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Effects of Stability in Sleep Timing on Sleep Quality, Cognitive
Performance and Mood

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Kathrin Holzer

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1. Abstract

Stability in sleep timing has long thought to be a hallmark of a healthy and successful life. In modern humans the natural solar day has to be synchronized with unnatural economic and social environments. This can often lead to disorganization between the internal circadian system and these environments and as a consequence produce irregularities in sleep timing and a loss of life quality. The present study addressed the question of how humans, who normally living in unstructured time schedules would react to a regulation of their sleep wake pattern in the form of regular bed times. The study focused on subjective and objective sleep parameters collected via sleep logs and actigraphy, vigilance performance changes (PVT, reaction time task), subjective well-being, as measured with Basler rating scales and finally a physiological parameter, urinary cortisol metabolites. Two weeks of undisturbed, irregular sleep schedules and timing were compared with two subsequent weeks of regulated sleep/wake schedules. The results revealed individual differences in the ability to adapt to preset sleep timing. Some subjects had extreme difficulties in conforming to the prescribed sleep wake schedule. In the regulated or regular condition, subjective sleep and awakening quality was either worse or showed no differences compared to the unstructured weeks. Subjects had longer sleep durations and, earlier bed and awakening times during the structured weeks. Vigilance performance did not differ between conditions. The same was true for cortisol metabolites. In the structured experimental phase, sleep/wake timing was negatively related to well-being and mood. During irregular conditions, mood interacted with vigilance performance, whereas under controlled regular conditions performance was more sensitive to subjective awakening quality, which may have been due to the earlier awakening times. These individual differences underline the idea that there may be different types of sensitiveness in an individual's ability to adapt to preset sleep schedules. Here it appears that, with regard to irregular sleep patterns, the data do not support the conclusion that stable sleep/wake patterns always improve life quality. Due to differences in individual types, stability may improve life and performance in one, but may also disturb the same parameters in another. Other factors like age and sex certainly play a role in the adaptation. Youth and gender might compensate an irregular life style easier. More studies concerning stability and instability in sleep timing are needed to unravel these effects.

2. Introduction

One prevailing characteristic of all living organisms is that they have an endogenous temporal organization or internal clock that controls many physiological processes and regulates their interactions with the environment. In light of this, the most pervasive temporal pattern on earth is the 24-hour light dark cycle. Therefore, it is not surprising that investigations of endogenous clocks in living organisms have demonstrated that these 24-hour clocks are ubiquitous in nature (Bünning 1973). In line with their connection to day/night cycles these cycles were defined as circadian rhythms by Halberg et al. (1959). Similar rhythms were also documented in humans (Aschoff 1965; Lewis and Lobban 1957). Being the case, medical research was then confronted with the issue of how modern humans with ancient biological clocks can live in a natural solar day with unnatural, economic and social, temporal environments that are not related to light: Is the endogenous clock that was tuned by evolution a help or hindrance?

Whole institutions have been created to examine these problems (see Dunlap et al. 2004). Nonetheless, the present study was designed to examine one aspect of this in a very simple way: The idea was to empirically compare how the human circadian system behaves in structured or unstructured, temporal environments in the field. Aschoff (1998) had pointed out that the expression of circadian traits in individuals were traits as stable as fingerprints. Both chronotype as discussed below and circadian stability are examples of these traits. If that is the case, it begs the question of how humans with unusual circadian traits fit into the natural or cultural environment. Again, this is a common question in human chronobiological research with no clear answers. This is also the specific theme of the study, for which some background information is necessary to formulate and understand the specific question.

2.1. Circadian rhythms components and entrainment

Circadian clocks are found at every level of organization within an organism. On a cellular level, circadian patterns of gene expression exist in all tissues even though the specific “oscillating” genes differ widely among cell types. The expression of these clock genes controls tissues of the circadian system (Takahashi 1991). One of the first of these genes to be discovered was *per* gene in flies (Konopka and Benzer 1971). Before then, circadian oscillators and pacemakers had been discovered on physiological levels in several biological systems, i.e. the eyes of amphibians, and pineal glands of fishes, reptiles and birds. There appeared to be a hierarchy in the system of oscillators, suboscillators, coupling factors and passive elements (see Dunlap et al. 2004). In mammals and humans this hierarchy has been described and the suprachiasmatic nuclei (SCN) of the anterior hypothalamus were found to be the pacemaker of the other numerous oscillators. Bilateral SCN-lesions often lead to disorganization of the circadian rhythm of physiological and behavioral activity (reviewed in

Nelson 2005). The proof of its pacemaker nature was actually the fact that in hamsters a transplantation of SCN tissue into a SCN-lesioned recipient activated a circadian rhythm that matched that of the donor (Ralph et al. 1990). In humans it has been known for a century that damage of the anterior hypothalamic region next to the optic chiasm was associated with daily sleep-wake and temperature cycle disturbances. The initial reports were published by the Viennese neurologist, Constantin von Economo in 1917. Later it was shown that this area contained an unusual group of neurons and that direct damage to this group, the SCN, lead to disruptions of temperature and sleep wake cycles and impairment of cognitive and behavioral functions. The latter may reflect an inability to coordinate and maintain permanent levels of arousal and/or attention (reviewed in Nelson 2005).

As mentioned above, human sleep/wake cycles are controlled by an endogenous clock. Experiments have shown that the free-running rhythms are stable but different among individuals, varying from 23.5 to 25.5 hours. Individual clock characteristics can be used to separate individuals into so-called chronotypes according to their phase relationship with the natural day: early, moderate or late chronotypes. Very late types are called ‘owls’ and very early types are called ‘larks’ (Roenneberg et al. 2007; 2003). The chronotype and its individual sleep-wake behavior are to an extent genetically determined (Archer et al. 2003; Ebisawa 2007; Katzenberg et al. 1998; Toh et al. 2001), while also showing variation with environmental factors, development and age (Roenneberg et al. 2004).

In humans the light/dark-cycle is an important Zeitgeber to entrain the endogenous circadian rhythm to the 24 hour day, although the importance of non-photic Zeitgebers like nutritional cues and even social Zeitgebers has been proposed for decades (reviewed in Nelson 2005). Studies that investigated the effect of living on non-24 hour days have shown that the ability of entrainment is limited to ranges of 18.5 to 33.5 hours (Engelmann 2007; Eriksen and Kecklund 2007; Schaefer et al. 1979; Wever 1989; Zulley and Knab 2003). Much is known about the mechanisms of light entrainment in mammals: As reviewed by Reppert and Weaver (2002) the SCN receives light information via the retinohypothalamic tract (RHT), a glutamatergic pathway (Pickard 1982), to entrain the clock to a 24 hour day. This is achieved by a recently discovered new photoreceptor, next to rods and cones, in the retina. When this specialized type of ganglion cell is excited by light, it interprets the information with a non rhodopsin type of photopigment ‘melanopsin’ and sends signals directly to the SCN (Berson 2003). A second indirect pathway, the geniculo-hypothalamic tract (GHT), also directs photic information to the SCN. Its neurochemical signal appears to be Neuropeptide Y, which could serve to phase-shift the endogenous circadian system (reviewed in Nelson 2005).

2.2. Sleep and a two process model of sleep regulation

Hands of the clock, like behavior, are controlled by the pacemaker, the oscillators and the interactions with Zeitgebers (Dunlap et al. 2004). These are often quite complex. Sleep wake

cycles are a particular expression of circadian rhythms that have been examined with regard to these interactions. A two-process model of sleep regulation was proposed (see Daan et al. 1984 in Beersma 1998) that attributed the timing of human sleep and wakefulness to an interaction between a homeostatic process, “**S**” and a circadian process, “**C**”. The homeostatic process **S** is a sleep-dependent component. It starts to increase during wakefulness, which can be depicted as exponentially increasing sleep pressure, also called sleep propensity or sleep drive. At a particular threshold, sleep is being initiated. During sleep the homeostatic component declines exponentially until a particular threshold that leads to wakefulness. In a parallel process, these thresholds underlie circadian fluctuations or gating that are determined by the sleep-independent component **C**. This process is controlled by the SCN (Fig.1), so sleep and wake thresholds vary systematically with the time of day, which actually determines the specific placement or phase of sleep in the cycle. The sleep components **S** and **C**, also control the timing of sleep phases. Slow wave or non-REM sleep is coupled to homeostatic sleep pressure, whereas REM sleep is neurologically controlled by the circadian pacemaker in the SCN (reviewed in Beersma 1998).

2.3. The Pacemaker: Suprachiasmatic nuclei and gene expression

The SCN is comprised of approximately 20000 neurons. Most of them are ‘clock cells’, which work in functionally distinct populations (Reppert and Weaver 2002; Welsh et al. 1995). As reviewed by Hastings et al. (2007) the pacemaker is controlled by clock control genes (CCK) that are expressed in clock cells of the SCN. These are responsible for gating effects that, among other things, enable sleep-onset or awakening. This circadian ‘sleep-gate’ should ideally be synchronized with the homeostatic sleep drive and other functions in our brains and bodies. Not surprisingly, clock genes are not only expressed in the SCN, but also in many other brain areas, including the cerebral cortex, hippocampus and cerebellum, as well as in peripheral tissues including the heart, lungs, adrenal glands and the liver (Hastings et al. 2007; Kyriacou and Hastings 2010; Mendoza and Challet 2009; Reppert and Weaver 2002). The SCN communicates with these peripheral organs and clocks directly to synchronize gene expression. Without SCN input or in the case of SCN-lesions these rhythms may continue but are invariably disorganized (reviewed in Hastings et al. 2007; Nelson 2005).

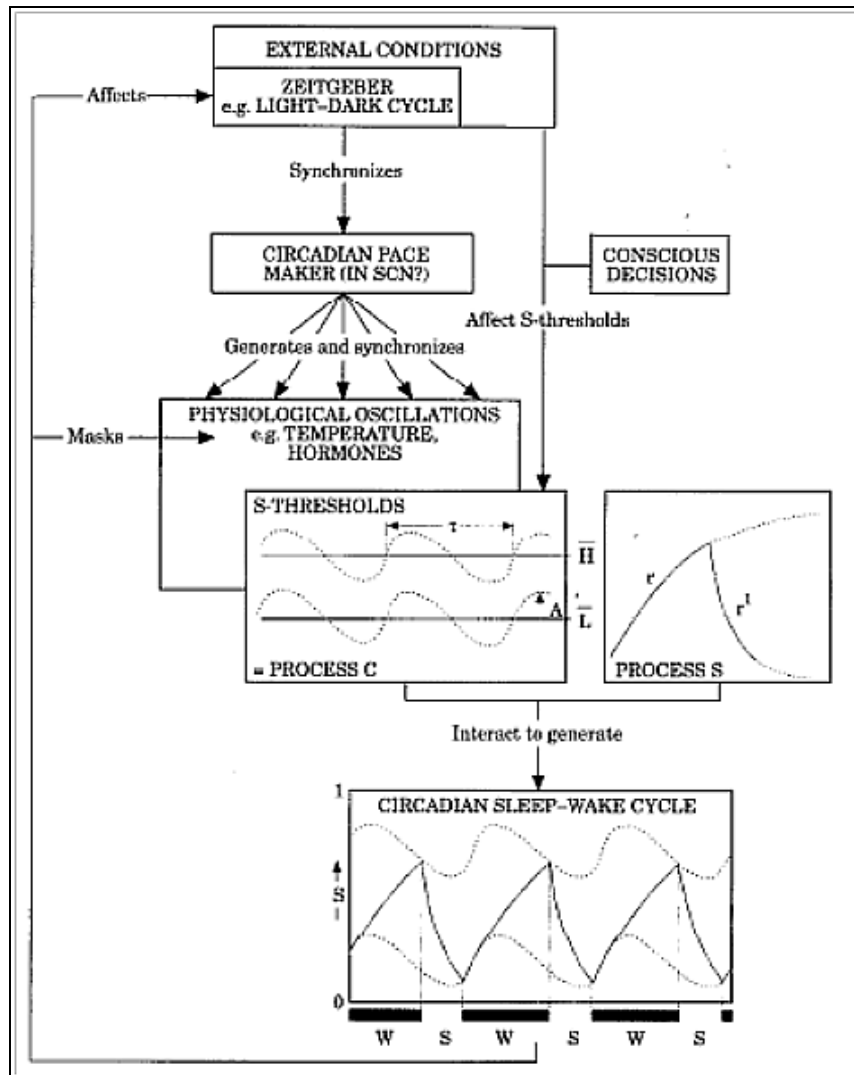


Figure 1: Model of human sleep regulation. A homeostatic process S increases exponentially during wakefulness (sleep drive) and decreases exponentially during sleep. S is limited by two thresholds. The upper threshold determines sleep onset, the lower threshold determines awakening. Both thresholds are controlled by the SCN in the hypothalamus and therefore vary systematically with time of day. The S thresholds run in parallel and are called process C . Other parameters influence the timing by modulating both thresholds, such as conscious decisions, pain, stress while process S remains unaffected. After Beersma 1998.

2.4. Sleep interactions with physiological and psychological functions

As mentioned above, physiological parameters can be directly coupled with process S or C . In humans cortisol begins to increase during sleep and attains its highest daily basal concentration prior to or immediately after awakening (Fig. 2). The secretion of melatonin from the pineal gland is another circadian process related to sleep that occurs only at night (Fig. 2). Its duration of secretion is related to the length of the night and therefore varies with

season. In humans, a short illumination of over 2500 lux at night can suppress melatonin secretion. Melatonin is considered to be a potent Zeitgeber for humans (reviewed in Nelson 2005).

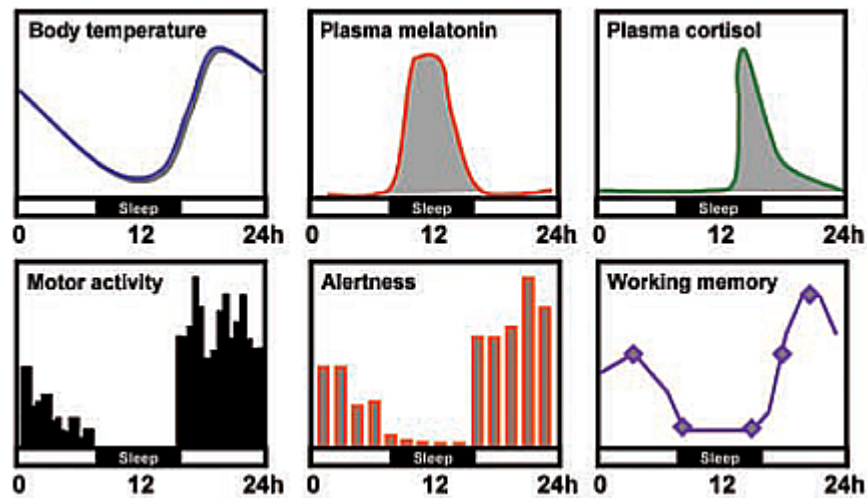


Figure 2: Circadian patterns of physiological (body temperature, plasma melatonin, plasma cortisol) and psychological (motor activity, alertness, working memory) parameters. During sleep body temperature sinks, plasma melatonin rises and cortisol rises around awakening time. Motor activity, alertness and working memory decrease during the night. After Mendoza and Challet 2009.

