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Capsaicin Increases Swimming Endurance Capacity in High-Fat-Fed Mice

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Abstract

Increase in fat mobilization by capsaicin (CAP) was investigated in high-fat-fed mice using an adjustable-current water pool. Male ICR 7-wk-old mice were fed a high fat diet [50% total energy content in the diet (E%) fat, 20 E% protein, 30E% carbohydrate] for 2 wk and one group (HCAP) was orally administered CAP at 2 h before swimming. After being accustomed to swimming, the mice were subjected to forced swimming every 2 d in the current water pool and the total swimming period until exhaustion was measured. The total swimming period was used as the index of swimming capacity. Swimming time to exhaustion of treated mice was significantly longer than that of the high-fat-fed control group (100.2±10.6 vs. 58.0±8.5 min, P<0.01) after 2 wk of training. The concentration of serum-free fatty acids gradually increased up to 2 h in CAP-administered mice. The perirenal adipose tissue weight of CAP-administered mice (HCAP) before swimming was lower than that of the high-fat-fed mice administered placebo solution (HP) which had not ingested CAP during the 2 wk. These results suggest that the increase of swimming capacity of CAP-administered high-fat-fed mice was due to an increase of fat mobilization that was induced by CAP.

Key words: capsaicin, swimming capacity, high-fat diet

INTRODUCTION

It is well accepted that exercise endurance is directly related to the amount of carbohydrate stored in muscle and that a low carbohydrate diet reduces glycogen storage and exercise performance. In the human exercise-nutrition studies, muscle glycogen storage was manipulated by both diet and exercise in order to determine the relationship between glycogen content of muscle and exercise endurance (1). It is generally accepted that exercise endurance is directly related to the glycogen concentration in muscle prior to beginning work and that glycogen content is directly related to the amount of carbohydrate consumed in the diet (2). In the study by Christensen & Hansen (3), when the trained subjects consumed either a fat-rich diet or a carbohydrate-rich diet for 3~5 d, exercise to exhaustion at 65~70% VO_2max revealed an average endurance time on the carbohydrate diet of 210 min, which was longer than that on the fat diet (90 min). Also, when intermittent exercise at 70% VO_2max was performed in the trained man, endurance performance time to exhaustion was significantly impaired after consuming a fat-rich diet for 4 d (62 min) compared with a carbohydrate-rich diet (106 min) (4). Thus, it is evident that fat-loading reduced endurance performance.

The interaction between training and diet was studied by Helge et al. (5,6) and when comparing the trained subjects exercising at the same relative workload, time to exhaustion after both 2- and 7-wk on a high-fat diet was found to be significantly shorter than that with a high-carbohydrate diet. But, it is not clear why prolonged elevated dietary fat intake reduces improvement in endurance performance in human subjects.

On the other hand, Kawada et al. have shown that capsaicin (CAP) supplement with a high fat diet lowers the weight of perirenal adipose tissue and serum triglyceride concentration in rats due to an increase in energy metabolism (7). An increased utilization of mobilized body fat by CAP had demonstrated by the R.Q. decreasing (about 0.75) at 2~3 h after the administration of CAP in high-fat-fed rats (8). Recently, Kim et al. showed that swimming capacity was increased by oral administration of CAP in mice, observed only when CAP was administered 2 h before swimming and also the oral administration of CAP produced a marked increase in serum adrenaline concentration of 2 h after ingestion (9). These results suggest that the effect of CAP is due to the enhancement of fatty acid metabolism via adrenaline secretion.

These findings led us to speculate that ingestion of CAP in high-fat-fed mice may promote a sparing of muscle glycogen and increase swimming endurance capacity by use of elevated plasma fatty acids due to the enhancement of fat metabolism and also decrease adipose tissue weight.

In the present study, we investigated the effect of CAP on swimming capacity and the amount of adipose tissue of high-fat-fed mice.

MATERIALS AND METHODS

Animals and diets

Male ICR mice (International Laboratory Animals Center,

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Korea) weighing about 28 g (7 wk old) were used in the present study. Mice were housed in standard cages (33×23×12 cm, 3 mice/cage) under controlled conditions of temperature (22~24°C), humidity (50%), and lighting. The room was lighted from 0700 to 1900 h. In the preliminary periods, they were given access to water and a commercial diet (Samyang Co., Seoul, Korea) containing the following (g/kg diet): moisture, 80; protein, 230; fat, 35; fiber, 50; carbohydrate, 600, and water *ad libitum*. The composition of the high fat experimental diet is presented in Table 1.

