Effects of Total Sleep Deprivation on Cardiovascular Parameters: An Absence of Biologically Significant Findings?

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Abstract The present study analyzes the variations of heart rate (HR) and systolic and diastolic blood pressure (SBP and DBP) during 60 h of total sleep deprivation (TSD). All variables were evaluated every 2 h in a resting condition, during the performance of a vigilance task. Thirty healthy volunteers (15 men and 15 women) from 18 to 24 years old participated in the experiment. The analyses of variance (ANOVA) with repeated measures showed some modifications of HR and SBP mean values mainly marked by circadian oscillations. The circadian oscillations had a smaller amplitude for SBP than for HR. HR showed a slight decrease on the second night of TSD and a slight increase on the third day of TSD. SBP decreased during the first 24 h of TSD and after that maintained its values without significant changes. DBP did not show any significant variations during TSD. In addition, there were no differences in function of gender for the TSD effect on the studied variables. All these statistically significant findings, however, seem to have no biological or clinical relevance. These aspects as well as the possible relationships between our results and activation or stress levels during TSD are discussed.

Introduction

Disturbances in the sleep-wake rhythm and/or sleep deprivation are frequent events in modern life. It is well known that total sleep deprivation (TSD) negatively impacts a wide range of cognitive, behavioral, physiological, and emotional measures. Several studies have stressed the relationships among habitual sleep deprivation and premature mortality, cardiovascular morbidity, and functional disability (Bliwise et al., 1994; Newman et al., 1997). However, very few investigations have systematically analyzed the TSD effects on the cardiovascular system.

Several earlier studies, revised by Horne (1978), analyzed the changes in heart rate (HR) or blood pressure (BP) at different periods of TSD. HR did not show any significant changes in nine studies (24–123 h of TSD), but did show a decrease in five studies (40–205 h of TSD) and an increase in another two studies (100 and 264 h of TSD). Similarly confusing results were found for BP, in which significant modifications were not found in the greater part of the collated studies (24–205 h of TSD). As Horne (1978) reported, many of these works suffered from methodological limitations (i.e., measurements were taken only once or twice during the TSD, there was no standardization of recording conditions, etc.). According to the most recent investigations, the situation is still not much clearer. Various studies did not report significant changes in HR or BP during periods of TSD from 24 to 65 h (Angus et al., 1985; Gauthier & Gottesmann, 1983; Meney et al., 1998), perhaps with the exception of a slight decrease in SBP (Kamphuisen et al., 1992; Webb et al., 1981). However, Kaneda et al. (1999) found that the R-R interval widens (i.e., HR decreases) in a discrimination task during 24 h of TSD. Similarly,
Muenster et al. (2000) did not observe any changes in the heart rate variability (HRV) in 10 subjects with partial sleep loss during four nights, but SBP increased (110 ± 6 vs 124 ± 3 mmHg) and HR decreased (108 ± 8 vs 49 ± 8 bpm).

Some authors have argued that TSD may increase sympathetic nervous system activity on the following day, generating high HR and BP and potentiating the responses to stressful stimuli (Lusardi et al., 1999; Toshikubo et al., 1996). Lusardi et al. (1999) analyzed 36 moderately hypertensive, nontreated, sleep-deprived patients during the first part of the night (period of sleep from 3 a.m. to 7 a.m.) and found an increase in the SBP, DBP, and HR daily values, accompanied by an increase in the urinary excretion of norepinephrine. However, Kato et al. (2000) observed an increase in mean BP after one night of TSD (measuring only once in the morning), but HR, forearm vascular resistance, plasma catecholamines level, and the autonomic and hemodynamic responses to stressful stimuli did not change.

On the other hand, although very few studies introduce frequent measurements in order to control rhythmic influences, some reports suggest that the TSD does not modify the HR circadian rhythm (Endo et al., 1981; Stefi kova et al., 1986) and others did not observe any rhythmicity for HR, BP, or other parameters (i.e., QRS, PQ, and QT intervals) (Ahrve et al., 1981; Ewing et al., 1991; Rechlín et al., 1995). Kerkhof et al. (1998) in a recent study of 26 h of TSD, applying rigorous “unmasking” conditions (bed rest, constant temperature and illumination, and hourly equilocal feeding) found that HR exhibited a significant circadian model, but BP did not.

