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Consequences of post-weaning sleep deprivation on behaviour and oxidative stress parameters in rat plasma and brain

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Abstract

Sleep is essential for health: Adequate sleep is essential for healthy development and sleep deprivation results in several consequences. Indeed, sleep deprivation early in life is associated with poor behaviour and cognition, as well as impaired mental and physical health. Preclinical studies have shown that sleep deprivation alters several physiological functions later in life such as the cardiovascular, immune and endocrine systems, resulting in altered oxidative states. Most of the preclinical literature is focused on adult animals, and little is known about oxidative alterations during development, especially in the context of sleep deprivation. Hence, we adapted a classic and well-documented model of sleep deprivation, paradoxical sleep deprivation using multiple platforms, for juvenile rats and explored central and peripheral oxidative parameters, as well as the behavioural consequences of sleep deprivation post-weaning. We showed that 96 h of paradoxical sleep deprivation induced a significant reduction in body weight, decreased sucrose preference—a behaviour suggestive of anhedonia—and increased glucose and decreased cholesterol in the plasma. In the brain, we observed a decrease in reduced glutathione levels in the medial prefrontal cortex and an increase in thiobarbituric acid reactive substance levels in the hypothalamus, indicating oxidative damage in these regions. Taken together, our findings suggest that paradoxical sleep deprivation during development induces anhedonic behaviour and promotes central and peripheral alterations in oxidative parameters.

KEYWORDS
behaviour, experimental model, oxidative stress, rats, sleep deprivation

Abbreviations: CAT, catalase; CEUA, Ethics Committee on Animal Use; GSH, glutathione; GPx, glutathione peroxidase; HC, homecage control; ICLAS, International Council for Laboratory Animal Science; mPFC, median pre frontal cortex; NREM, non-rapid eyes movements; PUCRS, Pontifical Catholic University of Rio Grande do Sul; REM, rapid eyes movements; SD, sleep deprivation; SOD, superoxide dismutase; TBARS, thiobarbituric acid reactive substance.

1 | INTRODUCTION

Sleep is a behavioural state that is essential for health considering the metabolic impairments that result from sleep deprivation (Knutson et al., 2007). Indeed, sleep deprivation activates neurobiological mechanisms involved in the stress response as well as oxidative parameters (Gopalakrishnan et al., 2004). Even though sleep is not yet fully understood, evidence suggests that it is closely related to several physiological functions, such as maintenance of the cardiovascular, immune and endocrine systems, and especially in the developing central nervous system (Liew & Aung, 2021). Adequate sleep is mandatory for optimal infant development, especially during the early developmental phases (Alrousan et al., 2022). Studies suggest that children who achieve the recommended amount of sleep have improved behavioural and cognitive functions, as well as improved physical and mental health (Maski & Kothare, 2013). On the other hand, sleep deprivation could be a risk factor for cognitive issues and early overweight/obesity (Taheri, 2006).

In addition, previous reports suggest increased oxidative stress and neuroinflammation following sleep deprivation (Atrooz et al., 2019; Villafuerte et al., 2015), and there is a hypothesis that sleep may induce antioxidant mechanisms, because, during wakefulness, we produce several free radicals as a result of neuronal metabolism (Gopalakrishnan et al., 2004). Therefore, sleep can play a protective role, as it acts against these agents. Among these mechanisms, it is worth mentioning reduced glutathione (GSH), which is especially active in tissues with a high metabolic rate, as well as catalase (CAT), glutathione peroxidase (GPx) and superoxide dismutase (SOD), enzymes that act to stabilize free radicals. These enzymes help attenuate oxidative stress, which is characterized by an imbalance between the prooxidant and antioxidant systems (Villafuerte et al., 2015).

Most of the literature on animal models of sleep deprivation has focused on adult animals, and little is known about oxidative alterations throughout development following sleep deprivation. Although other experimental studies have employed different sleep deprivation paradigms in juvenile rodents, this study contributes to the literature with the adaptation of a classic, inexpensive and well-documented model of sleep deprivation for juvenile rats. We explored metabolism and oxidative parameters in the blood and the brain, as well as the behavioural consequences of sleep deprivation during the post-weaning period.

