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Original Article

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Effect of Food Deprivation on a Delayed Nonmatch-to-place T-maze Task

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Food deprivation can affect performance on difficult cognitive task, such as the delayed nonmatch-to-place T-maze task (DNMT). The importance of food deprivation on maintaining high motivation for DNMT task has been emphasized, but not many studies have investigated the optimal conditions for depriving rodents to maximize performance. Establishing appropriate conditions for food deprivation is necessary to maintain DNMT task motivation. We applied different conditions of food deprivation (1-h food restriction vs. 1.5-g food restriction; single caging vs. group caging) and measured body weight and the number of correct choices that 8-week-old C57BL/6J mice made during the DNMT task. The 1.5-g food restriction group maintained 76.0±0.6% of their initial body weight, but the final body weight of the 1-h food restriction condition group was reduced to 62.2±0.8% of their initial body weight. These results propose that 1.5-g food restriction condition is effective condition for maintaining both body weight and motivation to complete the DNMT task.

Key words: food deprivation, motivation, cognitive ability, delayed nonmatch-to-place T-maze task

INTRODUCTION

The delayed nonmatch-to-place T-maze (DNMT) task can be used in a variety of ways to assess animal cognitive abilities. The natural tendency of mice in a DNMT task, however, is to alternate their choice of goal arm, which requires working memory. Alternation reflects the animal's motivation to explore its environment and locate the presence of reward. If two trials are performed consequently, mice tend to choose the arm not explored before, suggesting that they remember their choice on the first trial. This tendency of choosing the right arm can be reinforced by performing the trial while the animal is deprived and rewarding it with a reward if it alternates appropriately between the 2 arms [1].

Motivation plays a critical role in DNMT task performance. Food deprivation is directly correlated with motivation and is used to reinforce performance on tasks that require higher cognitive ability. Different laboratories have their own protocol to deprive mice to maintain a certain body weight. A 10 to 40% decrease of initial body weight is an ideal percentage that keeps the animal motivated to run the task [2-4]. Motivation and food deprivation are widely used in rewarding tasks, but few studies have been done on food deprivation to control mouse body weight for optimal DNMT task performance.

To identify the best food deprivation condition for the DNMT task, we employed two paradigms; 8-week-old mice were given 1.5 g of food pellets per mouse per day or given access to food for 1 h per day. To determine if a dominant mouse would control the

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food, we employed two groups, single and group caging, to assess a possible relationship between social isolation (housing condition) and food deprivation. We found that 1-h food restriction was harsh; two mice in the single caging condition of the 1-h group died of starvation, and the final body weight for the group caging of 1-h food restriction was reduced by 40%, which is close to starvation. Our findings suggest that the 1.5-g condition is more suitable to maintain DNMT task performance.

MATERIALS AND METHODS

Animals

We obtained 8-week-old male C57BL/6J mice from Orient Co. (Gyeonggi, Korea). Animals were housed singly and in group cages and both were maintained on a 12-h light/dark cycle. All behavioral experiments were conducted during the light phases. Food and water were provided ad libitum prior to the experiments. All animal procedures were conducted in accordance with the guidelines of the Institutional Animal Care and Use committee of Seoul National University.

Behavioral testing

Food deprivation condition

Two different food deprivation conditions were conducted, 1-h food restriction group and 1.5-g food restriction group. The 1-h food restriction group was allowed to consume food for 1 h per day, and the 1.5-g food restriction group was allowed 1.5 g of food pellets per day per mouse (1.5 g was given for a single cage, and 6.0 g was given for a group cage). The amount of 1.5 g was based on the nutritional needs of an 8-week-old mouse. Each group was subdivided into two group, single and group caging. Food was provided immediately after the last DNMT trial.

DNMT task

Mice were handled for 4 consecutive days, habituated for 2 days, and trained for 14 days. They were food deprived throughout the experiment. For the DNMT, food reward was placed at the end of each arm. Mice were placed in the starting arm of T-maze to perform a trial. Four trials were performed each day for 14 days of training. Every trial was composed of forced run and free run. At the beginning of the trial, rewards were placed the end of each arm and only one door was open. For the forced run, mice were placed in the starting arm and trained to enter the open arm. Then mice were placed back to the start box and the free run was performed 20 sec after the forced run. Both arms were open for the free run. Each trial was performed 15 min apart. Mice learned and formed working memory of new spatial information as the reward location randomly alternated between the 2 arms on every trial. Behavioral flexibility was required for choosing a correct choice [5, 6]. Individual mouse body weight was recorded before training trials, and the number of correct choices was also recorded.

