



Research report

Food restriction or sleep deprivation: Which exerts a greater influence on the sexual behaviour of male rats?

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ABSTRACT

The purpose of this study was to determine the effects of food restriction (FR) and paradoxical sleep deprivation (PSD), either alone or in combination, on sexual behaviours (mount, intromission and ejaculation) in adult male rats. Diet restriction began at weaning with 6 g/day of food, and the amount of food was increased by 1 g/week until it reached 15 g/day amount (in adulthood). During adulthood, rats under FR and those fed *ad libitum* were either subjected to PSD for 96 h or maintained in home-cage groups. The results indicated that both FR and *ad libitum* sleep-deprived groups showed a significant decrease in performance and motivation to initiate sexual behaviour, reflected by the increase in mount and intromission latencies and decreased copulatory rate. FR associated with PSD reversed the adverse effects of sleep deprivation on the number of ejaculations and inter-copulatory interval. Testosterone concentrations decreased after sleep deprivation, regardless of food availability; while progesterone was significantly higher in the FR-PSD group only. In light of the limited understanding of the link between secretion patterns and neural–hormonal control of food availability related to sexual behaviour, our data indicate that sleep loss affects sexual responses, and FR was able to restore some of the sexual parameters investigated.

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1. Introduction

Many studies have shown that a reduction in caloric intake is associated with lifespan extension. Evidence for this phenomenon first emerged in the 1930s, when McCay et al. [33] demonstrated that rats that were fed measured amounts of food after weaning lived much longer (about 80%) than the *ad libitum* group. In rodents, the effects of food restriction (FR) are extensive, including a decrease of anxiety-like behaviour in an open field test [30] and lower incidences of age-related tumors [16,34]. Although these nutritional strategies produced chronic under-nutrition (not malnutrition) by limiting caloric intake, they still provided adequate amounts of other dietary essentials [47].

There are some studies on behavioural alterations in rats undergoing FR; however, only a limited number focused specifically on sexual behaviour. Some authors reported that food deprivation reduced sexual motivation and delayed the onset of puberty in male rats [24,27,29]. For instance, after long periods of starvation, some males failed to achieve intromission or ejaculation [39]. Additionally, according to Larsson [28], when presented with a receptive

female in a Skinner box, rats deprived of food for 23 h tended to defer eating until after ejaculation. However, erectile responses were found to be substantially improved by caloric restriction in spontaneously hypertensive rats [26]. It has also been demonstrated that caloric restriction modulates gonadal steroids. Govic et al. [24] showed that long-term caloric restriction, initiated during adulthood, decreased testosterone levels in adult male rats. Recently, using the paradoxical sleep deprivation (PSD) paradigm that is known to facilitate genital reflexes in male rats [4–7,9–11], we observed a higher percentage of erections and ejaculations in the sleep-deprived group fed *ad libitum* than in the FR-PSD rats, indicating that PSD did not override the inhibitory effect of long-term FR on erectile function [3].

Since most adults have experienced sleep deprivation at some stage of their lives, the PSD method has been used to mimic sleep loss that results from our modern lifestyle. A number of studies have examined different behavioural changes [5,12,23,32,38,42,49] produced by PSD, but few have looked at its effects on sexual behaviour. For instance, increased sexual responses have been reported in cats [19], rats [2,4–7,11,43] and humans [50] after deprivation of sleep. In addition, patients with situational impotence presented a full erection after 24 h of sleep deprivation, following audiovisual stimulation [21]. The participation of steroid hormones has also been examined, as they play a modulating

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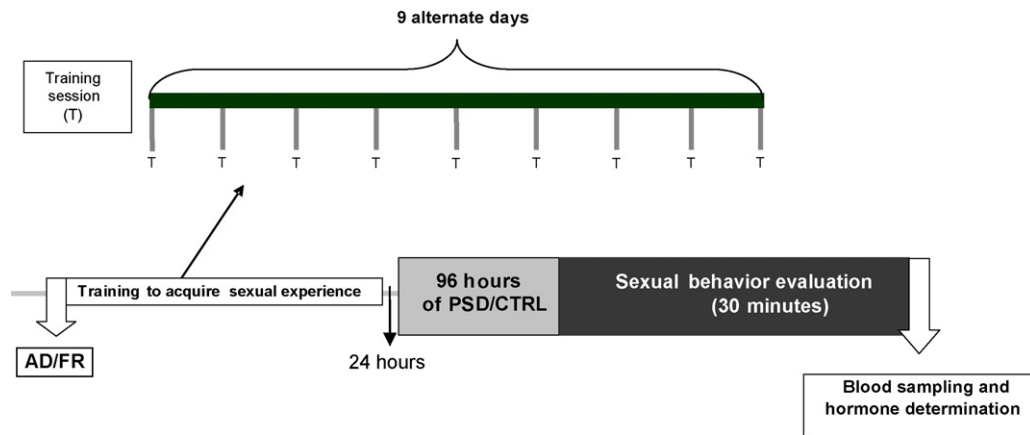


Fig. 1. Schematic representation of the test groups and protocol design.

effect on male sexual function [9]. In this sense, we have demonstrated that PSD reduced testosterone and enhanced progesterone concentrations in male rats, compared with the control group [6–9].

