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Brief communication

Effects of age on recovery of body weight following REM sleep deprivation of rats

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Abstract

Chronically enforced rapid eye (paradoxical) movement sleep deprivation (REM-SD) of rats leads to a host of pathologies, of which hyperphagia and loss of body weight are among the most readily observed. In recent years, the etiology of many REM-SD-associated pathologies have been elucidated, but one unexplored area is whether age affects outcomes. In this study, male Sprague-Dawley rats at 2, 6, and 12 months of age were REM sleep-deprived with the platform (flowerpot) method for 10–12 days. Two-month-old rats resided on 7-cm platforms, while 10-cm platforms were used for 6- and 12-month-old rats; rats on 15-cm platforms served as tank controls (TCs). Daily changes in food consumption ($g/kg^{0.67}$) and body weight (g) during baseline, REM-SD or TCs, and post-experiment recovery in home cages were determined. Compared to TCs, REM-SD resulted in higher food intake and decreases in body weight. When returned to home cages, food intake rapidly declined to baseline levels. Of primary interest was that rates of body weight gain during recovery differed between the age groups. Two-month-old rats rapidly restored body weight to pre-REM-SD mass within 5 days; 6-month-old rats were extrapolated by linear regression to have taken about 10 days, and for 12-month-old rats, the estimate was about 35 days. The observation that restoration of body weight following its loss during REM-SD may be age-dependent is in general agreement with the literature on aging effects on how mammals respond to stress.

Keywords: Food consumption; Body weight; REM sleep deprivation

1. Introduction

Many different pathologies develop when rats are chronically deprived of rapid eye movement (REM; paradoxical sleep) or total sleep [1,2]. Two prominent symptoms are hyperphagia and loss of body weight [1,2]. For food intake to increase manifold while losing body weight means that sleep deprivation (SD) leads to a state of negative energy balance. Consequently, energy expenditure increases significantly [3–5], as does resting metabolic rate [6]. The time course of increases in oxygen consumption approximately matches the development of hyperphagia [6], suggesting that food consumption is increased to fuel elevated energy metabolism. When SD is relieved and rats are returned to their home cages, within a day or two, hyperphagia is no longer evident [6] and there is a rapid decline of energy expenditure [7] and oxygen consumption [6] to baseline levels.

The regulation of food intake behavior is governed largely by the hypothalamus and brainstem [8]. Recently, it was shown that neuropeptide Y, the most potent orexigen known, is markedly increased within the arcuate nucleus of the hypothalamus; concurrently, there is a pronounced decrease in POMC, the anorexigenic counterpart to NPY [9]. Further, circulating levels of leptin, a satiety hormone secreted by white adipocytes that binds to receptors within the hypothalamus and brainstem to signal a blunting of appetite [10], decrease rapidly within the first several days of SD and remain suppressed [6,11,12].

Much remains to be learned about the pathophysiology of SD, but what has not been explored is how age may affect SD outcomes. Whereas an abundant body of research on aging has shown that responses to stressors decline with age [13–17], we are not aware of any study of SD and differently aged rats. Here,

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we report that while rats of 2, 6, and 12 months of age respond stereotypically to REM-SD by loss of body weight and hyperphagia, the ability to recover from the regimen, using restoration of body weight as an index, may be slowed with age.

2. Methods

2.1. Animals

Male Sprague-Dawley rats (Harlan) were housed individually in shoebox-style cages with ad libitum chow (TekLad) and water; ambient temperature averaged 24 °C and photoperiod was a 12:12 cycle with lights-on at 0800 h. Experimental procedures were approved by the Morgan State University Institutional Animal Care and Use Committee, and they comply with National Institutes of Health guidelines.

2.2. REM sleep deprivation paradigm

The platform (i.e., flowerpot) method was used to effect REM-SD. Two large Plexiglas tanks are each divided into five separate compartments of 30 × 30 cm; each compartment has a 10-cm high column onto which can be attached Plexiglas platforms of 7-, 10-, or 15-cm diameter. The tanks are fitted with inlet and outlet ports for continuous water flow-through to carry away feces and debris; water floods each chamber to a height of ~1 cm below the platform surface. A wire mesh covers the tank for ventilation.

