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Total sleep deprivation effect on disengagement of spatial attention as assessed by saccadic eye movements☆

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Abstract

Objective: Previous research has shown that total sleep deprivation (TSD) of short duration (one night) affects performance to some cognitive tasks subserved by a fronto-parietal network. The aim of our study was to assess the effects of TSD on visuo-spatial attention, which is a cognitive task involving this network. Specifically, the disengagement of spatial attention was investigated with gap and overlap paradigms of saccadic eye movements.

Methods: Ten healthy young male subjects performed the two tasks the morning after a normal night and after a TSD night. The study was conducted using a balanced, crossover design.

Results: TSD significantly increased the gap effect (difference of latency between overlap and gap).

Conclusions: This result can be interpreted as an impaired disengagement of attention after TSD. As the peak velocity, which is an indicator of alertness, was not altered by TSD, the impairment in the disengagement of spatial attention does not result from a decrease in alertness.

Significance: This study shows that saccadic eye movements enable studying alertness and disengagement of spatial attention simultaneously. The idea that specific brain areas are affected by TSD is confirmed by our results.

Keywords: Saccadic eye movements; Attention; Latency; Sleep deprivation; Healthy subjects

1. Introduction

Numerous studies have investigated the effects of sleep deprivation (SD) on various aspects of performance, arguing that sleep loss has a more deleterious effect on the performance of long, monotonous, boring tasks than it does on short and interesting ones (Dinges and Kribbs, 1991 for a review; Koslowsky and Babkoff, 1992 for a meta-analysis). Some authors maintain that sleep deprivation leads to a global decrease in arousal levels, the general idea being that impaired performance induced by total SD (TSD) is due to a decrease in alertness (Dinges and Kribbs, 1991; Wilkinson, 1992). Thus, based on several decades of research, Wilkinson (1992) concluded that "sleep deprivation reduces the non-specific arousal level of the body, but has no specific effect".

Several studies have, however, refuted Wilkinson's conclusion. Thus, it has been reported that TSD affects selective cognitive performance on short-lasting neuropsychological tasks that are believed to be subserved by the prefrontal cortex; for example, word fluency test (Horne, 1988), Haylings task (Harrison and Horne, 1998) and Trail-Making task (Muzur et al., 2002; Wimmer et al., 1992) (see Durmer and Dinges, 2005 for a review). Moreover, functional imaging studies during cognitive tasks have shown that TSD leads to modifications in specific brain areas. Among them, the frontal and parietal cortices are often affected (Drummond and Brown, 2001; Drummond et al., 1999, 2000; Portas et al., 1998; Thomas et al., 2000). For example, after a 24 h TSD it has been observed a decreased glucose metabolism in prefrontal and parietal

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cortices during performance of a difficult arithmetic working memory task (Thomas et al., 2000) and an increased bilateral cerebral blood oxygen level in both cortices during verbal learning and divided attention (Drummond and Brown, 2001). It seems likely that other cognitive tasks involving frontal-parietal network such as visuo-spatial attention (Posner et al., 1984) would also be affected after TSD. Among the visuo-spatial attention processes, disengagement of attention is of particular importance in many situations where it is necessary to treat in time an event, which has to be avoided (for example, during driving: bike, pedestrian, other vehicle) or in usual situations as reading or visual searching an information. A recent published study (Versace et al., in press) investigated the effect of sleep reduction on orienting of attention and showed reduction in the efficiency of the disengaging mechanisms using the cued reaction time task of Posner (1980). The authors concluded that this effect is independent of reduced alertness evaluated with a simple reaction time task. Nevertheless, as subjects realized the two tests at two different times and as alertness is fluctuating (Okawa et al., 1984), it is possible that alertness during the cued reaction time task differ from the alertness measured during the reaction time task. The aim of our study was to evaluate the effect of total sleep deprivation simultaneously on disengagement of attention and on alertness. Eye movements were used to assess this aspect of attention because they are in close functional and anatomical relationships (Corbetta et al., 1998; Nobre et al., 2000).

