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CIRCADIAN BIOLOGICAL CHARACTERISTICS AFTER SHIFTING SLEEP AND MEAL TIMES

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A b s t r a c t

In order to examine differences among individuals and among variables related to the rate of shift of the circadian system, nine male students were studied for 72 h under controlled physical environmental conditions. During this 3-day test, they were subjected to a 12-hour shift in the times of sleep and meals. Differences in the rate of shift from day 1 to day 3 were observed for blood pressure and urinary cortisol, norepinephrine and dopamine, but not for other urinary variables or for heart rate, temperature and body weight. Inter-individual differences in the rate and/or direction of adjustment were seen primarily for blood pressure and heart rate. The experimental design used in this study may detect differences in the suitability of a subject for shift-work.

K e y w o r d s

Circadian rhythm, Blood pressure, Sleep changes, Meal intake changes

INTRODUCTION

During most of our lives, the majority of components in a spectrum of physiological rhythms are locked into a spectrum of environmental cycles, with synchronised frequencies acceptable to (and resonant with) the organism *(1).* The spectrum of multifrequency rhythms is one element of the time structure, or chronome, of a given variable, with trends as a second element, and with both rhythms and trends superposed on probabilistic and other chaos, as a third element *(2, 3).* Environmental factors, synchronisers or influencers, such as sleep and meal schedules, may be manipulated so that rhythms are shifted in response to new schedules *(1-7).* Thus, one finds phenomena such as asymmetries (e.g., a delay of rhythms faster than an advance or vice versa) and polarities (e.g., some rhythms advance while others delay in the same organism, responding to the same synchroniser shift or the same physiological rhythms may advance in one individual and may delay in another in response to the same conditions) (*8-10).* Rhythms persist under certain conditions of isolation from society *(8).*

MATERIALS AND METHODS

Nine male students were studied for 72 h under controlled physical environmental conditions. Their characteristics (mean ± SD) are summarised in *Table 1*. Sleep hours were from 00:00 to 07:00 on the first day and from 12:00 to 19:00 on the third day; they did not sleep on the second day. They ate meals at 12:30, 18:30 and 08:00 on the first day, at 12:30, 18:30, 00:30 and 06:30 on the second day, and at 20:00, 00:30 and 06:30 on the third day. Snacks were consumed at 15:30 and 21:30 on the first day, at 15:30, 21:30, 03:30 and 09:30 on the second day, and at 03:30 and 09:30 on the third day.

The subjects measured their oral temperature every hour. Blood pressure and heart rate were measured every 15 minutes with an automatic device (ABPM-630, Nippon Colin Ltd., Komaki, Japan). Body weight was measured every 3 h after urine collection. Urine samples were frozen for the determination of cortisol, catecholamines and other examinations. The data were analysed by curve-fitting with linear least-square rhythmometry and the Halberg cosinor analysis (*8, 11, 12*).

RESULTS

In the whole group, the circadian rhythm was demonstrated with statistical significance in all variables except for urinary K^+ during the first day, and urinary Na^+ and Cl^- on the third day. On the sleepless day (day 2), the circadian rhythm was statistically significant at the 5% probability level for 12 of the 17 variables investigated (*Table 2).* The circadian acrophase was least affected by the shift in schedule for oral temperature and urinary cortisol values that varied by no more than 36° and 23 °C or 2.4 and 1.5 h, respectively. The largest and fastest changes in acrophase were found for heart rate, blood pressure and dopamine that increased from 36.8 to 107.2 μg/h on average from day 1 to day 2 *(Table 2).* A statistically significant reduction in the circadian amplitude of blood pressure from day 1 to day 2 was observed in association with the sleepless night (*Table 2*).

