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Study on emotion by rest time in mice with repetitive sleep deprivation

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Sleep deprivation (SD) inhibits normal biorhythms, causing physical and mental problems. To solve the problems caused by SD, fundamental measures are needed. I investigated change of recovery by rest time in psychological aspect after repetitive SD. The mice were divided into four groups: control 24-hr rest after 24-hr SD group, 48-hr rest after 24-hr SD group, and 72-hr rest after 24-hr SD group (n = 20 in each group). I carried out SD in the water cage included multiple platforms. Repetitive SD executes for 36 days. I measured weight every week after SD for 6 weeks. To check emotional condition, I carried out intruder-evoked aggression test and modified forced swimming test. In the present results, group treated 24-hr rest and 48-hr rest after 24-hr SD showed lower natural aggressiveness and high depression. However, group treated 72-hr rest after 24-hr SD indicated emotional changes to recover the normal conditions. In the weight change, all group showed significant decrease compared to control for 6 weeks. I suggest that appropriate rest time after SD can help to restore emotional change.

Keywords: Sleep deprivation, Depression, Aggressiveness, Rest time

INTRODUCTION

With regard to sleep, which is one of the vital functions of humans, sleep deprivation (SD) became to appear temporarily or chronically due to the changes in lifestyles resulting from the progression of high degrees of industrialization hindering the normal biorhythm thereby causing physical, mental, and even social problems. In particular, workers in the health care industry who should work 24 hr a day such as emergency medicine department doctors and nurses and shift workers that have occupations such as policemen and drivers are complaining of many problems due to chronic SD (Kim et al., 2000). It has been reported that although implementing shift work can provide the continuity and efficiency of work and economic benefits, related repetitive SD may increase the sense of fatigue thereby increasing the risk of related accidents, increase the risks of cardiovascular diseases, digestive system diseases, and reproductive dysfunctions, and cause the development negative emotions such as tension, depression, anger, and confusion (Kim et al., 2002; Ko and Joe, 2002; Lee et al., 1999).

Recently, as SD not only has hurt the health of individuals and disturbed job performance but also has reduced productivity and brought about fatal consequences that even led to industrial disasters or accidents, public awareness of and interest in sleep rhythm has been increasing (Choi et al., 2003). In particular, changes in mental states have been studied by many researchers with interest through animal experiments and human investigations. As the lengths of the time of SD, methods such as total, partial, selective, and fragmented SD were used and it has been reported that according to a meta-analysis using the results of existing studies regarding SD, partial SD deteriorated mood regulation much more greatly than total SD in the psychological aspect (Pilcher and Huffcutt, 1996). Bonnet (1989) reported that SD time dependently reduced the degree of awakedness and executive ability. In addition, Novati et al. (2008) reported that SD for long periods of time might lead to changes in the neurotransmitter system and neuroendocrine responses and may be regarded as one of the symptoms of mental diseases.

The decrease in the physical activities of night-shift workers

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Table 1. Change in weight

	0 Week	1 Week	2 Weeks	3 Weeks	4 Weeks	5 Weeks	6 Weeks
Control	28.90±0.36[a]	31.70±0.31[b]	35.95±0.49[c]	36.35±0.50[c]	39.50±0.48[c]	40.20±0.56[c]	40.55±0.55[c]
24-Hr rest after 24-hr SD	29.25±0.32[a]	29.00±0.30[a]	30.90±0.28[a]	31.90±0.36[b]	34.25±0.33[a]	33.75±0.33[b]	34.80±0.39[b]
48-Hr rest after 24-hr SD	29.00±0.27[a]	28.50±0.31[a]	31.15±0.29[a]	33.10±0.33[a]	33.65±0.41[a]	37.30±0.49[a]	37.85±0.50[a]
72-Hr rest after 24-hr SD	29.65±0.38[a]	28.55±0.32[a]	34.15±0.37[b]	33.65±0.37[a]	36.30±0.44[b]	36.40±0.53[a]	39.05±0.51[a]
F	0.964	23.54*	43.10*	22.16*	38.16*	29.22*	24.20*

Values are presented as mean±standard error (g).
SD, sleep deprivation.
*$P<0.05$. Duncan: a<b<c.

contributes to the decrease in physical fitness, which is a negative change in body composition, and furthermore, leads to declines in the efficiency of work due to fatigue and SD (Costa, 2004). Since night-shift workers should work at a certain time, their physical activities decrease. Because of these decreases in physical activities, night-shift workers showed chronic fatigue, sleeplessness, sleepiness, and, in particular, in the case of night shift workers that worked for more than 5 years, a 6 times higher rate of depression than daytime workers (Atkinson et al., 2008; Øyane et al., 2013). Although studies on physical and psychological states such as mood changes, fatigue, and sleepiness have been actively conducted, studies on how much rest is necessary for recovery are insufficient. Therefore, the present study was intended to examine changes in psychological aspect according to the rest time in mice repeatedly deprived of sleep.