Among eye movements, saccadic eye movements are of particular interest as two parameters give different information on performance. First, saccadic latency enable to evaluate attentional disengagement according the three-loop model of Fischer (1987) and Fischer and Weber (1993), by using two paradigms (gap and overlap). In both paradigms, a visual fixation point is first presented in a central, straight-ahead position, followed by a lateral target to which a saccade must be performed. In the gap paradigm, in which the central target disappears before the lateral target appears, attention is disengaged by the extinction of the central target, thus before the appearance of the lateral target. By contrast, in the overlap paradigm, in which the central target remains during the appearance of the lateral target, attention remains engaged on the central target when the lateral target appears. As subjects had to disengage from the fixation point before to perform a saccade toward the target, saccadic latencies are longer in the overlap paradigm than in the gap paradigm, inducing a gap effect (i.e. the difference in saccadic latencies between the two paradigms (Saslow, 1967)) which can be explained by the attentional disengagement process (Fischer and Weber, 1993). Increased gap effect thus reflects an impairment of attentional disengagement. Second, saccadic peak velocity is a parameter strongly dependent on the level of alertness (Crommelinck and Roucoux, 1976; Ron et al., 1972). This saccadic parameter is thus a convenient means to assess alertness during an oculomotor task. Thus, if TSD alters disengagement of attention, we should observe an increased gap effect and, if this impairment results from a decrease in alertness, we should also observe a decrease in saccadic peak velocity.

The aim of the present study is thus to assess the effects of TSD on visuo-spatial attention, and to determine whether a putative deficit would be related to a decrease in alertness as suggested by Wilkinson (1992).

2. Methods

2.1. Subjects

Ten young, healthy male adults participated in this study (age range 19–24 years, mean = 21). All were University students. Screening excluded those having sleep difficulties who napped regularly in the daytime, and were on medication that affected sleep or sleepiness. Subjects suffering from neurological, psychiatric, cardiovascular, respiratory, hepatic, renal or metabolic pathologies where excluded. They slept 7–8 h at night, were non-smokers with no history of alcohol abuse. All had normal, or corrected normal, vision. They had the procedures explained, signed consent forms, and were paid to participate. Experiments were approved by the local ethical committee.

2.2. Experimental design

The study was conducted using a balanced, crossover design. A 2-week interval separated the two experimental sessions, with half of the subjects starting by the sleep deprivation and the other half by the control night. Actimeters were used three nights prior each testing session to ensure that subjects sleep normally before the experiments.

Each session began at 7 p.m. where subjects had a standardized dinner. Subjects who were non-sleep-deprivated were escorted home at 10 p.m. and retired at their usual bedtime (between 11 and 12 p.m.). To monitor the times of both retiring to bed and rising as well as the quality of sleep, an actimeter was placed on the non-dominant wrist of subjects sleeping at home. Analysis of their actimetric profiles showed that all subjects respected instructions, i.e. they woke up between 7 and 7.30 a.m., they did not had nap the day before the experiment and they had normal sleep (mean duration of 6.50 ± 0.42 h). During sleep deprivation, subjects stayed the night at the laboratory under the supervision of an experimenter. No food was permitted to eat and no beverage other than water was available in the laboratory. They might carry out quiet activities such as reading, writing or discussing. The next morning, the subjects who slept at home were brought to the laboratory by an experimenter. All subjects ate the same breakfast at 8.30 a.m. All subjects performed saccadic eye movement tests between 10.00 and 12 a.m.

2.3. Saccade tests

Horizontal eye movements were recorded by an infrared photoelectric limbus eye tracking device (IRIS, SKALAR, Delft, The Netherlands) in a quiet, darkened room. Eye and target movements were sampled on-line at 200 Hz using a 12 bit analog-to-digital converter. Head movements were restricted using a bite bar.

Each recording session began and ended with a calibration test. This comprised light emitting diode (LED) jumps with amplitudes of 5, 10, 15, 20, 25° to and from the central position, in both directions.

