The Effect of Food Restriction on Learning and Memory of Male Wistar Rats: A Behavioral Analysis

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Article info:
Received: 17 October 2009
First Revision: 25 October 2009
Accepted: 15 November 2009

A B S T R A C T

Introduction: Social inequality may have a significant negative effect on health. There are some evidences that social inequality and stressful conditions could lead to development and progression of various disorders. On the other hand, the results of some research studies have shown that reducing the consumed calorie could prolong the lifetime. In addition, limiting the consumed calorie could produce beneficial changes in the level of some hormones including blood insulin and may reduce body temperature. Meanwhile, food restriction could reduce genetic damage and may have protective effect against external toxins. Therefore, the aim of the present study was to evaluate the effect of food restriction on learning and memory of male rats using passive avoidance and Y-maze tests.

Methods: For this purpose, male Wistar rats (n = 48) were divided into control, 3 experimental, and two negative and positive control groups. Control group received normal rat regimen for 6 weeks. The group with full restriction and non-isolated received 1/3 of the food regimen. The group with full restriction and isolation received 1/3 of the food regimen. The experimental group with two-weeks food restriction and non-isolated received 1/3 of the food regimen only for two weeks. Streptozotocin-diabetic rats with blood glucose higher than 250 mg/dl was considered as negative and positive control received vitamin E (10 mg/kg/day; i.p.) as an antioxidant. For evaluation of learning and memory, initial and step-through latencies and alternation behavior were analyzed using passive avoidance and Y-maze tests.

Results: Regarding initial latency, there was a reduction in diabetic, vitamin-E treated, and group with 2-weeks food restriction and there was an increase in groups with full restriction and isolated and with full restriction as compared to control. Meanwhile, there were no significant differences among the groups, indicating that there were no changes in behavior acquisition. With respect to step-through latency which indicates the ability for consolidation and recall of information, vitamin-E treated group and group with full restriction showed a slight non-significant increase as compared to control group. Diabetic group showed a significant reduction ($p<0.01$) in comparison with control group. Meanwhile, in groups with full restriction and isolated and with 2-weeks restriction showed a significant reduction in relation to control group ($p<0.05$ and $p<0.01$). In addition, these groups showed a significant higher index as compared to diabetic group ($p<0.05$). The results of Y-maze which indicated spatial memory capability of the animal showed that alternation was significantly lower in diabetic group as compared to control ($p<0.01$) and there was no significant differences for other groups as compared to control. On the other hand, vitamin E caused a slight increase in this regard.

Discussion: The results of this study showed that food restriction irrespective of intervention kind did not produce a significant change regarding behavior acquisition and full food restriction (non-isolated) also did not cause a significant change regarding animal ability for consolidation and recall of information in relation to control group. Meanwhile, 2-weeks restriction and full restriction with isolation caused a significant reduction in this respect. In addition, food restriction did not have an effect on spatial memory.

Key Words:
Food Restriction,
Learning,
Memory,
Rat

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1. Introduction

Social inequality may have a significant negative effect on health. There are some evidences that social inequality and stressful conditions could lead to development and progression of various disorders (1). On the other hand, dietary restriction (DR) a condition of reduced calorie intake with nutritional maintenance can extend life span in many organisms commonly used in biomedical research including mice and rats(2) and this also appears to be the case in humans (3). Conversely, overeating is a risk factor for cardiovascular diseases, many types of cancers, type-2 diabetes and stroke. Several such DR feeding regimens can extend lifespan, with the two most commonly used protocols being intermittent (every other day) feeding and paired feeding that employs feed pellets containing 30–40% less calories than pellets in control diet (4). In addition to slowing the aging process, DR may increase resistance of cells to acute metabolic and oxidative insults. As evidence, rats maintained on DR showed reduced susceptibility to myocardial infarction (5), and DR in adult rats results in reduced hippocampal and striatal damage and improved behavioral outcome following excitotoxic and metabolic insults (6).

The impact of diet on brain function and susceptibility to neuropsychiatric and neurodegenerative disorders is increasingly appreciated. It has also been proposed that prolonged low calorie intake may result in neuroprotection with respect to both chronic and acute brain pathologies (7). Recent experimental findings suggest profound neuroprotective effects of DR in animal models relevant to the pathogenesis of neurodegenerative disorders like Huntington's, Parkinson's, Stroke and Alzheimer's (8). It has also been reported that rats maintained under dietary restriction from second to the eighth month of age are fully protected towards degeneration of GABAergic neurons in the hippocampus and olfactory-entorhinal cortex caused by the systemic administration of the convulsant toxin, kainic acid (7). Available data suggests that much of the studies carried out involve long-term dietary restriction regimen in relation to aging. Recent studies involving short-term dietary restriction have documented the similar beneficial effects against vulnerability to excitotoxic and metabolic insults (9). A genomic profiling study of short and long-term caloric restriction also showed that short-term calorie restriction (4 weeks) reproduced nearly 70% of the effects of long-term calorie restriction on genes that changed expression with age (10).