MATERIALS AND METHODS

Animals and SD treatment

Male ICR mice weighing 30±1.5 g (n=80) were used in this experiment. All animal experimental procedures confirmed to the National Institutes of Health and the Korean Academy of Medical Science guidelines. All animals were housed under controlled temperature (20°C±2°C) and under a 12-hr light/12-hr dark cycle conditions and were supplied with food and water *ad libitum*. The mice were randomly divided into four groups: control group, 24-hr rest after 24-hr SD group, 48-hr rest after 24-hr SD group, and 72-hr rest after 24-hr SD group (n=20 in each group). SD was carried out using the multiple platform (3 cm in diameter) in water cage method, as previously described (Lee et al., 2012; Silva et al. 2004). Repetitive SD executes for 36 days. The weight was measured every week after SD for 6 weeks.

Intruder-evoked aggression test

Intruder-evoked aggression tests were conducted referring to a paper reported previously (Koike et al., 2009). Male ICR mice (13 weeks) had never seen the mice in the experimental group were used as intruders. The mouse in the experimental group was kept in the crystal cylindrical cage (50-cm diameter) for 10 min before the experiment. Thereafter, the intruder mouse was put into the cage and the aggressiveness of the experimental mouse was observed for 10 min. The aggression was analyzed with the latency to first attack, the number of attacks, the duration of attacks, the number of tail rattles, and the duration of tail rattles.

Modified forced swimming test

We performed a modified forced swimming test to investigate a depressed-like state in the SD mice as previously described (Sung et al., 2010). All mice conducted a pretest for 15 min to eliminate the acute stress by water. Twenty-four hr after the pretest, the mice were tested for 6 min. During the test session, the fasting and resting time were analyzed using a Smart version 2.5 video tracking system (Panlab, Barcelona, Spain).

Data analysis

The results are expressed as the mean±standard error. Statistical analyses were performed using one-way analysis of variance followed by Duncan *post hoc* test using IBM SPSS Statistics ver. 21.0 (IBM Co., Armonk, NY, USA). The significance level was set to $P<0.05$.

RESULTS

Changes in weight

The control group showed statistically significant difference to all groups after weight measurement ($P<0.05$). Forty-eight-hr rest after SD group and 72-hr rest after SD group showed no significant difference in weight from 5 weeks (Table 1).

Change in aggression

Latency to first attack was statistically increased in 24-hr rest

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Table 2. Change in aggression

	Latency to first attack (sec)	No. of attacks	Duration of attack (sec)	No. of tail rattles	Duration of tail rattle (sec)
Control	95.70±23.77[a]	3.90±1.08[a]	21.30±8.13[b]	3.00±1.12[a]	3.10±1.35[a]
24-Hr rest after 24-hr SD	279.30±71.50[b]	1.60±0.42[b]	5.60±2.77[a]	1.10±0.10[b]	1.10±0.10[a]
48-Hr rest after 24-hr SD	264.60±69.86[b]	1.30±0.15[b]	4.10±1.69[a]	1.50±0.26[a,b]	1.20±0.13[a]
72-Hr rest after 24-hr SD	77.30±23.72[a]	2.60±0.61[a,b]	7.70±2.81[a]	1.70±0.36[a,b]	1.20±0.13[a]
F	4.15*	3.10*	2.94*	1.82	1.99

Values are presented as mean±standard error.
SD, sleep deprivation.
*$P<0.05$. Duncan: a<b.

