 1, S3B, S3D, S4B, S4D, S5B, S6B, S7B, S8B, and S9–S11) for further analyses (eg, Tables 1, S2–S4).

Effects of the First and Second Experimental Condition on Locomotor Activity and Sleep

Figures S3 and S4 illustrate the effects of the first experimental condition on the time courses of locomotor activity and sleep, respectively, on weekdays the control condition. The levels of activity and sleep were changed both in the morning and evening hours. These changes, however, did not lead to change in daily means of locomotor activity and sleep reported in Table S2 and illustrated in Figure S11.

Figures S5–S9 illustrate the effects of the second experimental condition on the time courses of locomotor activity and sleep during weekdays and weekends. They show that, also the 24-h light/dark cycle remained unshifted on weekends, the 4-h weekday shift of the 24-h light/dark cycle modified these time courses not only on weekdays but also on weekends. For instance, biphasic daily rhythm was more clearly evident in the experimental flies both weekdays and weekends (Figures S5–S9). Thus, the 24-h weekday patterns of locomotor activity and sleep in the experimental flies did not fully resemble the 24-h weekday patterns of the control flies delayed for 4 h. Results of comparison of daytime and nighttime levels of activity and sleep illustrated in Figure S10 and reported in Tables S3 and S4 confirmed such a modifying effect of the weekend-weekday shifts of phase of the 24-h cycle of light exposure on the 24-h rhythms of locomotor activity and sleep. Any of the observed differences between experimental and control flies in the diurnal patterns of activity and sleep persisted over the generations (Figures S5–S9).

Moreover, Canton-S flies showed significant changes in daily levels of locomotor activity and sleep in any age and any generation (Table 1 and Figure 1). This strain always responded to the experimental regimen by a decrease in the daily level of locomotor activity and by an increase in the daily amount of sleep on weekdays. In contrast, daily level of sleep in Harwich did not increase in the experimental condition (Table 1 and Figure 1).

Effects of the Experimental Conditions on Fecundity, Rate of Development, and Longevity

Fecundity in the first experimental condition was not significantly different from that of the control condition (Table 2, upper part, and Figure S9), but flies from the Canton-S strain had a longer lifespan under these experimental conditions than in the control condition (Table 3, upper part, and Figure 3A).

In the second experimental condition, flies of both strains had a longer lifespan than flies in the control condition (Table 3, middle panel, and Figure 3B). Moreover, they developed slower under these experimental conditions, as indicated by the significant delay in their emergence (Table 2 and Figure 2C). Although this delay was not observed in offspring (Figure S10), offspring from the Harwich strain showed significantly decreased fecundity (Table 2, lower part, and Figure S10) and a shorter lifespan in the control than experimental condition (Table 3, lower part, and Figure 3C).

Overall, when the tested measures of sleep, reproductive health, and mortality in the experimental condition were significantly different from those in the control condition, the difference was in favor of the experimental conditions (Tables 1–3).

Discussion

It is difficult to separate the two hypothetical negative health impacts of early weekday wakeups: either weekday sleep reduction, light-induced weekday-weekend shifts of the circadian phase, or both can be blamed for compromising health of daytime workers/learners.[22] A *Drosophila* model can be used to clarify whether light-induced weekday-weekend shifts of the circadian phase, rather than weekday sleep insufficiency, are detrimental to reproductive health and survival. In the present study, we examined the effects of weekday-weekend shifts of the 24-h light/dark schedule on sleep, fecundity, and longevity of flies from two strains of *Drosophila melanogaster* at different speeds of the aging process. In light of

