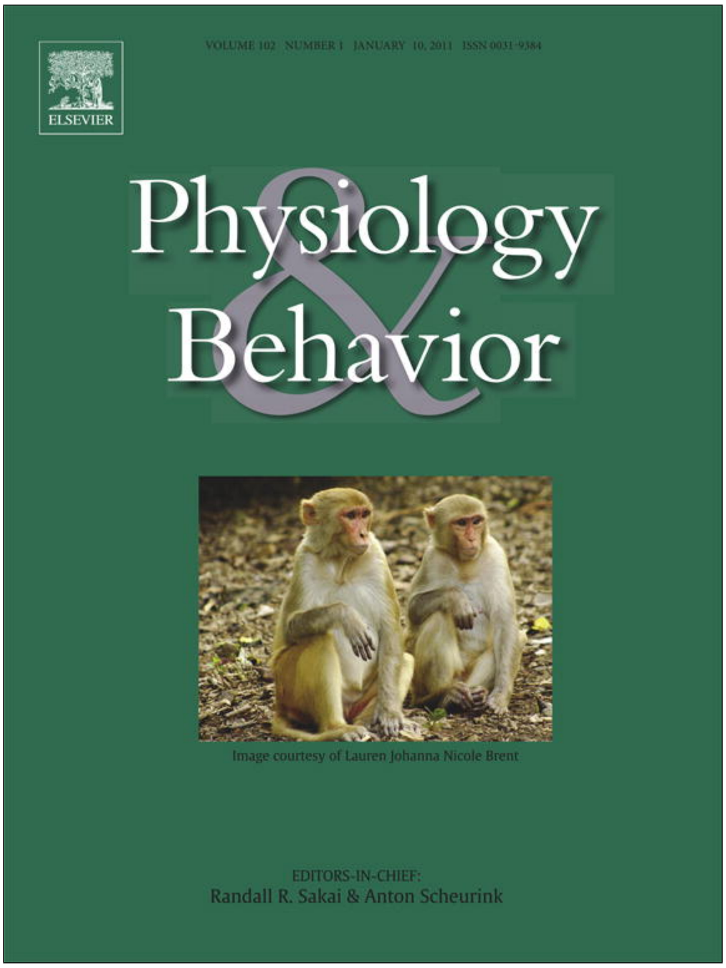
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A sex difference in the response to fasting

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ABSTRACT

We determined whether women and men would alter their pattern of food intake after they had deprived themselves of food. We found that women consumed 12% *less* food after fasting and that men ate 28% *more* food after fasting. Serving more food on the test day did not increase food intake of women. Women, who ate at a nearly constant rate (linear eaters), consumed less food than those eating at an initially high speed which decreased over the course of the meal (decelerated eaters). Women decreased their food intake after fasting as their eating pattern became more linear. After fasting, men increased their food intake, and the rate at which they ate became more decelerated. Food intake of both women and men was normalized after fasting by providing feedback that encouraged them to eat according to the pattern they showed in the non-fasted condition. The results support the hypothesis that linear eating, and the dieting that elicits linear eating, are risk factors for the development of the abnormal linear eating pattern that characterizes patients with *anorexia nervosa*. The data also provide additional support for the use of behavioral feedback to normalize the pattern of eating for individuals who have difficulty maintaining their body weight.

1. Introduction

The normal pattern of eating a meal starts with a rapid acceleration of food intake, followed by an eventual deceleration of the rate of food intake before termination of the meal [1,2]. Those individuals who maintain this normal eating pattern are likely to maintain a normal body weight [3–5]. Abnormal eaters consume food at a nearly constant rate and these eaters have difficulty maintaining a normal body weight [3]. Following the suggestion by Westerterp-Plantenga et al. [6,7], we refer to these two types of eaters as decelerated and linear eaters, respectively [3–5]. When eating rate is experimentally decreased, linear eaters eat less food, and we have therefore hypothesized that they are at risk of developing the disordered eating pattern associated with *anorexia nervosa* [3–5]. In support of this hypothesis, the cumulative food intake pattern of women who were linear eaters, and who were tested at a reduced eating rate, was similar to that of anorexic patients [3]. Moreover, they felt as satiated as anorexics, despite the fact that their food intake was reduced [3]. These changes were not seen in men [8]. Dieting by food restriction, which is more common among women than among men [9] is a risk factor for *anorexia nervosa*, a condition that affects mainly women.

On the hypothesis that linear eaters are at risk of developing anorexic eating behavior when challenged with a brief period of fasting, we predicted that women who were linear eaters would eat less food after fasting, and women who were decelerated eaters would eat the same amount of food as when they were not food deprived. Given the clear difference in the probability of men and women developing eating disorders, we predicted that men and women would respond differently to food restriction. Therefore, we tested the effect of fasting on the pattern of food intake during a meal in both women and men. We also tested the corollary hypothesis that feedback with the normal pattern of eating during a meal would be capable of restoring the normal pattern of food intake in both men and women after fasting.