RESULTS

Food restriction for 1 h

Food restriction is a critical variable for successful DNMT task performance because it increases motivation to run the task. Social isolation (single caging/group caging) and food restriction (1-h food restriction or 1.5 g food per day) are two important factors affecting the motivation of mice to perform the DNMT task. Thus, two measures of food deprivation were conducted to maximize motivation. Mice were divided into four groups: single caging with 1-h food restriction (n=4), group caging with 1-h food restriction (n=4), Single caging with 1.5-g food restriction (n=4), Group caging with 1.5-g food restriction (n=33). The goal of both measures was to maintain body weight at approximately 85% of the initial weight.

We determined that only allowing mice to eat for 1 h per day was excessively harsh, especially for mice housed singly. In single cages, two mice died due to starvation on the third day of handling, and the other two mice were near death. The average body weight of single-caged mice was reduced to 75.5±3.7% of their initial average body weight after 3 days of food restriction. None of mice in the group cages died, but their final body weights were reduced nearly 40%. The final average body weight of group-caged mice was reduced to 62.2±0.7% of their initial average body weight. Moreover, the body weight curve of the group caging group continued to decline (Fig. 1B), but they did achieve a stable plateau in behavioral performance throughout the task. All the mice made correct choices during the last 7 days of training (Fig. 2C).

Food restricted to 1.5 g

None of mice died from starvation in the 1.5-g food restriction condition. The final body weight of group caged mice was reduced to 76.0±0.6% of the initial value, and the singly caged group was reduced down to 69.1±0.8%. Both groups maintained their final lower body weights. In the single caging group, body weight reduced abruptly during habituation and handling, and their final body weight was reduced to nearly 70% of their initial body weight (Fig. 1A). Similar to the 1-h food restriction conditioned group, the 1.5-g group reached a stable plateau in behavioral performance (Fig. 2B).

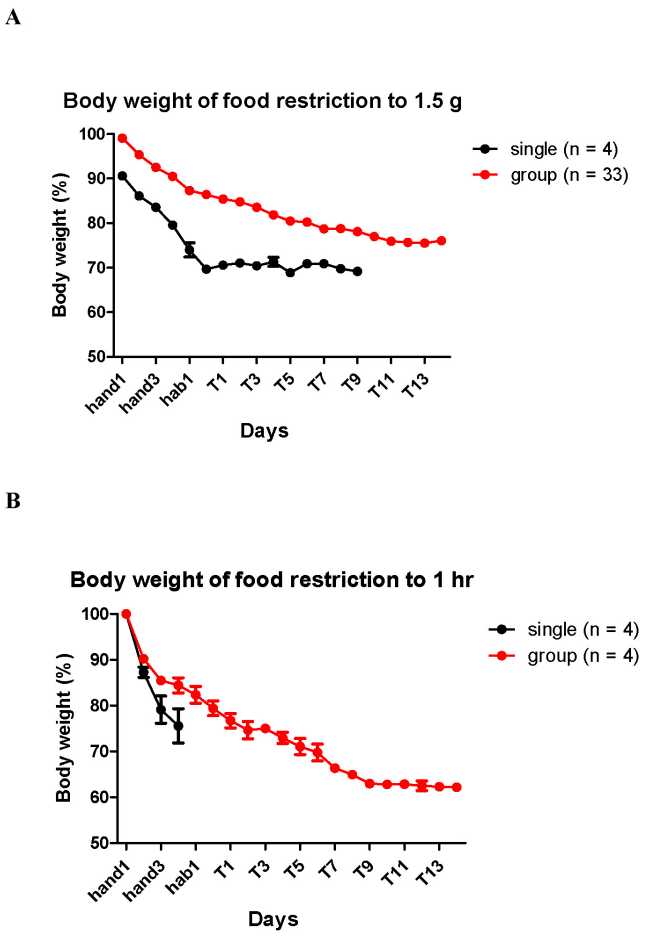

Fig. 1. (A) Average body weight (%) of 1.5-g food restriction-conditioned mice from handling (4 days) to habituation (2 days) to training (14 days). (B) Average body weight (%) of 1-h food restriction-conditioned mice from handling (4 days) to habituation (2 days) to training (14 days).