Table 1

Data characterising the nine subjects investigated in the study

Characteristic	Mean ± SD	Range
Age (years)	21.8 ± 0.8	20.6 — 22.8
Height (cm)	171.0 ± 4.4	165.0 — 177.7
Weight (kg)*	62.7 ± 4.3	54.0 — 69.0
BMI (kg/m^2)	21.5 ± 1.5	18.8 — 23.7
% Fat (%)	13.5 ± 2.0	10.7 — 16.2
Oral temperature (°C)*	35.8 ± 0.3	35.3 — 36.1
Systolic BP (mm Hg)	121 ± 4	112 — 125
Diastolic BP (mm Hg)	75 ± 3	69 — 79
Heart rate (beats/min)	74 ± 11	59 — 92

BMI, body mass index; BP, blood pressure; *, measured at 7:00 after the first sleep.

A number of urinary variables, such as volume, Cl^-, Na^+ and K^+, showed an intermediate shift that was smaller than shift in blood pressure, creatinine, dopamine or norepinephrine, but greater than that in oral temperature and urinary cortisol. Urinary epinephrine showed a larger shift on day 2 than on day 3.

The results of the group as a whole could not be applied to individuals, particularly when day 2 or day 3 values were compared with day 1 values. In three of nine subjects, the day 2 values for blood pressure showed only a small shift as compared to day 1 values. In these subjects, a larger shift occurred on day 3 and had a slow initial and a faster subsequent stage. In the remaining six subjects, the situation was opposite. Inter-individual differences in adjustment to the shifts were established by one-way analyses of variance (ANOVA) for systolic and mean arterial pressure. These inter-individual differences were only of borderline statistical significance for diastolic blood pressure, urinary cortisol, urinary creatinine and heart rate, and were not statistically significant for oral temperature, body weight, urine volume, urinary Na^+, K^+, Ca^{++}, glucose, noradrenaline, adrenaline or dopamine.

DISCUSSION

As reported earlier (*8, 13*), some variables (e.g., body core temperature or cortisol) shift slowly, while others (e.g., blood pressure and heart rate) shift rapidly. For the latter variables, the shift was immediately seen but, by curve-fitting procedures, the shift, even when fast on the average, was found to occur gradually. Moreover, there were inter-individual differences in the rate and/or direction of shift with a slow initial phase found in three and fast initial stage in six subjects when systolic and diastolic pressure was measured.

These results are in keeping with earlier findings. The response to a schedule change by 6 or more hours was found to be incomplete after one day, with residual adjustment taking several additional days, as shown by the analyses of data from published graphs (*14*). More specifically, the cosinor fit of a 24-hour cosine curve showed that the 95% confidence interval of the acrophase did not cover the target phase within a day but it did so by the third day. Earlier chronobiometric studies (*9, 15)* also suggested an incomplete adjustment on the first day after a shift in schedule. Inter-individual differences in the rate of adjustment have also been observed in the experimental laboratory (*16*) as well as in shift-workers (*17, 18*).

The experimental design used herein may detect differences in the suitability of a subject for shift-work within 3 days by mere monitoring of blood pressure. If the shift rate was studied in relation to mental state and performance, it could be possible to test whether those who shift rapidly are better adjusters and more apt to perform well on certain shift work schedules. Of particular interest will be the adjustability of subjects in terms of psychological and performance variables

Table 2

Circadian rhythm characteristics and sleep schedule in nine male students.
Results of the population-mean analysis

Day 1 (sleep from 00:00 to 07:00)