A lot of studies have investigated the effects of sleep restriction or deprivation on performance and mood. In line with these studies, the duration of sleep has been assumed to be an important factor for neurobehavioral functioning. For example, a chronic restriction of sleep duration, even a relatively moderate one, can produce pronounced cognitive performance deficits in individuals. This is common. In some cases the affected subjects may not even be aware of their problems (Van Dongen et al. 2003). Taub and Berger (1974) investigated the effects of shifting bed-time on performance and mood, when subjects were allowed to maintain their natural sleep-duration of 7 to 8 hours. Following 2 to 4 hour sleep displacements in both directions there were pronounced decreases in performance and mood. within 24-hours The authors suggested that in addition to the factor sleep duration the placement of sleep in the circadian rhythm may have been important to insure efficient psychological and behavioral functions (Taub and Berger 1974). Other studies have investigated the effect of extended sleep on performance and mood (Kamdar et al. 2004; Taub et al. 1971). Kamdar et al. (2004) showed, that sleep extension beyond the habitual sleep duration improved multiple sleep latency test (MSLT) scores, vigilance performance and mood. Despite the influence of sleep on alertness and performance, these psychological parameters also underlie a circadian rhythm that reaches a minimum just after the minimum of body temperature (Fig. 2) (Czeisler et al. 1980; Johnson et al. 1992). Nonetheless, these

variables show free-running periodicities that are often shorter than 24 hours. In an entrained state there is a nadir in the afternoon compared to morning and evening alertness and performance (reviewed in Broughton 1975). In line with this, Dijk et al. (1992) postulated that in addition to sleep inertia, a state of lowered alertness and decrement in performance immediately after awakening (reviewed in Tassi and Muzet 2000), subjective alertness and performance may also be regulated by the interaction of process **S** and **C**.

As reviewed by Kyriacou and Hastings (2010), optimal cognitive performance depends on the temporal alignment between sleep propensity and clock-driven mechanisms. This concept is very important because it can shed light on the effects of shift work or jet lag: They disrupt the circadian clock or its entrainment, which disturbs sleep and leads to physiological and cognitive malaise. Still, there are other context, and experience, dependent factors as Hull et al. (2003) have postulated in their work on human performance that are independent of circadian phase and hours awake. Despite these disclaimers, it is a common belief that stable sleep is a prerequisite for health, happiness and longevity. Many studies have also supported this. For instance, Birchler-Pedros et al. (2009) documented that both the circadian phase and sleep pressure play crucial roles in subjective well-being. The effects of high sleep pressure were invariably negative and women and older subjects showed greater sleep-related mood vulnerability. In addition, sleep/wake patterns were found to change with age in that they became more disrupted while sleep time regularity increased (Kramer et al. 1999). Nonetheless, the sleep related psychic problems were more pronounced in the elderly than in younger adults even though they have more variability in their sleep times. This exemplifies the complexity of sleep regulation and its interactions with health and psychological well-being.

Hallmarks of aging are neurodegeneration that are often linked to sleep and the circadian system. For instance, in Alzheimer's disease (AD) pathological changes are found in the SCN (Stopa et al. 1999), that parallel sleep and mood disorders and disruption of circadian rhythms (Volicer et al. 2001). Even the behavioral symptoms of dementia in patients appear to have an **S** or **C** component in that they peak in the afternoon and evening. One phenomenon is called 'sundowning' (Little et al. 1995). For instance, AD patients show less diurnal activity, higher percentages of nocturnal activity, and later activity and temperature acrophases. Sundowning could then be related to desynchronization in the circadian system as it is paralleled by a phase delay in body temperature (Volicer et al. 2001). On the other hand, restructuring or reinforcement of environmental Zeitgebers has been shown to help patients. Exposure to extended bright light during daytime was found to increase the stability of the sleep/wake cycles in Alzheimer patients and slow down the progress of dementia (Van Someren et al. 1997).

This may also be the case in younger adults. Czeisler et al. (1987) showed, that the intensity of environmental light can modulate the amplitude of circadian rhythms in young adults.

Different rhythms have different light intensity thresholds for entrainment. In low illumination some rhythms may free-run and other rhythms remain entrained, which leads to desynchronization and the concomitant sleep, eating or mood disorders. Seasonal affective disorders (SAD) i.e. those occurring during the darker winter season are associated with dysfunctional timekeeping and may be an expression of this kind of disorder that one finds in the elderly. They are related to both the circadian system and sleep timing while being expressed in all age groups (Lewy 2007; Nelson 2005).

In cases of other types of clinical depressions, two types of sleep disturbances have been reported. As reviewed by Wehr (1990), insomnia and early awakening occur in older, agitated and/or psychotic patients, whereas younger, lethargic, and/or bipolar patients have excessive sleep. Different manipulations of sleep have been shown to modify depression and mania. For instance, in some depressions, REM sleep occurs abnormally early. In these cases a shift in the timing of the sleep schedules of 6 hours from its usual schedule was found to produce improvement in patients. The opposite type of phase-shift, later sleep, in healthy individuals caused depressive symptoms.

If stable sleep-wake patterns are hallmarks of a healthy and successful life (Monk et al. 2003; Zulley and Knab 2003), then why don't we prescribe it for all humans? The problem here is the individuality in the circadian system and the generalities of what the society calls stable sleep. Some studies also maintain on the contrary that sleep disruption or the variability in sleep is not unhealthy and may even be an important component in creative processes (Healey and Runco 2006; Sladeczek and Domino 1985; Stickgold and Walker 2004). The debate is unresolved due to the lack of empirical data.

The present study was designed to add some information to this on-going discussion. The goal was to recruit healthy subjects with unstable or variable sleep habits and to examine the potential effects of stable or unstable periods of sleep on the subjects' mental and physical state. The aim was to test whether stable sleep patterns in individuals could contribute to or detract from an individual's subjective and objective condition and performance.

Specific objectives of the study:

- 1) Examine potential effects of stability and instability in sleep timing on sleep quality in instable sleepers.
- 2) Monitor the effects of regular and irregular schedules of sleep timing on daytime cognitive performance and well-being.
- 3) Compare a physiological marker (cortisol) changes for circadian rhythms during phases of regular or irregular sleep.

3. Material & Methods

3.1. Subjects

Twelve healthy male subjects with a mean age of 24.8 (SD 2.4; range 21-30) participated in the study. The subjects had no history of medical treatment for sleep disorders, which was controlled for by applying the Pittsburgh Sleep Quality Index (score ≤ 5). Subjects were selected that had so-called *indifferent* Chronotypes. These included moderate morning- or evening types, according to the Morningness-Eveningness-Questionnaire by Horne and Oestberg (1976). A third prerequisite for participation was a documented instability or irregularity in their past sleep-wake-patterns. Here subjects were chosen that reported a regular variability in bedtimes of more than 30 minutes in both directions of their “preferred” average sleep onset. Finally, a subject could only participate if they had no temporal restrictions on sleep timing, e.g. work or study schedules. All subjects signed informed consent forms before the beginning of the study.

3.2. Study design

3.2.1. Actigraphy and sleep logs

During the study the participants’ sleep and wake patterns were recorded by actigraphy (Fig. 1) for 4 weeks. For this purpose, an Actiwatch™ was worn on the wrist of the non-dominant hand. In the first two weeks (Condition 1) the subjects maintained their natural irregular sleep-wake-pattern, in the subsequent two weeks (Condition 2) a regular sleep phase was kept from 00:00 to 08:00 (1 subject 23:00 to 07:00). Two subjects switched the sequence of conditions, by starting with Condition 2. To assess the participants’ subjective sleep and awakening quality, a sleep-log was filled out every morning and evening. The evening protocol consisted of bipolar rating scales and questions to assess the subjective mood, effectiveness and health. The morning protocol comprised: a) a self-assessment questionnaire (Saletu et al. 1987) for subjective sleep quality, subjective awakening quality, somatic complaints and any nocturnal disturbances; b) the documentation of bed times (BT, e.g. beginning of bed rest or time of lights out) and the time of awakening (GUT, get up time) for the Actiwatch analyses, the number of awakenings and finally the estimated sleep duration.

3.2.2. Cognitive performance and mood

A Psychomotor Vigilance Task (PVT) was used to assess the subjects’ cognitive performance. It is based on Wilkinson and Houghton's Unprepared Reaction Time Task (1982) and is available as part of the PEBL Test Battery (Mueller 2008). This program can be downloaded from the internet. The subjects installed the program on their own computers. The PVT is a stimulus-response task that is used in sleep-related and circadian studies. The task takes about

15 minutes with 121 stimuli (red dot) appearing in random intervals of 1 and 9 seconds on a black screen. As soon as the stimulus appears the participants have to press the spacebar of their keyboard as quickly as possible. The participants in this study were advised to perform the PVT on the same computer. During each task the subjects had to hold their hand and fingers in a fixed position in front of the spacebar and return to that position after each task. The PVT was performed in each condition on seven mornings and evenings. In the morning, the subjects had to wait for an hour after waking before taking the test. The test also had to be performed in a fasted state. In the evening, a second PVT was performed between 15:00 and 22:00. No preconditions were stipulated for this session.

To assess the subjects' mood and psychological well-being at each test point, a Basler rating scale (Basler Befindlichkeits-Skala, BBS) (Hobi 1985) was filled out immediately before each PVT. The subjects characterized their well-being on 16 bipolar, 7-point scales. These scales were then grouped into the 4 factors: Intra-psychoic Balance (IB), Vitality (VT), Social Extroversion (SE), and Vigilance (VG). Additionally the total sum (SU) of the numerical values was used as a measure for overall well-being.

3.2.3. Cortisol

Paired evening and morning urine samples were collected five times in each condition to measure the levels and diurnal patterns of cortisol metabolites. The samples were collected in plastic scintillation vials, in the evening before getting into bed and the next morning immediately after getting out of bed. They were frozen immediately and stored so until analysis. Urine samples were analyzed with a specific enzyme immunoassay in the laboratory of the Department of Behavioural Biology of the University of Vienna. Urine samples were diluted 1:20 with deionised water and then further diluted to 1:200 with assay buffer. The assay was done using an antibody against cortisol-3-CMO (Palme and Mostl 1997). Cortisol and its metabolites were detected using the cortisol-3-CMO antiserum, a DADOO-biotinylated cortisol-3-CMO label (dilution 1:250) and bovine serum albumin-coupled antibodies (dilution 1:20). The procedure had been described earlier by Palme and Möstl (1997). A Labsystems Multiscan® MCC/340 photometer was used to detect the bound fraction. These values were corrected for urine concentration by monitoring creatinine content. The assay for creatinine was based on the standard Jaffe method in a dilution of 1:20 with deionised water (Slot 1965). With these two data sets cortisol/creatinine-ratios were calculated for each sample and used in the analysis.

A summary of the experimental protocol is shown in Figure 3.

Week 1	Irregular	Actiwatch	Sleep Log	PVT	Paired Urine Samples
Week 2				7 x morning + evening	5 x evening + morning
Week 3	Regular (0:00 - 8:00)			PVT	Paired Urine Samples
Week 4				7 x morning + evening	5 x evening + morning

Figure 3: The experimental protocol: Sleep-wake patterns were monitored in 12 subjects with ActiwatchTM and sleep logs for 4 weeks. Two weeks (Condition 1) were self selected sleep times and in Condition 2 (2 weeks) the subjects were required to keep regular sleep times (0:00-08:00). Psychomotor Vigilance Tests (PVTs) were done on seven of the mornings and evenings in each condition. Paired, evening/morning urine samples were collected on five of the days in each condition.

3.3. Statistical analyses

In order to document the degree of regularity or irregularity in sleep timing the mean deviation from the median ($MD_{\tilde{x}}$) of bed times (lights out, BT) and awakening times (AT) were calculated for each subject in Conditions 1 and 2 using the formula

$$MD_{\tilde{x}} = 1/n \sum |x_i - \tilde{x}|$$

with n representing the number of nights, x_i bed time or awakening time of the individual night and \tilde{x} representing the median of the bed or awakening time of one condition.

In Condition 1 (the irregular condition) an $MD_{\tilde{x}}$ of at least 30 minutes was the threshold for use in the study. In Condition 2 (regular condition) an $MD_{\tilde{x}}$ of 15 minutes or less was a prerequisite for inclusion in the study. Actiwatch data were analysed using the Software ActiwatchTM Sleep Analysis Software 5.32 (Cambridge Neurotechnology, Cambridge, UK). The parameters chosen for analysis were sleep duration (actual sleep time) and fragmentation index (FI). These are treated as so-called objective sleep parameters in the study. Subjective sleep quality (SSQ), subjective awakening quality (SSQ) and subjective sleep efficiency (SSEFF) were used as subjective sleep parameters. SSEFF was the percentage of time the subjects thought they had slept during the time they spent in bed. The parameters were recorded daily in the sleep logs.

Due to non-normal distribution of the data, non-parametric tests were carried out using SPSS 15.0 for Windows. Wilcoxon rank-sum tests were used to compare bed times, awakening times and the sleep parameters in both conditions. Global alpha criterion (α) was set at $P = 0.05$, but because multiple comparisons of mutually correlating values were performed, alpha-

level was corrected using a modified Bonferroni correction after Cross and Chaffin (1982) with the formula $\alpha^* = \alpha / (k - x + 1)$ for every participant separately. k represented the number of tests and x the number of tests fulfilling the global alpha criterion. P-values were considered as tendencies when $\alpha^* < P \leq \alpha$.

During each PVT performance 121 reaction times (RTs) were recorded. In the programme, each RT was classified into one of 4 categories of answer types: Type 1, the spacebar was pressed too early; type 2, correct answer; type 3, lapse (RT ≥ 500 ms); type 4, sleep attack (RT $\geq 30\,000$ ms). Due to the fact, that the subjects performed the PVT on their own computers with their computer-specific system speeds, the reaction types among individuals actually varied with the computer of the subject making cross subject comparisons difficult. In this study we have placed emphasis on the middle types of reactions and the reaction times. For this reason the type 1 and 4 reactions were not directly brought into the analyses. A premature reaction (type 1) was not considered as relevant for the PVT. Type 4 reactions or complete lapses did not occur. In the evaluation, the mean RT for each PVT performance was calculated for the combined type 2 and type 3 answers. To assess performance variability of each PVT session the 10th to 90th interpercentile range (difference between the fastest 10% and slowest 10% RT's) was calculated. A z-transformation of mean PVT and interpercentile range values were used for each subject and their morning and evening tests. Then, a one-way repeated measurement (within subject) ANOVA with z-transformed morning and evening PVT data was calculated using SPSS 15.0 for Windows. Additionally t-tests for paired samples with original PVT data were performed for every subject separately to assess individual differences between conditions and morning and evening performance. Alpha-level was corrected using a modified Bonferroni correction after Cross and Chaffin (1982) as mentioned above.

The relationship between PVT performance and psychological well-being was analysed in one dataset of all individuals for each condition. This was possible using the z-transformed mean PVT results for each test and the normed Basler scores. Spearman's rank correlations were calculated to document the correlative interactions. T-tests on the paired samples were used to compare the differences between the conditions. Finally, in order to assess the relationships among PVT performances and the sleep parameters of the previous nights, Spearman's rank correlations were calculated between z-transformed PVT data and subjective and objective sleep parameters. For the cortisol data, the cortisol/creatinine-ratios were z-transformed for every subject to make them comparable among subjects. Then a one-way repeated measurement (within subject) ANOVA was calculated for z-transformed morning and evening cortisol/creatinine-values to compare Conditions 1 and 2. Additionally z-transformed morning and evening cortisol/creatinine-values were compared in each condition using a t-test for paired samples.

4. Results

4.1. Actigraphy and sleep log data - Basic statistics

The basic statistics of the sleep patterns in the subjects are shown in Table 1. To begin with, the conformance of each subject to the desired sleep-timing schedule was examined. Among the subjects only 10 showed the desired mean deviations from the median of bed times and awakening in Conditions 1 and 2 (Tab. 1). This meant that some subjects failed to produce desired irregularity in normal self-selected sleep patterns while others had difficulty accepting the imposed sleep schedules. In effect, subjects 3 and 8 did not show enough regularity in Condition 2 and were therefore excluded from the comparison of conditions.