Table 3. Change in depression

	Resting	Fasting
Control	29.48±6.35[a]	167.51±13.02[c]
24-Hr rest after 24-hr SD	69.76±10.67[b]	79.57±6.86[a]
48-Hr rest after 24-hr SD	68.93±9.28[b]	83.37±7.18[a]
72-Hr rest after 24-hr SD	42.58±4.03[a]	112.51±11.47[b]
F	6.20*	16.48*

Values are presented as mean±standard error (sec).
SD, sleep deprivation.
*$P<0.05$. Duncan: a<b<c.

after 24-hr SD group and 48-hr rest after 24-hr SD compared to control group ($P<0.05$). However, 72-hr rest after 24-hr SD group was not significant difference ($P>0.05$). The number of attacks and duration of attacks were significantly decreased in all groups than in the control group ($P<0.05$). The number of tail rattles and duration of tail rattles decreased in all groups, however, not statistically significant in all group ($P>0.05$) (Table 2).

Change in depression

Fasting was significant decreased in all group except control group ($P<0.05$). Resting was statistically significant in 24-hr rest after 24-hr SD group and 48-hr rest after 24-hr SD compared to control group ($P<0.05$). However, 72-hr rest after 24-hr SD group was not significant difference ($P>0.05$) (Table 3).

DISCUSSION

Changes in sleep rhythm, such as repeated SD, are known to alter biorhythm, affecting not only mere physical fatigue but also mental aspects such as aggression, anxiety, and depression, leading to various social problems (Lee et al., 2014). In particular, shift workers are known to experience insomnia, anxiety and depression more frequently than nonshift workers (Lee et al., 2013). To solve the problems caused by SD, more fundamental measures are necessary to restore normal body rhythm after SD. Kim and Wang (2005) reported that when 300 mg of caffeine was administered after SD in normal adults, daytime sleepiness was considerably improved and the improvement of cognitive functions was helped. However, since these study results were obtained from total SD for one night, repeated SD may show different results. Lim and Kim (2000) reported that when exercise was applied after SD, the ability to perform exercise was reduced due to physical fatigue resulting from the shortage of sleep. Negative emotions increased after exercise so that the negative emotions recognized due to SD were aggravated by the stimulation of exercise. As such, various methods presented for physical recovery after SD were reported to be not helpful for fundamental recovery. Therefore, to normalize the body rhythm after SD, an appropriate rest time is necessary and discussion on how much rest time is appropriate is necessary. Recently, Lee et al. (2012) reported that factors associated with apoptosis significantly increased in the hippocampus of mice that took a rest for 24 hr or 48 hr after 24-hr SD compared to the control group. The significant results were shown in behavioral tests that checked cognitive functions too. They also suggested that recovery time should be considered because a rest for at least 72 hr is helpful for the recovery of cognitive functions.

In a study regarding body weight and SD, Rechtschaffen et al. (1983) reported that weights decreased despite of increases in food intake in mice deprived of sleep. They advised that the reason was increases in the ratios of catabolism and anabolism. In addition, they found that the adrenal glands of mice deprived of sleep were hypertrophied demonstrating that SD is a great stress. These stress situations should have affected body metabolism so that the weight decreased in reverse proportion to the increase in food intake. The results of the present study also showed that weights statistically significantly decreased from one week to 6 weeks after weight measurement in all experimental groups compared to the control group. However, it could be seen that when 5 weeks had passed after repetitive SD, a rest for 48 hr and a rest for 72 hr did not show any big difference.

As SD progresses, the mood state changes negatively. In particular, when the time of SD has exceeds 20 hr, rapid mood changes appear due to the influence of the daily cycle (Kim et al., 2000). Due to the imbalance of the daily cycle, the central body temperature, which is one of the indicators of biorhythm, shows low values, the secretion of growth hormone reaches the peak, and the secretion of cortisol increases mainly leading to a sense of fatigue and depression (Boivin et al., 1997; Kim et al., 2000). In the present study, the group treated a rest for 24 hr and 48 hr after 24-hr SD showed higher depression and lower aggressiveness than the control group. However, the group treated a rest for 72 hr after 24-hr SD showed no significant difference compared to the control group. Due to the nature of rodents, when new individuals enter their territory, rodents become to show aggressiveness. However, inappropriate rests after SD did not help recovery from natural aggressiveness and depression. These results indicated that a rest for 72 hr is necessary for such a behavioral change to be restored to the normal state.

The present results taken together, it can be seen that repetitive SD can act as great stress on the body, which can lead to decreased body weight, decreased aggression, and increased depression. However, a rest for 72 hr after repetitive SD for 24 hr relieves the negative changes of the body caused by stress. It should be considered as a solution to the social and economic problems caused by SD.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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