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Research report

Effects of paradoxical sleep deprivation on the performance of rats in a model of visual attention

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Abstract

In the present work we sought to evaluate the effects of paradoxical sleep deprivation (PSD) on the performance of rats in the five-choice serial reaction time task, a test designed to assess attentional function. Adult male Wistar rats were trained to detect a brief (1 s) light stimulus randomly presented in one of five locations in a box specially designed for the task. After achieving stable performance, the animals were submitted to 96 h of sleep deprivation by the platform technique, in which the rats are placed on top of small platforms in a tank filled with water. During sleep, particularly during the paradoxical stage, the loss of muscle tone make the animals fall into the water, thus awakening them and so depriving of sleep. Performance in the task was assessed daily during the 96 h deprivation period and also during seven recovery days afterwards. Paradoxical sleep deprivation reduced accuracy on the on the third (72 h) and fourth (96 h) days of sleep deprivation compared to home-cage controls, and this impairment reverted soon after the beginning of the recovery period. Sleep-deprived animals also showed an increase in omissions in the first day of PSD and a reduction on the number of trials started on the fourth day of sleep deprivation. No significant group differences were observed in premature and perseverative responses, correct response latency and reward latency. Our results thus indicate that paradoxical sleep deprivation impairs attentional function.

Keywords: Sleep deprivation; Paradoxical sleep deprivation; Attention; Five-choice serial reaction time task; Rat

1. Introduction

It is known that sleep deprivation has detrimental effects on human cognitive functioning. Attention and performance are greatly impaired in subjects deprived or restricted of sleep, either experimentally [64,22,11,56,10] or due to sleep disorders [46,63]. This is a matter of great concern since sleepy subjects with reduced attentional capabilities are more accident prone in traffic or workplace situations [1,7,28].

The mechanisms of sleep have largely been studied in animals such as rats and mice. Sleep in the rat has a stage of gradual slowing of cortical electroencephalographic activity, which can be divided in superficial or light sleep and deep sleep, and a stage of cortical reactivation accompanied by loss of muscle tone, namely paradoxical sleep [57]. Sleep deprivation, and particularly paradoxical sleep deprivation (PSD), have long been regarded as a useful model for the study of sleep. In rats, PSD can lead to behavioural and cognitive alterations such as reduced fear and less anxiety-like behaviour [19,35,54,32], altered response rates in active (operant) avoidance tests [52,18] and impaired learning and memory processes [5,51,9,36]. These observations are indicative of impairments in brain physiology, and indeed many studies have found alterations in neurotransmitter systems induced by PSD [58,42,41,13,45,21,20,4]. It is interesting to note that these systems affected by sleep deprivation are involved in the arousal and attention mechanisms [48,31], thus being a possible interaction factor in the attentional deficits found in sleep-deprived individuals.

Among the various paradigms for assessing attention in rodents [38,6], the five-choice serial reaction time task

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(5-CSRTT) has been extensively used in studies of the neurobiological mechanisms of this cognitive function [47]. This task involves rats being trained to detect a brief light stimulus randomly presented at one location in an array of five possible spatial targets, and to respond appropriately with a nose-poke to receive a food reward. In this format, the 5-CSRTT contains elements of a sustained attention or vigilance test and also requires subjects to divide their attention across multiple spatial locations [38]. By evaluating several parameters such as latency to respond (correctly or incorrectly), accuracy in responding, number of omissions, premature and perseverative responses, it is possible to assess attentional function and at the same time rule out confounding factors such as motivation, motor impairments or speed/accuracy trade-off [38,47].

Despite the studies in humans, the effects of sleep deprivation in attention are not well studied in animal models so far. To our knowledge, the only published work in this regard was performed in monkeys submitted to a visual choice reaction test continuously during 48 h (thus depriving the animals of sleep, since errors and omissions in the task were punished with electric shocks), displaying a reduction in percent correct responses to the target but not the correct rejection of the non-target stimulus [34]. Animal models allow different aspects of disorders to be investigated in detail [38], and rodents are a species commonly used to investigate the alterations induced by PSD and also the neurobiology substrates of attention, so it is important to determine the effects of PSD on a widely used attention paradigm in these animals as a first step into the development of a model with predictive value to human sleep and attention pharmacology.