Table 1: Mean bed (BT) and awakening (GUT) times of the different subjects in the two conditions. Medians are shown along with the mean deviation of the median (MD) for both parameters. The threshold for inclusion in the analyses were irregularities of over 30 minutes in Condition 1 and less than 15 minutes in Condition 2. The subjects that did not fulfil these prerequisites are shaded grey in the table.

Subject	Condition	Median BT	MD _{BT} (min)	Median GUT	MD _{GUT} (min)
1	1	24,25	32	7,83	31
	2	24,00	0	7,75	9
2	1	25,04	49	10,13	54
	2	24,10	1	8,17	6
3	1	23,00	76	10,50	148
	2	23,25	76	11,00	122
4	1	25,17	67	9,08	23
	2	24,09	12	8,17	6
5	1	26,92	51	11,5	119
	2	23,13	4	7,21	5
6	1	26,25	68	9,71	78
	2	24,00	3	8,33	4
7	1	23,92	62	8,50	63
	2	24,00	5	8,15	9
8	1	27,00	87	10,18	82
	2	24,20	49	8,50	43
9	1	25,92	62	10,67	24
	2	24,04	3	8,00	5
10	1	25,89	69	10,92	45
	2	23,42	8	8,33	15
11	1	24,75	46	8,79	42
	2	24,00	8	8,17	4
12	1	27,00	72	8,50	81
	2	24,42	9	8,42	21

An example of a subject (6) with acceptable changes in sleep timing is shown in Figure 4. In this actogram one can recognize the irregular sleep-wake pattern during the first two weeks (Condition 1) and the regular pattern over the second two weeks (Condition 2).

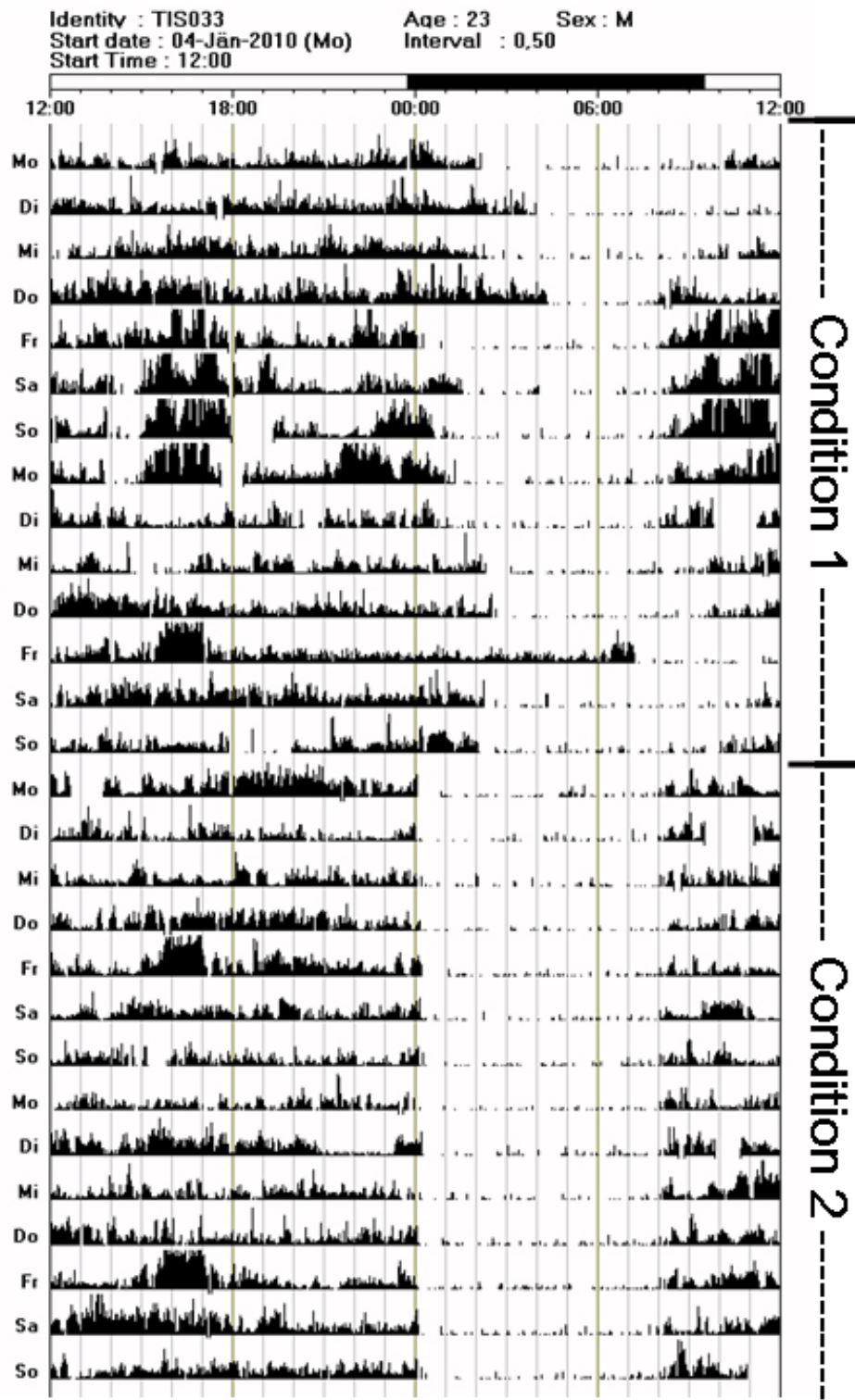


Figure 4: Actogram of subject 6 showing an irregular sleep-wake pattern in the first two weeks (Condition 1) and regular sleep times from 0:00 to 8:00 in the subsequent two weeks (Condition 2).

The mean deviations from the set BT's and GUT's were calculated for each subject in Condition 2 and are shown as a measure of the subjects' ability to maintain a stable sleep/wake pattern (Tab. 2). The variability was high here. Subject 1 went to bed exactly at the set bedtime, but got up on average 17 minutes earlier. Subjects 4, 7 and 9 were able to conform their sleep habits to the set times. Subjects 2 and 5 went to bed and got up slightly later than had been prescribed. Subjects 6, 10 and 11 showed irregular phase shifts in their BT's and GUT's. Subjects 6 and 11 went to bed slightly earlier, but got up later than prescribed. Subject 10 showed the same pattern, although more distinct with earlier BT's and later GUT's. Subject 12 showed a regular phase shift with on average 24 minutes later BTs and GUT's than preset.

Table 2: Phase advance and delays (-) in sleep. Deviations in minutes from the prescribed BT 24:00 (subject 5 23:00) and GUT of 8:00 (subject 5 7:00) in

Subject	Deviation from set time	
	Bed Time	Getup Time
1	0	-17
2	7	10
4	1	7
5	6	10
6	-2	16
7	5	4
9	3	4
10	-37	26
11	-3	10
12	24	24

The point is more clearly made when one graphically compares the overall mean sleep patterns in the subjects. BT's are in Figure 5 and GUT's in Figure 6. Intra-subject analyses showed that five of the ten subjects (5, 6, 9, 10 and 11) had significantly earlier bed times and awakenings in Condition 2 than in Condition 1, the irregular phase. This did not parallel the data on so-called ability to conform as shown in the previous table (2). With regard for the other subjects here, in Condition 2, two of them (4, 12) had a tendency to go to bed earlier times and three (2, 4 and 7) only had earlier mean awakening times.

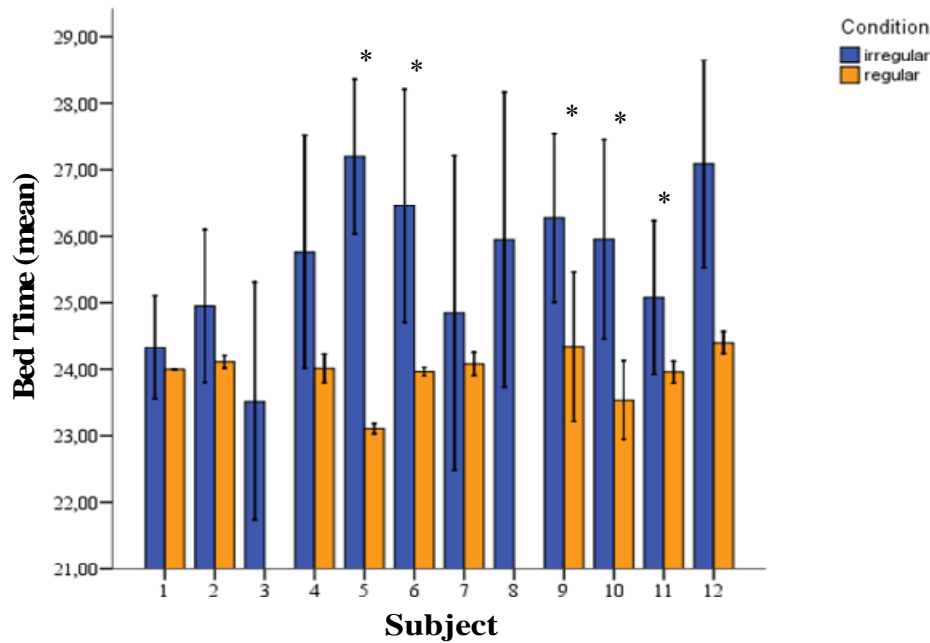


Figure 5: Comparisons of mean bed times in Condition 1 (irregular) and 2 (regular). In Condition 1, subjects showed later bed times with higher variation. *significant differences between conditions; bars are standard deviation of the mean.

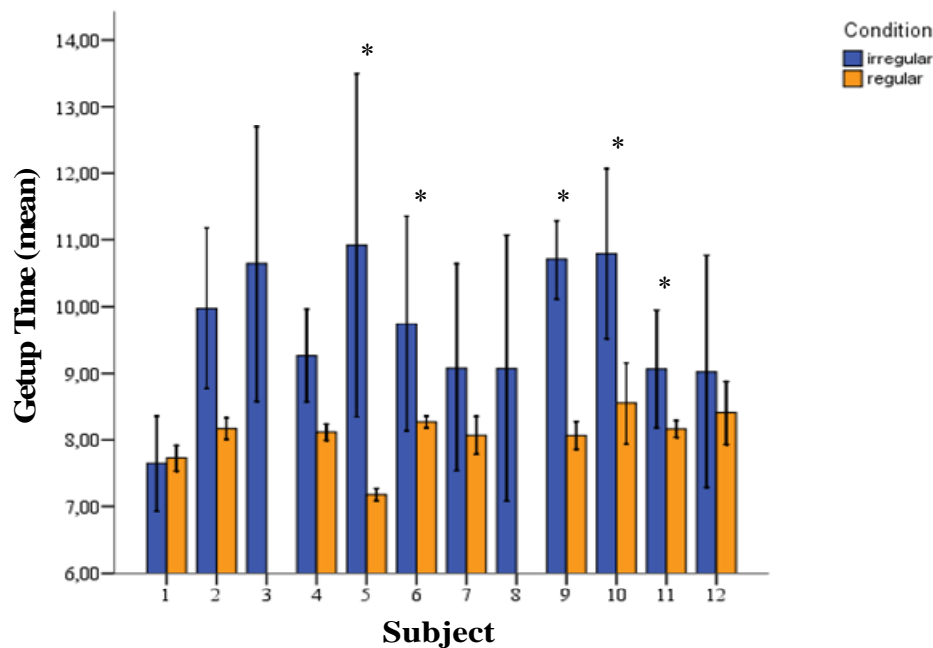


Figure 6: Comparison of mean getup times in Condition 1 (irregular) and 2 (regular). In Condition 1, subjects showed later getup times with higher variations. *significant differences between conditions; bars are standard deviation of the mean.

Following the description of the basic sleep/wake cycles, the analysis went on to examine characteristics of the sleep patterns documented in both objectively and subjectively assessed parameters. In Tables 3 and 4, the results of the analyses and statistics of comparisons are shown for each subject. Note that for subjects 3 and 8 only the datasets for Condition 1 were included.

Table 3: Mean values of subjective and objective sleep parameters for Conditions 1 and 2 (regular sleep times). High scores in subjective sleep quality (SSQ) and subjective awakening quality (SAQ) indicate poorer sleep! SSQ scores varied between 7 and 28, SAQ scores between 8 and 32. Subjective Sleep Efficiency (SSEFF) was the subjectively sensed percentage of time spent in bed, in which the subjects thought they had slept. Actual Sleep Time (ST, Actiwatch) is shown in minutes. Fragmentation Index (FI, Actiwatch) scores reflect sleep fragmentation. The higher the score, the more fragmented or disturbed the sleep.

Subject	Condition	SSQ	SAQ	SSEFF (%)	Actual ST (min)	FI
1	1	11	11	87	363	42
	2	11	11	90	367	45
2	1	8	13	91	459	32
	2	10	15	87	386	29
3	1	10	15	64	512	39
4	1	11	15	88	426	34
	2	11	15	89	392	33
5	1	10	13	93	410	25
	2	11	16	92	426	33
6	1	8	17	92	372	43
	2	8	15	95	422	42
7	1	13	19	81	383	48
	2	13	19	89	377	38
8	1	10	17	92	339	28
9	1	8	10	97	466	27
	2	11	17	94	428	31
10	1	9	14	88	419	30
	2	12	17	79	412	34
11	1	12	15	88	440	29
	2	13	14	86	430	27
12	1	7	17	87	322	22
	2	9	13	88	424	22

The analyses produced a cocktail of results for sleep duration, subjective assessments of sleep awakening and sleep efficiency and finally the objective measurement of their sleep. To begin with, in subjects 6 and 12 significantly longer actual sleep times were found in Condition 2, in subject 2 there was a tendency toward decreased sleep time. In addition, statistical analyses of subjective sleep parameters showed that subjects 2, 9 and 12 all had significantly worse SSQ assessments in Condition 2 than 1. For subject 5 the SSQ tended to be lower (Tab. 3 and 4, Fig. 2) but was not quite statistically significant. For subjects 5 and 9 there were significantly worse SAQ assessments in Condition 2 than in 1. Here again, for subjects 2 and 10 this was present but only as a trend. Subject 12 was unusual among the experimental group. He had significantly better SAQ assessments in Condition 2 than 1. A similar trend without significance was found in subject 6. The subject assessment of sleep efficiency varied in a similar way. In Condition 2, subjects 9 and 10 had a significantly worse SSEFF and in subject 2 this was only a tendency. Subject 6 had a significant better SSEFF here and for two other subjects (1, 7) this was a trend (Tab. 4). Finally with regard to the objective measure of sleep, two subjects (5, 10) showed a significant higher FI in Condition 2, while in subject 7 the FI was significantly lower FI (Tab. 4).

Table 4: Wilcoxon rank-sum test of conditions using Z-values for sleep parameters Subjective Sleep Quality (SSQ), Subjective Awakening Quality (SAQ), Actual Sleep Time (ST), Fragmentation Index (FI), Bed Time (BT) and Getup Time (GUT). Bold values with asterisks indicate significant differences between conditions or tendencies (without).

Subject	SSQ	SAQ	Actual ST	FI	SSEFF	BT	GUT
1	-1.066	-0.257	-0.118	0.000	-1.977	-1.437	-0.089
2	-3.074*	-2.298	-2.201	-0.105	-2.040	-1.183	-2.366
4	-0.039	-0.079	-0.931	-0.338	-1.177	-2.201	-2.371
5	-2.104	-2.631*	-0.510	-2.824*	-0.863	-3.061*	-2.981*
6	-0.642	-2.139	-2.418*	-0.251	-2.417*	-3.297*	-2.671*
7	-0.280	-1.368	-0.863	-2.589*	-2.341	-0.235	-2.511
9	-2.984*	-3.188*	-1.664	-1.067	-2.417*	-3.108*	-3.296*
10	-1.433	-2.089	-0.157	-2.480*	-2.903*	-3.170*	-3.170*
11	-1.145	-0.158	-0.785	-0.408	-0.874	-2.921*	-3.041*
12	-2.521*	-2.484*	-2.543*	-0.126	-0.245	-3.110	-1.015

4.2. Cognitive performance and mood

The next step in the analysis was the investigation of the subjects' performances in the morning and evening PVT's. The basic statistics for original PVT data are shown in Table 5. From these data an overall analysis of the results from a one-way repeated measurement (within subject) ANOVA is shown in Table 6. In short, this analysis revealed no effect of irregular or regular sleep conditions on PVT performance. This was true for both, morning

and evening tests. However, interactions among condition, subject and evening performances yielded significant interactions among mean reaction times (RTs) ($F_{8,50} = 6.05$; $P < 0.01$) and interpercentile ranges ($F_{8,50} = 2.63$; $P = 0.017$). Still, there were no interactions found between morning and evening performance as can be seen from the results of the t-test for paired samples in Table 7.