Therefore, the aim of the present study was to evaluate the effect of food restriction on learning and memory of male rats using passive avoidance and Y-maze tests.

2. Methods

2.1. Animals

Male Wistar rats (n = 48) were divided into control, 3 experimental, and two negative and positive control groups. Control group received normal rat regimen for 6 weeks. The group with full restriction and non-isolated received 1/3 of the food regimen. The group with full restriction and isolation received 1/3 of the food regimen. The experimental group with two-weeks food restriction and non-isolated received 1/3 of the food regimen only for two weeks. Streptozotocin-diabetic rats with blood glucose higher than 250 mg/dl was considered as negative and positive control received vitamin E (10 mg/kg/day; i.p.) as an antioxidant. For evaluation of learning and memory, initial and step-through latencies and alternation behavior were analyzed using passive avoidance and Y-maze tests as follows:

2.2. Y-maze Task

Working short-term memory performance was assessed by recording spontaneous alternation behavior in a single session in Y-maze. The maze was made of black-painted Plexiglas. Each arm was 40 cm long, 30 cm high, and 15 cm wide. The arm converged in an equilateral triangular central area that was 15 cm at its longest axis. The procedure was basically the same as that described previously as follows: each rat, naive to the maze, was placed at the end of one arm and allowed to move freely through the maze during an 8-min session. The series of arm entries was recorded visually. Arm entry was considered to be completed when the base of the animal's tail had been completely placed in the arm. Alternation was defined as successive entries into the three arms on overlapping triplet sets. The alternation percentage was calculated as the ratio of actual to possible alternations (defined as the total number of arm entries minus two).

2.3. Single Trial Passive Avoidance Test

This test was always conducted 2-3 days after Y-maze task. The apparatus (BPT Co., Tehran) consisted of an illuminated chamber connected to dark chamber by a guillotine door. Electric shocks were delivered to the grid floor by an isolated stimulator. On the first and second days of testing, each rat was placed on the apparatus and left for 5 min to habituate to the apparatus. On the third day, an acquisition trial was performed. Rats were individually placed in the illuminated chamber. After a habituation period (2 min), the guillotine door was opened and after the rat entering the dark chamber, the door was closed and an inescapable scrambled electric shock (1 mA, 2 s once) was delivered. In this trial, the initial latency (IL) of entrance into the dark chamber was recorded and rats with ILs greater than 60 s were excluded form the study. Twenty-four hours later, each rat was placed in the illuminated chamber for retention trial. The interval between the placement in the illuminated chamber and the entry into the dark chamber was measured as step-through latency (STL up to a maximum of 600 s as cut-off).

2.4. Statistical Analysis

All values were given as mean ± S.E.M. Statistical analysis was carried out using repeated measure ANOVA and non-parametric Kruskall-Wallis and Mann-Whithney tests. Statistical P value less than 0.05 was considered significant.

3. Results

Figure 1 shows body weight changes in different groups. In this respect, except for 2-week restricted group, other restricted groups showed a significant reduction in body weight.

Regarding initial latency, there was a reduction in diabetic, vitamin-E treated, and group with 2-weeks food restriction and there was an increase in groups with full restriction and isolated and with full restriction as compared to control. Meanwhile, there were no significant differences among the groups, indicating that there were no changes in behavior acquisition (Fig. 2). With respect to step-through latency which indicates the ability for consolidation and recall of information, vitamin-E treated group and group with full restriction showed a slight non-significant increase as

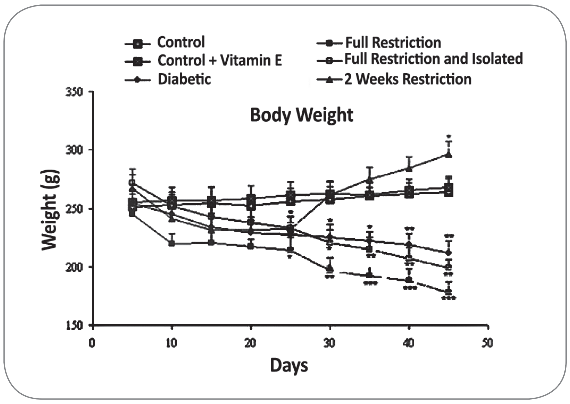

Figure 1. Body weight changes in different groups
*P<0.05, ** P<0.01, *** P<0.005