Considering the effects of sleep deprivation in humans and in rodents, we hypothesise that attention will be impaired in sleep-deprived rats. In order to test this hypothesis, we deprived the rats of sleep using a variation of the multiple platform technique [55], in which groups of rats are placed on top of small (6.5 cm diameter) circular platforms, in a tank filled with water up to 1–2 cm below the platforms level. During paradoxical sleep, the loss of muscle tone make the animals fall into the water, thus depriving them of sleep. This method is widely used in experimental sleep deprivation research and is known to cause total deprivation of the paradoxical (REM) stage of sleep and also to some extent the slow-wave stage [31]. We then evaluated their performance on the five-choice serial reaction time task.

2. Materials and methods

2.1. Subjects

The subjects were 24 male Wistar rats from the department vivarium, housed in groups of six under controlled light–dark cycle (lights on 7:00 h and off 19:00 h) and 22 ± 2 °C room temperature. Rats were 3-month-old and approximately 300 g body weight at the beginning of the procedures. They were allowed ad libitum access to water but food was restricted to 12–14 g of standard rodent chow per rat per day, given during 1 h after each daily training session (sufficient for the rats eat the daily amount of food). All experimental procedures were performed during the first two-thirds of the light phase, and we counterbalanced the order of testing between control and deprived animals throughout this period. All procedures used in this research were approved by the local ethics committee, based on international guidelines for animal use and care.

2.2. Apparatus

Two five-choice chambers (Med Associates Inc., USA) were used. The test apparatus consisted of a 25 cm × 25 cm aluminium chamber illuminated by a houselight located on top of the front wall. The rear wall of each chamber was curved and contained five 2.5 cm × 2.5 cm × 2.5 cm square holes (apertures) located 2.5 cm above a stainless steel grid floor. Each aperture had an infrared photocell beam monitoring its entrance and a small lamp located at the rear for delivery of the visual signal. Food pellets were delivered automatically into a magazine located at the front of the chamber (25 cm equidistant from each hole), which also had an infrared photocell beam on its entrance. The rat was placed in the chamber through a lateral door. To minimise environmental noise, the chamber was encased in a dark, sound-attenuating compartment with a ventilator fan providing low-level background noise. Each chamber was automatically controlled, and data were collected via a microcomputer (IBM/MS-DOS compatible) using Med-PC software (Med Associates Inc., Georgia, USA).

2.3. Behavioural training

On the first day of training, rats were placed in the chambers for 15 min with all lights off and allowed free access to some reward pellets placed in the food tray. On the next 2 days, 2–3 pellets were placed in each aperture, 10–15 food pellets were placed in the food tray, and the houselight, nose-poke holes, and magazine lights were lit throughout the session. The rats were kept in the chamber for 15 min. On the fourth and fifth days, they were placed in the chambers for 20 min and a pellet was delivered every 20 s to habituate the rats to collecting the dispensed reward and associate the mechanical sound of the dispenser with the presence of food. Finally, on days 6–8 one hole was illuminated and the rats received food after responding to it in a FR-1 schedule, and session length was extended to 30 min.