Table 5: Basic statistics of original PVT data. The mean values for morning and evening mean reaction times (ms) and interpercentile ranges (10th-90th percentile, ms) of irregular Condition 1 and regular Condition 2 are shown. Values in brackets are standard deviation of the mean.

Subject	Condition	PVT Performance		Interpercentile Range	
		morning	evening	morning	evening
1	1	543 (46)	564 (43)	174 (35)	211 (35)
	2	543 (27)	545 (27)	189 (34)	204 (38)
2	1	512 (75)	542 (63)	236 (101)	532 (294)
	2	402 (19)	470 (92)	182 (16)	255 (104)
4	1	345 (15)	324 (18)	162 (31)	146 (23)
	2	351 (13)	326 (22)	173 (14)	155 (25)
5	1	437 (19)	472 (22)	164 (27)	194 (41)
	2	493 (37)	494 (18)	220 (58)	231 (33)
6	1	306 (8)	307 (10)	81 (11)	81 (15)
	2	299 (16)	290 (18)	83 (22)	75 (24)
7	1	368 (17)	360 (6)	114 (17)	111 (8)
	2	370 (21)	373 (13)	131 (35)	144 (18)
9	1	351 (9)	349 (5)	66 (15)	69 (13)
	2	370 (9)	365 (8)	71 (7)	71 (11)
10	1	418 (15)	396 (14)	177 (42)	172 (20)
	2	458 (28)	428 (28)	187 (46)	207 (50)
11	1	334 (13)	333 (14)	95 (21)	90 (20)
	2	365 (31)	355 (19)	130 (28)	124 (27)
12	1	395 (29)	337 (17)	148 (32)	71 (18)
	2	354 (39)	327 (35)	106 (33)	80 (38)

Table 6: Results of a one-way repeated measurement (within subject) ANOVA using the z-transformed mean reaction times (RT) and 10th-90th interpercentile ranges (IR).

Effect	d.f.	z (Mean RT)		z (10th-90 th IR)	
		F-value	P-value	F-value	P-value
irregular-regular					
Morning	1, 50	0.001	0.980	0.320	0.859
Morning X subject	8, 50	0.071	1.000	0.460	1.000
Evening	1, 50	3.313	0.075	3.513	0.067
Evening X subject	8, 50	6.044	0.000	2.635	0.017
Morning X evening	1, 50	0.126	0.724	0.453	0.504
Morning X evening X subject	8, 50	1.140	0.354	1.070	0.399

Subjects 9, 10 and 11 had significantly worse morning RT's in Condition 2 (irregular) and for subject 2 there was a tendency towards faster RT's in the same condition. In the evening subjects 9 and 11 had significantly worse PVT performances in Condition 2 and subjects 5 and 10 tended to have worse PVT's (Tab. 6 and 7). In subject 11 the interpercentile ranges in the morning and the evening were significantly larger in Condition 2, for subject 7 this was a tendency in the evening tasks (Tab. 6 and 7).

Table 7: Results of the t-test for paired samples of PVT performance (mean reaction times) and mean values of interpercentile ranges (10th-90th percentile). *T*-values are shown. Bold values with * reflect significant differences between conditions and without reflect tendencies.

Subject	PVT Performance		Interpercentile Range	
	morning	evening	morning	evening
1	-0.021	1.394	-0.672	0.396
2	3.395	1.525	1.187	2.114
4	-0.818	-0.175	-0.931	-0.558
5	-2.015	-3.201	-1.662	-1.815
6	1.019	1.927	-0.144	0.524
7	-0.169	-1.963	-1.405	-3.729
9	-6.025*	-3.806*	-0.844	-0.334
10	-4.924*	-3.093	-0.641	-1.553
11	-3.584*	-2.391*	-3.485*	-2.673*
12	2.188	0.700	2.177	-0.559

The final parameter of psychological state in the subjects was the Basler Befindlichkeits scale. The mean sum scores of these scales are presented in Table 8. Higher scores indicate better moods or psychological wellbeing. The samples were compared over the whole groups. A T-test for paired samples demonstrated that there was a significant difference between Conditions 1 and 2 in the morning and in the evening. Scores were higher in Condition 1.

Table 8: Results of Basler Befindlichkeits scales: The means of the sum of scores for morning and evening scales in Conditions 1 and 2. Standard deviation from the mean is shown in brackets. The results of the T-tests for paired samples for morning scores and evening scores are on the right.

	Basler Score		T-test for paired samples		
	Condition 1	Condition 2	T	df	P-value
morning	81 (14)	74 (12)	4.312	66	0.000
evening	81 (12)	77 (11)	2.501	64	0.015

Table 9: Interactions among PVT performance, subjective and objective sleep parameters and mood. Shown are the coefficients of the non-parametric Spearman's rank correlations for (irregular) Condition 1 and (regular) Condition 2. Fat values with ** reflect highly significant correlations ($P \leq 0.01$), fat values with * reflect significant correlations ($P \leq 0.05$).

Correlations - Spearman-Rho										
Condition 1	morning PVT	morning PVT	evening PVT	SSQ	SAQ	SSEFF	Actual ST	FI	Basler morning	Basler evening
	morning PVT	-	0.461**	0.074	0.234*	-0.006	-0.188	0.189	-0.247*	-0.034
	evening PVT	0.461**	-	-0.075	0.077	-0.126	-0.209*	0.258*	-0.184	-0.029
	SSQ	0.074	-0.075	-	0.357**	-0.358**	-0.095	0.182	-0.317**	-0.283**
	SAQ	0.234*	0.077	0.357**	-	-0.336**	-0.129	<i>0.201*</i>	-0.472**	-0.175
	SSEFF	-0.006	-0.126	-0.358**	-0.336**	-	-0.168	-0.342**	0.452**	0.356**
	Actual ST	-0.188	-0.209*	-0.095	-0.129	-0.168	-	-0.141	0.046	-0.044
	FI	0.189	0.258*	0.182	0.201*	-0.342**	-0.141	-	-0.404**	0.001
	Basler morning	-0.247*	-0.184	-0.317**	-0.472**	0.452**	0.046	-0.404**	-	0.420**
	Basler evening	-0.034	-0.029	-0.283**	-0.175	0.356**	-0.044	0.001	0.420**	-
Condition 2	morning PVT	-	0.529**	0.194	0.333**	0.126	0.14	0.206	-0.11	-0.045
	evening PVT	0.529**	-	0.093	0.374**	-0.031	0.054	0.084	-0.232	-0.188
	SSQ	0.194	0.093	-	0.326**	-0.358**	-0.155	0.197	-0.503**	-0.365**
	SAQ	0.333**	0.374**	0.326**	-	-0.098	-0.028	-0.005	-0.428**	-0.315**
	SSEFF	0.126	-0.031	-0.358**	-0.098	-	0.064	0.104	0.045	0.088
	Actual ST	0.14	0.054	-0.155	-0.028	0.064	-	-0.228	0.316**	0.314**
	FI	0.206	0.084	0.197	-0.005	0.104	-0.228	-	-0.13	-0.138
	Basler morning	-0.11	-0.232	-0.503**	-0.428**	0.045	0.316**	-0.13	-	0.583**
	Basler evening	-0.045	-0.188	-0.365**	-0.315**	0.088	0.314**	-0.138	0.583**	-

morning PVT - z-transformed morning PVT performance (mean Reaction Time in ms), evening PVT - z-transformed evening PVT performance (mean Reaction Time in ms), SSQ - Subjective Sleep Quality, SAQ - Subjective Awakening Quality, SSEFF - Subjective Sleep Efficiency, Actual ST - Actual Sleep Time, FI - Fragmentation Index, Basler morning - sum score of Basler Befindlichkeits scale before morning PVT, Basler evening - sum score of Basler Befindlichkeits scale before evening PVT

In a final analysis of sleep and the cognitive and psychological parameters in Conditions 1 and 2 correlative statistics were employed to identify possible interactions among circadian stability, sleep quality and mental performance. The data have been summed up in Table 9. Non-parametric Spearman's rank correlations revealed interactions between morning PVT performance and SAQ in both conditions (Tab. 9). In Condition 1 a significant correlation between morning PVT performance and SAQ occurred ($\rho = 0.234$; $P = 0.022$). In Condition 2 a highly significant correlation was found between SAQ and morning PVT performance ($\rho = 0.333$; $P = 0.006$) as well as between SAQ and evening PVT performance ($\rho = 0.374$; $P = 0.002$). Further interactions were found in Condition 1 that did not occur in Condition 2 (Tab. 9). Morning PVT performance showed a significant negative correlation with morning Basler scores ($\rho = -0.247$; $P = 0.022$). Evening PVT performance showed a significant negative correlation with actual sleep time ($\rho = -0.247$; $P = 0.05$) as well as a significant positive correlation with Fragmentation Index ($\rho = 0.258$; $P = 0.015$). In both conditions Basler scores correlated negatively with SSQ (Tab. 9). SAQ correlated negatively with Basler morning scores in Condition 1 and Basler morning and evening scores in Condition 2 (Tab. 9). In Condition 1, Basler scores correlated with SSEFF and morning scores were correlated with FI. These interactions did not occur in Condition 2. Otherwise in Condition 2, Basler scores were correlated with actual sleep time, which did not occur in Condition 2. In both conditions morning and evening PVT performance showed highly significant interactions (Tab. 9).

4.3. Cortisol urine metabolites

In Table 10 the means of original cortisol/creatinine-ratios of each subject in both conditions are shown. A one-way repeated measurement (within subject) ANOVA using z-transformed cortisol/creatinine-ratios revealed no effect for phases of regular or irregular sleep patterns (Tab. 11). Variation of urinary cortisol levels did not interact with any sleep parameter (see Appendix Table 14). Nonetheless, a t-test for paired samples using z-transformed cortisol/creatinine-ratios revealed significant differences between morning and evening cortisol values in both conditions (Tab. 12), with higher urinary cortisol concentration in the morning than in the evening (Fig. 7).

Table 10: Mean Cortisol/creatinine-ratios (ng Cortisol / μg Creatinine) found in Conditions 1 and 2.

Subject	Condition	Morning Cortisol	Evening Cortisol
1	1	0.994	0.287
	2	1.379	0.141
2	1	1.244	0.181
	2	1.044	0.568
3	1	0.931	0.443
4	1	0.613	0.216
	2	2.046	0.124
5	1	1.306	0.877
	2	1.634	0.821
6	1	0.666	0.119
	2	0.976	0.234
7	1	0.802	0.035
	2	1.282	0.043
8	1	0.419	0.303
9	1	0.754	0.236
	2	0.701	0.421
10	1	0.447	0.221
	2	0.470	0.327
11	1	0.594	0.135
	2	0.643	0.159
12	1	0.800	0.278
	2	0.675	0.184

Table 11: Results of the one-way repeated measurement (within subject) ANOVA using z-transformed cortisol/creatinine-ratios comparing irregular and regular phases of sleep.

Effect irregular-regular	d.f.	<i>F</i> -value	<i>P</i> -value
Morning Cortisol	1, 36	2.127	0.153
Morning Cortisol x subject	9, 36	0.787	0.630
Evening Cortisol	1, 36	0.054	0.817
Evening Cortisol x subject	9, 36	0.857	0.570

Table 12: Results of the t-test for paired samples comparing morning and evening z-transformed cortisol/creatinine-ratios (ng Cortisol / μg Creatinine) in irregular Condition 1 and regular Condition 2.

Condition	N	T-value	d.f.	P-value
1	71	7.31	70	0.000**
2	51	8.29	50	0.000**

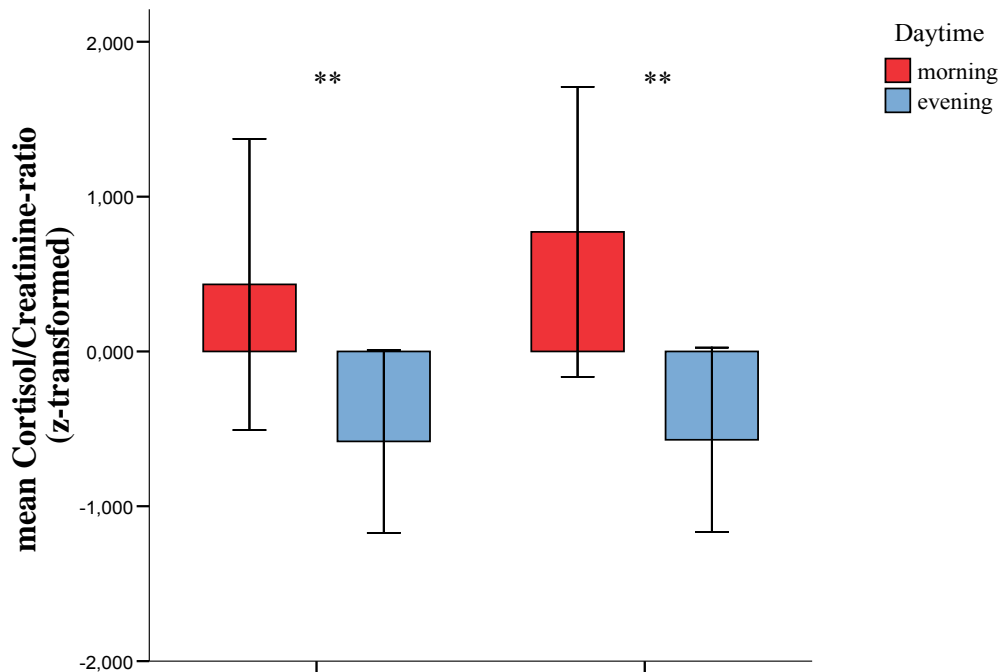


Figure 7: Comparison of z-transformed morning and evening urinary cortisol/creatinine-ratios (ng Cortisol / μg Creatinine) in Conditions 1 and 2. ** show significant differences; error bars show 1 standard deviation from the mean.

5. Discussion

Regulating sleep timing of healthy irregular sleepers with moderate chronotypes revealed individual differences among subjects. Some adapted to the set bedtime from 00:00 to 08:00 in Condition 2 better than others. Subjects 4, 7 and 9 seemed to have no problems in adapting to the preset sleep timing. Subject 1 went to bed on time, but could not maintain a sleep duration of eight hours, which was also obvious already in Condition 1. Subjects 2, 5 and 12 could not go to bed on time and therefore got up too late. Subjects 6, 10 and 11 seemed to need more sleep than eight hours, because they went to bed early and got up too late.

Although subjects were moderate chronotypes (see Appendix Tab. 13) their average sleep timing was earlier, in both bed and awakening times, in regular Condition 2 compared to irregular Condition 1. Four subjects had a worse SSQ and 4 subjects had a worse SAQ. Although 2 subjects showed a better SAQ in Condition 2, it seems that regulating the sleep timing of irregular sleepers might have had no or even a negative effect on subjective sleep and awakening quality. Especially SAQ appeared to be worse because subjects were not willing to get up at 8 o'clock.