Two paradigms of reflexive visually guided saccades were successively tested. In each paradigm, one lateral LED was randomly presented 15° to either the right or left of the central LED on the horizontal meridian in each of the sixty trials. In the gap paradigm, subjects fixated a central fixation target illuminated for 2–4 s. Two hundred milliseconds after the central target was extinguished, a lateral target was switched on for 500 ms. Subjects were asked to move their eyes to the lateral target as quickly as possible when it appeared. Trials were separated by a 2000 ms intertrial interval, during which no stimuli were presented. In the overlap paradigm, the central fixation target remained switched on during presentation of the lateral target. All other conditions were the same as for the gap task.

2.4. Data analysis

Eye movement velocity was calculated digitally using the two-point central difference algorithm (20 ms step size). Saccades were then detected by an algorithm using velocity and acceleration thresholds, then systematically checked and corrected manually as required (Denise et al., 1996). Each saccade was visually inspected and excluded from analysis if the subject blinked.

In the gap paradigm, human subjects may generate saccades with short reaction times, named 'express saccades' (Fischer and Ramsperger, 1984). From animal lesions studies, it appears that express saccades analysis in human provides a way of testing collicular function (Leigh and Kennard, 2004). The percentage of express saccades (80–130 ms range; Fischer and Weber, 1993) was calculated for both tasks.

We also calculated for gap and overlap tasks the number and the latency of errors, i.e. saccades made in the opposite direction to the lateral target.

Saccades with latency less than 80 ms, suggesting an anticipatory saccades (Fischer and Weber, 1993; Wenban-Smith and Findlay, 1991), were excluded from the following analysis. Saccadic parameters analyzed were: (1) saccadic latency (ms), which is the period of time from lateral target illumination to initiation of eye movement; (2) saccadic accuracy (%), i.e. amplitude of the saccade divided by the lateral target amplitude (15°) and (3) saccadic peak velocity (°/s), which is the highest velocity reached during the saccade. As this parameter is a function of saccade amplitude and because many saccades undershoot, we used the known linear relationship between peak velocity and saccade amplitude for saccade amplitude under 20° (Bahill et al., 1975) to determine the peak velocity value. We plotted the peak velocity value of each of the 60 trials to determine the parameters of the linear relationship for each subject and each condition. With these parameters we calculated the peak velocity value for our requested 15° saccade. Finally, we calculated the gap effect (ms) as the latency difference between the overlap and gap conditions.

2.5. Statistical analysis

Saccadic latency, accuracy, and peak velocity were analyzed using a 2 (sleep: normal vs TSD) by 2 (paradigms: gap vs overlap) repeated measures ANOVA. TSD effect on number of errors was evaluated with a chi-square test. A Wilcoxon test was used to test TSD effect on percent of express saccades and an unpaired t test evaluated TSD effect on errors latency. Significance was accepted at the $P<0.05$ level. Mean $\pm$ SD were given in the text.

3. Results

The ANOVA performed on the saccadic latency showed a significant paradigm [$F(1,9)=152.91$; $P<0.000001$], sleep [$F(1,9)=17.3$; $P=0.00242$] and paradigm $\times$ sleep effect [$F(1,9)=25.466$; $P=0.00069$]. t Tests showed that TSD significantly increased saccadic latency (in ms) in both the gap [NN: 187 ± 23; TSD: 198 ± 27; $t_9=2.31$; $P=0.046$] and overlap [NN: 290 ± 20; TSD: 327 ± 30; $t_9=4.937$; $P<0.001$] paradigms (Fig. 1). As the interaction was significant, t test showed that the gap effect (in ms) was significantly higher after TSD as compared to normal night (NN) [NN: 103 ± 27; TSD: 129 ± 34; $t_9=5.046$; $P=0.0007$]. The increased gap effect was found in each individual subject (see Fig. 2).