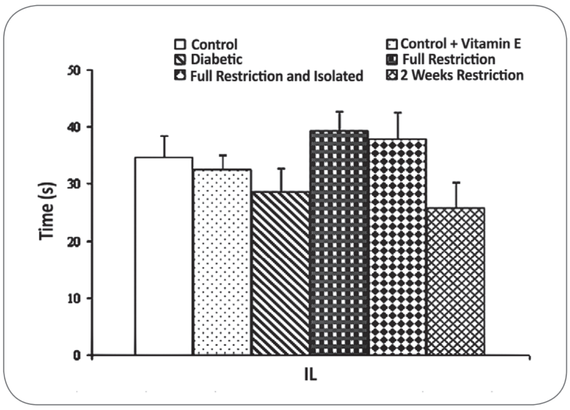

Figure 2. Initial latency in passive avoidance test in different groups

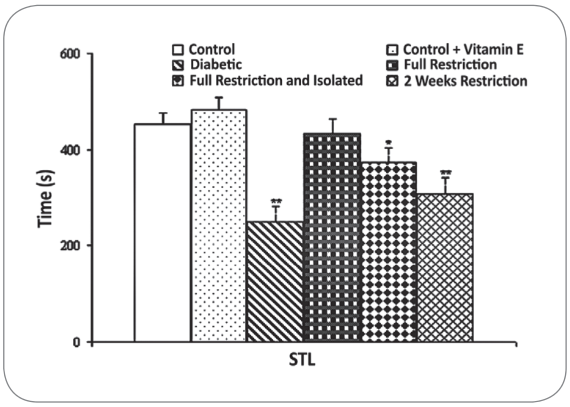

Figure 3. Step-through latency in passive avoidance in different groups
*P<0.05, ** P<0.01 (as compared to control)

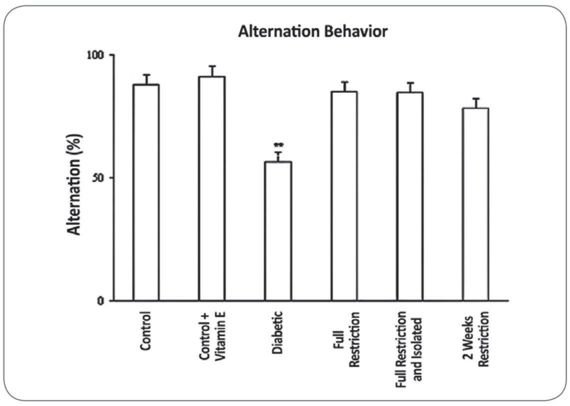

Figure 4. Spatial memory in Y-maze test in different groups
*P<0.01 (as compared to control)

compared to control group. Diabetic group showed a significant reduction ($p<0.01$) in comparison

with control group. Meanwhile, in groups with full restriction and isolated and with 2-weeks restriction showed a significant reduction in relation to control group ($p<0.05$ and $p<0.01$). In addition, these groups showed a significant higher index as compared to diabetic group ($p<0.05$) (Fig. 3). The results of Y-maze which indicated spatial memory capability of the animal showed that alternation was significantly lower in diabetic group as compared to control ($p<0.01$) and there was no significant differences for other groups as compared to control. On the other hand, vitamin E caused a slight increase in this regard (Fig. 4).

4. Conclusion

Dietary restriction (DR) a condition of reduced calorie intake with nutritional maintenance can extend life span in many organisms commonly used in biomedical research including mice and rats (2) and this also appears to be the case in humans (3). Conversely, overeating is a risk factor for cardiovascular diseases, many types of cancers, type-2 diabetes and stroke. Several

such DR feeding regimens can extend lifespan, with the two most commonly used protocols being intermittent (every other day) feeding and paired feeding that employs feed pellets containing 30–40% less calories than pellets in control diet (4). In addition to slowing the aging process, DR may increase resistance of cells to acute metabolic and oxidative insults. As evidence, rats maintained on DR showed reduced susceptibility to myocardial infarction (5) and DR in adult rats results in reduced hippocampal and striatal damage and improved behavioral outcome following excitotoxic and metabolic insults (6).

The results of this study showed that food restriction irrespective of intervention kind did not produce a significant change regarding behavior acquisition and full food restriction (non-isolated) also did not cause a significant change regarding animal ability for consolidation and recall of information in relation to control group. Meanwhile, 2-weeks restriction and full restriction with isolation caused a significant reduction in this respect. In addition, food restriction did not have an effect on spatial memory.

Acknowledgement

This work was supported by a grant from Research Council of Shahed University (Tehran).

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