After these procedures, the 5-CSRTT training began. At the beginning of the session, the houselight came on and a reward pellet was delivered in the magazine. Each trial was initiated when the rat collected the pellet at the magazine. After a 5 s inter-trial interval (ITI), a light was turned on in one of the five apertures and the rat was required to locate the stimulus and make a nose-poke response in the appropriate aperture. Responses made on the illuminated aperture when the stimulus was lit or within 5 s of its presentation (the limited hold (LH) period) were registered as correct and rewarded with food (45 mg sucrose pellets). Responses in the other non-illuminated apertures were punished with suspension of the reward and a period of lights off (the time out (TO) period) lasting for 4 s. On the other hand, if no response was detected within the LH, the rat was punished with the TO and an omission registered. Additional responses made in any of the apertures after a correct response but before the retrieval of the reward were recorded as perseverative and punished in the same way as an omission. Finally, any responses made during the ITI period (i.e., before the presentation of the stimulus) were recorded as premature and also punished with TOs. The next trial was initiated by the rat nose-poking at the food magazine, either to collect a reward or after a TO period. Any additional responses during the darkness period reinitiated the TO. The computerised data-collecting system also recorded any perseverative responses in the magazine (additional responses after the collection of the reward) but they had no consequences. The latency to respond correctly was registered as the time between the onset of the stimulus and the detection of a correct response. The magazine latency was the time between a correct response and collecting the reward. Each session lasted 30 min, or until the completion of 100 trials. At the end of each session, all lights were switched off, the animals were put into individual shoe-box cages for 1 h, during which they consumed their daily amount of food, and were then returned to their home cage.

The initial parameters were: stimulus duration: 60 s; LH and IET: 5 s; TO: 4 s. The LH, IET and TO were kept constant all the time, and the stimulus duration was gradually reduced each time the rats performed the task with at least 80% accuracy and less than 20% omissions on two consecutive days. Rats selected for testing were those that showed over 70% accuracy and less than 20% omissions on four out of five consecutive days with 1 s stimulus duration. Sixteen animals were selected based on these criteria, resulting in a final *n* of 8 rats per group (control and deprived). The mean performance over these 5 days was used as baseline, and following this the PSD procedures began.

Performance of the task was assessed using the following behavioural measures.

- Accuracy: the number of correct responses/total number of correct plus incorrect responses, expressed as a percentage.
- Total number of trials started: the sum of correct, incorrect, omissions and premature responses.
- Omissions: number omissions/total trials started, as percentage.
- Premature responses, expressed as percentage (premature responses/total trials started).
- Perseverative responses in the apertures.
- Correct response and magazine latencies.

2.4. *Sleep deprivation*

Sleep deprivation was obtained using a slight variation of the original multiple platform technique [55]. In the present experiment, 12 narrow (6.5 cm diameter) platforms were placed inside a water tank made of white tiles. Water was filled up to 1 cm below the platforms. Each tank was divided in half by a metal plate, so there were six platforms on each side. Three rats from the same cage (with six) were placed in each half tank (so each half functioned as an independent tank). These modifications were made because the experimental groups were counterbalanced based on training/testing time and performance level, so in each cage there were animals both form the deprived (DEP) and Control (CON) groups. Animals were placed in the tanks following their testing order and time to ensure precise sleep deprivation periods. Control animals were kept in their home cages in the vivarium room, where the light and temperature conditions were the same as the deprivation room. In the tanks, water was available ad lib but food was restricted to free-feeding for 1 h, 30–50 min after each 5-CSRTT testing session.

2.5. *Experimental design*

After recording baseline performance, rats were adapted in the deprivation tanks for 40–60 min on three consecutive days before beginning the deprivation procedure. Performance on the 5-CSRTT was assessed daily during the 96 h deprivation period and during the 7 days after the end of deprivation (recovery days). During deprivation, rats were taken from the deprivation tank, gently dried with a soft paper towel and then put into the test chamber. After testing animals were returned to their respective tank. After the fourth deprivation day (96 h), animals were returned to their home-cages for recovery testing.

2.6. *Data analysis*

Data were analysed by two-way ANOVA with Group (control: CON or deprived: DEP) × Days (basal, 1st–4th days; PSD, 1st–7th day of recovery) as main factors. When necessary for best homogeneity of variance, arcsine transformation was applied to the percentage measures, logarithmic to the latencies and square root for perseverative responses using the formulae described by Zhar [65]. Post hoc analysis was carried out using the Duncan post hoc test assuming differences with $p \leq 0.01$ to be significant. The frequency of animals that completed 100 trials on the fourth day of PSD was compared by the Fisher Exact Test (one-tailed), and the correlation between the number of trials started and percentage correct response in this day was calculated using Pearson's correlation.