The mice were administered CAP (10 mg/kg body weight) or a placebo solution containing 3% ethanol and 10% Tween 80 in saline *via* a stomach tube at 2 h before swimming (9). CAP was purchased from Fluka AG (Buchs, Switzerland; Lot No. 258397 186) and suspended in placebo solution.

Current swimming pool

An adjustable-current water pool was used to determine swimming capacity. The details were described previously (10): the acrylic plastic pool (90×45×45 cm) filled 35 cm deep with water was maintained at 34°C. The current in the pool was generated by circulating water with a pump, and the strength of the current was adjusted to 8 L/min by controlling the voltage supplied to pump and was monitored with a water flowmeter (type F45500, Blue white Co, Westminster, CA, USA). Fig. 1 shows the design of the swimming system used.

Evaluation of the swimming endurance capacity of mice

To avoid circadian variation in physical activity, experiments were carried out from 1100 to 1700, a period in which minimal variation of swimming capacity was confirmed (10). Mice were assessed as fatigued when they failed to rise to the surface of the water to breathe within a 7-s period. Periods of longer than 7-s frequently resulted in drowning while less than 5-s reduced the reproducibility of the test (10). The total swimming time until exhaustion was used as the index of swimming capacity.

Table 1. Composition of the high-fat diet (g/100 g diet)

Nutrient	High-fat diet
Casein	26.2
Corn starch	27.6
Sucrose	10
Lard	22.4
Soybean oil	4
Mineral mixture[1)]	3.5
Vitamine mixture[2)]	1
Cellulose	5
L-Methionine	0.3
Total energy (kcal)	475
Percent of calories (per total energy)	
Fat	50
Carbohydrate	30
Protein	20

[1)]Composition of mineral mixture was as follows (g/kg): $CaPO_4 \cdot 2H_2O$, 145.6; KH_2PO_4, 257.2; NaH_2PO_4, 93.5; NaCl, 46.6; calcium lactate, 350.9; ferric citrate, 31.8; $MgSO_4$, 71.7; $ZnCO_3$, 1.1; $MnSO_4 \cdot 4H_2O$, 1.2; $CuSO_4 \cdot 5H_2O$, 0.3; KI, 0.1.
[2)]Vitamin mixture: ICN Vit. mixture (No 904654,1999)

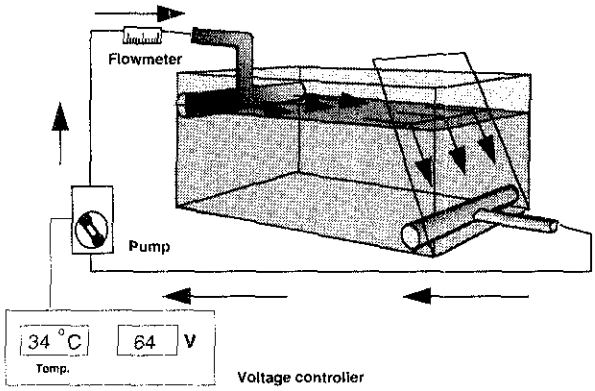

Fig. 1. Side-view illustration of adjustable-current pool (10).

Effect of CAP on swimming capacity of the high-fat-fed mice

The mice were fed a commercial diet during the preliminary period. They were forced to swim for 30 min at a flow rate 6 L/min to be accustomed to swimming. On the last day of the preliminary period, the mice were subjected to swimming until exhaustion at a current strength of 8 L/min, and then the swimming capacity was measured. Mice were then separated into two groups (HP and HCAP group) with mean swimming time before the experiment. During the next 2 wk, both groups were fed high-fat diet with free access to water and the same energy intake for the mice of two groups, but only HCAP group was administered CAP at 2 h before swimming. The swimming capacity was measured in the same way during forced swimming every 2 d for 2 wk. Food intake and body weights were monitored daily. On the last day of the experimental period, each mouse was killed by decapitation and was removed and weighed, quickly.

Serum fatty acid analysis

Thirty μl of mouse blood was taken from the tail at 1 h interval for 3 h after administration of CAP (or vehicle) in mice of each group. Serum free fatty acid was measured by an acyl CoA-synthetase and acyl CoA oxidase enzyme method with a commercial kit (NEFA test Eiken Chemical Industries, Japan).

Statistics

Data were expressed as mean±SEM. Comparisons between means of the high-fat-fed group administered CAP (HCAP) and placebo solution (HP) before swimming determined by the unpaired *t*-test. Statistics were calculated with the INSTAT software package (Macintosh version 2.00, GraphPad Software Inc., San Diego, CA) and a level of $p<0.05$ as the criterion for statistical significance.