The present investigation is the first to analyze the variations of two of the most representative cardiovascular activity indexes, HR and BP, during 60 h of TSD, including frequent measurements (every 2 h) and to determine possible differences in function of gender.

Method

Subjects

A total of 30 healthy subjects (15 men and 15 women) from 18 to 24 years old (mean age = 20.06 and SD = 4.38) participated in the study. The final sample was selected by means of a questionnaire elaborated for this purpose which explored such areas as physical and psychological health, consumption of tobacco, medication, alcohol, and other drugs, ingestion of coffee, tea, and other stimulants, menstrual cycle regularity in the case of women, regularity in sleep schedules, and the possible existence of sleep disorders. The Horne and Östberg Morningness-Eveningness Scale for determining each subject’s circadian type was administered along with the selection questionnaire. Subjects who obtained scores superior to 21 (“clearly morning-type”) or scores inferior to 8 (“clearly evening-type”) were not admitted. The Beck Depression Inventory (BDI), the State-Trait Anxiety Inventory: Trait Scale (STAI), and the Eysenck Personality Questionnaire (EPQ-A) were also administered. The basis for exclusion was a score superior to 9 on the BDI or a direct score on the STAI and in the neuroticism and psychoticism dimensions of the EPQ-A over the centile 70. These last exclusions were established to assure that the subjects did not exhibit extreme variations in mood or personality characteristics that might indicate the presence of a possible behavior disturbances or an uncommon response to TSD.

All of the selected participants presented good health and did not consume any type of medication. Each subject had a regular sleep pattern of 7–9 h, with a common bedtime hour between 11:30 p.m. and 2:30 a.m. and a wake up time hour between 7:30 a.m. and 10:30 a.m. Only those subjects who did not consume more than three cups of coffee per day were admitted. Subjects who presented high tobacco consumption (more than 15 cigarettes per day) or low tobacco consumption (five cigarettes or less per day) were excluded in an attempt to even out the effects of the nicotine by impeding an excessive or minimal nicotine habituation. The final sample included 10 smokers (5 women and 5 men). Finally, the females were given a date that did not coincide with their premenstrual, menstrual, or ovulation periods. That is, one week between the last day of their menstruation and the following 7–10 days (preovulation phase).

Apparatus and Procedure

Participants received instructions concerning the week prior to the study, indicating them to sleep according to their normal schedules. The day before the investigation subjects were assessed from 9:00 a.m. to 3:00 p.m. (each 2 h) to familiarize them with the devices and the experimental protocol. On the first day of the study, subjects (always a mixed group of 5–7) were reminded of the participation rules of the experiment and signed a written consent binding them to such norms. Subjects were free to withdraw from the experiment at any time. They were not allowed to consume coffee, tea, or cola refreshments, alcohol, or any medication. They could not shower (they could freshen up and change clothing) or do any physical exercise that could facilitate activation. Smoking was only allowed immediately after finishing each data recording (every 2 h) to prevent a nicotine effect on psychophysiological variables.

The investigation began at 9:00 a.m. on Tuesday.
morning and continued until 9:00 p.m. Thursday evening. Throughout the 60 h of TSD the subjects remained in a large room that could only be abandoned to go an adjacent laboratory every 2 h. A total of 30 recordings were completed always at the same time of day: 9:00 a.m., 11:00 a.m., 1:00 p.m., 3:00 p.m., etc. The room temperature in both areas was maintained at a thermoneutral level (22–25 °C), the lighting was constant, and there was isolation from any noise. Each recording session in the laboratory consisted of a reaction time task, which lasted about 3 min in length. Following the RT task, a longer vigilance task was initiated (to estimate time intervals during 5–7 min) in which the HR (the average value of the second min) was recorded in order to standardize the recording context. The photoplethysmograph for the HR recording was placed on the index finger of the left hand (all of the subjects were right handed). A Biociber (Barcelona, Spain), Model Cardioback CY-15, polygraph module for sanguineous pulse provided the measure for HR (filter 0.5–5 Hz). This device shows the HR in a digitalized display or in a computerized recording by means of a Windows 95 software program. After finishing the vigilance task, SBP and DBP were obtained under carefully standardized conditions using a Nissei (Tokyo, Japan), Model DS-155E, digital blood pressure monitor that uses the oscillographic method. A standard cuff automatically inflated to a maximum pressure of 190 mmHg was placed over the brachial artery of the left arm, with a deflation rate of 3–4 mmHg/s. Subjects were seated in an armchair on which their left arm was immobilized to reduce artefacts, and no verbalization was allowed from the participants to eliminate potential confusing effects.