Considering that inadequate sleep and poor nourishment are prevalent in many populations and that both interfere with hormonal mechanisms that control sexual behaviour, it is important that the consequences of their interactions with respect to sexual responses and hormonal profiles be documented. Thus, in this study, we expanded our previous finding on the effects of PSD and FR on the complete repertoire of sexual behaviours (mount, intromission and ejaculation) in adult male rats. To the best of our knowledge, this is the first investigation of the effects of PSD on sexual behaviours in rats subjected to long-term FR.

2. Methods

2.1. Subjects

Male Wistar rats were bred and raised in the animal facility of the CEDEME of Universidade Federal de São Paulo. The animals were housed in a colony maintained at 22 °C in 12:12 h light–dark cycle (lights on at 07:00 h) and allowed free access to water inside standard polypropylene cages. The experimental protocol was approved by the Ethical Committee of UNIFESP (CEP N. 05/434).

2.2. Food restriction (FR)

From weaning (at 30 days of age), rats were fed 6 g of chow daily. This amount of food was increased by 1 g/week until it reached 15 g/week in the 8th week. This amount of food represents 40–50% of the *ad libitum* intake in the control group. The animals were kept apart in separate cages during feeding and remained there until all food was completely ingested (approximately 60 min). The protocol used for the calculation of chow was established in compliance with our previous studies [2,3]. The animals were distributed into two groups:

- Ad libitum* (AD): animals were allowed to eat and drink, *ad libitum*, from weaning to the end of the experiment.
- Food restriction (FR): animals were fed under the dietary restriction protocol described above. Water was offered *ad libitum*. Since we found no statistically significant effects of feeding time on the sleep–wake pattern of diurnal periods [2], the FR rats were fed at approximately 19:00 h.

2.3. Protocol designs

After 8 weeks of FR or AD, the animals were randomly distributed into the following groups ($n = 18/19$ per group):

- AD-CTRL: AD control rats maintained in the home cage.
- AD-PSD: AD rats submitted to 96 h of PSD.
- FR-CTRL: FR control rats maintained in the home cage.
- FR-PSD: FR rats submitted to 96 h of PSD.

2.4. Sexual behaviour evaluation

After the 7 weeks of FR or feeding *ad libitum*, the rats were trained to acquire sexual experience and were still following their respective food programs. The protocol consisted of exposing the male rat to a receptive female during 9 alternate days for 30 min (Fig. 1). Since sexually inexperienced male rats can display low performance, we followed this protocol because it allowed standardization of the degree of copulatory activity and avoided possible bias. This criterion was based on the expertise of Javier Velázquez-Moctezuma and his group on sexual behaviour in male rats. Indeed, Chu and Agmo [17] reported that all experimental groups displayed a very low level of sexual behaviour during the pre-test. The number of rats displaying mount, intromission and ejaculation was so low that no meaningful analysis of these parameters could be performed. Rats that did not display any intromission or ejaculation until 15 or 30 min after exposure to the female, respectively, were excluded from this study. The total number of rats excluded between the first and second days of the training session was 20 out of 95. Beginning 24 h after the last training, the rats were subjected to PSD for 96 h. Immediately after this period, sexual behaviour was evaluated.

Sexual behaviour tests were performed using a Plexiglas cylinder (45 cm diameter) arena. Dim red lights were shone during the dark phase of the light/dark cycle. The male was introduced into the arena 5 min before the female. The female rats were brought into sexual receptivity by administering estradiol benzoate (Sigma Chemical Co., St. Louis, MO, USA, 10 µg/0.1 ml of sesame oil, sc) 48 and 24 h before the sexual test, and progesterone (Sigma Chemical Co., St. Louis, MO, USA, 500 µg/0.1 ml of sesame oil, sc) 4 h prior the test. The test lasted for 30 min. On the day of the experiment, after the introduction of the female, the following parameters were recorded: the first mount, intromission and ejaculation latencies, the total number of mounts (mounts with the pelvic thrusting), intromissions (mounts with the pelvic thrusting and penile insertion) and ejaculations. The copulatory rate [(number of intromission)/(number of mounts + number of intromissions)] and the inter-intromission [ejaculation latency/number of intromissions] and inter-copulatory [ejaculation latency/(number of intromissions + number of mounts)] intervals were also evaluated.

2.5. Paradoxical sleep deprivation (PSD)

After the training sessions (Fig. 1), the rats were distributed in two groups: CTRL and PSD. The experimental groups were subjected to 96 h of PSD, using the modified multiple platform method. We used this PSD period because it has been shown that most genital reflexes are produced during this time span [5]. In total, six rats were placed inside a tiled water tank (143-cm length × 41-cm width × 30-cm depth), containing 12 circular platforms, each 6.5 cm in diameter, with water within 1 cm of the upper surface. The rats could, therefore, move around inside the tank by jumping from one platform to another. When they reached the paradoxical phase of sleep, muscle atonia set in, and they fell into the water and were awakened. Throughout the study, the experimental room was maintained at a controlled temperature (22 ± 1 °C) with a light–dark cycle (lights on at 07:00 h and off at 19:00 h). Food and water were provided with free access to the AD group by placing chow pellets and water bottles on a grid located on top of the tank. The water in the tank was changed daily throughout the PSD period. The FR groups were fed at approximately 19:00 h in individual cages, and, after 60 min, they were returned to the water tank after having eaten all of the food pellets. Lastly, the cage control (AD and FR) groups were maintained in separate cages in the same room as the experimental rats during the sleep deprivation procedure. By housing both groups in the same room, we maintained control over housing conditions between the two groups. All animals were subjected to PSD at 19:00 h (at the beginning of the dark phase of the light–dark cycle) [2,3]. Since we elected not to