Sleep duration was longer in all subjects in Condition 2, with one exception, although only two subjects showed significant longer sleep times. This indicates that irregular sleepers may have had shorter average sleep durations with much higher variation, than regular sleepers. Irregular sleepers may have needed variation in sleep length and longer, stable sleep durations may have had negative consequences for their subjective well-being and their sleep and awakening quality.

With regard to vigilance performance, no general effect of sleep quality was found. Instead, large inter-individual differences were documented in this study. Only one subject seemed to benefit slightly from regular sleep timing, tending to perform better in the morning. Other subjects showed worsened performance or no RT differences in Condition 2. An ANOVA analysis demonstrated significant interactions in evening performance within subjects between conditions. This might have been due to inter-individual difference and intra-individual consistency in performance variation and additionally due to a larger time frame in which the PVT had to be completed (15:00 - 22:00). The results and the consideration of the PVT duration need to be studied and discussed in more detail. There are concerns that 15 minutes of vigilance testing were not sufficient to document PV. Moreover, giving feedback about the reaction time during test performance as was the case in this paradigm, may have had effects on motivation. Motivation could have masked the effect of sleep restriction on PVT performance (Harrison and Horne 2000).

The sum of Basler rating scores, an indicator for subjective well-being and mood, was significantly lower in Condition 2 in the morning and in the evening. This indicates better

mood or over all wellbeing, when subjects were able to maintain their natural sleep timing. So sleep timing and duration might influence an individual's mood the whole next day.

Significant interactions were found between SAQ and morning PVT performance in both conditions, indicating that the better the subjects' awakening quality was the faster the subject's RT turned out to be. In Condition 2 this interaction was even stronger than in Condition 1. Subjects' performance may have been more sensitive to SAQ when they had to sleep outside their own irregular pattern. Additionally, morning PVT performance showed significant interactions with morning Basler scores in Condition 1. The better mood ratings the subjects had, the faster their RT's were. This indicates that performance might be more affected by mood under 'natural' conditions. To this, subjective awakening quality, when subjects are forced to get up (Condition 2) might have dominated the effect of general mood on performance. Nonetheless, the results show that the Basler scores correlated with SSQ and SAQ in both conditions, so subjectively sensed sleep quality might have affected mood and mood could have then affected performance.

In both conditions morning and evening performances were significantly correlated. In irregular Condition 1, evening performance interacted with actual sleep time and with sleep fragmentation; otherwise not. Due to irregular sleep schedules sleep duration varied and tended to be reduced in Condition 1 compared to 2. This could have had more effects in the evening. Although actual sleep time and FI did not correlate, FI interacted with evening performance in Condition 1. A higher fragmentation index was indicative of more waking periods and more disturbances during the night. As a result, subjects might have sensed it as bad sleep and actual sleep time would have been lowered, which could have negatively affected evening performance the next day. Due to irregular sleep schedules, vigilance performance especially in the evening might have been more sensitive to sleep duration and fragmentation. A daily sleepiness scale would have given more information about the subjects waking state combined with its mental state in the evening. It was not assessed in this study.

Finally with regard to physiological parameters regulating sleep timing, the urinary cortisol-levels did not show any significant effect of condition on their pattern. Cortisol-levels were simply higher in the morning than in the evening, which is as expected the normal circadian pattern (Fig. 2).

According to the findings of Birchler-Pedros et al. (2009) circadian phase has a crucial role on subjective well-being. Results of Taub and Berger (1974) moreover have shown that even a moderate shift in bed time can produce performance and mood deficits. These ideas were not substantiated in the present study. It can be assumed that some participants in this study might have suffered similar negative effects because mean bedtimes and getup times were earlier in Condition 2 than in 1. The effects were not, however, as pronounced as one might have expected from the literature. The age or sex of the participants may have had a role here. To see if there is any general effect of regulating bedtime on irregular sleepers more people

should be investigated, also women and elderly. There may also be different types of sensitiveness in different people to ‘forced’ sleep schedules. For instance, subjects 5, 9 and 10 all had a similar pattern showing worse sleep quality and worse performance in Condition 2. Still even if there were reaction types, the number of participants used in this study was too small to allow any classification of types.

One disadvantage of the presented study was that subjects participated from November 2009 till June 2010. This unscheduled long duration was due to the fact that some subjects quit participation over the period of the four study weeks and that the number of available Actiwatch was limited. Seasonal effects on mood i.e. seasonal affective disorder (Nelson 2005) in the months of winter can therefore not be excluded. The study design could also have been improved by analyzing daily sleepiness using sleepiness scales at different time points during the day, daily mood and daily performance. Additionally there should have been a stricter temporal window for completing evening PVT sessions to avoid performance variability due to different PVT time points. To make PVTs comparable among subjects it would have been better if subjects had had the same computer to perform. Other types of performance have not been analyzed. Tests on verbal/numeric learning might show additional information about the effect of irregular and regular sleep timing.

In general, finding appropriate subjects with irregular sleep times but no sleep disorder (PSQI) and a moderate chronotype (MEQ) was very difficult. Most of the interested candidates had very high PSQI scores that indicated sleep disorders or at least subjectively sensed bad sleep and/or were very late chronotypes. It seems that a healthy moderate chronotypes with irregular sleep schedules is more the exception than the rule. In this case age might have played an additional role because younger individuals are known to be able to compensate irregular life styles more easily than elderly subjects.

The bottom line is that even though it is inherently obvious that both circadian physiology and sleep quality interact with normal behavior and physiology of individuals, the interactions among Zeitgebers, health, wellbeing and performance appear to be both quite variable and individually dependent. So the general recommendation to use regular sleep patterns, as a method to improve life quality and expectancy should be taken with a grain of salt. Some might need stability to gain optimal performance, others might need a kind of irregularity, as mentioned above to produce a desired creative process (Healey and Runco 2006; Sladeczek and Domino 1985; Stickgold and Walker 2004). As Aschoff postulated in 1967, there appears to be a fingerprint like character in the circadian system of individual humans, which might be added here to say that the character extends to the interactions of the system with the environment.

6. References

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7. Appendix

7.1. Tables

Table 13: Subject demographics showing age, the scores of the Pittsburgh Sleep Quality Index (PSQI), and the scores of the Morningness-Eveningness-Questionnaire (MEQ) by Horne and Oestberg (1976). PSQI scores under and until 5 are considered as good sleep quality. MEQ scores beneath 30 classify an extreme evening-type, scores from 31 to 41 characterize a moderate evening-type, scores from 42 to 58 classify an indifferent type, scores from 59 to 69 characterize a moderate and over 70 an extreme morning-Type.

Subject	Age	PSQI	MEQ	Chronotype Classification
1	26	5	56	indifferent type
2	27	3	39	moderate evening type
3	22	5	44	indifferent type
4	30	3	51	indifferent type
5	21	1	39	moderate evening type
6	23	5	45	indifferent type
7	25	5	38	moderate evening type
8	24	2	48	indifferent type
9	24	2	38	moderate evening type
10	25	3	52	indifferent type
11	22	4	51	indifferent type
12	24	2	45	indifferent type

Table 14: Interaction of urinary cortisol levels (z-transformed cortisol/creatinine-ratios in ng Cortisol / μg Creatinine) and sleep parameters. Shown are the coefficients of the non-parametric Spearman's rank correlations for irregular Condition 1 and regular Condition 2. No significant correlations were found.

Correlations - Spearman-Rho		SSQ	SAQ	SSEFF	BT	GUT	ActualST	FI	morning Cort	evening Cort
Condition 1	SSQ	1	0.182	-0.212	-0.185	-0.334	-0.18	0.167	-0.016	0.053
	SAQ	0.182	1	-0.163	-0.233	-0.373	-0.4	0.018	-0.164	-0.151
	SSEFF	-0.212	-0.163	1	0.379	0.04	-0.034	-0.516	-0.025	-0.024
	BT	-0.185	-0.233	0.379	1	0.549	-0.043	-0.269	0.133	-0.196
	GUT	-0.334	-0.373	0.04	0.549	1	0.677	-0.172	0.237	-0.183
	Actual ST	-0.18	-0.4	-0.034	-0.043	0.677	1	-0.164	0.15	-0.026
	FI	0.167	0.018	-0.516	-0.269	-0.172	-0.164	1	-0.04	-0.127
	morning Cort	-0.016	-0.164	-0.025	0.133	0.237	0.15	-0.04	1	-0.168
	evening Cort	0.053	-0.151	-0.024	-0.196	-0.183	-0.026	-0.127	-0.168	1
Condition 2	SSQ	1	0.347	-0.451	-0.039	-0.375	-0.335	0.253	0.05	0.062
	SAQ	0.347	1	-0.049	-0.102	0.039	-0.062	0.255	-0.148	0.203
	SSEFF	-0.451	-0.049	1	0.086	-0.107	0.323	-0.011	0.267	-0.217
	BT	-0.039	-0.102	0.086	1	0.207	-0.153	-0.175	0.017	-0.12
	GUT	-0.375	0.039	-0.107	0.207	1	0.092	0.005	0.046	-0.004
	Actual ST	-0.335	-0.062	0.323	-0.153	0.092	1	-0.293	-0.013	-0.23
	FI	0.253	0.255	-0.011	-0.175	0.005	-0.293	1	0.213	-0.036
	morning Cort	0.05	-0.148	0.267	0.017	0.046	-0.013	0.213	1	-0.063
	evening Cort	0.062	0.203	-0.217	-0.12	-0.004	-0.23	-0.036	-0.063	1

SSQ - Subjective Sleep Quality, SAQ - Subjective Awakening Quality, SSEFF - Subjective Sleep Efficiency, BT - Bed Time, GUT - Getup Time, Actual ST - Actual Sleep Time, FI - Fragmentation Index, Cort - ng Cortisol / μg Creatinine

7.2. Actograms

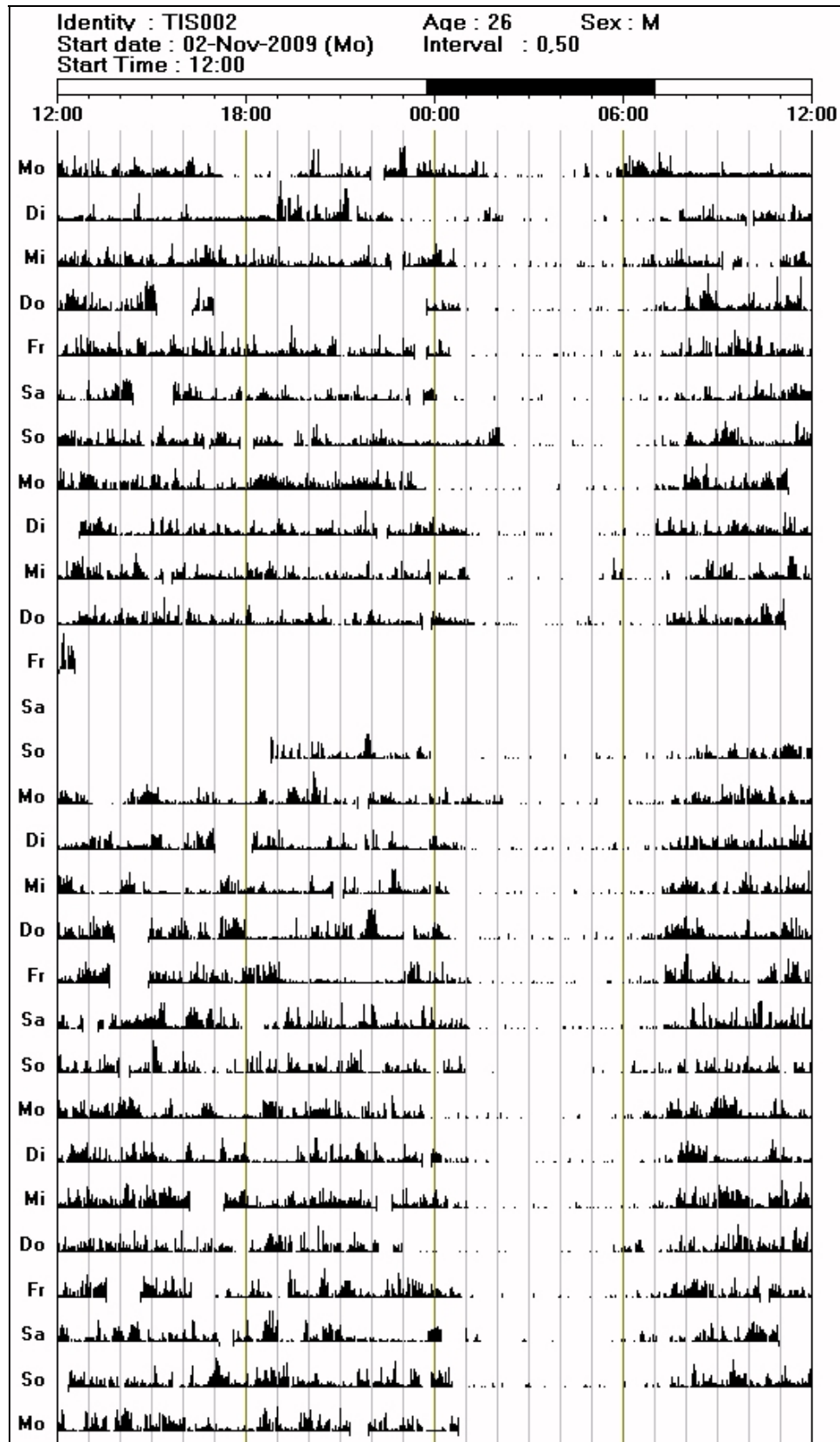


Figure 8: Actogram of subject 1.

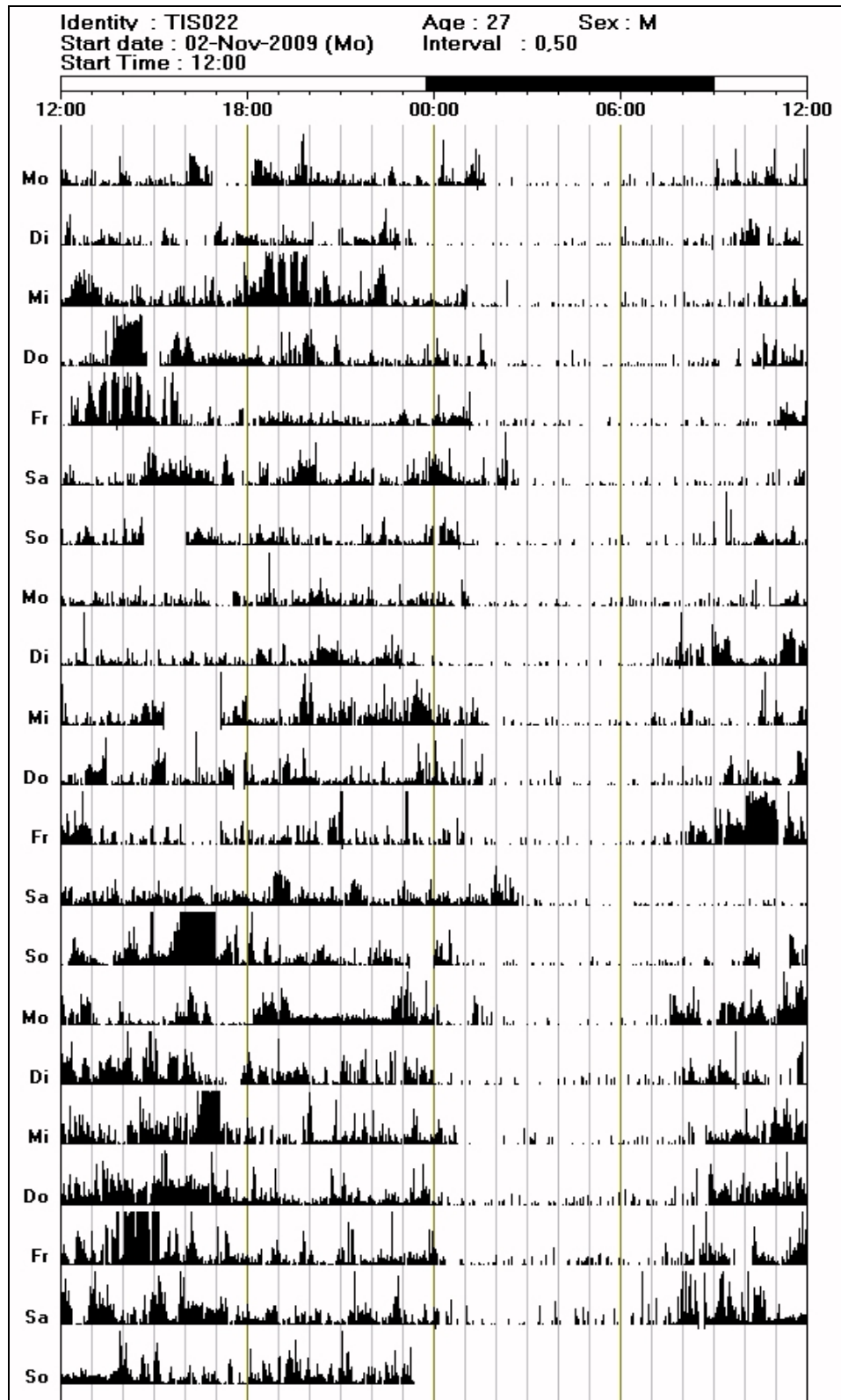


Figure 9: Actogram of subject 2.