2 | METHODS

2.1 | Animals

The present study was conducted following the guidelines of the International Council for Laboratory Animal Science (ICLAS) and was approved by the Ethics Committee on Animal Use (CEUA) of Pontifical Catholic University of Rio Grande do Sul (PUCRS), Brazil (registration #9389). Male Wistar rats were acquired from the Center for Laboratory Animals at our university (CeMBE, PUCRS), Brazil. All animals were housed in standard plastic rat cages (22 × 16 × 14 cm) and kept under constant room temperature (21 ± 1°C), relative humidity (55% ± 5%) and ventilation. The rats were maintained on a 12-h photoperiod (lights on from 7 a.m. to 7 p.m.) and supplied with rat food and water ad libitum. The animals were placed in groups of six per cage (with same-sex littermates). After P21, the rats were weaned, and from P23 to P26, the rats were subjected to the sleep deprivation protocol for 96 h. They were randomly assigned to two experimental conditions, sleep deprivation or home-cage controls (Suchecki & Tufik, 2000). Moreover, the animals were weighed after weaning and before the behavioural battery (P31). To investigate the behavioural effects of sleep deprivation, the rats were evaluated from P31 to P34 in the sucrose preference, chocolate intake and social interaction tests. The behavioural battery is described in detail below. The rats were euthanized by guillotine 48 h after the end of the protocols, and the brain and blood were processed quickly for further analysis.

2.2 | Sleep deprivation

The rats were exposed to the paradoxical sleep deprivation paradigm for 96 h in groups of six animals in a tank with 15 platforms to avoid movement restriction and the effects of social isolation (Alvarenga et al., 2008). This method consists of placing a rat on a narrow platform (in this study, adapted to 4 cm in diameter) surrounded by water. In this condition, when animals lose muscle tone when they reach paradoxical sleep, they fall into the water, thus being awakened. In this model of selective rapid eye movement (REM) sleep deprivation, animals can achieve non-rapid eye movement (NREM) sleep ad libitum, and, when falling into the water, the animal is able to return to the platform. Throughout the duration of this experimental protocol, a grid with food and water was attached to the tank to allow animals to have food and water ad libitum.

Two days before the behavioural battery, the rats were handled by a researcher who performed all the animal manipulations during the following days. The rats were acclimated in the room for 30 min before the tests. All tests were performed during the light cycle (9 a.m. to 2 p.m.). All apparatuses were cleaned with 70% ethanol between rats to avoid any odour cues. Video was recorded using a professional camera and then analysed in the ANY-Maze software version 4.9 (ANY-Maze, Inc., Greensburg, PA, USA).

2.3 | Behavioural tests

2.3.1 | Sucrose preference test

To measure sucrose preference, the rats were water restricted the night before the test during the light phase (12 h of water restriction). On the following morning, the rats were placed in individual cages for 1 h before starting the test for habituation. Then, two bottles were placed in the cage for 3 h, one with water and another with sucrose solution (1%). To measure consumption, the bottles were weighted before and after test, and sucrose preference was calculated as [sucrose consumption/ (water consumption + sucrose consumption)] × 100.

2.3.2 | Chocolate intake test

For the chocolate intake test, the rats were food restricted the night before (12 h of food restriction) to motivate them to consume chocolate, which is highly palatable. The rats were habituated to chocolate for two consecutive days in the home-cage environment to avoid novelty-induced stress. Specifically, the rats were placed in individual cages and exposed to small pieces of chocolate in a small bottle lid. For 3 h, the rats were allowed to consume the chocolate that had been weighed before and after this period. To determine the intake, the body weight was measured with a high precision balance before and after the tests.

2.3.3 | Social interaction test

During this test, the rats were exposed for 2.5 min to an empty cage in the centre of an open field. To avoid novelty-induced stress, the rats were previously habituated for 30 min. Immediately after the 2.5-min exploration period, a stranger animal (same sex, age and weight) was added to the cage, and the total time spent interacting with the stranger animal was measured. Interaction was considered to be sniffing, nose poking and rearing in the cage. The interaction ratio was defined as the time spent interacting with the stranger divided by the time spent interacting with the empty cage.

2.4 | Biochemical analysis

Biochemical analysis was performed on whole blood samples collected in tubes with heparin. Blood was centrifuged at 1000 g for 10 min, and plasma was removed and frozen at −80°C until analysis. The levels of glucose, cholesterol and triglycerides were determined with commercial kits (Labtest Diagnóstica, Brazil), according to manufacturer's instructions, and a spectrophotometer (Spectronic GENESYS 8, Thermo Scientific).