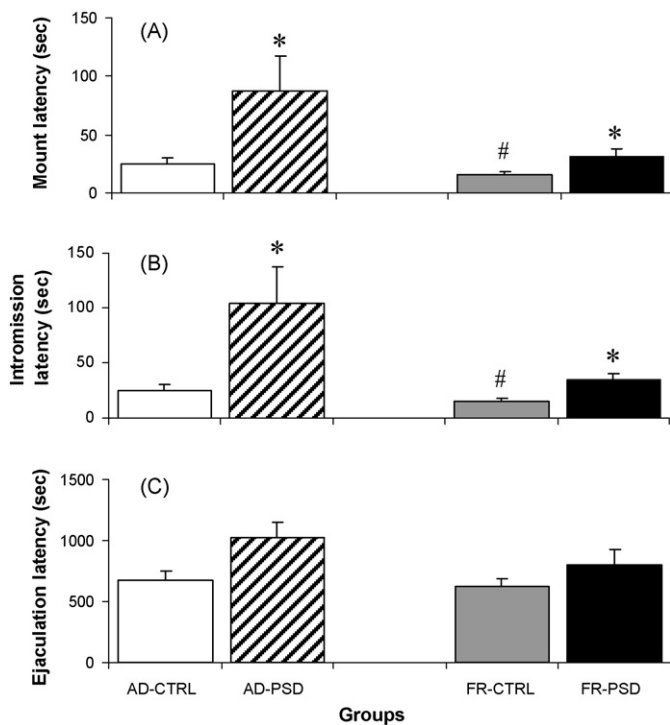


Fig. 2. Effect of FR and PSD on latencies of mount (panel A), intromission (panel B) and ejaculation (panel C). The latencies of three distinct events were expressed as mean \pm SEM of 18–19 rats per group. *Different from respective control rats and #different from AD-CTRL group. See text for *p* values.

invert the light–dark cycle, the rats were also trained and tested during the dark phase.

2.6. Blood sampling and hormone determination

As shown in Fig. 1, immediately after the behavioural tests, rats from the PSD and CTRL groups were taken to an adjacent room and decapitated. Blood samples were collected and stored individually. Blood was collected in glass tubes and centrifuged at $3018.4 \times g$ for 15 min at room temperature, then frozen at -20°C until required. Intra-assay coefficients of variations are given in parentheses. The serum testosterone (7.7%) and progesterone (6.5%) were measured by a chemiluminescent enzyme immunoassay (Advia Centaur, Bayer Corporation, Tarrytown, NY, USA). Duplicate serum aliquots were used.

2.7. Statistical analyses

The sexual behaviour data were analyzed using the nonparametric Kruskal–Wallis test followed by Mann–Whitney *U*-test. Hormonal data and the copulatory rate were analyzed using a one-way ANOVA test followed by a Duncan test for the comparison between groups. Values are expressed as mean \pm SEM. The level of significance was set at $p < 0.05$.

3. Results

3.1. Sexual behaviour parameters

3.1.1. Mount, intromission and ejaculation latencies

The latencies to the first mount (Fig. 2A) and intromission (Fig. 2B) were increased in AD-PSD and FR-PSD groups compared with the respective control groups (both $p < 0.01$). However, the size of the increment observed in the FR-PSD group was not as large as the AD-PSD group. The AD-CTRL group had statistically higher latencies than the FR-CTRL group ($p < 0.05$). All rats were sufficiently trained to reach ejaculation during testing. Thus, the ejaculation latencies refer to all animals. The statistical analyses did not reveal any statistical significance among the groups (Fig. 2C).