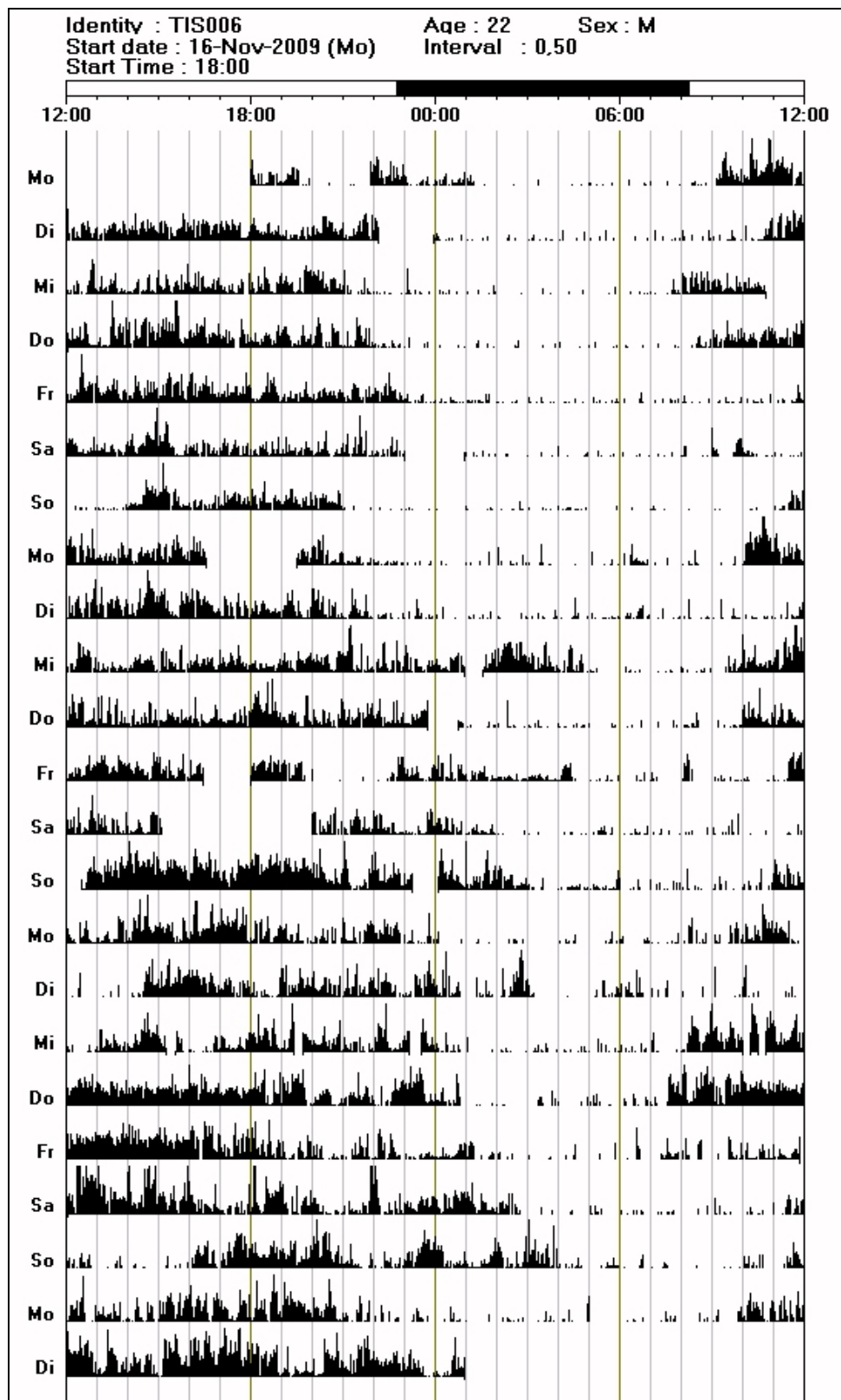


Figure 10: Actogram of subject 3.

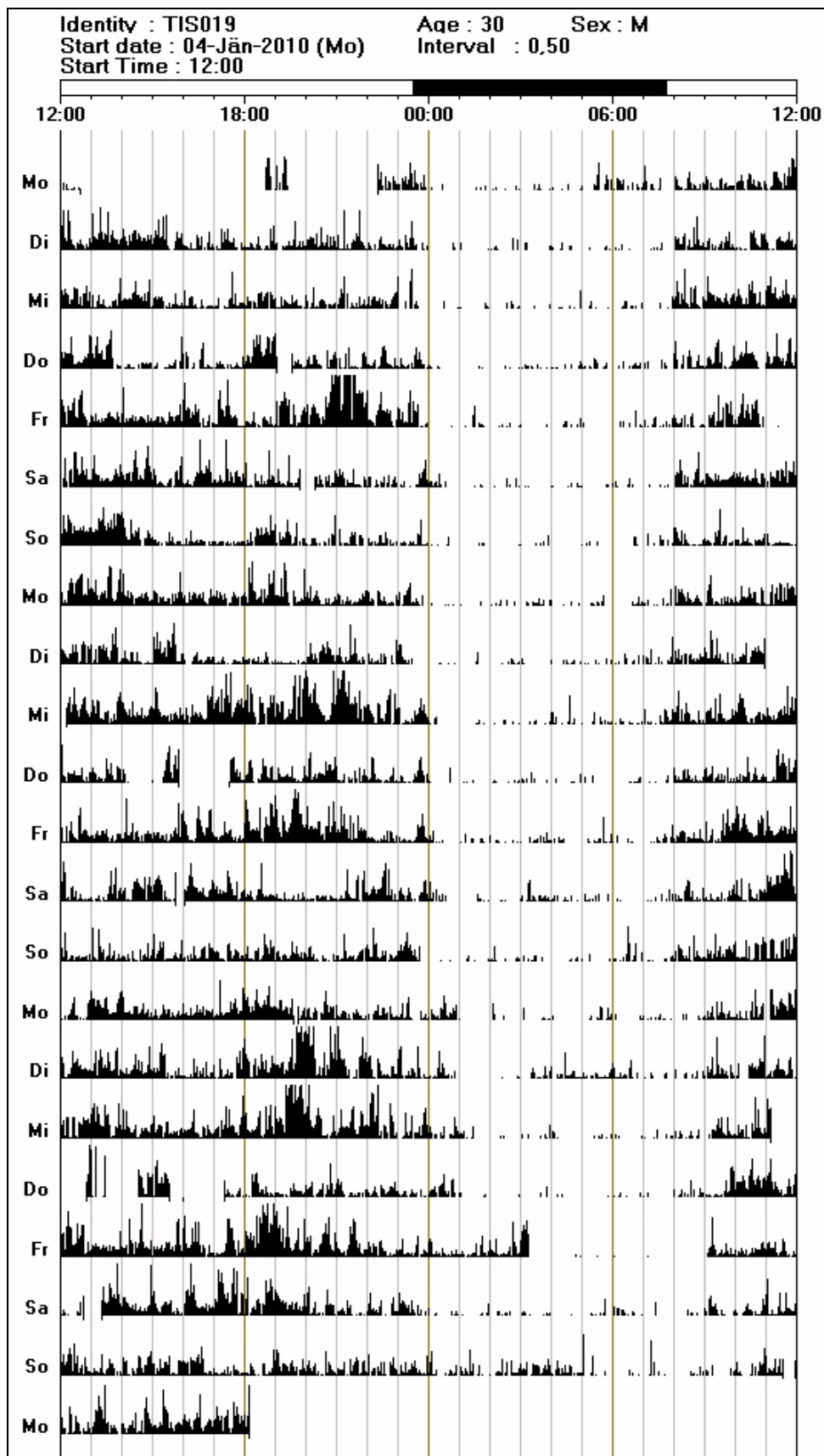


Figure 11: Actogram of subject 4.

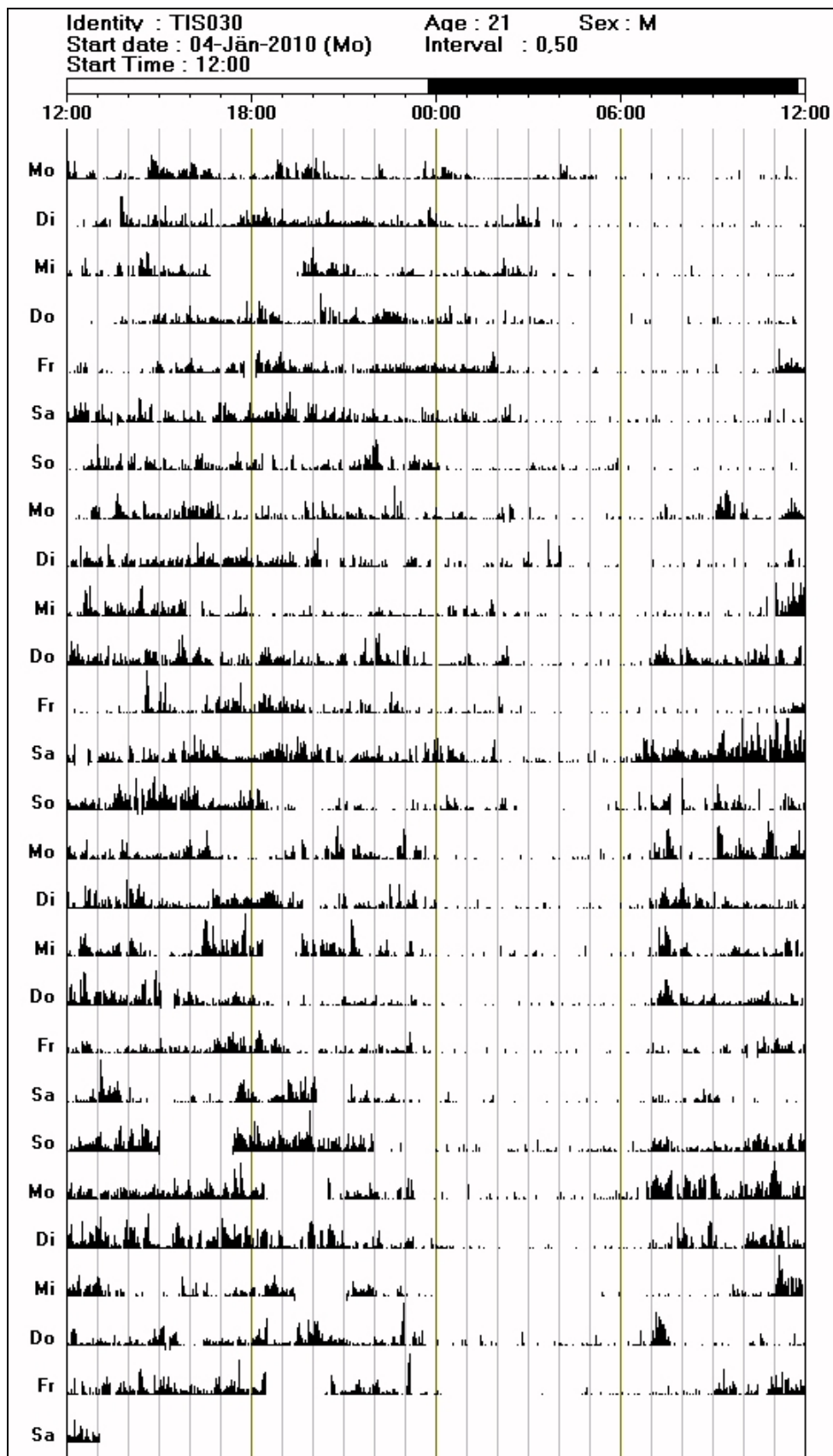


Figure 12: Actogram of subject 5.

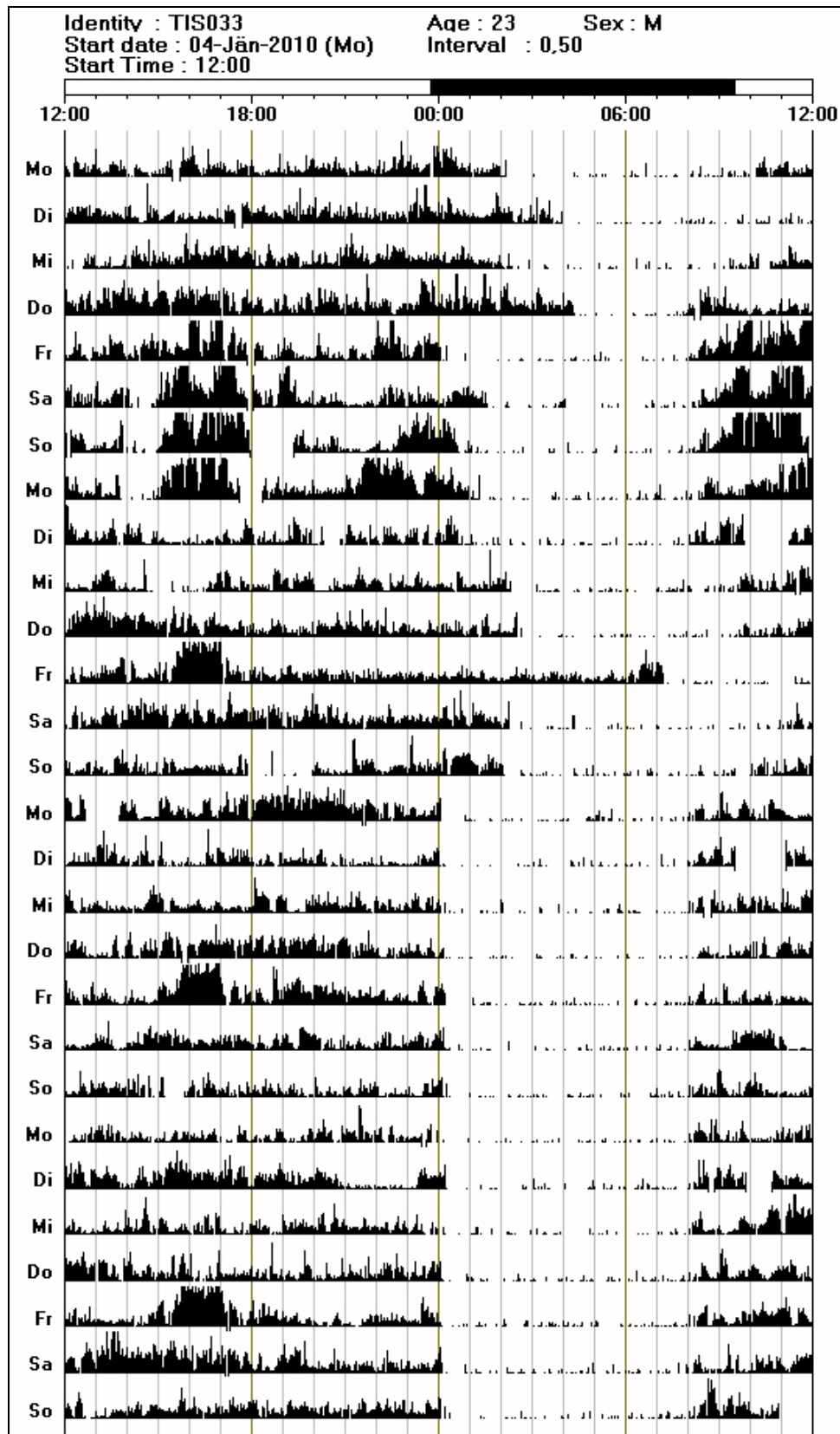


Figure 13: Actogram of subject 6.