When subject 1 completed a data recording session in the laboratory and returned to the room, subject 2 arrived, and this process was repeated until the entire group had finished a recording session. Free time between data recordings could be spent on reading, listening to music, playing board games, etc. Subjects were under the constant supervision of two female laboratory technicians. The technicians worked 8-h shifts. Breakfast was provided at 8:30 a.m., the main meal at 2:30 p.m., dinner at 8:30 p.m. and a snack at 2:30 a.m., with the same menu for all subjects.

Data Analysis

A comparison of the average of the measurements taken before the experiment on Monday (four recordings from 9:00 a.m. to 3:00 p.m.) with the average of the four measurements taken on the first day of the study at the same times yielded information about the stabilization of the measures. The first recording of both days was discarded to eliminate artefacts. Paired t-test confirmed that there were no significant differences for any variables in these comparisons. A two-way analysis of variance (ANOVA) for repeated measures was performed to assess the effects of TSD and gender as well as their interaction on each parameter. ANOVAS had the duration of TSD as one within-subject factor (with a total of 30 measures) and gender as the other factor, with significance levels corrected for sphericity by the Greenhouse-Geisser ε.

The data collected during TSD are subjected to inherent rhythmic oscillations along with effects related to the sleep loss per se. It has been established that a linear or monotonic function would be related to the cumulative effect of TSD, while the circadian and/or ultradian rhythmicity would be specified in other types of functions (Bakoff et al., 1991). In those variables where the ANOVA was significant, we determined by means of planned complex comparisons whether the effects attributable to TSD were exhibited across the diurnal periods, on the one hand, and the nocturnal periods, on the other hand. Complex comparisons corrected by Bonferroni were done on the following periods of time: DAY 1 (9:00 a.m. to 7:00 p.m.), NIGHT 1 (9:00 p.m. to 7:00 a.m.), DAY 2 (9:00 a.m. to 7:00 p.m.), NIGHT 2 (9:00 p.m. to 7:00 a.m.), and DAY 3 (9:00 a.m. to 7:00 p.m.). For each period, the scores of each variable were averaged. If the TSD produces a significant alteration in HR or BP, the effects will be greater, DAY 2 than DAY 1, DAY 3 than DAY 2, and logically, DAY 3 than DAY 1. On the other hand, it is expected that all of the variables reach their greatest level of deactivation on NIGHT 2. NIGHT 1 vs DAY 2 and NIGHT 2 vs DAY 3 will be compared in order to verify up to what extent the maintenance of the circadian rhythm can produce a recovery of the scores in the diurnal periods.

Furthermore, trend analyses were performed on data for which there were significant variation across the TSD days. This analysis was applied to the 30 measurements of HR and BP and yielded information about the nature of the relationship between TSD and each parameter. In addition, the percentage of variance accounted for by each significant trend was estimated. The maximum order for the trend components was limited to nine, after previously applying an analysis with components up to the 29th order and verifying that the significant trends were the same in both cases.

Results

Heart Rate

The ANOVA for repeated measurements indicated a significant main effect for the tso factor (F(29, 812) = 5.79,
Table 1. Planned complex comparisons corrected by Bonferroni between the different periods of TSD established for the data analysis. The table shows the mean scores of each period of analysis for HR (heart rate) and SBP (systolic blood pressure).