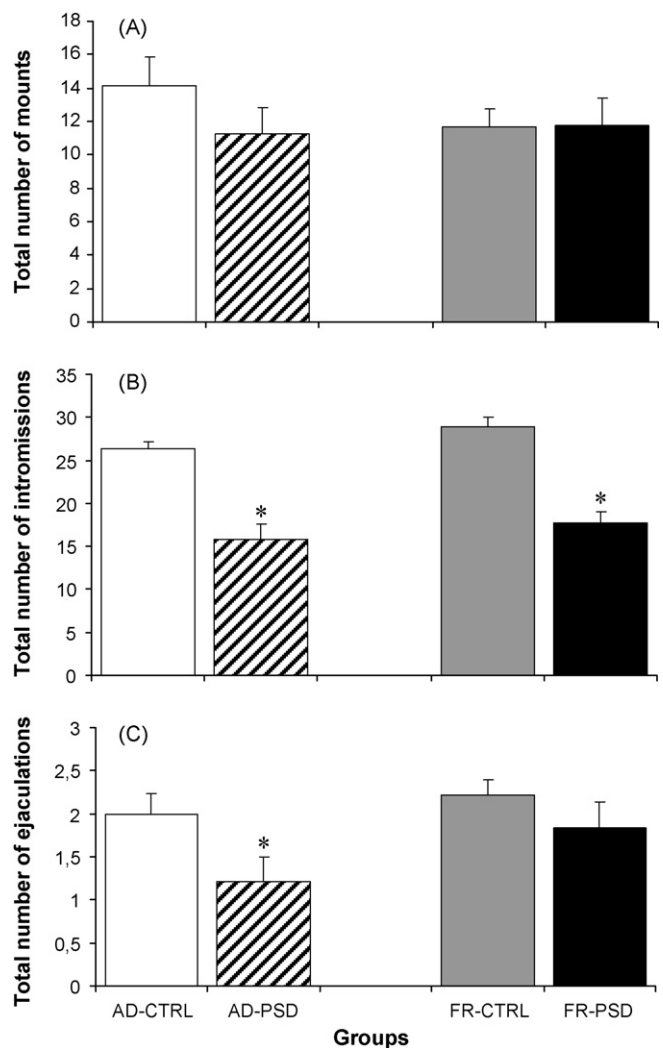


Fig. 3. Effects of FR and PSD during the entire sexual behavioural test on the total number of mounts (panel A), intromissions (panel B) and ejaculation (panel C). *Different from respective control rats.

3.1.2. Total number of mounts, intromissions and ejaculations

The total number of mounts was similar among the groups. Neither PSD nor FR exerted any significant effect on this parameter (Fig. 3A). As depicted in Fig. 3B, the total number of intromissions was significantly reduced after sleep deprivation in both AD and FR groups (both $p < 0.001$). Moreover, only the AD-PSD group showed a decrease in the total number of ejaculations when compared to the CTRL group ($p < 0.05$). Sleep deprivation had no significant effect on the FR group, as shown in Fig. 3C.

3.1.3. Inter-copulatory and inter-intromission intervals

In the inter-copulatory interval, only the AD-PSD group presented a statistical increase when compared to its control group ($p < 0.01$). Sleep deprivation had no significant effect on the FR group, as shown in Table 1. However, the inter-intromission interval was significantly higher after sleep deprivation in both AD and FR groups ($p < 0.001$ and $p < 0.05$, respectively), compared with the respective control groups.

3.1.4. Copulatory rate

The ANOVA test for copulatory rate indicated significant differences among groups (Table 1). The post hoc Duncan test revealed that PSD groups showed a significant decrease in the copulatory

Table 1

Effect of food restriction (FR) and/or paradoxical sleep deprivation (PSD) on inter-copulatory interval; inter-intromission interval and copulatory rate.

Parameters	AD-CTRL	AD-PSD	FR-CTRL	FR-PSD
Inter-copulatory interval	29.4 ± 2.6	80.6 ± 23.9 ^a	31.2 ± 2.5	41.8 ± 6.7
Inter-intromission interval	41.3 ± 3.7	136.8 ± 35.4 ^a	38.7 ± 2.8	68.6 ± 11.2 ^a
Copulatory rate	0.7	0.6 ^a	0.8	0.6 ^a

^a Different from respective control rats.

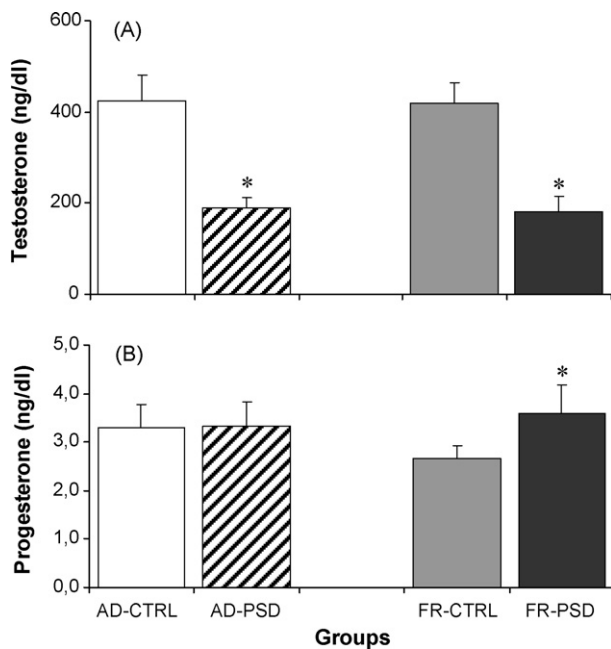


Fig. 4. Concentrations of serum testosterone (ng/dL; panel A) and progesterone (ng/mL; panel B) in FR/AD-CTRL and PSD male rats. Concentrations are represented as the mean ± SEM. *Different from respective control rats.

rate in both AD ($p < 0.05$) and FR ($p < 0.01$) rats, compared with their respective control groups.

3.2. Hormonal concentrations

3.2.1. Testosterone

The ANOVA test for testosterone concentrations revealed significant differences among groups (Fig. 4A). The post hoc test indicated that sleep-deprived rats (AD-PSD and FR-PSD) presented a significant reduction in testosterone compared to respective CTRL groups ($p < 0.01$).