RESULTS AND DISCUSSION

Body weight

Body weight changes are shown in Fig. 2. There was no difference between the groups administered CAP (HCAP)

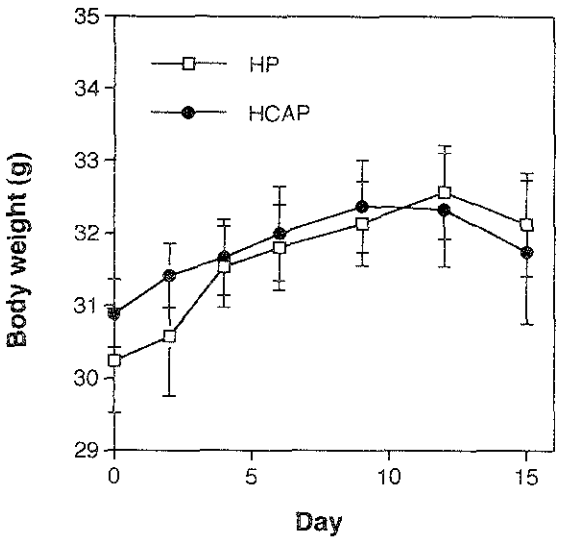

Fig. 2. The change of body weight of HP or HCAP group for 2 wk. HP: high-fat-fed mice administered placebo solution, HCAP: high-fat-fed mice administered CAP solution (10 mg/kg body wt) 2 h before swimming.

and placebo solution (HP) at 2 h before swimming during the 2 wk training period.

Effect of CAP administration on swimming endurance capacity

CAP (10 mg/kg, HCAP group) or placebo solution (HP group) was orally administered to high-fat-fed mice 2 h before the start of swimming and the time to fatigue at a flow rate of 8 L/min was measured. As shown in Fig. 3, the endurance of mice administered CAP (HCAP) had a significantly greater swimming capacity than did HP group at 12 d after the start

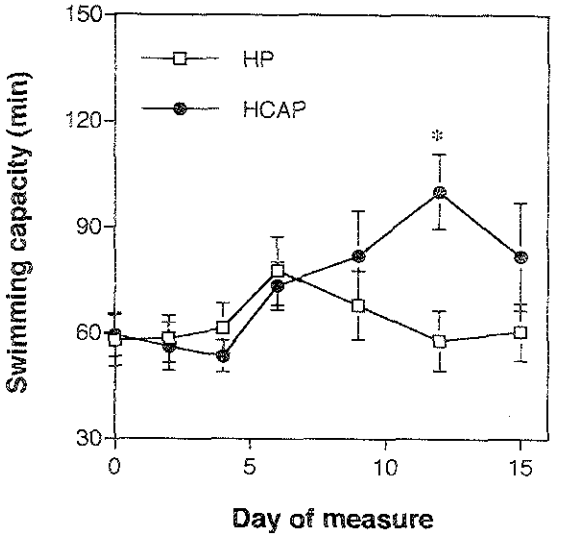

Fig. 3. The change in swimming capacity of HP or HCAP mice for 2 wk. Mice swam to exhaustion, and the swim capacity was measured in a current strength 8 L/min every 2 d for 2 wk. Mice of HCAP group are administered CAP (10 mg/kg) at 2 h before swimming. Value are means ± SEM for 11 ~ 15 mice. *Significantly different from the corresponding value for HP group at the same time, by unpaired *t*-test ($p<0.01$).

of the training period. The swimming capacity on 12 d was 100.19 ± 10.61 min in the HCAP group and 57.97 ± 8.52 min in the HP group ($p<0.01$). The swimming time of the high-fat-fed mice administered placebo solution instead of CAP was neither increased nor maintained for the 2 wk- training period and this result suggests that a lower storage glycogen by feeding high-fat diet decreases swimming capacity. But swimming capacity of high-fat-fed mice administered CAP is increased by enhanced fat mobilization and its utilization via an action of CAP. It has often been demonstrated that fatigue during prolonged strenuous exercise is correlated with depleted muscle glycogen stores and has also been shown that the more glycogen stored in the muscle before exercise, the longer one can endure work (11,12). Several studies have shown that a high-fat diet decreased endurance exercise compared with carbohydrate rich diet, apparently through lowering of muscle glycogen concentration (5,6,13,14) and these results are consistent with that of our study.