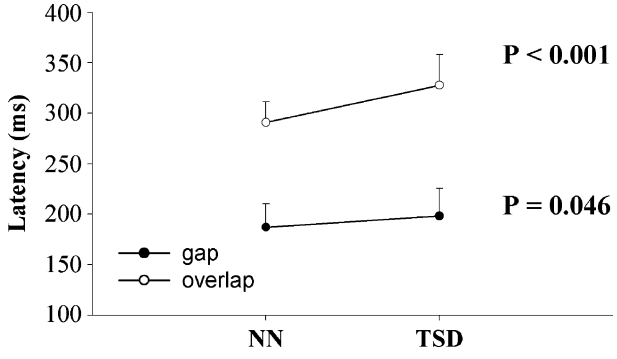

Fig. 1. Effects of TSD on latency (ms) in gap and overlap paradigms. Mean $\pm$ SD are represented. NN, normal night; TSD, total sleep deprivation night.

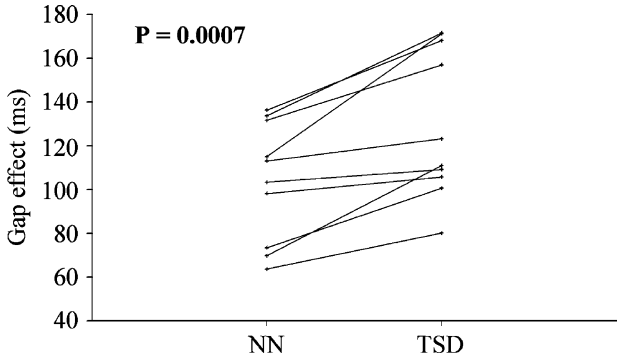

Fig. 2. Effects of TSD on gap effect (ms). Ten individual values are represented. NN, normal night; TSD, total sleep deprivation night.

ANOVA performed on saccadic accuracy (in percentage) (Fig. 3) showed a significant main effect of paradigm [gap: 82±7.2; overlap: 87.3±5.7; $F(1,9)=20.005$; $P=0.00155$], of sleep [NN: 87.6±4.7; TSD: 81.7±7.7; $F(1,9)=13.368$; $P=0.00527$] but no paradigm×sleep interaction [$F(1,9)=1.3$; $P=0.28$].

On saccadic peak velocity (in °/s), ANOVA showed a significant main effect of paradigm [gap: 314.8±38.2; overlap: 307.6±36.9; $F(1,9)=6.52$; $P=0.003$] but no sleep effect [$F(1,9)=3.008$; $P=0.11$] and no paradigm×sleep interaction [$F(1,9)=1.65$; $P=0.23$] (Fig. 4).

Express saccades were analyzed only in the gap paradigm because no sufficient express saccades or errors were made in overlap paradigm to serve for analysis. TSD significantly decreased the percentage of express saccades (in percentage) [12.5±9.4 for NN; 7.87±7.61 for TSD; $Z=1.98$; $P=0.04$]. The number of errors occurring before 130 ms was compared by a chi-square test to the total number of saccades [number of errors: 30 for NN and 15 for TSD; number of saccades: 556 for NN and 524 for TSD; $X^2=3.99$, $P=0.045$). Errors latency (in ms) was not affected by TSD [71±31 for NN and 75±25 for TSD: $t_{43}=0.385$; $P=0.7$].

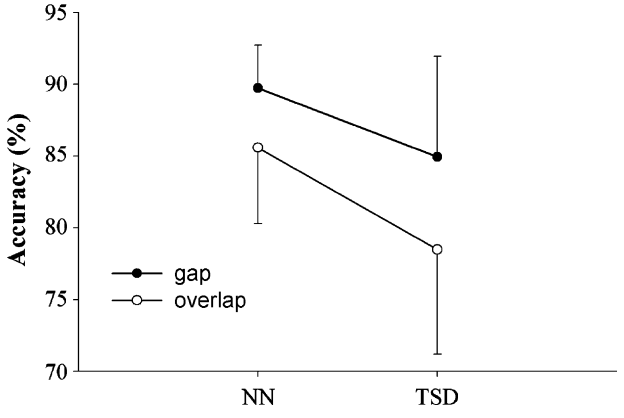

Fig. 3. Effects of TSD on accuracy (%) in gap and overlap paradigms. Mean±SD. NN, normal night; TSD, total sleep deprivation night.