3.2.2. Progesterone

Fig. 4B shows the effects of sleep deprivation on progesterone concentrations. The Duncan test indicated that progesterone was significantly higher in FR-PSD animals than in controls ($p < 0.05$). There were no significant differences among the other groups.

4. Discussion

This study was designed to examine the effects of FR and PSD, either alone or in combination, on sexual behaviours of adult male rats. FR had no marked effect on sexual behaviour, whereas sleep deprivation had significant, but heterogeneous, effects on male sexual behaviour. Our data showed that sexual motivation and performance, reflected by increased mount and intromission latencies, were decreased in both sleep-deprived groups, compared with respective control groups. Furthermore, the total number of ejaculations in the FR-PSD group was not significantly lower than the

control group. Similar observations were noted for the AD-PSD group. Interestingly, testosterone concentrations decreased after PSD, while progesterone was significantly higher in the FR-PSD group only. Manipulations of such variables have been conceived and performed in an attempt to expand the comprehension of the complex interactions underlying the regulation of mammalian sexual behaviour.

In our previous study, we examined the influence of different long-term FR schedules on genital reflexes in PSD males [3]. The experiments revealed that, in contrast to the AD group, sleep deprivation did not exert any significant effects on penile erection in FR rats. In an attempt to reverse this inhibitory effect of FR on erections, we provided freely available food to the restricted group during the period of PSD. The data showed that the effects of FR can be reversible, as 80% of FR rats displayed penile erection. Furthermore, we also sought to investigate motivational behaviour by placing food in the behavioural cage during the evaluation of genital reflexes. As a result, the FR group preferred to eat rather than exhibit penile erection. Collectively, these findings suggest that food availability can influence the occurrence of erectile events, which consequently affects the initial arousal.

In this study, both AD and FR groups, when sleep-deprived, displayed a decrease in sexual performance, reflected by a reduction in the total number of intromissions, an increased inter-intromission interval and decreased copulatory rates. However, the FR group did not show a decrease in the total number of ejaculations. This demonstrated that FR reverses the adverse effects of sleep deprivation on the total number of ejaculations (Fig. 3C). Such a response from the FR group may have been influenced by the presence of a receptive female, which may have prompted a more intense urge to survive by means of species perpetuation. It is known that such drives (e.g., eating and sex) are subjected to modulation by many different environmental variables. Survival in extreme conditions dictates that feeding should be guaranteed initially, thus allowing future reproduction. This is seen during FR and sleep deprivation. Thus, food availability is an important cue in the regulation of reproduction [14]. Nevertheless, our previous studies showed that hyperphagia after the PSD paradigm was not necessarily associated with shorter periods of sleep loss [31,32].

We have consistently demonstrated that 96 h of PSD, viewed as a motivational reflex (for review see [10]), facilitates erection. In humans, augmented sexual fantasy [18], increased penile tumescence and masturbation [21] have also been reported after sleep deprivation. A distinction can be made between appetitive and consummatory aspects of copulatory behaviour, where latency until the first mount putatively reflects some of the appetitive aspects and sexual motivation [1]. Consummatory aspects of sexual behaviour (intromission and ejaculation latencies, mount and intromission frequencies) may all affect ejaculatory behaviour.

PSD, as used in this study, resulted in decreased number of intromissions. Although this result could be indicative of increased copulatory performance/proficiency or an enhancement of sympathetic arousal, we believe that this parameter is consistent with lower copulatory rates, increased latencies to mount, and intromission displayed by the PSD rats. Therefore, this suggests that copulatory activity declines in response to lower sexual performance and motivation. As the intromission ratio is sensitive to changes in erectile function [17], the increased inter-intromission interval for both PSD groups, appears to support this hypothesis.

In view of these findings, we speculated that PSD had a more pronounced effect on the initial triggering mechanisms for sexual motivation (e.g., spontaneous erection), than on the actual intensity of sexual activity, after a period of sleep deprivation. The presence of a female, in addition to the repertoire of behaviours intrinsic to copulatory activity and fatigue, could compromise both appetitive and consummatory aspects of copulatory behaviour. In this sense,

sleep deprivation resulting from sleep disorders, such as obstructive sleep apnea, can induce erectile dysfunction, ejaculatory problems and/or diminished libido [25]. Decreased androgen secretion that is associated with this sleep disorder in middle-aged men supports this notion (for review [10]).

The study of hormone determinants of genital reflexes induced by PSD rats demonstrated that sleep-deprived rats presented with significantly lower testosterone concentrations, in contrast to the high frequency of erections seen at different ages [5–10]. However, reduced testosterone in sleep-deprived males that were exposed to females paralleled the low sexual behaviour observed in this study. Collectively, these findings indicate that decreased androgen secretion after PSD does not govern sexual responses in sleep-deprived male rats.