3. Results

3.1. *Accuracy*

We found a significant Interaction ($F_{11,154} = 2.58$; $p < 0.005$) between Group and Days. The animals deprived of sleep showed less accuracy than controls on day 3 ($p = 0.007$) and day 4 ($p < 0.001$) of PSD (Fig. 1). Intra-group comparisons showed that for the DEP animals accuracy on the third ($p = 0.005$) and fourth ($p = 0.008$) days of PSD was lower than the group baseline performance. No main effects of Group or Days (Group $F_{1,14} = 2.88$; $p = 0.11$; Days $F_{11,154} = 1.60$; $p = 0.10$) were found.

3.2. *Omissions*

There was a significant main effect of Days ($F_{11,154} = 4.34$; $p < 0.001$) and a significant Interaction ($F_{11,154} = 2.29$; $p < 0.013$). Analysis of the Interaction revealed that the percentage of omissions was greater in the DEP than in controls only on the first day of sleep deprivation ($p < 0.01$; Fig. 2). Post hoc analysis of Days showed no significant differences in performance on baseline compared to sleep deprivation or recovery days (in all cases $p > 0.01$). The Group main effect was not significant ($F_{1,14} = 0.73$; $p = 0.41$).

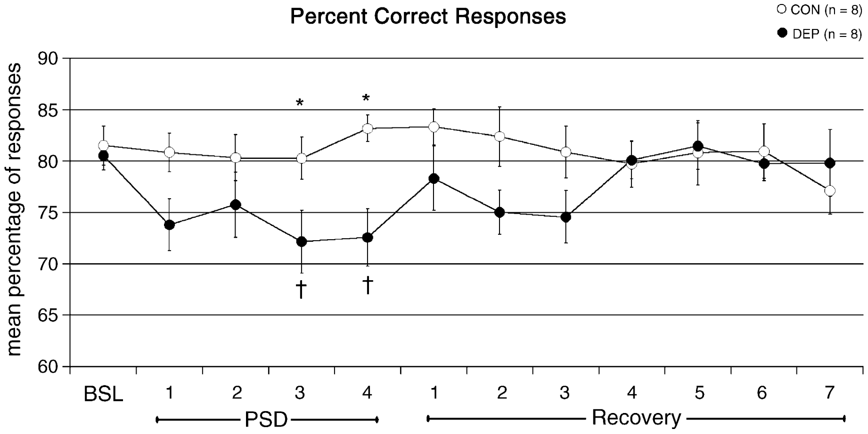

Fig. 1. Percentage of correct responses (accuracy). Data displayed as mean ± S.E.M. The Interaction was significant ($F_{11,154} = 2.58$; $p < 0.005$). Sleep-deprived rats were less accurate than controls on PSD days 3 and 4 ($^{*}p < 0.01$, Duncan test). Also, DEP rats showed reduced accuracy on PSD days 3 and 4 relative to the group baseline ($^{\dagger}p < 0.01$, Duncan test).

3.3. Premature and perseverative responses

Data are displayed in Table 1. For both parameters the main factor Days was significant ($F_{11,154} = 2.32$; $p = 0.011$ for premature (PRE) and $F_{11,154} = 2.21$; $p < 0.017$ for perseverative (PER) responses). Post hoc analysis showed that premature responding was higher on day 3 of sleep deprivation than baseline ($p < 0.007$) and perseverative responses more frequent on the first day of sleep deprivation than baseline ($p = 0.008$). There was no Group effect ($F_{1,14} = 0.56$; $p = 0.46$ and $F_{1,14} = 0.06$; $p = 0.80$ for PRE and PER, respectively) and no Interaction ($F_{11,154} = 1.18$; $p = 0.30$ for PRE and $F_{11,154} = 1.00$; $p = 0.56$ for PER).