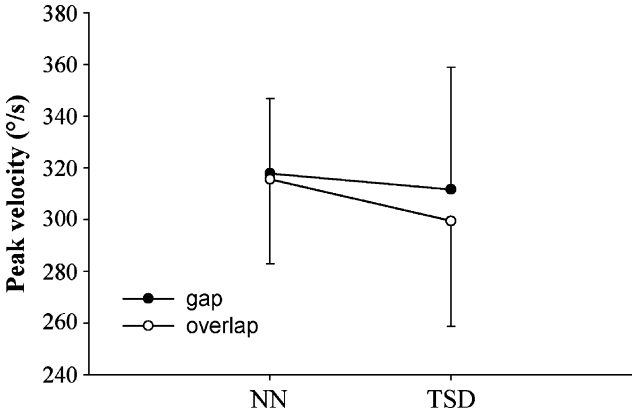

Fig. 4. Effects of TSD on peak velocity (°/s) in gap and overlap paradigms. Mean±SD. NN, normal night; TSD, total sleep deprivation night.

4. Discussion

In our study, we investigated a possible impairment of disengagement of attention induced by TSD. We found, in the TSD condition, an increase in saccade latency both in the gap and in the overlap paradigms, which is in agreement with earlier studies using a single oculomotor test (De Gennaro et al., 2000; van Steveninck et al., 1999) but not with Zils et al. (2005) who did not found an increase in saccade latency in the gap paradigm after one sleep deprivation night. We also found that the TSD effect was of greater magnitude in the overlap condition, which results in an increased gap effect in TSD in comparison with NN. As overlap latencies are longer than gap latencies one might hypothesize that a general slowing of all processes due to TSD would also result in larger effects for the overlap saccades, which could explain the gap effect increase. An overall delay in oculomotor responses could also explain the decrease in frequency of express saccades in the gap paradigm after TSD. However, after TSD the increase in latency is significantly higher in the overlap condition (>12%) than in the gap condition (6%) [$t_9=-3.6$; $P=0.006$], indicating that the gap effect increase (+24.7%) observed after TSD cannot be explained by a simple general slowing. Thus, our results show that the triggering of saccades after TSD is much more affected in the oculomotor paradigm that requires disengagement of attention (overlap) than in the one in which attention (gap) is already disengaged. Moreover, a simple general slowing cannot explain the decreased number of errors and the not delayed errors after TSD found in the gap condition. We may conclude that, in line with our initial hypothesis, disengagement of visuo-spatial attention is impaired after TSD.

Our results could be explained by impaired function of one or several brain structures that are known to be involved in visuo-spatial attention; mainly the superior colliculus, the dorsolateral prefrontal cortex (DLPFC) and the parietal cortex. In monkeys, it has been shown that during gap paradigm cells in the superior colliculus decrease their activity during the gap, thereby weakening their normal

state of inhibition on the saccade generator, allowing for faster saccadic reaction times to peripheral targets (Dorris and Munoz, 1995). In TSD condition, a prolonged activity of the fixation cells in the superior colliculus, linked to persistent engagement of attention, might occur after the extinction of the central target. This phenomenon could explain the decreased errors and the increased saccadic latency observed in the gap paradigm after TSD. Consequently, the impairment of disengagement of attention may be mediated by such persistent engagement of attention which should be necessarily much more strong in overlap paradigm.