2.5 | Oxidative stress

To analyse oxidative stress parameters in the brain, the hypothalamus, medial prefrontal cortex (mPFC) and hippocampus were dissected on an iced-chilled plated using a free-hand dissection method according to atlas coordinates (Paxinos & Watson, 2014). The regions were stored at −80°C until molecular analysis. The tissue was homogenized in 15 volumes (1:15, w/v) of sodium phosphate buffer, pH 7.4, and the homogenates were centrifuged at 750 g for 10 min at 4°C. The supernatant of the sample was used for the GSH, thiobarbituric acid reactive substance (TBARS) and CAT analyses. Total protein was measured using a NanoDrop 1000 spectrophotometer (Thermo Scientific).

2.5.1 | TBARS

TBARS is an index of lipid oxidation and indicates the levels of malondialdehyde in the tissues. For the test, 10 μl of the brain region homogenate or plasma was added to 10 μl of 12.4-mM sodium dodecyl sulphate and 400 μl of thiobarbituric acid. The mixture was warmed for 30 min and centrifuged at 750g for 10 min at 25°C. Then, the supernatant was collected and measured spectrophotometrically at 532 nm.

2.5.2 | Cat

CAT activity was determined based on the conversion of hydrogen peroxide (H_2O_2) into water and oxygen. A

reaction medium containing 102 µl of 30% H_2O_2 and 100 µl of Triton X-100 was pipetted with 10 µl of plasma and the hippocampus samples. The reaction was measured at 240 nm immediately and after 1 min, in a semiautomatic spectrophotometer. One CAT unit is characterized as 1 µmol of H_2O_2 consumed per minute.

2.5.3 | GSH

The reaction of GSH with the superoxide radical ($\cdot O_2^-$) produces an increase in oxygen consumption and the formation of oxidized glutathione. For the analyses, 250 µl of metaphosphoric was added to 10 µl of the brain region homogenate or plasma. The mixture was centrifuged at 750g for 10 min at 4°C. Then, 650 µl of Na_2HPO_4 and 100 µl of the colour reagent (5,5′-dithiobis-2-nitrobenzoic acid) were added to 250 µl of the supernatant. The reaction was read at 412 nm in a semiautomatic spectrophotometer.

2.6 | Statistical analysis

All statistical analyses were performed using SPSS 20.0 (IBM Corp., Armonk, NY, USA), and the graphs were prepared using Prism GraphPad 6.0 (GraphPad Software, La Jolla, CA, USA). The normality of the variables was verified using the Shapiro–Wilk test. To investigate the effect of sleep deprivation on dependent variables, an independent *t* test was executed for each dependent variable. To analyse the effects of sleep deprivation on weight gain, a repeated-measures analysis of variance was performed using the two groups as the between-subjects variable and weight measures over time as the repeated-measures variable. The data are expressed as mean