3.4. Latencies

Latencies are shown in Table 1. A main effect of Days was found for correct ($F_{11,154} = 3.01$; $p = 0.001$) and reward latencies ($F_{11,154} = 3.36$; $p < 0.001$). Duncan's test showed that rats were faster to respond correctly in the sixth day of recovery than during baseline ($p < 0.01$) and slower to collect the reward on the first day of S.D. compared to baseline ($p < 0.001$). No Group or Interaction effects were found. For correct latency, Group $F_{1,14} = 1.99$, $p > 0.1$ and Interaction $F_{11,154} = 0.53$, $p > 0.8$. For reward latency, Group $F_{1,14} = 0.32$, $p > 0.5$ and Interaction $F_{11,154} = 1.57$, $p > 0.1$.

3.5. Trials started

The mean number of trials started and the number of animals that completed 100 trials/day in each group are shown in Table 2. A Fisher Exact Test was performed to compare the number of animals that completed 100 trials on day 4 of sleep deprivation, and a significant difference was found ($p < 0.04$, one-tailed test). A correlation analysis between the mean total of trials started and the percentage of correct responses on day 4 of PSD was also performed, but was not significant (Pearson's $r = -0.15$, $p = 0.7$).

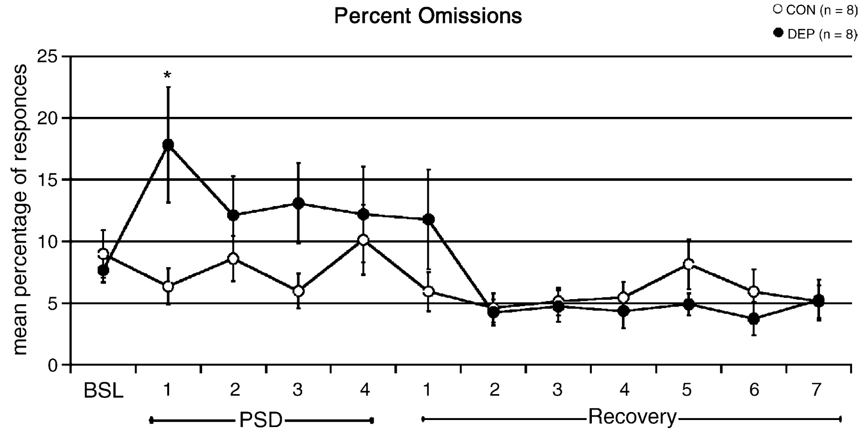

Fig. 2. Percent omissions. Data displayed as mean ± S.E.M. We found a significant Interaction ($F_{11,154} = 2.29$; $p < 0.05$), and post hoc test showed that PS-deprived rats omitted more than controls on PSD day 1 ($^{*}p < 0.01$, Duncan test). There was also an effect of Days ($F_{11,154} = 4.35$; $p < 0.0001$), but no significant differences relative to baseline in post hoc test were found.