Variable (unit)	PR	*P*	MESOR ± SE	Amplitude **(95% CI)**	Acrophase **(95% CI)**
SBP (mm Hg)	31	<0.001	115.7 ± 1.2	10.9 (6.4, 15.4)	-239°(-231,-251)
MAP (mm Hg)	26	<0.001	86.8 ± 1.1	8.9 (5.2, 12.9)	-235°(-228, -251)
DBP (mm Hg)	34	<0.001	65.6 ± 1.2	8.3 (5.6, 11.1)	-232°(-223, -247)
HR (beats/min)	39	<0.001	71.3 ± 1.3	12.2 (7.9, 16.7)	-241°(-226, -252)
Oral temp. (°C)	61	0.001	36.60 ± 0.07	0.44 (0.21, 0.67)	-283°(-273, -299)
Body weight (kg)	51	<0.001	62.64 ± 1.45	0.27 (0.18, 0.40)	-359°(-316, -25)
Urine:					
Volume (ml/h)	56	0.002	39.5 ± 2.3	15.4 (6.8, 24.1)	-216°(-197, -227)
Cortisol (µg/h)	54	<0.001	3.22 ± 0.23	1.93 (1.07, 3.00)	-154°(-124, -200)
Glucose (mg/dl)	41	0.035	4.22 ± 0.96	1.54 (0.08, 4.80)	-230°(-200, -7)
Creatinine (mg/h)	54	<0.001	70.2 ± 1.9	4.5 (2.8, 6.6)	-251°(-214, -273)
Cl^- (mEq/h)	55	0.005	8.7 ± 0.8	3.3 (1.2, 5.4)	-190°(-169, -219)
Na^+ (mEq/h)	56	0.002	8.9 ± 0.8	3.2 (1.3, 5.3)	-214°(-196, -256)
K^+ (mEq/h)	57	0.186	2.19 ± 0.23	0.41	-199°
Ca^{++} (mEq/h)	54	<0.001	0.68 ± 0.06	0.35 (0.28, 0.42)	-179°(-160, -197)
E (µg/h)	90	<0.001	0.81 ± 0.08	0.59 (0.31, 0.89)	-262°(-249, -285)
NE (µg/h)	73	<0.001	5.1 ± 0.4	1.0 (0.7, 1.3)	-256°(-236, -274)
Dopamine (µg/h)	48	<0.001	36.8 ± 1.9	6.6 (4.4, 9.1)	-280°(-252, -316)

Day 2 (no sleep)

Variable (unit)	PR	*P*	MESOR ± SE	Amplitude **(95% CI)**	Acrophase **(95% CI)**
SBP (mm Hg)	10	0.077	119.3 ± 1.8	1.6	-36°
MAP (mm Hg)	10	0.053	90.0 ± 1.7	2.4	-50°
DBP (mm Hg)	11	0.005	69.0 ± 1.6	2.1 (0.8, 4.0)	-58°(-348, -100)
HR (beats/min)	4	0.444	71.3 ± 1.2	0.8	-24°
Oral temp. (°C)	50	0.004	36.52 ± 0.05	0.23 (0.09, 0.38)	-303°(-267, -350)
Body weight (kg)	25	<0.001	63.05 ± 1.46	0.20 (0.07, 0.37)	-75°(-9, -89)
Urine:					
Volume (ml/h)	50	0.001	46.4 ± 2.6	16.5 (6.6, 27.2)	-166°(-153, -200)
Cortisol (µg/h)	65	<0.001	3.29 ± 0.13	2.41 (1.60, 3.45)	-161°(-141, -193)
Glucose (mg/dl)	36	0.563	4.78 ± 1.12	0.68	-204°
Creatinine (mg/h)	17	0.459	69.1 ± 1.7	0.4	-274°
Cl^- (mEq/h)	64	0.001	9.1 ± 0.5	3.2 (1.5, 4.9)	-181°(-161, -209)
Na^+ (mEq/h)	56	0.019	9.6 ± 0.5	2.2 (0.4, 4.3)	-187°(-155, -258)
K^+ (mEq/h)	63	0.008	2.31 ± 0.17	0.56 (0.14, 1.08)	-180°(-157, -251)
Ca^{++} (mEq/h)	66	<0.001	0.73 ± 0.07	0.26 (0.18, 0.34)	-152°(-136, -167)
E (µg/h)	37	<0.001	0.93 ± 0.09	0.66 (0.42, 0.91)	-156°(-146, -168)
NE (µg/h)	66	<0.001	10.3 ± 0.4	9.7 (6.6, 12.8)	-96°(-89, -104)
Dopamine (µg/h)	53	<0.001	107.2 ± 5.6	75.0 (50.3, 109.5)	-73°(-41, -89)

Day 3 (sleep from 12:00 to 19:00)