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>SBP</th>
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</thead>
<tbody>
<tr>
<td>DAY1–DAY2</td>
<td>71.25–71.54</td>
<td>11.69–11.42**</td>
</tr>
<tr>
<td>DAY2–DAY3</td>
<td>71.54–72.19</td>
<td>11.42–11.40</td>
</tr>
<tr>
<td>DAY1–DAY3</td>
<td>71.25–72.19</td>
<td>11.69–11.40**</td>
</tr>
<tr>
<td>NIGHT1–NIGHT2</td>
<td>70.32–69.22</td>
<td>11.40–11.41</td>
</tr>
<tr>
<td>NIGHT1–DAY2</td>
<td>70.32–71.54</td>
<td>11.40–11.42</td>
</tr>
<tr>
<td>NIGHT2–DAY3</td>
<td>69.22–72.19**</td>
<td>11.41–11.40</td>
</tr>
</tbody>
</table>

**P < .01

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Table 2. Summary of the trend analysis for HR (heart rate) and SBP (systolic blood pressure) in relation to 60 h of TSD. The determination coefficients ($R^2$) of polynomial regression express the variability accounted for by each one of the significant trends.

<table>
<thead>
<tr>
<th></th>
<th>TRENDS</th>
<th>$R^2$ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>Cubic**</td>
<td>23.37 %</td>
</tr>
<tr>
<td></td>
<td>Quintic***</td>
<td>49.01 %</td>
</tr>
<tr>
<td></td>
<td>Septic***</td>
<td>16.51 %</td>
</tr>
<tr>
<td>SBP</td>
<td>Linear*</td>
<td>24.73 %</td>
</tr>
<tr>
<td></td>
<td>Quadraticc</td>
<td>15.72 %</td>
</tr>
<tr>
<td></td>
<td>Quintic**</td>
<td>28.51 %</td>
</tr>
<tr>
<td></td>
<td>Septic**</td>
<td>18.60 %</td>
</tr>
</tbody>
</table>

$P < .05$ **P < .01 ***P < .001

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Figure 1. The mean scores of heart rate (HR) for the total sample are plotted on the ordinate as a function of 60 h of total sleep deprivation (TSD). At the top, the five periods of TSD included and some indications of the hours of the day that correspond to the accumulated hours of TSD.

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$P < .001$. There was no significant main effect for the gender factor, nor for the interaction between gender and TSD. Table 1 shows a summary of the planned complex comparisons carried out between the mean values of HR in the different periods of TSD. Results were significant for the comparison between NIGHT 2 vs DAY 3 ($F(1, 28) = 7.78, P < .01$). The remaining planned complex comparisons did not prove to be significant. There seems to be a tendency in which the mean values of HR increase during the daily periods, DAY 1 (71.25 ± 12.41 bpm), DAY 2 (71.54 ± 11.23 bpm), and DAY 3 (72.19 ± 13.88 bpm), and decrease during both nights, NIGHT 1 (70.32 ± 12.33 bpm) and NIGHT 2 (69.22 ± 10.83 bpm), but these very small variations are not significant. HR increased significantly only from NIGHT 2 (69.22 ± 10.83 bpm), the period in which the lowest HR values are reached at 5:00 a.m., to DAY 3 (72.19 ± 13.88 bpm).

Table 2 shows a summary of the trend analysis for the HR in relation to the period of TSD. The trends found to be significant are the cubic ($F(1, 28) = 17.27, P < .001$), quintic ($F(1, 28) = 38.14, P < .001$), and septic trends ($F(1, 28) = 28.83, P < .001$). The polynomial trend that explains a greater percentage of the variance (49.01 %) in HR during the TSD is a quintic function, which, just as the septic trend (16.51 %), must be understood as ap-
proximating to the rhythmicity of the data (see Fig. 1). The cubic trend accounted for a 23.37% of the HR variability throughout the TSD. This trend appears to be related to the two main direction changes that the HR shows during the 60 h of TSD, as was also reflected by the comparisons. HR shows no important changes during the first 36 h of TSD (DAY 1, NIGHT 1, and DAY 2), a decrease in average on NIGHT 2, and an increase on DAY 3.