We reported that the swimming capacity was increased by a single oral dose of CAP in the commercial diet fed mice using an adjustable-current swimming pool (9). In that experiment, the mean swimming time was significantly prolonged by CAP administered 2 h before swimming and we showed that this effect of CAP (10 mg/kg body wt) is due to CAP-induced adrenaline secretion that results in sparing muscle glycogen due to enhancement of fat metabolism (9). And also, Kawada et al. (8) have shown that the R.Q. decreased after injection of CAP in high-fat-fed rats together with the serum free fatty acid level gradually increased to 3 h after CAP-injection. The decrease in R.Q. indicated the use of fatty acid as a fuel by CAP between 90 to 150 min. From all these results, we suggest that in our study, the increase of swimming capacity in high-fat-fed mice administered CAP may increase the utilization and/or uptake of serum FFA by an enhancement of CAP-induced fat metabolism.

Effect of CAP administration on body fat content

As shown in Table 2, there was no difference between the groups (HP and HCAP) in the wet mass of gastrocnemius muscle, quadriceps muscle, and liver. However, the wet size of the epididymal fat and the perirenal fat pads were smaller relative to body weight, in high-fat-fed mice administered CAP, especially the perirenal adipose tissue in HCAP group which was significantly reduced ($p<0.05$, Table 2) and also this result corresponds to Kawada's study (7). It indicates that absorbed CAP induces the quick mobilization of body fat for fuel use rather than storing it in adipose tissues in high-fat fed mice.

Effect of CAP on serum free fatty acids

To confirm that the enhancement of CAP-induced swimming capacity result from an increase of fatty acid metabolism, the concentrations of serum free fatty acids were measured at 1 h interval after oral-administration of CAP (10 mg/wt body wt) in HCAP group. Serum free fatty acid concentrations gradually increased by CAP administration, reaching maximum 2 h before slowly decreasing as shown in Fig. 4.

Table 2. Relative organ weights of HP or HCAP mice for 2 wk (g/100 g body wt)

Organ	Group	
	HP	HCAP
Liver	4.69±0.16	4.70±0.14
M. Gastrocnemius	0.94±0.01	0.94±0.01
M. Quadriceps	0.90±0.02	0.98±0.02
Perirenal fat pad	1.01±0.06	0.70±0.09*
Epididymal fat pad	2.70±0.17	2.12±0.29

Values are mean±SEM for 9~19 mice.
*Significantly different from the corresponding value for the HP group, by unpaired *t*-test ($p<0.05$).
HP: high-fat-fed mice administered placebo solution 2 h before swimming
HCAP: high-fat-fed mice administered CAP (10 mg/kg) 2 h before swimming

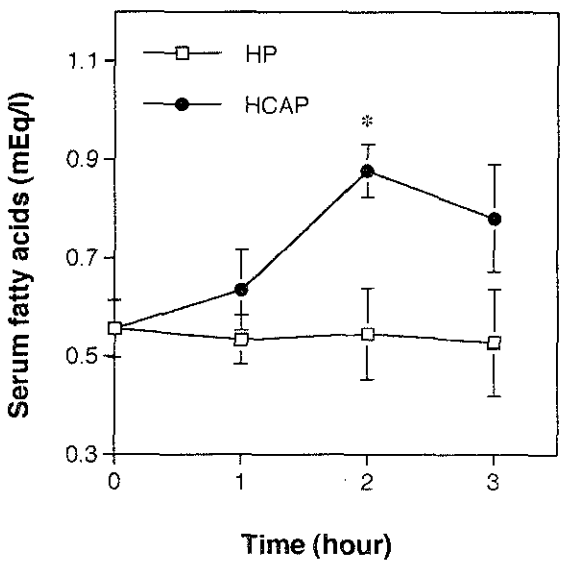

Fig. 4. Course of serum free fatty acid concentration after CAP administration in HCAP mice. CAP (10 mg/kg) was administered to HCAP mice under conscious. Blood was taken form the tail at 1 h intervals and the data analyzed by unpaired t-test. Values are mean±SEM for 10~15 mice. *Significantly different from the corresponding value for HP group at the same time, by unpaired *t*-test ($p<0.05$).

From this result, we have demonstrated that the increase of swimming capacity in the HCAP group is caused by an increase in fatty acid utilization due to an enhancement of CAP-induced fat metabolism, in spite of lowering of muscle glycogen stores generally showed in high-fat-fed animals. In addition, the liver and muscle glycogen stores in high-fat-fed mice were lower than that of high-carbohydrate fed mice in our preliminary experiment (data not shown). The increase of swimming endurance capacity by CAP has been demonstrated by Kim et al. (9). They have shown that the residual glycogen concentration of the muscle after swimming was significantly higher in the CAP-administered mice than in control mice, suggesting that use of the serum free fatty acids spares muscle glycogen consumption.

From our study, it was suggested that the enhancement of swimming capacity of CAP-administered high-fat fed mice results from the increase of CAP-induced fat mobilization and its use as energy substrate during exercise.

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