Table 1
Premature and perseverative responses and latencies

	Prematures (%)		Perseveratives		Correct latency (s)		Reward latency (s)	
	CON	DEP	CON	DEP	CON	DEP	CON	DEP
Baseline	6.4 ± 1.5	4.9 ± 0.7	4.3 ± 1.4	6.5 ± 1.1	0.88 ± 0.05	0.85 ± 0.03	1.72 ± 0.16	1.81 ± 0.13
PSD								
1	8.1 ± 1.5	5.7 ± 1.6	13.3 ± 5.1§	14.0 ± 4.9§	0.87 ± 0.05	0.87 ± 0.05	2.86 ± 0.88§	3.82 ± 1.06§
2	5.3 ± 2.1	8.8 ± 2.9	7.6 ± 2.1	7.0 ± 2.0	0.89 ± 0.05	0.85 ± 0.07	2.03 ± 0.20	1.88 ± 0.23
3	9.5 ± 1.1§	14.2 ± 3.4§	5.3 ± 1.4	7.5 ± 2.8	0.84 ± 0.04	0.79 ± 0.03	1.87 ± 0.19	1.69 ± 0.14
4	6.8 ± 2.3	10.0 ± 3.9	6.1 ± 1.6	7.6 ± 1.7	0.90 ± 0.05	0.82 ± 0.06	1.86 ± 0.22	2.50 ± 0.32
Recovery								
1	7.2 ± 1.5	6.5 ± 2.0	8.6 ± 3.2	6.5 ± 2.6	0.90 ± 0.04	0.80 ± 0.02	2.21 ± 0.30	1.53 ± 0.15
2	7.5 ± 2.0	11.4 ± 1.2	3.6 ± 1.5	5.3 ± 2.1	0.80 ± 0.04	0.76 ± 0.02	1.55 ± 0.11	1.58 ± 0.17
3	7.9 ± 1.5	9.6 ± 2.1	6.6 ± 1.1	2.4 ± 0.8	0.88 ± 0.05	0.77 ± 0.04	1.94 ± 0.16	1.35 ± 0.08
4	6.6 ± 1.9	8.8 ± 2.2	7.6 ± 2.3	6.8 ± 1.8	0.85 ± 0.05	0.76 ± 0.04	2.09 ± 0.25	1.73 ± 0.15
5	5.1 ± 1.4	8.0 ± 1.5	4.4 ± 0.9	6.4 ± 2.1	0.83 ± 0.04	0.76 ± 0.02	1.83 ± 0.16	1.59 ± 0.13
6	10.3 ± 2.3	8.6 ± 1.1	8.0 ± 2.2	9.0 ± 3.0	0.79 ± 0.04§	0.70 ± 0.03§	3.05 ± 1.17	1.91 ± 0.22
7	5.7 ± 1.6	4.6 ± 1.1	3.4 ± 0.9	8.0 ± 3.1	0.83 ± 0.05	0.78 ± 0.05	1.71 ± 0.15	1.98 ± 0.23

CON and DEP groups made more premature responses in PSD day 3, and perseveration was more frequent on PSD day 1, both relative to baseline (BSL). Rats were faster to respond on recovery day 6 and slower to retrieve the reward on PSD day 1, relative to baseline (§ in all cases $p < 0.01$, Duncan test for the Days main factor of the ANOVA). Values are mean ± S.E.M.

Table 2
Number of trials started

	CON		DEP	
	Trials	Frequency 100	Trials	Frequency 100
Baseline	99.4 ± 0.3	–	99.5 ± 0.3	–
PSD				
1	100 ± 0	8	88.9 ± 7.5	6
2	100 ± 0	8	95.6 ± 2.7	5
3	100 ± 0	8	90.6 ± 6.1	6
4	100 ± 0	8	84.9 ± 7.8	4[*]
Recovery				
1	98.5 ± 1.5	7	95.3 ± 3.1	6
2	100 ± 0	8	100 ± 0	8
3	100 ± 0	8	100 ± 0	8
4	98.5 ± 1.5	7	100 ± 0	8
5	96.1 ± 2.8	6	99.4 ± 0.6	7
6	97.0 ± 3	7	100 ± 0	8
7	98.8 ± 1.3	7	100 ± 0	8

By the fourth day of sleep deprivation, significant less rats could complete 100 trials in the DEP group when compared to the control group (*Fisher Exact Test $p < 0.05$, one-tailed). Values are mean ± S.E.M. (trials) and the number of rats that completed 100 trials in each day (frequency 100).

[*] Different from control ($p < 0.05$, Fisher test).