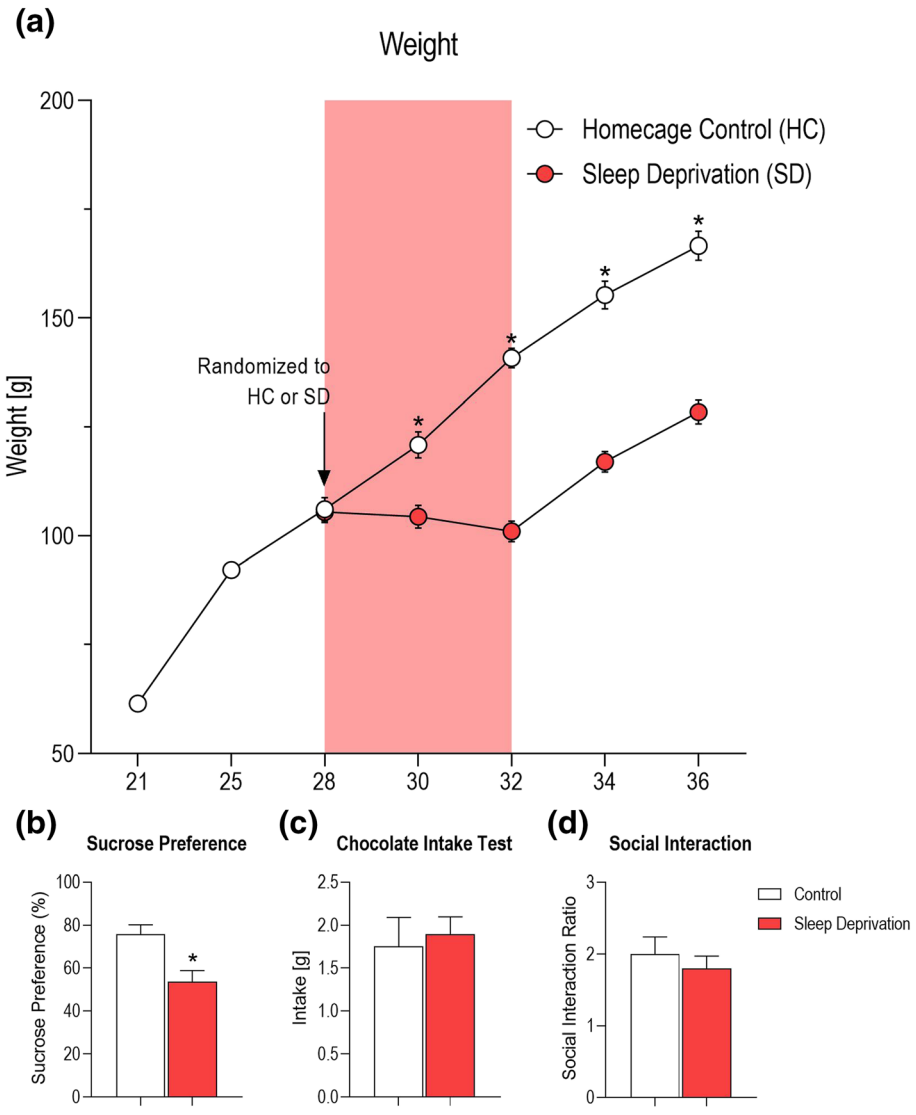

FIGURE 1 (a) Body weight (g) at postnatal day 21 (P21), P25, P28, P30, P32, P34 and P36. (b) Analysis of the sucrose preference test. (c) Analysis of the chocolate intake test. (d) Analysis of the social interaction test. * $p < 0.05$. The results are expressed as mean ± standard error of the mean.

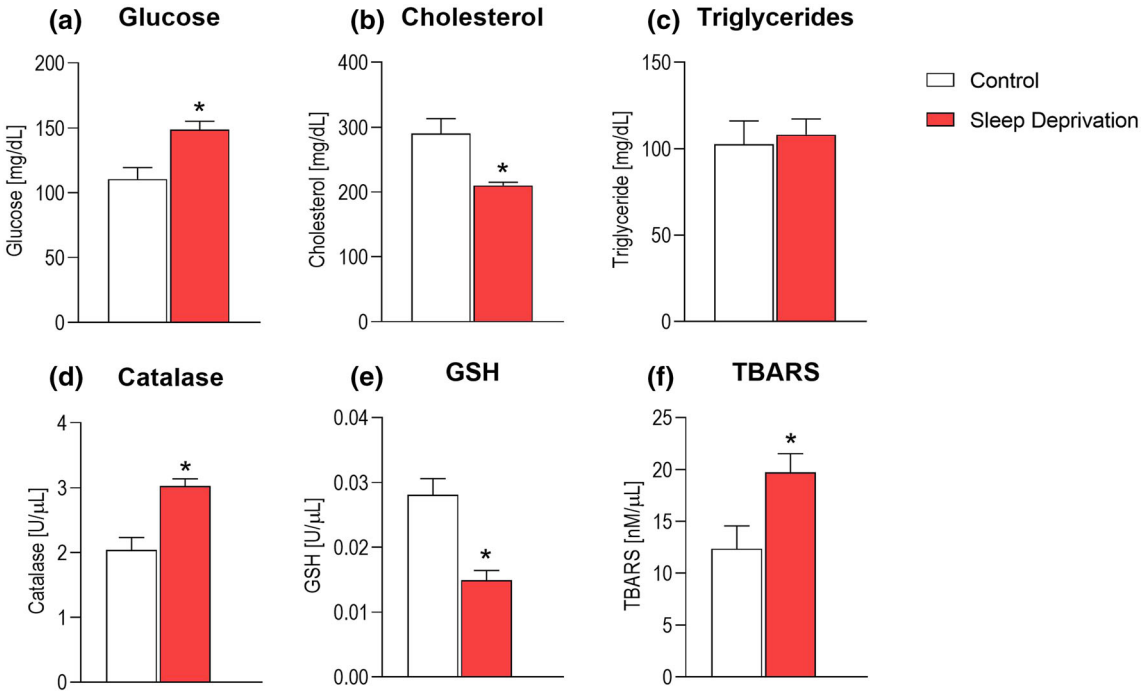

FIGURE 2 Comparison of peripheral metabolic markers and oxidative stress: (a) plasma glucose, (b) plasma cholesterol, (c) plasma triglycerides, (d) plasma catalase activity, (e) plasma reduced glutathione (GSH) concentration and (f) plasma thiobarbituric acid reactive substances (TBARS). * $p < 0.05$. The results are expressed as mean ± standard error of the mean.