Based on the following: (1) increased progesterone concentrations verified by our previous studies; (2) participation of progesterone in the induction of erection in castrated rats [7]; and (3) progesterone-dependent mechanisms can influence neurochemical pathways involved in copulation [48], we proposed that progesterone is important for erectile function in PSD males [10]. In fact, the pre-treatment with mifepristone significantly reduced the percentage of rats displaying erections and erection frequency, compared to control rats [9]. In the current study, progesterone was significantly higher in the FR-PSD group only, but not affected in rats fed *ad libitum*. Our data cumulatively suggest that the sexual response in sleep-deprived rats may be dependent on progesterone secretion and may not be primarily influenced by testosterone availability. These data contribute to the growing body of literature indicating that progesterone influences male sexual behaviour. For instance, it has been reported that supplementation with progesterone in castrated male rats can initiate the full complement of sexual behaviours, even in the absence of other gonadal steroids [48]. These authors showed that testosterone alone could not completely restore typical sexual responses in all males unless progesterone concentrations were elevated. Although the role of testicular androgen in male sexual behaviour cannot be completely excluded, there is a need for further studies to clarify the interaction of these hormones with sexual mechanisms, especially in sleep-deprived conditions.

We acknowledge that sleep deprivation is inherently stressful, so it may not be possible to completely extricate its effects from those of general stresses. However, several aspects of our findings argue against the possibility that non-specific stress could account for our observations [8]. Besides PSD, different types of stress can promote distinct responses to sexual behaviour. Retana-Marquez et al. [37] showed that the level of stress can change the sexual response. In addition to the effects of PSD on stress, several components of the hypothalamus–pituitary–adrenal (HPA) axis are also modulated by gonadal steroids [22], and activation of the HPA axis can similarly alter reproductive function [41]. It is important to stress that in our previous studies, we investigated the effects of PSD in naïve (sexually inexperienced) rats. Inconsistencies with the current findings may be explained, in part, by the fact that the hormonal profile was investigated in the present study after a sexual behaviour session (plus 9 days in training). In the present experiment, all rats were exposed to a specific mating situation that, we believe, influenced the hormones in a markedly different manner compared with our previous work.

Sexual behaviour may be influenced by several conditions which the animal are exposed, including different degrees of receptivity of the female, promoting different hormonal responses [15,37]. Another factor contributing to the different responses of sexual behaviour is if the animal is sexually experienced or naïve. Recently, Edinger and Frye [20] reported that sexually experienced rats demonstrated less anxiety-like behaviour in the open field and had increased plasma and hippocampal testosterone levels compared

with animals that never were exposed to any sexual stimulation. Thus, the repeated exposure to a female might cause a reversal of hormonal increases related to the sexual stimuli and stress responses [15,20,37], since corticosterone levels were not statistically different between the home-cage and PSD rats, regardless of the diet paradigm (AD-CTRL: 423.6 ± 58.7 vs. AD-PSD: 323.0 ± 41.1 and FR-CTRL: 234.6 ± 38 vs. FR-PSD: 159.9 ± 27.1). These findings, although speculative, might suggest that sleep loss, rather than stress, may influence sexual performance in this paradigm.

Concerning sexual behaviour associated with hormonal profiles, few studies in the literature have reported the effect of FR [13]. In this sense, a shortage of food generally inhibits reproductive development or causes regression of the reproductive system in adult male and female rats [44,45]. In young and adult male rodents, decreased food availability inhibits somatic growth, gonad and accessory organ size, spermatogenesis, and steroidogenesis [12,46]. In fact, there are some studies that have showed the effects of FR on sexual behaviour [24,27,35,36] and testosterone levels [24,40].

Our data on the effects of FR alone on sexual behaviour contradict previous studies [24,37] probably due to protocol design discrepancies. For instance, the FR protocol used in this present study started at weaning whereas in the Govic's study [24] the FR started after 8 weeks of age. Govic's et al. [24] reported that moderate caloric restriction (25%) did not result in impairment in sexual behaviour. Nevertheless, sexual performance was affected by a substantial caloric restriction, as the caloric restriction 50% group (similar to that used in the present study) exhibited a longer latency to the first intromission, indicating alteration in sexual arousal. Collectively, these findings suggest that the food is an important factor that can modulate the sexual behaviour probably in dose-dependent manner, and such sexual response depends of the protocol design of food regimen in which the animal were exposed.

Santos et al. [40] reported that a 30-day period of protein-restriction in male rats did not change their sexual behaviour compared with control rats, thus the component of the diet can also promote different responses. Furthermore, testosterone concentrations were within the normal range as also observed in our study using a long-term FR protocol. In contrast, a suppression of circulating serum testosterone was found in male rats 25% and 50% of caloric restriction [24]. Therefore, it can be speculated that duration of the FR/caloric restriction as well as adult-onset caloric restriction regimen influence the neuroendocrine profile, suggesting that male copulatory parameters might be related to discrete, but important hormonal changes. As depicted in Fig. 4, testosterone was markedly decreased in both PSD groups, regardless of the food availability, whereas progesterone was significantly higher in the FR-PSD group only. This latter result, together with the absence of significant inter-copulatory interval decreases in FR-PSD rats, might be related to the associated reversal of sleep deprivation effects on the number of ejaculations; a possible evolutionary, survival strategy. Taken together, the increase in progesterone may not only exert an important role in erectile reflex, but also in ejaculatory and reproductive mechanisms. A previous study stated that the effect on reproduction may be more closely related to caloric restriction than to reduced protein intake [40].