REM-SD is enforced by selecting a platform size appropriate to body weights [18]. For animals of up to 350 g body weight, the 7-cm platform was used; 10-cm platforms are employed with rats greater than 350 g. Rats have free access to chow (pellet hopper) and water (standard water bottle); they can groom themselves and engage in limited exploratory behavior. Rats can rest by lying down and eventually enter into slow-wave sleep. As they proceed into REM (paradoxical) sleep, muscle atonia causes them to make facial contact with or fall into the water. The rat abruptly awakens and the cycle begins again. Thus, the platform method is selective for abolishing REM sleep and has been validated by electroencephalography [19–22], although it also perturbs non-REM sleep [23,24]. Larger platforms of 15-cm size were used for tank control (TC) rats. The size is large enough so that within 1 day, rats learn to position themselves to obtain sleep; however, these rats may also experience fragmentation of sleep [21].

For 2 weeks, rats were accustomed to routine handling and the novel environment of the SD tanks by placement onto the platforms for ~1 h each day. Three age groups of rats were tested. For REM-SD, rats were 2 ($n=10$), 6 ($n=5$), and 12 ($n=10$) months of age; for TCs, rats were 3 ($n=10$), 6 ($n=4$), and 12 ($n=10$) months of age.

2.3. Experimental design

Baseline data were collected for ~5 days before experimentation. Rats were weighed and 24-h food consumption was determined; they continued the daily ~1-h stay in the tanks for acclimation. Rats were then placed into the tanks for 10 to 12 days. Food consumption was normalized as grams per day per kg body weight taken to the 0.67 power to correct for differences in metabolic rate as a function of body mass [25]. At the conclusion of REM-SD or TC experiments, rats were returned to home cages and observed for no less than 5 days of recovery.

2.4. Data analyses

For simplicity, data are shown as percent changes from baseline (mean ± S.E.), which was assigned a value of 100%. Statistical analyses of food intake (as g/day per $kg^{0.67}$) were done by comparing the averages during baseline and REM-SD or for TCs, across all three age groups, using 2-way ANOVA followed by the Bonferroni's post hoc test. Similar analyses were used for body weight in g except that averages of the final day of baseline were compared to average mass on the final day of the experiment (i.e., days 10–12), and by linear regression. Analyses were conducted using GraphPad Prism, version 4.03 (www.graphpad.com).

3. Results and discussion

3.1. Food consumption

Food consumption data are shown in Fig. 1 of individual 2- or 3-, 6-, and 12-month-old REM-SD (A, C, and E, respectively) and TC rats (B, D, and F, respectively) to illustrate overall variability. The data are given as percent change from each rat's baseline average (100%).

Two-month-old rats had the highest daily baseline food consumption of 54.5 ± 0.9 g/$kg^{0.67}$, which was not surprising because young rats undergo rapid growth. At 6 months of age, it decreased by about one-half to 25.5 ± 0.9 g/$kg^{0.67}$, and this level of daily food intake continued for 12-month-old rats (33 ± 0.8 g/$kg^{0.67}$). Consistent with the findings of others, the transition from home cages to REM-SD resulted in hyperphagia [1,2,6,12,26,27]. Two-way ANOVA revealed significant effects of treatment (i.e., REM-SD or TC; $F_{(1,284)}=13.56$, $P=0.0003$) and age ($F_{(2,284)}=4.36$, $P=0.0136$). Post hoc testing showed that REM sleep-deprived rats at 2 months of age significantly increased average daily food consumption by 1.7-fold to 94.3 ± 6 g/$kg^{0.67}$ ($P<0.05$), and for 6-month-old rats, it was increased by more than 3-fold to 84 ± 6.1 g/$kg^{0.67}$ ($P<0.05$). Twelve-month-old rats had a modest increase to 44.2 ± 1.6 g/$kg^{0.67}$, but this was not statistically significant.

Average daily food consumption of TC rats at 3, 6, and 12 months of age during baseline was 49.2 ± 0.9, 27.5 ± 0.8, and 37.3 ± 1 g/$kg^{0.67}$, respectively. On the other hand, on the larger platforms for 10–12 days, treatment was significant with 2-way ANOVA ($F_{(1,274)}=9.82$, $P=0.0019$). The only age group to have a statistically significant increase by post hoc testing was the 6-month-old rats (77.5 ± 5.9 g/$kg^{0.67}$, $P<0.05$).

While there was hyperphagia during REM-SD, many instances of increased food consumption were also noted