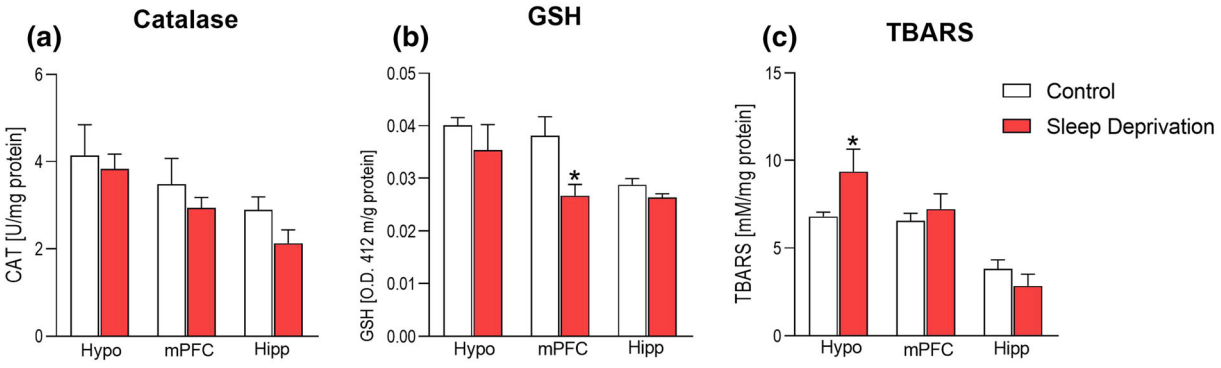

FIGURE 3 Comparison of oxidative stress markers in the brain: (a) catalase (CAT) activity, (b) reduced glutathione (GSH) concentration and (c) thiobarbituric acid reactive substances (TBARS) concentration. Hipp = hippocampus, Hypo = hypothalamus, mPFC = medial prefrontal cortex. * $p < 0.05$. The results are expressed as mean ± standard error of the mean.

± standard error of the mean. The level of significance was set at 5%.

3 | RESULTS

First, we looked at body weight gain between the groups from P28 to P36. We found a significant group effect, with rats exposed to sleep deprivation showing a decreased body weight compared with rats from control group [$F(4, 112) = 43.571$, $p < 0.001$; Figure 1a]. We observed a significant reduction in sucrose preference in sleep-deprived rats [$t(28) = 3.016$, $p = 0.0054$; Figure 1b]. However, sleep-deprived rats showed no differences in chocolate intake or social interaction when compared with control rats [$t(28) = 0.388$, $p = 0.700$, Figure 1c, and $t(28) = 0.687$, $p = 0.497$, Figure 1d, respectively].

To investigate sleep deprivation effects on overall metabolism and peripheral oxidative stress parameters, we looked at circulating glucose, triglycerides, cholesterol, CAT, GSH and TBARS in the plasma. We found a significant increase in glucose levels of sleep-deprived

rats compared with control rats [$t(14) = 3.439$, $p = 0.004$; Figure 2a]. We also found a significant reduction in cholesterol levels [$t(14) = 3.395$, $p = 0.004$; Figure 2b] but no differences in plasma triglycerides [$t(14) = 0.346$, $p = 0.734$; Figure 2c]. CAT activity in the plasma was significantly different between the groups [$t(14) = 4.405$, $p = 0.0006$; Figure 2d]. We also found a significant reduction in the GSH concentration in the plasma of sleep-deprived rats [$t(14) = 4.555$, $p = 0.0004$; Figure 2e] together with an increase in TBARS [$t(14) = 2.584$, $p = 0.0216$; Figure 2f] compared with control rats.

In the brain, there were no differences between the groups in CAT in the hypothalamus, mPFC and hippocampus [$t(14) = 0.389$, $p = 0.7026$; $t(14) = 0.841$, $p = 0.4143$; and $t(14) = 1.797$, $p = 0.0939$, respectively, Figure 3a]. In addition, the GSH concentration in the hypothalamus [$t(14) = 0.930$, $p = 0.3681$; Figure 3b] and hippocampus [$t(14) = 1.822$, $p = 0.0899$; Figure 3b] were not different between the groups, but the sleep-deprived rats showed a significant reduction in GSH in the mPFC [$t(14) = 2.714$, $p = 0.0168$; Figure 3b]. Finally, there was a significant increase in TBARS levels in the hypothalamus of sleep-deprived rats compared with control rats [$t(14) = 2.164$, $p = 0.0482$, Figure 3c], with no differences in the mPFC and hippocampus [$t(14) = 0.668$, $p = 0.5147$ and $t(14) = 1.181$, $p = 0.2573$, respectively].