In summary, food intake and sex behaviours are dependent on a combination of factors that integrate into a complex and contextual cascade of hormones. Although FR leads to increased life span with decreased mount and intromission latency, when combined with sleep deprivation, the body can overcome the reduction in sexual performance by increasing the latencies of mount and intromission. This can be counteracted by maintaining the number of ejaculations as compensation for the effects of PSD, possibly to continue perpetuation of the species in adverse situations. In this study, we explored the role of FR and PSD, individually and in combination, on sex-

ual behaviour and hormonal profiles. Limited understanding of the link between secretion patterns and the neural–hormonal control of food availability under different sleep-deprived paradigms warrants further investigation to completely understand the complex interactions involved.

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References

- Agmo A. Sexual motivation—an inquiry into events determining the occurrence of sexual behaviour. *Behav Brain Res* 1999;105(November 1 (1)):129–50.
- Alvarenga TAF, Andersen ML, Papale LA, Antunes IB, Tufik S. Influence of long-term food restriction on sleep pattern in male rats. *Brain Res* 2005;1057:49–56.
- Alvarenga TA, Andersen ML, Papale LA, Tufik S. Effects of long-term food restriction on genital reflexes in paradoxically sleep-deprived male rats. *Brain Res* 2006;1115:148–54.
- Andersen ML, Tufik S. Distinct effects of paradoxical sleep deprivation and cocaine administration on sexual behaviour in male rats. *Addict Biol* 2002;7:251–3.
- Andersen ML, Bignotto M, Tufik S. Cocaine-induced genital reflexes during paradoxical sleep and recovery. *Physiol Behav* 2003;78:255–9.
- Andersen ML, Bignotto M, Papale LA, Tufik S. Age-related effects on genital reflexes induced by paradoxical sleep deprivation and cocaine in rats. *Exp Gerontol* 2004;39:233–7.
- Andersen ML, Bignotto M, Tufik S. Hormone treatment facilitates penile erection in castrated rats after sleep deprivation and cocaine. *J Neuroendocrinol* 2004;16:154–9.
- Andersen ML, Martins PJ, D'Almeida V, Bignotto M, Tufik S. Endocrinological and catecholaminergic alterations during sleep deprivation and recovery in male rats. *J Sleep Res* 2005;14:83–90.
- Andersen ML, Tufik S. Effects of progesterone blockade over cocaine-induced genital reflexes of paradoxical sleep-deprived male rats. *Horm Behav* 2005;47:477–84.
- Andersen ML, Tufik S. Does male sexual behaviour require progesterone. *Brain Res Rev* 2006;51:136–43.
- Andersen ML, Perry JC, Papale LA, Tufik S. Effects of different substance misuse in genital reflexes of paradoxical sleep deprived male rats. *Scand J Psychol* 2007;48:191–5.
- Antunes IB, Andersen ML, Baracat EC, Tufik S. The effects of paradoxical sleep deprivation on estrous cycles of the female rats. *Horm Behav* 2006;49:433–40.
- Bergendahl M, Veldhuis JD. Altered pulsatile gonadotropin signaling in nutritional deficiency in the male. *Trends Endocrinol Metab* 1995;6:154–9.
- Bronson FH, Heideman PD. Seasonal regulation of reproduction in mammals. In: Knobil E, Neill JD, editors. *The physiology of reproduction*, vol. 2, 2nd ed. New York: Raven; 1994. p. 541–84.
- Bonilla-Jaime H, Vázquez-Palacios G, Arteaga-Silva M, Retana-Márquez S. Hormonal responses to different sexually related conditions in male rats. *Horm Behav* 2006;49:376–82.
- Bruce-Keller AJ, Umberger G, McFall R, Mattson MP. Food restriction reduces brain damage and improves behavioural outcome following excitotoxic and metabolic insults. *Ann Neurol* 1999;45:8–15.
- Chu X, Agmo A. Sexual incentive motivation in old male rats: the effects of sildenafil and a compound (Impaza) stimulating endothelial NO synthase. *Pharmacol Biochem Behav* 2008;89:209–17.
- Dement W. The effect of dream deprivation. *Science* 1960;131:1705–7.
- Dement WC. Recent studies on the biological role of rapid eye movement sleep. *Am J Psychiatry* 1965;122:404–8.
- Edinger KL, Frye CA. Sexual experience of male rats influences anxiety-like behavior and androgen levels. *Physiol Behav* 2007;92:443–53.
- Ferrini-Strambi L, Oldani A, Zucconi M, Castronovo V, Montorsi F, Rigatti P, Smirne S. Sleep-related painful erections: clinical and polysomnographic features. *J Sleep Res* 1996;5:195–7.
- Figueiredo HF, Dolgas CM, Herman JP. Stress activation of cortex and hippocampus is modulated by sex and stage of estrus. *Endocrinology* 2002;143:2534–40.