conflicting results in the literature, we hypothesized that these shifts would have either negative or non-significant effects on the sleep, reproductive health, and mortality of flies. The results showed that the daily levels and circadian patterns of locomotor activity and sleep, fecundity, rate of development from egg to imago, and longevity of *Drosophila* can be significantly changed in response to the 4-h weekday-weekend shifts of the light/dark regimen. However, they also showed that, in contrast to the study hypothesis, these changes are mostly beneficial for sleep, reproductive health, and survival in *Drosophila*. These are novel results allowing the conclusion that weekday sleep reduction, rather than light-induced weekday-weekend shifts in the circadian phase in response to shifts in the 24-h light/dark schedule, can explain the negative health impacts of early weekday wakeups. This conclusion of *Drosophila* study is in line with the result of our previous human study that showed a link of reduced self-perceived health of university students with weekday sleep insufficiency rather than with a large weekday-weekend gap in the circadian sleep timing.[22]

Interestingly, the present results suggest that, despite the full identity of the weekend light/dark cycle in the control and experimental conditions, the 24-h weekday patterns of locomotor activity and sleep in the experimental flies did not fully resemble the 24-h weekday patterns of the control flies delayed for 4 h. The reorganization of the 24-h pattern of sleep under the second experimental condition resulted in an increase in the amount of weekday sleep in Canton-S. It has to be noted, however, that we tested sleep only in male flies that sleep more than female flies during the daytime in constant darkness.[23,24] Therefore, it is necessary to examine whether the sleep lengthening effect that is reliably observed in Canton-S is sex-specific.

It is also necessary to point at the paradoxical impacts of shifts in the 24-h pattern of illumination on sleep duration and timing in response to weekday-weekend shifts of wakeups in daytime workers/learners. On the one hand, artificial light sources can be blamed for the unhealthy delay of the circadian phase experienced by people living in modern post-industrial societies on free days.[25,26] On the other hand, these sources provide the possibility of a partial reduction of this delay after early wakeups on weekdays by exposing them to light immediately after early awakening.[2,3,27] Indeed, experimental human studies have confirmed the substantial influence of risetime, likely via associated morning light exposure, on the timing of the human circadian clocks.[28–30] Moreover, the findings of these experimental studies were additionally supported by the results of "natural experiments" on weekday shifts of risetimes relative to weekend risetimes.[31–34] Therefore, the analysis of sleep times on weekdays and weekends reported by daytime workers/learners suggests that weekday sleep duration is reduced after early weekday wakeups, but this reduction is partially compensated by an advance in the circadian sleep timing caused by an advance in the phase of the circadian clocks in response to an advance in exposure to the 24-h cycle of darkness and light emitted by natural and artificial light sources.[2,3] Recently, we showed that an additional advance in weekday rise time is equal to the sum of an additional advance in the circadian sleep phase and additional sleep loss on weekdays.[2,3] Therefore, the results suggesting an increase of amount of sleep on weekdays in Canton-S also can have practical implications. The previously proposed light interventions[35–37] can be used to change the ratio between the two terms of this equation. Appropriately timed exposure to artificial and natural bright light sources can increase the contribution of the advancing shift in the circadian sleep phase at the expense of weekday sleep loss. For instance, earlier and more extensive morning light exposure combined with earlier termination and less intensive evening light exposure may be recommended to reduce weekday sleep loss. Moreover, the reorganization of the 24-h pattern of sleep after earlier wake-ups can be made by, for instance, allowing daytime naps for reduction of the negative health impact of insufficiency of nighttime sleep on weekdays.

Under the first experimental condition, a large shift of the circadian phase is expected after two-h advance of morning light. However, this advance lead to increase of the length of photoperiod on two hours on weekdays in this experimental condition. It is known that adaptation of *Drosophila melanogaster* to long photoperiod at higher latitudes is limited by the inability of flies of this fruit fly species to delay a position of evening peak of activity relative to the position of morning peak for more than 16-h interval.[15,38–40] Since such delay required under the first experimental condition is not larger than 16 h, an extension of photoperiod to 16 h cannot compromise the functioning of the circadian clock. Therefore, it cannot, in turn, compromise health of *Drosophila melanogaster*. Indeed, mostly non-significant differences between the control and experimental flies were found. The only significant difference was beneficial for health of flies in the experimental condition (ie, under this condition, flies from one strain, Canton-S, was found to live longer).