4 | DISCUSSION

In the present study, paradoxical sleep deprivation induced significant alterations in peripheral and neuronal oxidative stress parameters. We also found alterations in the sucrose preference test compared with control rats, a behaviour suggestive of anhedonia. In the brain of sleep-deprived rats, we observed a decrease of GSH in the mPFC and an increase in TBARS levels in the hypothalamus, indicating oxidative damage in these cerebral areas. In the plasma of sleep-deprived animals, we found a significant decrease in GSH levels and an increase in TBARS levels and CAT activity. Moreover, compared with control rats, sleep-deprived rats showed weight loss and increased glucose and decreased cholesterol levels in the plasma.

Researchers have already reported brain damage following sleep deprivation. Khadrawy et al. (2011) reported the effect of paradoxical sleep deprivation for 72 h on oxidative stress parameters in the cortex and hippocampus of adult rats. Even though our study differs regarding the hippocampus results, we did find a significant reduction in GSH levels. D'Almeida et al. (2000) used adult rats and found that GSH levels in the hypothalamus were significantly decreased in vehicle-treated animals submitted to sleep deprivation compared with cage control rats. Paradoxical sleep deprivation increases lipid peroxidation in brain regions such as the PFC and hippocampus (Lima et al., 2014). Moreover, Alzoubi et al. (2016) found a reduction in hippocampal CAT activity with no differences in TBARS and GSH levels in that region. Notably, those studies were carried out with adult animals. In juvenile animals, we only found increased lipid peroxidation in the hypothalamus, suggesting some time-dependent alterations in brain lipid peroxidation. Elevated CAT activity and TBARS levels and decreased GSH levels in the plasma during the initial stages of restorative sleep indicate that the body's homeostatic mechanisms are impacted by sleep deprivation. Increased lipid peroxidation in brain regions results in free radical production and, consequently, free radical-induced neuronal damage (Villafuerte et al., 2015).

Consistent with our study, body weight variance is an important effect of metabolic alterations following sleep deprivation. Researchers have found significant body weight loss on day 5 of sleep deprivation (Machado et al., 2005). In addition to body weight variance, a reduction in the sucrose preference ratio in experimental animals relative to control animals is indicative of anhedonia (Liu et al., 2018). An anhedonic condition constitutes the core manifestation of depressive states (Rygula et al., 2005). In agreement with the present study, Andersen et al. (2009) analysed adult mice and also reported reduced sucrose preference in sleep-deprived animals, proposing that in a particular case of circadian disruption, chronic sleep deprivation can lead to depressive symptoms. The interplay between mental illness such as depression and bipolar disorder and disruptions in circadian rhythms has been observed (Aydin et al., 2013; Durmer & Dinges, 2005). Clinical research indicates that acute sleep deprivation affects negative mood states in adults (Babson et al., 2010). Indeed, wake cycle alterations are by far the most widely reported circadian disturbances related to depression (Berger et al., 2003). Abundant evidence bolsters the view that the sleep disorders give rise to the development of depression (Geoffroy & Palagini, 2021; Roberts & Duong, 2014). In addition, sleep deprivation has been studied as a trigger of some mental disorders in humans (Wehr, 1992).

Antioxidative stress mechanisms are important for cognitive functions. Although we did not find alterations in the hippocampus, chronic paradoxical sleep deprivation has been demonstrated to result in mood-related monoaminergic network fluctuations in the hippocampus and striatum, as well as cognitive impairment. Numerous animal and human studies have described memory deficits following sleep deprivation (Alhaider

et al., 2011; Alzoubi et al., 2016; Jiang et al., 2009; Smith & Kelly, 1988; Vollert et al., 2011).