4. Discussion

In this study, we sought to assess the effects of paradoxical sleep deprivation (PSD) on the attentional performance of rats in the five-choice serial reaction time task (5-CSRTT). Based on analogous continuous performance studies in human subjects [11,22,64], we hypothesised that this manipulation would impair sustained visual attentional performance. Thus, PS-deprived animals showed a reduction in choice accuracy, the main parameter of the task reflecting sustained spatial attention [47], on the third (72 h) and fourth (96 h) days of PSD. Recovery from this impairment occurred soon after the end of the PSD. PS-deprived animals also showed increased omissions on the first day of PSD, and a reduction of the number of trials started occurred on the last (fourth) day of PSD. There were no significant group differences or interactions in premature and perseverative responses, suggesting that PSD per se had no effect on impulsivity or response control. The same occurred in the measures of speed: correct-response latency and food-reward retrieval latency were not affected by PSD itself, indicating an absence of motor and motivational impairments due this manipulation.

We found a clear effect on response accuracy and there were a number of alterations that were potentially causes of this attentional impairment. For example, PSD may cause alterations in cholinergic [58,42,49] and dopaminergic transmission [59,17,41] and it is known that accuracy is highly dependent on these two neurotransmitter systems [33,8,15,43]. Nevertheless, as no direct manipulation of the neurotransmitters was conducted in this study, this suggestion may be overly speculative. The specific mechanisms involved have to be investigated in future studies.

Recovery in performance is also interesting. In rats, the first 24 h after PSD are marked by a paradoxical sleep rebound and a reduction in wakefulness and slow-wave sleep. After this period, the sleep pattern of the rats does not differ from the pre-deprivation baseline [30]. The absence of statistically significant differences in accuracy or other measures during the first 24 h of recuperation from the sleep deprivation period suggest a fast recuperation of the attention deficits at least when using the parameters adopted in the present paper. However, it should be noted that significant alterations during recovery could have been found with the use of shorter stimuli or other more attention-demanding manipulations, like high event rates.

The reduction in accuracy may have been caused by impairments in the visual system. In humans, Krull and colleagues [25,26] observed a lengthening of reaction time correlated with alterations in event-related evoked potentials in sleep-deprived subjects, and suggested that sleep deprivation may delay target detection. Such a phenomenon, if present in PS-deprived rats, may have contributed to the accuracy deficit. So, while the hypothesis of a sensorial deficit can not be ruled out altogether, little can be stated in this regard in the present experiment due to the lack of studies about the effects of PSD on the visual system of rodents.

Paradoxical sleep deprivation induced an increase in omissions, but it was statistically significant only on the first day of PSD. It seems unlikely that this effect was due to initial contact of the animals with PSD procedures, since they had been adapted to the tanks and platforms for 3 days before deprivation began. There are data suggesting that some early effects of the PSD may not be present later in the deprivation period; for example, the binding to the benzodiazepine-type GABA receptors is increased after 24 h of PSD [44] but not after 96 h of PSD [37].

It was also observed that PSD reduced the number of trials started. During the experiments, it was noted that some PS-deprived rats stopped responding or greatly reduced their rate of response after 40–50 trials. After 96 h of PSD, four out of eight DEP animals failed to complete 100 trials in the maximum period of 30 min, while all control rats completed the task. Accuracy is calculated as the proportion of correct responses over the total number of correct plus incorrect responses, not the total number of trials; thus, those measures are calculated independently. However, we have raised the hypothesis that the drowsiest animals, which could have stopped responding and tended to fall asleep, could be the same animals that showed the worse response accuracy. A correlation analysis between the number of trials started and response accuracy was performed and, interestingly, this correlation was not significant and had a small *r* value (see Section 3). This suggests that the attentional deficit was present regardless of the animals' readiness or capacity to continue the task. It should be taken into account that the motivational state of the PS-deprived rats could be a possible confound in the present findings. The literature concerning the effect of sleep deprivation on motivation for food is somewhat confusing. First, PSD increases food consumption [27] and preference for sweet solutions [53], which would enhance and not decrease the motivation for the sucrose pellets given as food reward. However, Kennedy [23] and Kirby and Kennedy [24] have shown that following 96 h, but not 48 h of PSD the rewarding properties of food pellets are significantly reduced. That is, after 96 h of PSD, animals respond less on food-motivated tasks. After 96 h of PSD, our animals showed a reduction in the number of trials started which could mean diminished interest for food. On the other hand, the other measure that could reflect the reduction in motivation for food is the latency for retrieve the reward, but it was not found to be increased in our deprived animals. Additionally, omissions were affected by PSD only on the first day of deprivation when no accuracy deficit was observed. Nevertheless, it is not possible to discard the alternative interpretation of a motivational alteration in addition to the attentional impairment induced by PSD.