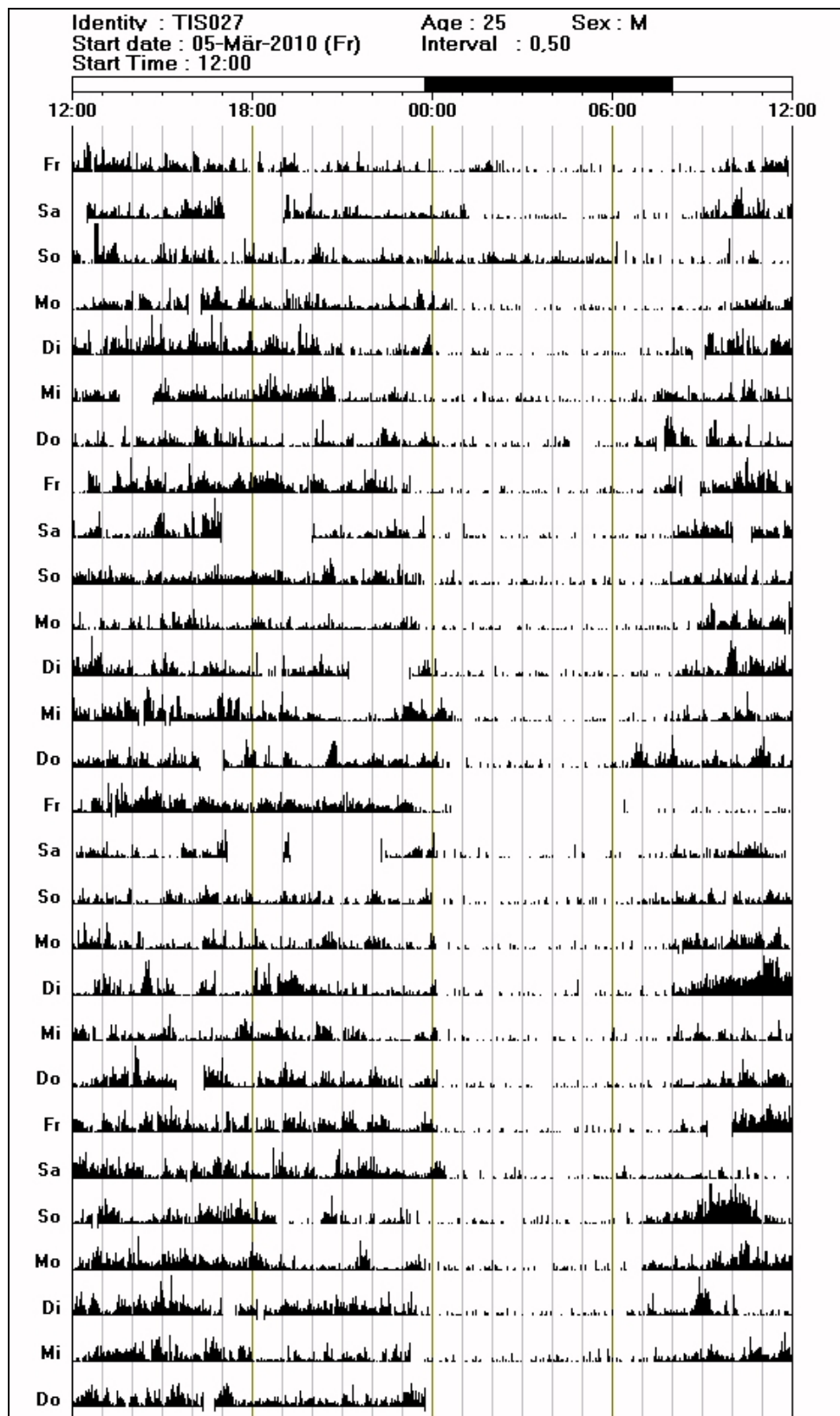


Figure 14: Actogram of subject 7.

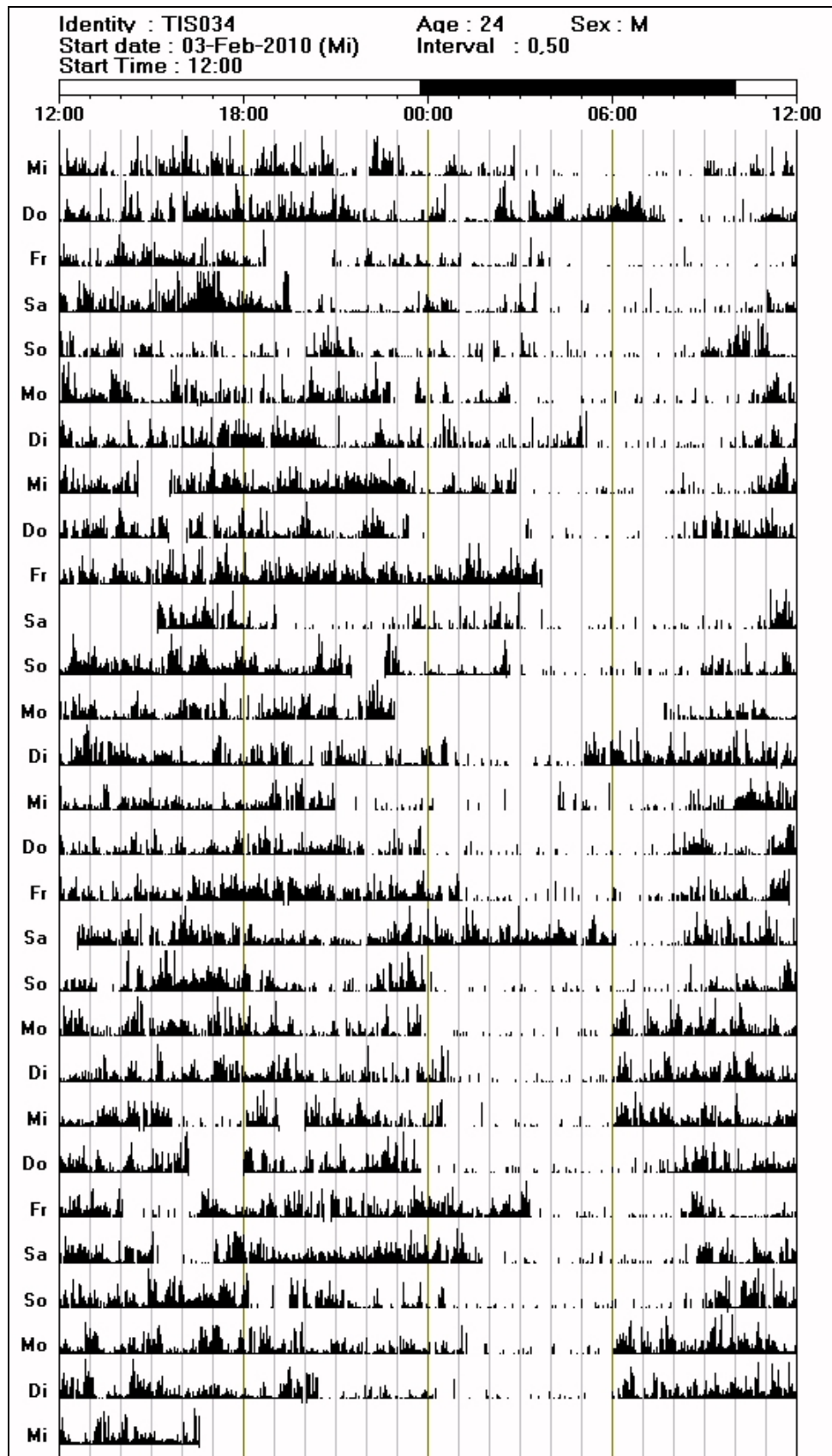


Figure 15: Actogram of subject 8.

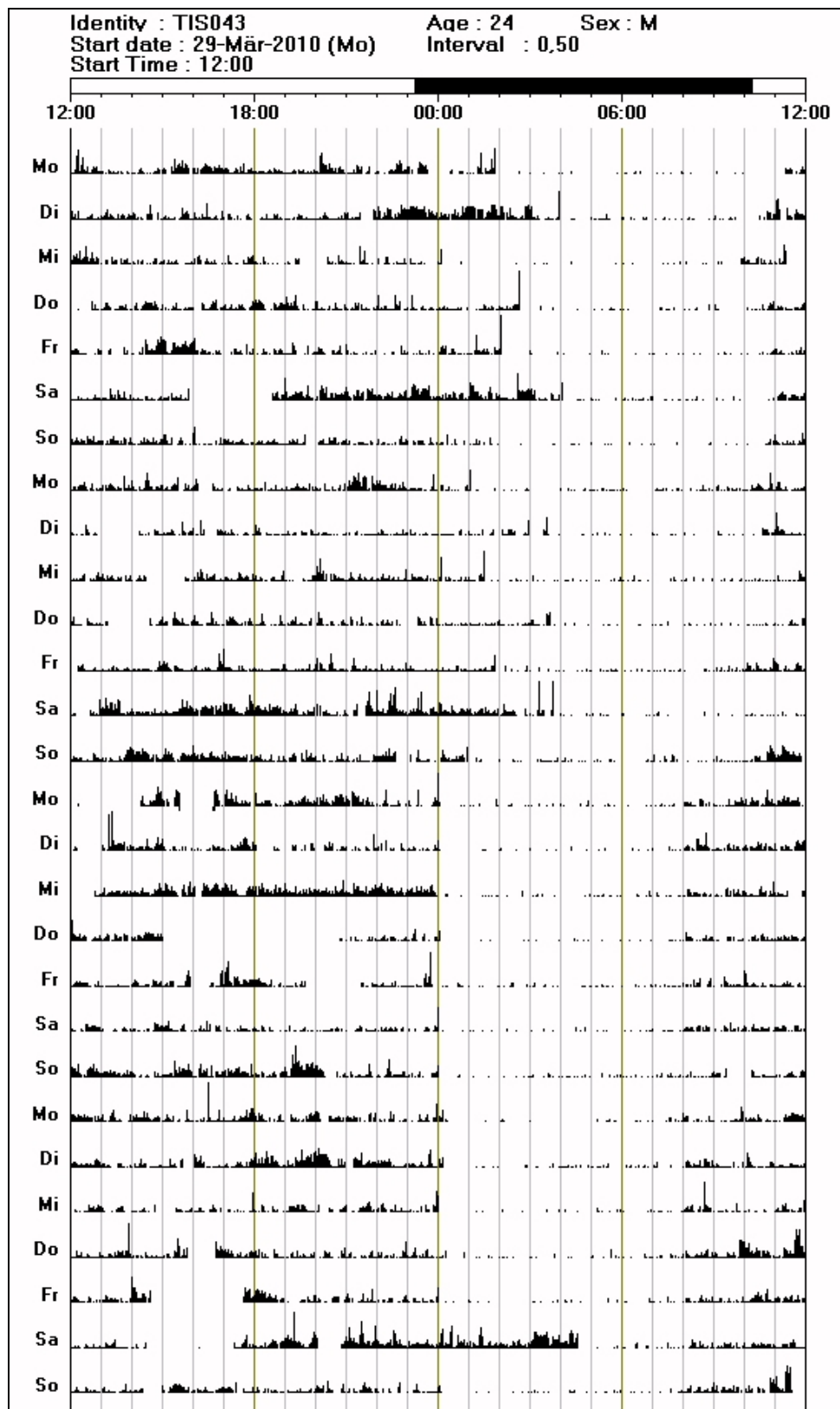


Figure 16: Actogram of subject 9.

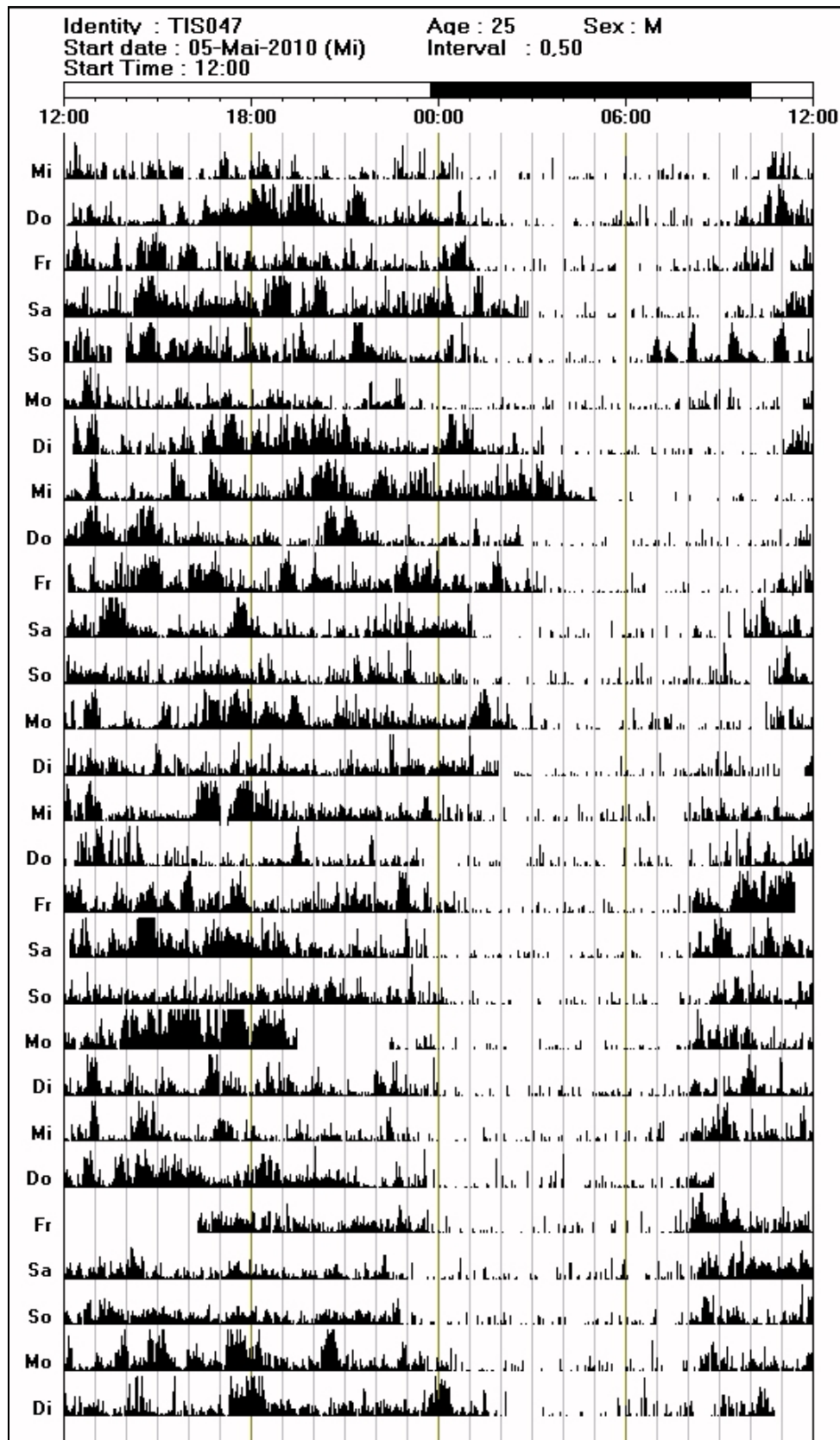


Figure 17: Actogram of subject 10.