Diastolic Blood Pressure

The ANOVA for repeated measures revealed a significant main effect for gender ($F(1, 28) = 7.68, P < .01$), but not for the TSD factor, nor for the interaction between gender and TSD. Males have a higher DBP (7.14 ± 1.05 mmHg) than females (6.43 ± 0.81 mmHg). However, DBP shows no significant changes during 60 h of TSD.

Systolic Blood Pressure

The results of the ANOVA indicated that for SBP there was a significant main effect for the TSD factor ($F(29, 812) = 2.19, P < .001$), and for the gender factor ($F(1, 28) = 38.53, P < .001$). As in the case of HR, the interaction between gender and TSD was not significant. The average SBP for males (12.33 ± 1.72 mmHg) is higher than for females (10.60 ± 1.23 mmHg), and these SBP values showed a small downward trend during 60 h of TSD. The planned complex comparisons that were found to be significant (see Tab. 1) were those carried out between DAY1 and DAY2 ($F(1, 28) = 9.61, P < .01$), and between DAY1 and DAY3 ($F(1, 28) = 6.95, P < .01$). SBP decreases from DAY 1 (11.69 ± 1.46 mmHg) to DAY 2 (11.42 ± 1.36 mmHg), and after that shows a nonsignificant decrease of a smaller magnitude from DAY 2 (11.42 ± 1.36 mmHg) to DAY 3 (11.40 ± 1.39 mmHg).

The trend analysis (see Tab. 2) was significant for the linear ($F(1, 28) = 4.93, P < .05$), quadratic ($F(1, 28) = 4.63, P < .05$), quintic ($F(1, 28) = 10.60, P < .01$), and septic trends ($F(1, 28) = 7.37, P < .01$). A descending linear function attributable to the accumulated sleep loss effect accounted for a 24.73% of the variance of SBP during the TSD. Similarly, the quadratic trend explains a 15.72% of the variance of SBP. This quadratic trend appears to reflect (as the comparisons also indicated) the decrease in SBP that occurs on the first 24 h of TSD followed by a stabilization with small nonsignificant variations during the remaining periods of TSD (see Fig. 2). Significant trends of a greater order are associat-
ed with rhythmic aspects (see Tab. 2). For example, it highlights the percentage of variance of the SBP accounted for by the quintic trend (28.51%), as in the case of HR.

Discussion

A TSD of 60 h produces some modifications in HR and SBP, although the clinical significance of these changes are probably null as we will discuss below. HR shows few changes attributable to sleep loss during the first 36 h of TSD (i.e., 71.25 bpm on day 1 and 71.54 bpm on day 2). After that, HR decreases on the second night (69.22 bpm) and increases on the third day (72.19 bpm). The slight decrease found in HR on night 2 is consistent with some recent reports (Kaneda et al., 1999; Muenter et al., 2000). However, it is not easy to interpret the HR variation pattern during the TSD. In the daily periods a progressive decrease of the HR is not observed. Instead, HR appears to increase on day 3. This highlights the importance of including frequent measurements during the whole period of TSD as in the present study (every 2 h). The TSD could simultaneously produce a decrease of the HR in the nocturnal periods, which is coherent with the intense deactivation related with the TSD combined with the rhythmic influence, which reaches its minimum here (Bakoff et al., 1991; Miró et al., 2002), and an increase during the daily periods. The organism can respond with a slight HR acceleration in a context in which a subject must remain awake with increasing fatigue, sleepiness, and decreased alertness. The enhanced effort or the active coping magnifies cardiovascular responses during normal wakefulness without TSD (Bongard & Hodapp, 1997; Müller et al., 1998). Furthermore, TSD might represent a stressful condition promoting the synthesis of catecholamines and increasing sympathetic nervous activity (lusardi et al., 1999; Tochikubo et al., 1996). But this is not clear, considering the absence of any consistent effect on the levels of stress-related hormones such as cortisol (Gary et al., 1996). Perhaps this pattern of changes in the HR during the TSD imply that the circadian amplitude (distance between the troughs and peaks) could be enhanced as the TSD progresses. Further studies are needed to test this hypothesis.