Regarding the latency to respond correctly, our results do not suggest a specific effect of PSD on this measure. Some authors propose that the correct latency can be interpreted as a measure of speed of decisional processes during simple visual discrimination tasks [39] or in the 5-CSRTT itself [40,47]. Accordingly, PSD did not seem to impair the rats' decisional speed in the 5-CSRTT as used here. Also, when taken in conjunction with the absence of specific effects in the latency to collect the reward, this indicates an absence of motor impairments [38] in sleep-deprived rats.

Some studies suggest that PSD may lead to an activated behavioural state characterized by reduced fear and anxiety-like behaviour [54,32], increased locomotion [62,9,32] and increased response rates in operant active avoidance tasks [52,18]. One may assume that this behavioural pattern could affect the response control and/or behavioural inhibition of the rats, changing premature and perseverative responses. However, in the present experiment we found no effect of paradoxical sleep deprivation on premature or perseverative responses. In this regard, Kennedy [23], considering the changes in response rates for appetitive operant tasks following PSD, raised the hypothesis that the behavioural activation observed in PSD rats is related to the type of task employed. Accordingly, tests involving aversive or anxiogenic components, like open-field, plus-maze or avoidance tasks would tend to increase activity or response rate, whereas appetitive tasks would not favour this behavioural pattern. On this hypothesis, the 5-CSRTT is an appetitive task, performed in an environment well known to the rats, and would not tend to induce increased activity or exploratory behaviour in the PSD rats.

Sleep deprivation is a stressful condition, which lead some authors to consider the contribution of stress on the cognitive impairments induced by sleep deprivation [50]. The platform method for sleep deprivation induces increased levels of ACTH and corticosterone [54,55], and alters CRH levels and CRH receptor binding in many brain areas [12]. It has recently been reported that transgenic mice overproducing CRH have impaired acquisition of autoshaping and a mild accuracy impairment in a version of the 5-CSRTT slightly different from the one used here [61]. Thus, the alterations on the HPA axis due to PSD could have been involved in the attentional deficit. Nevertheless, there is a need for further research onto the biological importance of sleep deprivation-related stress on the observed effects, and also the role of stress in attentional function in rodents.

Human studies with normal subjects that made use of simple reaction time tests usually report lengthened reaction time, increased errors and increased omissions or lapses following total sleep deprivation [14,29,11] or when daily sleep time is reduced to a few hours per night during several days [2,60]. Although the method of sleep deprivation used in the present study cannot be considered a limited sleep restriction, our data correlate to these observations in the sense that we found reduced accuracy of response indicating abnormal attentional processing in sleep-deprived rats. But contrary to the commonly related in human literature, response latency or omissions were not consistently increased. In this regard, it should be noted that differently from most human studies, there is a need for the animals to respond, since the animals are punished with a delay of the next opportunity for reinforcement, which usually does not happen in human experiments. It is also possible that the use of versions of the 5-csrtt with greater focus on stimulus detection (e.g. [16,3]) could reveal speed and omission impairments in sleep-deprived rats more close to those observed in humans.

Our study found that rats deprived of sleep, and in particular, the paradoxical stage of sleep, showed impaired attentional function. We have made some points regarding the nature of the attentional impairment, but there are a number of lines to follow in order to understand how the interaction of the neurobiological effects of paradoxical sleep deprivation could lead to such an effect. More research is required, and the study of attentional performance in sleep-deprived animals is a promising field for future studies.

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