Variable (unit)	PR	P	MESOR ± SE	Amplitude **(95% CI)**	Acrophase **(95% CI)**
SBP (mm Hg)	29	<0.001	115.5 ± 1.4	8.6 (5.8, 11.5)	-48°(-26, -67)
MAP (mm Hg)	22	<0.001	86.1 ± 1.5	7.0 (4.2, 9.8)	-55°(-30, -77)
DBP (mm Hg)	33	<0.001	64.6 ± 1.4	7.7 (5.7, 9.9)	-55°(-36, -71)
HR (beats/min)	27	<0.001	69.5 ± 0.8	8.0 (4.9, 11.1)	-38°(-24, -54)
Oral temp. (°C)	52	0.004	36.43 ± 0.07	0.23 (0.09, 0.38)	-319°(-269, -352)
Body weight (kg)	64	<0.001	62.90 ± 1.40	0.35 (0.27, 0.43)	-136°(-117, -151)
Urine:					
Volume (ml/h)	50	0.009	45.2 ± 2.7	14.7 (4.5, 25.0)	-196°(-149, -244)
Cortisol (μg/h)	69	<0.001	3.65 ± 0.21	2.30 (1.56, 3.21)	-177°(-154, -210)
Glucose (mg/dl)	28	0.020	4.53 ± 0.94	0.56 (0.08, 1.22)	-39°(-7, -139)
Creatinine (mg/h)	32	0.005	68.0 ± 1.8	2.5 (0.9, 4.6)	-27°(-354, -91)
Cl^- (mEq/h)	42	0.074	9.1 ± 0.5	1.8	-167°
Na^+ (mEq/h)	40	0.147	9.7 ± 0.5	1.7	-141°
K^+ (mEq/h)	75	0.039	2.20 ± 0.12	0.47 (0.03, 0.96)	-226°(-161, -312)
Ca^{++} (mEq/h)	29	0.023	0.64 ± 0.06	0.13 (0.02, 0.24)	-158°(-119, -225)
E (μg/h)	54	0.014	0.76 ± 0.08	0.19 (0.03, 0.54)	-304°(-187, -338)
NE (μg/h)	43	0.429	4.6 ± 0.3	0.2	-343°
Dopamine (μg/h)	66	<0.001	58.7 ± 2.6	40.0 (27.4, 52.2)	-2°(-350, -17)

PR, Percentage rhythm (average proportion of overall variance accounted for by the fit of a 24-hour cosine curve to individual data series); P, *P*-value from the zero-amplitude test; MESOR (midline-estimating statistic of rhythm), rhythm-adjusted mean value; Amplitude, measure of the extent of a predictable rhythm within a day; Acrophase, measure of timing of overall high values occurring each day; SE, standard error; CI, confidence interval; SBP, systolic blood pressure; MAP, mean arterial pressure; DBP, diastolic blood pressure; HR, heart rate; E, epinephrine; NE, norepinephrine

when there is polarity in the system, so that some variables delay whereas other variables in the same circadian system advance.

A c k n o w l e d g e m e n t s

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CIRKADIÁNNÍ BIOLOGICKÁ CHARAKTERISTICKA PO PŘESUNU ČASU SPÁNKU A ČASU PŘIJMU POTRAVY

S o u h r n

Abychom zjistili rozdíly v rychlostech posunu cirkadiánního rytmu mezi jedinci a mezi veličinami, devět studentů (mužů) bylo vyšetřováno 72 hodin za stejných fyzikálních podmínek. V průběhu třídenního testu byli studenti vystaveni 12-hodinovému posunu času spánku a jídla.

Rozdíly v rychlosti posunu z dne jedna na den tři jsme pozorovali u krevního tlaku a kortizolu v moči, noradrenalinu a dopaminu, ale ne u ostatních močových exkretů nebo u srdeční frekvence, teploty a tělesné hmotnosti. Inter-individuální rozdíly v rychlosti posunu byly nalezeny u krevního tlaku a srdeční frekvence. Experimentální podoba protokolu použita v této studii by měla odhalit následky posunů činnosti a spánku u pracovníků v třísměnném provozu.

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