- Frussa-Filho R, Gonçalves MT, Andersen ML, de Araújo NP, Chinen CC, Tufik S. Paradoxical sleep deprivation potentiates amphetamine-induced behavioural sensitization by increasing its conditioned component. *Brain Res* 2004;1003:188–93.
- Govic A, Levay EA, Hazi A, Penman J, Kent S, Paolini AG. Alterations in male sexual behaviour, attractiveness and testosterone levels induced by an adult-onset calorie restriction regimen. *Behav Brain Res* 2008;190:140–6.
- Guilleminault C, Eldridge FL, Tilkian A, Simmons FB, Dement WC. Sleep apnea syndrome due to upper airway obstruction: a review of 25 cases. *Arch Intern Med* 1977;137:296–300.
- Hannan JL, Heaton JP, Adams MA. Recovery of erectile function in aging hypertensive and normotensive rats using exercise and caloric restriction. *J Sex Med* 2007;4:886–97.
- Herberg IJ. Seminal ejaculation following positively reinforcing electrical stimulation of rat hypothalamus. *J Comp Physiol Psychol* 1963;56:679–85.
- Larsson K. Conditioning and sexual behaviour in the male albino rat. *Acta Psychol Gothob* 1956;1:261–9.
- Larsson K, Carlsson SG, Sourander P, Forsström B, Hansen S, Henriksson B, Lindquist A. Delayed onset of sexual activity of male rats subjected to pre- and postnatal undernutrition. *Physiol Behav* 1974;13:307–11.
- Levay EA, Govic A, Penman J, Paolini AG, Kent S. Effects of adult-onset calorie restriction on anxiety-like behaviour in rats. *Physiol Behav* 2007;92:889–96.
- Martins PJ, D'Almeida V, Nóbrega JN, Tufik S. A reassessment of the hyperphagia/weight-loss paradox during sleep deprivation. *Sleep* 2006;29:1233–8.
- Martins PJ, Nóbrega JN, Tufik S, D'Almeida V. Sleep deprivation-induced gnawing relationship to changes in feeding behaviour in rats. *Physiol Behav* 2008;93:229–34.
- McCay CM, Crowell F, Maynard LA. The effect of retarded growth upon the length of life span and upon the ultimate body size. *J Nutr* 1935;18:63–79.
- Mattson MP, Duan W, Guo Z. Meal size and frequency affect neural plasticity and vulnerability to disease: cellular and molecular mechanisms. *J Neurochem* 2003;84:417–31.
- Olds J. Discussion. In: Wolstenholme GEW, O'Connor CM, editors. *Ciba foundation symposium. Neurological basis of behaviour*. Boston: Little Brown; 1958. 219 p.
- Olds J. Effects of hunger and male sex hormone on self-stimulation of the brain. *J Comp Physiol Psychol* 1958;51:320–4.
- Retana-Márquez S, Bonilla-Jaime H, Vázquez-Palacios G, Martínez-García R, Velázquez-Moctezuma J. Changes in masculine sexual behaviour corticosterone and testosterone in response to acute and chronic stress in male rats. *Horm Behav* 2003;44:327–37.
- Ruiz FS, Andersen ML, Zager A, Martins RCS, Tufik S. Sleep deprivation reduces the lymphocyte count in a non-obese mouse model of type 1 diabetes mellitus. *Braz J Med Biol Res* 2007;40:633–7.
- Sachs BD. Sexual behaviour of male rats after one to nine days without food. *J Comp Physiol Psychol* 1965;60:144–6.
- Santos AM, Ferraz MR, Teixeira CV, Sampaio FJ, da Fonte Ramos C. Effects of undernutrition on serum and testicular testosterone levels and sexual function in adult rats. *Horm Metab Res* 2004;36:27–33.
- Schimpl PA, Rissman EF. Effects of gonadotropin-releasing hormones, corticotropin-releasing hormone, and vasopressin on female sexual behaviour. *Horm Behav* 2000;37:212–20.
- Velázquez-Moctezuma J, Monroy E, Cruz ML. Facilitation of the effect of testosterone on male sexual behaviour in rats deprived of REM sleep. *Behav Neural Biol* 1989;51:46–53.
- Verma S, Chhina GS, Kumar VM, Singh B. Effect of rapid eye movement sleep deprivation on sexual behaviour of male rats. *Indian J Exp Biol* 1989;27:892–4.
- Wade GN, Jones JE. Neuroendocrinology of nutritional infertility. *Am J Physiol Regul Integr Comp Physiol* 2004;287:1277–96.
- Wade GN, Schneider JE. Metabolic fuels and reproduction in female mammals. *Neurosci Biobehav Rev* 1992;16:235–72.
- Wayne NL, Wade GN, Rissman EF. Effect of food restriction and social cues on sexual maturation and growth in male musk shrews (*Suncus murinus*). *J Reprod Fertil* 1991;91:385–92.
- Weindruch RH, Suffin SC. Quantitative histologic effects on mouse thymus of controlled dietary restriction. *J Gerontol* 1980;35:525–31.
- Witt DM, Young LJ, Crews D. Progesterone modulation of androgen-dependent sexual behaviour in male rats. *Physiol Behav* 1995;57:307–13.
- Zager A, Andersen ML, Ruiz FS, Antunes IB, Tufik S. Effects of acute and chronic sleep loss on immune modulation of rats. *Am J Physiol Regul Integr Comp Physiol* 2007;293:504–9.
- Zarcone V, Zukowsky E, Gulevich G, Dement W, Hoddes E. Rorschach responses subsequent to REM deprivation in schizophrenic and nonschizophrenic patients. *J Clin Psychol* 1974;30:248–50.