Overall, the present study does not provide evidence for the negative health impact of weekday-weekend shifts of the light/dark regimen. In daytime workers/learners, a reduction in weekday sleep duration can lead to sleep insufficiency, but this reduction is partially compensated by an advance in the circadian sleep timing caused by an advance in the circadian phase of the body clock in response to an advance in exposure to the 24-h cycle of light emitted by natural and artificial light sources. By using a Drosophila model, we found that such weekday-weekend shifts in the circadian phase can further compromise health in addition to insufficient sleep.

Several limitations of the present experiments require acknowledgement. The molecular and physiological mechanisms underlying the observed benefits were not tested in the present study and might be explored in future research. This is a laboratory study on old wild-type strains that was not designed to account for the possible differences between control and experimental flies in their response to additional typical stresses that are common to flies living in natural settings. Although these shifts can positively rather than negatively influence the health and survival of animals in the absence of such stressors, they can magnify the disturbing actions of these stressors. Some animal studies mentioned in the Introduction vote for such a possibility. For instance, rapid shifts in the light/dark cycle can evoke circadian neural network desynchrony[13] that can lead to a magnified response to endotoxin,[8] impairment of short-term memory, and a shift in temperature preference,[12] etc., especially in unhealthy[6] and old organisms.[7] Therefore, future studies on *Drosophila melanogaster* model can be aimed at evaluating the interaction of the effects of weekday-weekend shifts of the light/dark regimen with the responses of an organism to typical stressors for this species, such as resisting Wolbachia infection and the efficacy of its pharmacological treatment, responses to exposure to hot and cold temperatures, and feeding with low caloric and hyperhydrate-reach food. Moreover, the literature pointed at the effects of the weekend-weekend shifts on memory, immune responses, metabolic state, neuronal circadian networks, etc. that were not tested in the present study. Therefore, future studies can be also aimed on elaboration of these effects.

Conclusion

Here, we examined the effects of weekday-weekend shifts of the 24-h light/dark schedule on locomotor activity, sleep, fecundity, rate of development from egg to imago, and longevity of two *Drosophila* strains. The results showed that each of the tested parameters - the daily levels and circadian patterns of locomotor activity, sleep, fecundity, rate of development from eggs to imago, and longevity - can be significantly changed in response to the 4-h weekday-weekend shifts in the light/dark regimen. The novelty of these findings was in documenting positive rather than negative effects of these shifts on the sleep duration, reproductive health, and longevity of *Drosophila*. Therefore, we showed that, in the absence of additional stressors, sleep, reproductive health, and longevity cannot be compromised by light-induced weekday-weekend shifts of the circadian timing.

Institutional Review Board Statement

This study has been approved by Bioethics Commission of the Institute of Cytology and Genetics, approval number 185 (23.09.24).

Abbreviations

7:00-7:00 and 5:00-7:00, the 0-h and 2-h weekday shift of morning light, respectively; 7:00-7:00 and 3:00-7:00, the 0-h and 4-h weekday shift of the 24-h light/dark cycle, respectively; LR, log-rank (Mantel–Cox) test; GW, Breslow (Generalized Wilcoxon) test; T-W, Tarone-Ware test; HR, hazard rate.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the first author upon reasonable request.

Author Contributions

Conceptualization, L.P.Z. and A.A.P.; methodology, L.P.Z., D.V.P., and A.A.P.; software, D.V.P. and A.A.P.; validation, A.A.P.; investigation, L.P.Z.; resources, L.P.Z.; writing—original draft preparation, A.A.P.; writing—review and editing,

A.A.P., L.P.Z., and D.V.P. All authors gave final approval of the version to be published, agreed on the journal to which the article was submitted, and agreed to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work. During the preparation of this work the authors did not use AI.

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