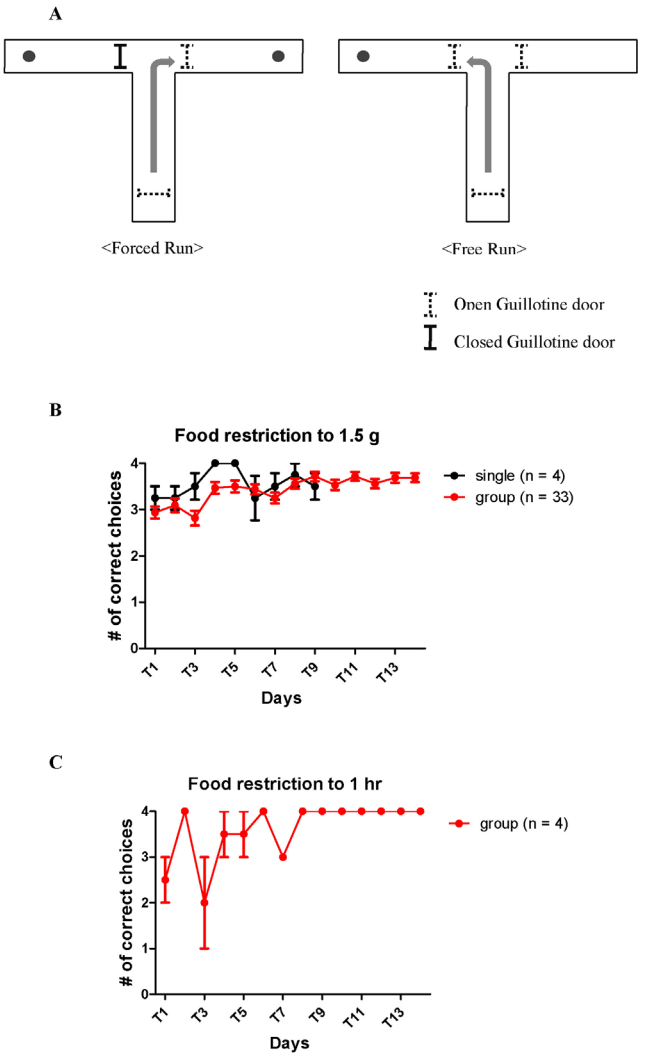

Fig. 2. (A) DNMT task schematic. The reward is placed at the end of each arm. For the forced run, mice are placed in the starting arm of the T-maze and forced to enter open arm. After mice entered the open arm and received the reward, mice were placed back in the starting arm to perform the free run. Entering the arm not visited on the forced run was considered as a correct choice. (B) Average number of correct choices (mean±s.e.m) in the DNMT task following 1.5 g-food restriction for single (n=4) and group caging (n=33). (C) Average number of correct choices (mean±s.e.m) in the DNMT task following 1-h food restriction for single (n=4) and group caging (n=4).

DISCUSSION

Single vs. group caging (relationship between social isolation and food deprivation)

Social isolation was conducted to exclude the possibility that dominant mice might monopolize the food supply. Lower final body weight was observed in the single caging groups for both conditions. This could be due to several reasons. Previous studies on the influence of isolation on behavioral characteristics showed that socially isolating mice induces depression, which can lead to increased food intake [7]. Exposure to stressful experiences during early developmental stage can alter cognition, motivation, and emotion of behavioral responses. [8, 9]. Habituation to novel stimuli is impaired in subjects exposed to social isolation, who show increased excitability response to stressful events. Social deprivation increases the possibility of altered neuronal function and could facilitate the development of neuropsychiatric disorders in adulthood [10, 11]. According to previous studies, social interaction is necessary for appropriate behavioral development [12], which supports the hypothesis that group caging is more suitable for mice subjected to the DNMT task.

Comparing food deprivation conditions

Even though both types of restriction led to a stable plateau in

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behavioral performance on the DNMT task, the use of 1-h food restriction should be considered carefully. Compared to the 1.5-g food restriction group, which maintained 75% of their initial body weight, the 1-h food restriction group was reduced to near 60% of their initial body weight regardless of single or group caging conditions (Fig. 1). Although 1-h food restriction succeeded in maintaining high motivation, it failed to keep the mice healthy.

Food deprivation is essential to increase and maintain motivation for mice to perform the DNMT task, but our findings suggest that severe food deprivation can lead to depression and eventually death. We found that the 1-h food restriction condition turned out to be too harsh for mice to maintain healthy condition and that the 1.5-g food restriction condition was more suitable for the DNMT task.

Successful completion of the DNMT task requires mice to explore their environment and obtain food, and motivation is known to play a critical role in task completion. The relationship between motivation and fear of the maze is considered important for running the DNMT task. Handling and habituation are useful for overcoming excessive fear and increasing motivation [13, 14]. The influence of food deprivation on task performance is less studied. Few investigations have assessed the impact of food deprivation on motivation. Our data suggest that giving 1.5 g of food per 8-week-old mouse in group caging conditions is better for maintaining final body weight to maintain high motivation on the DNMT task. Future studies are needed to identify conditions for specific behavior tasks that require reward seeking for task performance.

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