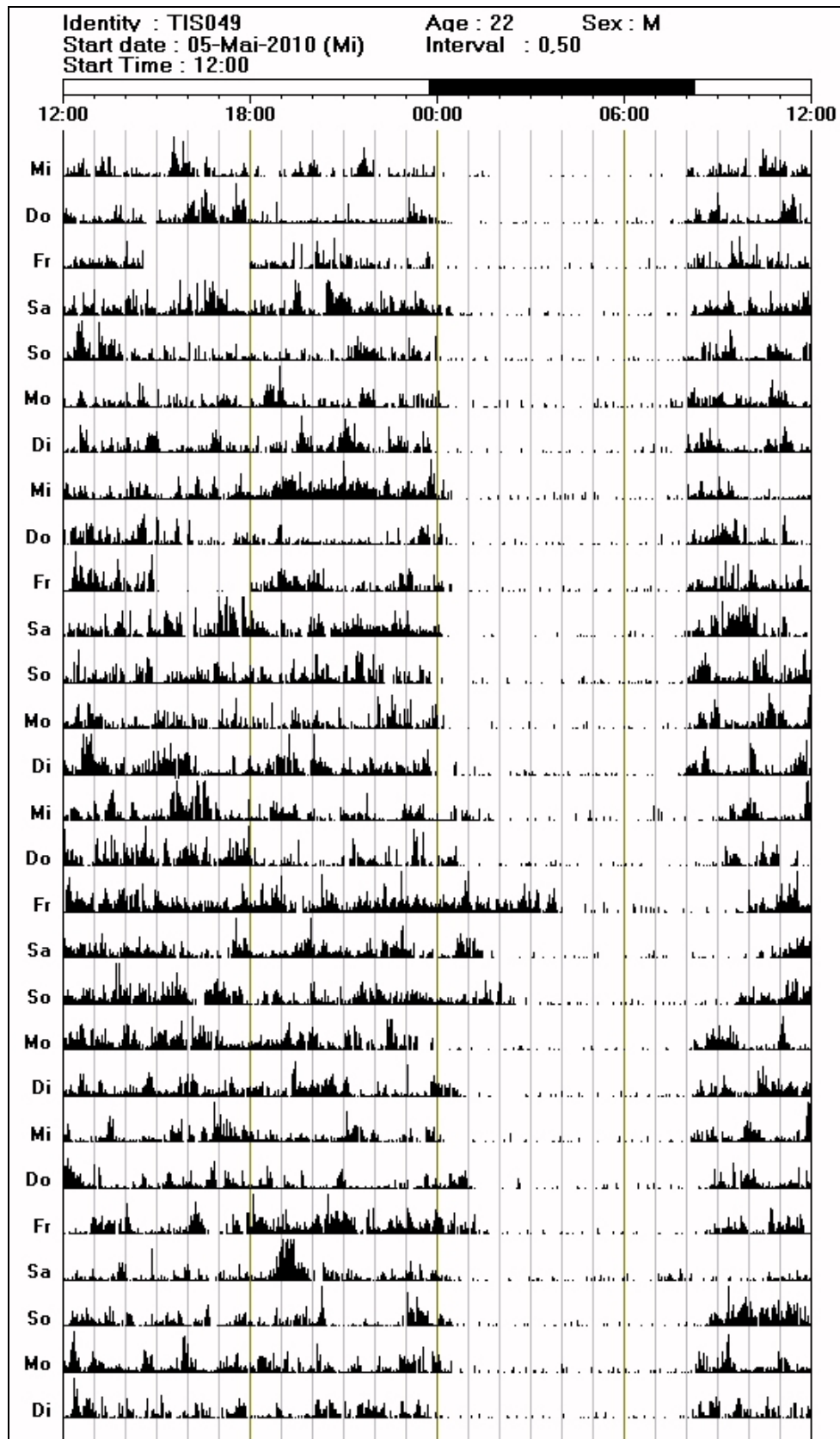


Figure 18: Actogram of subject 11.

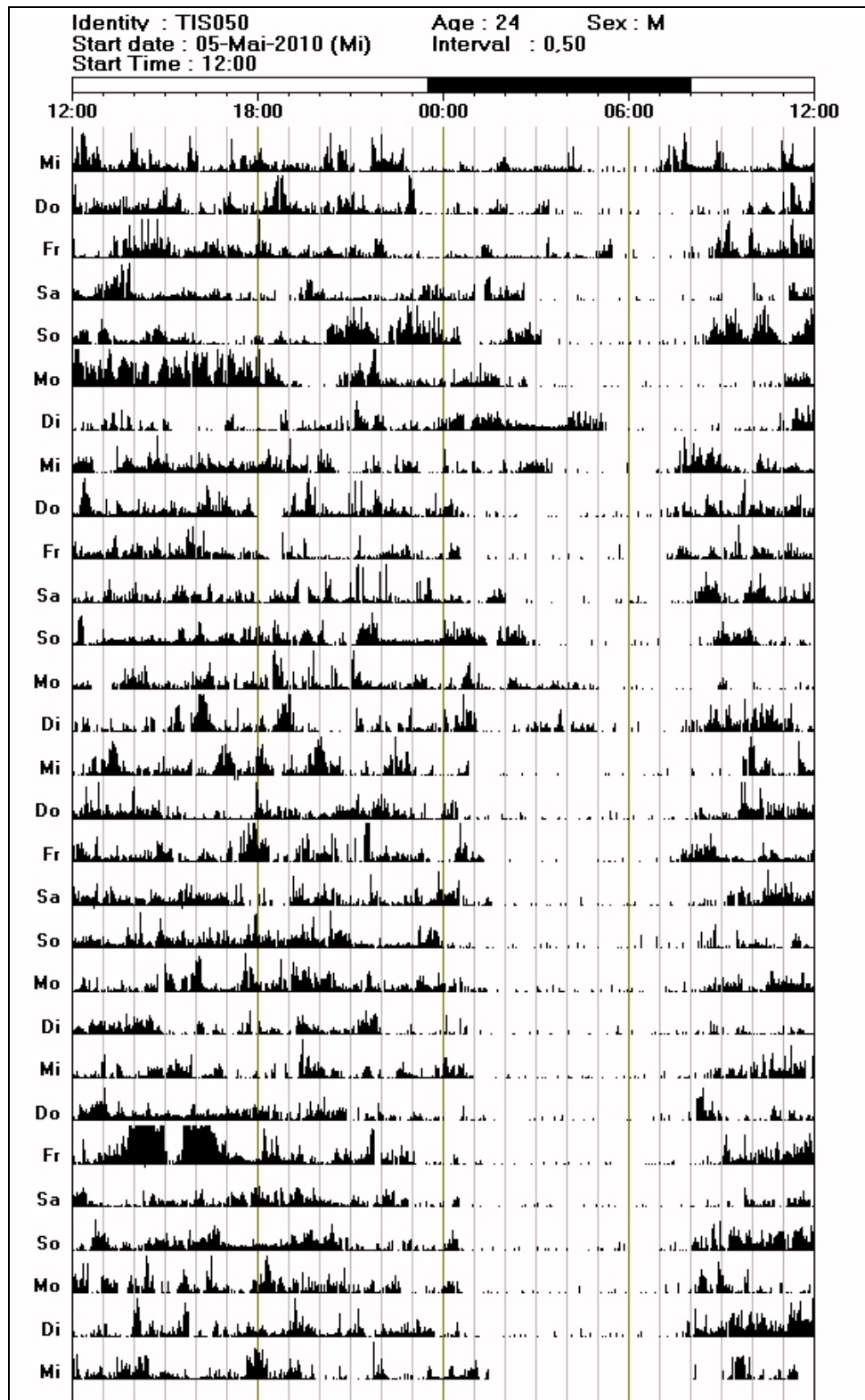


Figure 19: Actogram of subject 12.

7.3. Abstract

Stability in sleep timing has long thought to be a hallmark of a healthy and successful life. In modern humans the natural solar day has to be synchronized with unnatural economic and social environments. This can often lead to disorganization between the internal circadian system and these environments and as a consequence produce irregularities in sleep timing and a loss of life quality. The present study addressed the question of how humans, who normally living in unstructured time schedules would react to a regulation of their sleep wake pattern in the form of regular bed times. The study focused on subjective and objective sleep parameters collected via sleep logs and actigraphy, vigilance performance changes (PVT, reaction time task), subjective well-being, as measured with Basler rating scales and finally a physiological parameter, urinary cortisol metabolites. Two weeks of undisturbed, irregular sleep schedules and timing were compared with two subsequent weeks of regulated sleep/wake schedules. The results revealed individual differences in the ability to adapt to preset sleep timing. Some subjects had extreme difficulties in conforming to the prescribed sleep wake schedule. In the regulated or regular condition, subjective sleep and awakening quality was either worse or showed no differences compared to the unstructured weeks. Subjects had longer sleep durations, and earlier bed and awakening times during the structured weeks. Vigilance performance did not differ between conditions. The same was true for cortisol metabolites. In the structured experimental phase, sleep/wake timing was negatively related to well-being and mood. During irregular conditions, mood interacted with vigilance performance, whereas under controlled regular conditions performance was more sensitive to subjective awakening quality, which may have been due to the earlier awakening times. The individual differences mentioned above underline the idea that there may be different types of sensitiveness in an individual's ability to adapt to preset sleep schedules. Here it appears that, with regard to irregular sleep patterns, the data do not support the conclusion that stable sleep/wake patterns always improve life quality. Due to differences in individual types, stability may improve life and performance in one, but may also disturb the same parameters in another. Other factors like age and sex certainly play a role in the adaptation. Younger might compensate an irregular life style easier. More studies concerning stability and instability in sleep timing are needed to unravel these effects.

7.4. Zusammenfassung

Regelmäßige Schlafzeiten wurden stets als Merkmal für ein gesundes und erfolgreiches Leben angesehen. In der heutigen modernen Gesellschaft muss der natürliche Sonnentag mit einem unnatürlichen, nicht am Tageslicht orientierten, ökonomischen und sozialen Umfeld in Einklang gebracht werden. Dies führt oftmals zu einer Störung zwischen dem internen circadianen System und der Umwelt, was des Weiteren zu unregelmäßigen Schlafzeiten und eingeschränkter Lebensqualität führen kann. In dieser Studie wurde untersucht, wie Menschen mit natürlichen unregelmäßigen Schlafzeiten auf eine Regulierung dieser reagieren. Zwei Wochen mit natürlichen unregelmäßigen Schlafzeiten wurden verglichen mit zwei darauffolgenden Wochen, in denen ein vorgegebener regelmäßiger Schlaf-Wach-Rhythmus eingehalten werden musste. Augenmerk wurde dabei auf durch Schlaftagebücher und Aktigrafie ermittelte subjektive und objektive Schlafparameter, die kognitive Leistungsfähigkeit durch Psychomotorische Vigilanz Tests (PVT, Reaktionszeittest), die subjektive Befindlichkeit erfasst mittels Basler Befindlichkeitsskalen und schließlich auf die Konzentration von Cortisol-Metaboliten im Harn als physiologischen Marker gelegt. Das Ergebnis zeigte individuelle Unterschiede in der Fähigkeit der Probanden sich an einen vorgegebenen Zeitplan anzupassen. Einige Teilnehmer hatten sogar extreme Schwierigkeiten die vorgegebenen regelmäßigen Schlafzeiten einzuhalten. Subjektive Schlaf- und Aufwachqualität waren in der regulierten Studienphase entweder schlechter oder zeigten keine Unterschiede. Des Weiteren zeigten die Probanden in derselben Phase längere Gesamt-Schlafzeiten, sowie durchschnittlich frühere Zu-Bett-Geh- und Aufstehzeiten. Die Vigilanz-Leistung der Teilnehmer zeigte in unregelmäßigen und regelmäßigen Phasen keine Unterschiede. Die Konzentration der Cortisol-Metabolite im Harn zeigte ebenso keine Unterschiede zwischen den Phasen. Die Wochen mit regulierten Schlafzeiten wirkten sich negativ auf die Befindlichkeit aus. In der unstrukturierten Phase interagierte die Befindlichkeit mit der Leistung der Probanden. In der strukturierten Phase zeigte die Leistung einen stärkeren Zusammenhang mit der subjektiven Aufwachqualität, was auf frühere Aufstehzeiten zurückzuführen sein könnte. Die in dieser Studie gefundenen individuellen Reaktionen auf eine Regulierung der Schlafzeiten deuten darauf hin, dass es unterschiedlich sensible Typen gibt, welche sich mehr oder weniger gut an vorgegebene Schlafzeiten anpassen bzw. gewöhnen können. Die Schlussfolgerung, ein regelmäßiger Schlaf-Wach-Rhythmus verbessere die Lebensqualität scheint sich im Falle dieser Studie und in Anbetracht der Ergebnisse während unregelmäßiger Schlafzeiten, nicht zu bestätigen. Aufgrund von Unterschieden in den individuellen Typen kann Stabilität das Leben und die Leistungsfähigkeit des einen verbessern, aber eines anderen auch verschlechtern. Zusätzliche Faktoren wie Alter und Geschlecht spielen sicherlich ebenso eine Rolle in der Fähigkeit sich anzupassen. Jüngere könnten möglicherweise einen unregelmäßigen Lebensstil leichter

kompensieren. Weitere Studien werden nötig sein um die Auswirkung regelmäßiger und unregelmäßiger Schlafzeiten zu ergründen.

Curriculum vitae



Personal Information

Name: Kathrin Holzer, née Palkovics
Date of birth: January 28th, 1983
Nationality: Austria
Address: Krottenbachstrasse 42-46/3/15, 1190 Vienna
Tel: +43 / 650 / 901 38 21
Email: a0203475@unet.univie.ac.at
Marital status: Married to Dieter Holzer since June 18th, 2010

Education

Since 06/2006 Dipolma study in Zoology at the University of Vienna
Major topics:
Chronobiology
Endocrinology
Neurobiology
10/2002-06/2006 Diploma study in Biology at the University of Vienna
09/1993-06/2002 GRG Zirkusgasse, 1020 Vienna
09/1989-06/1993 VS Wehlistrasse, 1020 Vienna

Working Experience

Since 02/2008 Natural History Museum of Vienna, Employee in the Shop
03/2011-07/2011 Tutor for “Animal Physiology Laboratory 1 - Reproduction, Metabolism and Immunology” at the University of Vienna, Faculty of Life Science / Department of Behavioural Biology
03/2010-07/2010 Tutor for “Animal Physiology Laboratory 1 - Reproduction, Metabolism and Immunology” at the University of Vienna, Faculty of Life Science / Department of Behavioural Biology
09/2009-02/2010 Study Assistant at the University of Vienna, Faculty of Life Science / Department of Behavioural Biology
11/2003-02/2008 Employed at Eduscho/Tchibo as salesperson
08/2001 Summerjob as salesperson at Ankerbrot AG
07/2000 Summerjob at Price Waterhouse Coopers

Skills

Languages: German – native speaker
English – in speech and writing
French – basic skills
PC knowledge: MS Office (Acces, Excel, Word, Power Point)
SPSS for Windows