HR variations during TSD are mainly characterized by circadian oscillations as shown by the significant adjustment to quintic and septic trends, which together explain 65.52% of its variance. HR reaches its acrophase at 3:00 p.m. during the daily periods (i.e., 79.30 bpm on day 3) and its nadir at 5:00 a.m. during both nights (i.e., 65 bpm on night 2). The HR rhythm is very sensitive to the external zeitgebers (Buela-Casals & Sierra, 1994; Rechlin et al., 1995), so that in some studies a HR circadian rhythm is not observed (Ahnve et al., 1981). However, the maintenance of the circadian rhythmicity of the HR agrees with two studies of 24–26 h of TSD (Endo et al., 1981; Kerkhof et al., 1998) and with another study of 60 h of TSD (Stefikova et al., 1986).

In addition, we found no gender differences in the TSD effect on HR or BP. To the best of our knowledge there are no investigations that can be directly compared with our results. On the other hand, coinciding with previous reports (Horne, 1978; Kamphuisen et al., 1992; Muenter et al., 2000; Webb et al., 1981) DBP did not show significant modifications during the TSD. SBP shows a decrease from the first 24 h of TSD (11.69 mmHg on DAY 1 to 11.42 mmHg on DAY 2) and is then maintained without notable variations across all the remaining periods of TSD. The slight descending linear trend in SBP is consistent with other investigations of 48–60 h of TSD (Kamphuisen et al., 1992; Webb et al., 1981). Also, a number of studies have found comparable effects without TSD using "bored" or "sleepy" mood states (Shapiro et al., 2001). Other studies report an increase in SBP, but in middle-age adults or moderately hypertensive subjects (Kato et al., 2000; Lusardi et al., 1999). These changes in SBP during the TSD are also accompanied by rhythmic oscillations. It highlights the percentage of variance in SBP accounted for by a quintic trend (28.51%). SBP shows the acrophase at 9:00 p.m (i.e., 11.78 mmHg on day 1) and the nadir around 5:00–7:00 a.m. (i.e., 11.01 mmHg on night 1). But the circadian rhythmicity for SBP is not as clear as for HR. In fact, several authors have stressed that because of its small amplitude, BP rhythm is not easily detectable (Ikonomov et al., 1998). The origin of BP variation is still under debate, and the bulk of the available evidence favors a predominant role of exogenous factors in determining its modifications, especially the intensity and the timing of the sleep-wake cycle (Baumgart, 1991; Kerkhof et al., 1998). Our results suggest that the existence of an endogenous circadian factor cannot be excluded.

It should be mentioned that in our design single readings of BP were obtained every 2 h. Assessing only one each time could have limited the validity of the measures. However, it has been suggested that the low reproducibility of the BP measures is not explained by a limited number of hourly measurements, rather than by differences in conditions between recordings, a limitation that may be mitigated by stricter standardization (Mancia et al., 1992). In standardizing recording conditions, as in the present study, the reproducibility of BP improves (Musso et al., 1997; Zakopoulos et al., 2001). In fact, we did not find differences between measurements taken on the pre-TSD day and on the first day of the experiment.

In short, HR and SBP seem to undergo some varia-
tions during 60 h of TSD; but it is very important to ask whether these significant statistical differences are of biological impact. A comparison of the values obtained here with the normal range for HR (70 bpm) or for SBP (80–120 mmHg) reveals that the most likely answer is that they are not. In fact, it has been stressed that the deficits following the TSD are mainly cognitive, of activation and of mood, supporting, from a functional perspective, that sleep mainly serves the brain, at least in humans (Horne, 1988; Harrison & Horne, 1998). However, subjects in our study were young and healthy. Thus, our findings may underestimate the impact of TSD in older subjects and in subjects with cardiovascular disease. Future investigation could clarify the relationships between cardiovascular parameters and activation levels during TSD, as well as the impact on health from different sleep restriction manipulations.

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References