In conclusion, our data indicate that paradoxical sleep deprivation in juvenile rats induces anhedonic behaviour and reduces body weight throughout development. Furthermore, increased glucose and decreased cholesterol in the plasma of sleep-deprived animals support the possibility of an altered metabolic condition that could increase the risk for physical and mental illnesses later in life. In addition, increased levels of oxidative markers in the brain suggest that sleep deprivation induces peripheral alterations as well as oxidative damage in key brain regions involved in the regulation of several cognitive and behavioural functions.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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REFERENCES

Alhaider, I. A., Aleisa, A. M., Tran, T. T., & Alkadhi, K. A. (2011). Sleep deprivation prevents stimulation-induced increases of levels of P-CREB and BDNF: Protection by caffeine. *Molecular and Cellular Neurosciences*, *46*, 742–751. https://doi.org/10.1016/j.mcn.2011.02.006

Alrousan, G., Hassan, A., Pillai, A. A., Atrooz, F., & Salim, S. (2022). Early life sleep deprivation and brain development: Insights from human and animal studies. *Frontiers in Neuroscience*, *16*, 833786. https://doi.org/10.3389/fnins.2022.833786

Alvarenga, T. A., Patti, C. L., Andersen, M. L., Silva, R. H., Calzavara, M. B., Lopez, G. B., Frussa-Filho, R., & Tufik, S. (2008). Paradoxical sleep deprivation impairs acquisition, consolidation, and retrieval of a discriminative avoidance task in rats. *Neurobiology of Learning and Memory*, *90*, 624–632. https://doi.org/10.1016/j.nlm.2008.07.013

Alzoubi, K. H., Mayyas, F. A., Khabour, O. F., Bani Salama, F. M., Alhashimi, F. H., & Mhaidat, N. M. (2016). Chronic melatonin treatment prevents memory impairment induced by chronic sleep deprivation. *Molecular Neurobiology*, *53*, 3439–3447. https://doi.org/10.1007/s12035-015-9286-z

Andersen, M. L., Hoshino, K., & Tufik, S. (2009). Increased susceptibility to development of anhedonia in rats with chronic peripheral nerve injury: Involvement of sleep deprivation? *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *33*, 960–966. https://doi.org/10.1016/j.pnpbp.2009.04.022

Atrooz, F., Liu, H., Kochi, C., & Salim, S. (2019). Early life sleep deprivation: Role of oxido-inflammatory processes. *Neuroscience*, *406*, 22–37. https://doi.org/10.1016/j.neuroscience.2019.02.021

Aydin, A., Selvi, Y., Besiroglu, L., Boysan, M., Atli, A., Ozdemir, O., Kilic, S., & Balaharoglu, R. (2013). Mood and metabolic consequences of sleep deprivation as a potential endophenotype' in bipolar disorder. *Journal of Affective Disorders*, *150*, 284–294. https://doi.org/10.1016/j.jad.2013.04.007

Babson, K. A., Trainor, C. D., Feldner, M. T., & Blumenthal, H. (2010). A test of the effects of acute sleep deprivation on general and specific self-reported anxiety and depressive symptoms: An experimental extension. *Journal of Behavior Therapy and Experimental Psychiatry*, *41*, 297–303. https://doi.org/10.1016/j.jbtep.2010.02.008

Berger, M., Van Calker, D., & Riemann, D. (2003). Sleep and manipulations of the sleep-wake rhythm in depression. *Acta Psychiatrica Scandinavica*, *108*, 83–91. https://doi.org/10.1034/j.1600-0447.108.s418.17.x

D'Almeida, V., Hipólide, D. C., Lobo, L. L., De Oliveira, A. C., Nobrega, J. N., & Tufik, S. (2000). Melatonin treatment does not prevent decreases in brain glutathione levels induced by sleep deprivation. *European Journal of Pharmacology*, *390*, 299–302. https://doi.org/10.1016/S0014-2999(99)00924-3

Durmer, J. S., & Dinges, D. F. (2005). Neurocognitive consequences of sleep deprivation. *Seminars in Neurology*, *25*, 117–129. https://doi.org/10.1055/s-2005-867080

Geoffroy, P. A., & Palagini, L. (2021). Biological rhythms and chronotherapeutics in depression. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, *106*, 110158. https://doi.org/10.1016/j.pnpbp.2020.110158

Gopalakrishnan, A., Ji, L. L., & Cirelli, C. (2004). Sleep deprivation and cellular responses to oxidative stress. *Sleep*, *27*, 27–35. https://doi.org/10.1093/sleep/27.1.27

Jiang, F., Cui, Q. L., Jiang, J. H., Cui, M. L., Zhang, Y., Wang, C., Yu, X. G., & Yan, C. H. (2009). Effects of chronic partial sleep deprivation on growth and learning/memory in young rats. *Chinese Journal of Contemporary Pediatrics*, *11*, 599–600.