Spatial attention involves a fronto-parietal network in which the DLPFC acts on superior colliculus thus inhibiting the generation of express saccades (Muri et al., 1999). Increased activity in DLPFC resulting in an increased action on superior colliculus would also explain the observed inhibition of express saccades and error saccades. However, an increased activity in DLPFC is unlikely because TSD induces a decrease in glucose metabolism in the prefrontal cortex and a decrease in performance in prefrontal-oriented cognitive tasks (Drummond et al., 1999; Thomas et al., 2000). Nevertheless, this hypothesis could be tested in a further study by means of an antisaccade paradigm, in which prosaccade errors are known to be subserved by the DLPFC (Pierrot-Deseilligny et al., 2003). As it has been proposed that disengagement of attention could mainly depend on the parietal cortex (Posner et al., 1984), the impaired disengagement of attention found in the present study could thus result from a parietal cortex alteration induced by TSD. This hypothesis would be in agreement with reduced activation in the parietal regions reported after TSD, which was associated with reduced performance in serial subtraction (Drummond et al., 1999; Thomas et al., 2000) and increased reaction time during working memory tasks (Chee and Choo, 2004; Habeck et al., 2004). This hypothesis would also agree with the correlations reported between relative preservation of divided attention performance and greater activation in the bilateral parietal lobes after TSD (Drummond and Brown, 2001; Drummond et al., 2000). Finally, the similarity between the reaction time parameter used in the above working memory tasks and our saccadic latency parameter further supports our hypothesis. fMRI studies of eye movements after TSD would be very useful to further confirm the involvement of a parietal dysfunction in the impaired disengagement of attention after TSD.

The present study also shows that TSD does not decrease the peak velocity of saccades while De Gennaro et al. (2000), van Steveninck et al. (1999) and Zils et al. (2005) reported decreased peak velocity following TSD. This discrepancy probably arises from differential calculation of this parameter. Indeed, when the peak velocity is calculated for uncorrected amplitude of saccades as in De Gennaro et al. (2000) and van Steveninck et al. (1999) studies, we also found a decrease after TSD. Zils et al. (2005) corrected their data but the recording method (EOG) and the function used to correct peak velocity data (exponential) were different and may explain the discrepancy. Our results for a 15° saccade show that structures that generate peak velocity are not affected by TSD. Consequently, as peak velocity is supposed to reflect the level of alertness (Crommelinck and Roucoux, 1976; Ron et al., 1972), we can conclude that the increase in latency observed in our study did not result from a decrease in alertness. The particular interest of using saccadic eye movements is that it permits to record simultaneously two parameters that reflect different processes, which is not the case in Versace et al. (in press) study. Indeed, in that work, disengagement of attention and alertness were evaluated with a time reaction parameter used in two different tasks (simple reaction time task and cued reaction time task). Our results clearly indicate that the impairment of disengagement of attention following TSD is independent of any decrease in alertness.

A third saccadic eye movement parameter, saccadic accuracy, was analyzed despite it had no relation with main objective of this study. In agreement with Zils et al. (2005), we found significant impairment of saccadic accuracy after TSD. De Gennaro et al. (2000) did not find accuracy decrease after 40 h of SD with their stepwise jumps of pseudo-random amplitude paradigm. This discrepancy between their results and ours may be linked to the fact that we used a single amplitude (15°) whereas De Gennaro et al. (2000) used amplitude comprised between 5 and 30°. This result could arise from impairment in motor programming, as it has been shown that TSD induces deactivation in cerebellum (Bell-McGinty et al., 2004; Wu et al., 1991), a structure known to control saccadic accuracy (Leigh and Zee, 1999). This decrease in saccadic accuracy could also result from impairment in processing target location as it has been shown that TSD impairs areas that are known to be implicated in this function (Bell-McGinty et al., 2004) in particular parietal areas. As lesions of parietal eye field lead to both a reduced accuracy and an increased latency of reflexive saccade (Heide and Kompf, 1998) most of our results can be explained by a parietal dysfunction.

5. Conclusion

Using two oculomotor paradigms, we found that TSD impairs disengagement of attention and that this impairment, contrary to usual interpretation of the effects of TSD, appears to be independent of any decrease in alertness. This finding is probably, at least partially, related to a parietal dysfunction and leads to future investigations to evaluate possible dysfunction in other brain regions after TSD. This impairment would have dangerous effects on everyday life situations as car driving. Moreover, this study shows that attention and alertness can be assessed simultaneously with saccadic latency and peak of velocity.

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