Khadrawy, Y. A., Nour, N. A., & Aboul Ezz, H. S. (2011). Effect of oxidative stress induced by paradoxical sleep deprivation on the activities of Na+, K+-ATPase and acetylcholinesterase in the cortex and hippocampus of rat. *Translational Research*, *157*, 100–107. https://doi.org/10.1016/j.trsl.2010.11.005

Knutson, K. L., Spiegel, K., Penev, P., & Van Cauter, E. (2007). The metabolic consequences of sleep deprivation. *Sleep Medicine Reviews*, *11*, 163–178. https://doi.org/10.1016/j.smrv.2007.01.002

Liew, S. C., & Aung, T. (2021). Sleep deprivation and its association with diseases- a review. *Sleep Medicine*, *77*, 192–204. https://doi.org/10.1016/j.sleep.2020.07.048

Lima, A. M. A., De Bruin, V. M. S., Rios, E. R. V., & De Bruin, P. F. C. (2014). Differential effects of paradoxical sleep deprivation on memory and oxidative stress. *Naunyn-*

Schmiedeberg's Archives of Pharmacology, *387*, 399–406. https://doi.org/10.1007/s00210-013-0955-z

Liu, M. Y., Yin, C. Y., Zhu, L. J., Zhu, X. H., Xu, C., Luo, C. X., Chen, H., Zhu, D. Y., & Zhou, Q. G. (2018). Sucrose preference test for measurement of stress-induced anhedonia in mice. *Nature Protocols*, *13*, 1686–1698. https://doi.org/10.1038/s41596-018-0011-z

Machado, R. B., Suchecki, D., & Tufik, S. (2005). Sleep homeostasis in rats assessed by a long-term intermittent paradoxical sleep deprivation protocol. *Behavioural Brain Research*, *160*, 356–364. https://doi.org/10.1016/j.bbr.2005.01.001

Maski, K. P., & Kothare, S. V. (2013). Sleep deprivation and neurobehavioral functioning in children. *International Journal of Psychophysiology*, *89*, 259–264. https://doi.org/10.1016/j.ijpsycho.2013.06.019

Paxinos, G., & Watson, C. (2014). *The rat brain in stereotaxic coordinates* (7th ed.). Elsevier Academic Press.

Roberts, R. E., & Duong, H. T. (2014). The prospective association between sleep deprivation and depression among adolescents. *Sleep*, *37*, 239–244. https://doi.org/10.5665/sleep.3388

Rygula, R., Abumaria, N., Flügge, G., Fuchs, E., Rüther, E., & Havemann-Reinecke, U. (2005). Anhedonia and motivational deficits in rats: Impact of chronic social stress. *Behavioural Brain Research*, *162*, 127–134. https://doi.org/10.1016/j.bbr.2005.03.009

Smith, C., & Kelly, G. (1988). Paradoxical sleep deprivation applied two days after end of training retards learning. *Physiology & Behavior*, *43*, 213–216. https://doi.org/10.1016/0031-9384(88)90240-5

Suchecki, D., & Tufik, S. (2000). Social stability attenuates the stress in the modified multiple platform method for paradoxical sleep deprivation in the rat. *Physiology & Behavior*, *68*, 309–316. https://doi.org/10.1016/S0031-9384(99)00181-X

Taheri, S. (2006). The link between short sleep duration and obesity: We should recommend more sleep to prevent obesity. *Archives of Disease in Childhood*, *91*, 881–884. https://doi.org/10.1136/adc.2005.093013

Villafuerte, G., Miguel-Puga, A., Murillo Rodríguez, E., Machado, S., Manjarrez, E., & Arias-Carrión, O. (2015). Sleep deprivation and oxidative stress in animal models: A systematic review. *Oxidative Medicine and Cellular Longevity*, *2015*, 234952. https://doi.org/10.1155/2015/234952

Vollert, C., Zagaar, M., Hovatta, I., Taneja, M., Vu, A., Dao, A., Levine, A., Alkadhi, K., & Salim, S. (2011). Exercise prevents sleep deprivation-associated anxiety-like behavior in rats: Potential role of oxidative stress mechanisms. *Behavioural Brain Research*, *224*, 233–240. https://doi.org/10.1016/j.bbr.2011.05.010

Wehr, T. A. (1992). Improvement of depression and triggering of mania by sleep deprivation. *Journal of the American Medical Association*, *267*, 548–551. https://doi.org/10.1001/jama.1992.03480040096038

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