2. Methods

2.1. Subjects

Twenty-one women participated in the first experiment. Their median (range) age was 17.2 (16.8–19.1) years and their body mass index (BMI, kg/m^2) was 22.2 (21.4–24.1). Thirteen other women (age = 19.6 (18.3–21.2), BMI = 21.2 (19.6–24.2)) and 9 men (age = 17.9 (17.1–19.2), BMI = 21.2 (19.6–24.2)) participated in the second experiment. The differences in the age and BMI between the groups are not statistically significant. The subjects were healthy college students who were non-smokers, free from food allergies, did not have a history of eating disorders and did not use medication known to affect food intake. Athletes and pregnant and lactating women were excluded. Three women who did not meet these criteria, assessed by a questionnaire, did not participate.

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2.2. Apparatus

Mandometer® is a scale (IDEMA 750, IDEMA, Gävle, Sweden) built into a table and connected to a computer that reads the scale every second to the nearest gram. After placing a plate on the scale, the computer tars the weight of the plate, after which time the subjects weigh food on the plate and then eat the food while the plate remains on the scale. As the weight of the plate decreases, the software calculated the rate of food consumption. Data for the curve of cumulative food intake thus generated are then stored by the computer.

Feedback on the normal eating pattern is provided via a 15 in. TFT touch screen, which is part of the system. Subjects see their own rate of eating appearing on the screen and can mimic the normal eating pattern when it is simultaneously displayed of the screen [3–5]. Thus, Mandometer® expands on the capabilities of similar devices [10–12] by making it possible to normalize the rate of eating, a feature of the device that is used clinically [13,14].

2.3. Procedure

2.3.1. Serving fasted women more food

We first determined whether the decrease in food intake sustained by women who have fasted [8] could be reversed by serving more food to them. The 21 women who participated were tested under three conditions. In the control condition, they were tested for their food intake pattern during a meal without being deprived of food, although they were asked not to snack and drink anything but water after breakfast. In the fasting condition, they were asked to refrain from eating dinner the day before testing and also refrain from eating breakfast in the morning of the test meal. In the fasting + more food condition, 25% more food than the women had consumed in the control condition was placed on the plate for the test meal. The women ate as much as they wanted in both the control test and in the fasting test without being able to see the rate at which they were eating. The two fasting conditions were presented in random order.

2.3.2. Providing feedback after fasting to women and men

We attempted to replicate the sex difference in food intake in response to fasting that we had found previously [8] and we then determined whether the change in food intake after fasting in both women and men can be normalized by providing feedback during the meal. The 13 women and 9 men who participated in this study were tested as described above, with the exception that in a fasting + feedback condition, they were asked to mimic the pattern of food intake that they demonstrated during the control meal. We showed this pattern of eating by displaying two lines on the Mandometer® screen and the subjects were informed that their rate of eating, which appeared as a dot on the screen, should be kept between those lines, which were 15% above and below the value of the curve of cumulative food intake generated by each subject in the control test. If the subjects deviated from the proper rate of eating, the following message appeared on the screen: “you are eating too slow” or “you are eating too fast”. Compliance to the feedback procedure was estimated by counting the number of messages appearing on the screen during the meal [4].

2.3.3. Time of testing and preparation of food

In both experiments, subjects were tested individually at 11:30, 12:00 or 12:30 h, with one week between meals. The food (sliced chicken, rice and vegetables; Findus, Bjuv, Sweden; 400 kJ, 4.5 g protein, 18 g fat and 15 g carbohydrate/100 g) was freshly prepared before each meal, was served at a temperature of about 65 °C, and 1.3 kg additional food was available from a serving plate on an adjacent table. It is sufficient to test subjects in only one meal, as the intra-individual variation between tests is quite low with these procedures [4,6,7].

2.3.4. Information to participants

Participants were told that the goal of the study was to examine if women and men eat different amounts of food. All subjects gave written consent to participate and they were informed that they could leave the study at any time without giving a reason. These procedures were approved by the Ethics Committee of the Karolinska Institute.

2.4. Statistical analysis

In a previous experiment, 17 women ate 20% less food after a period of fasting of the same duration as in the present study, and 13 men ate about 30% more food, yielding statistically significant sex differences in food intake [8]. For these reasons, the number of subjects recruited for the present experiment was estimated suitable for testing the relevant hypotheses.

Data are presented as box plots in the figures and as median (range) in the text. The curve of cumulative food intake was calculated by: $y = kx^2 + lx + n$ [4,6,7,11,15]; where y is food intake and x is time. Individuals differ in the rate at which the speed of eating changes over the course of a meal (k-coefficient) and in the initial speed of eating (l-coefficient), but intake at the start of a meal (n) is, obviously 0; hence, $y = kx^2 + lx$. The influence of the k-coefficient and the l-coefficient in the control condition on the response to fasting was analyzed by calculating the change in food intake as percent of the intake in the control condition. In the analysis of the sex difference in the effect of fasting, the k-coefficient, the l-coefficient, food intake and meal duration were outcome variables; in the analysis of the effect of fasting + feedback, food intake was the only outcome variable. Because the k-coefficient is ≤ 0 in most cases it will be referred to as “the rate of deceleration” and the l-coefficient will be referred to as “the initial speed of eating” to facilitate understanding. The effect of fasting on the curve of cumulative food intake in women and men was analyzed separately from the effect of fasting + feedback; for analyzing the latter, the data on food intake in Fig. 3 are re-plotted in Fig. 4. ANOVA was used to compare differences between women and men and testing conditions and t-tests were used for subsequent group comparisons. Multiple regression analysis was used to understand the relationship between the k-coefficient, the l-coefficient and food intake. ANCOVA was used to determine how the k-coefficient and the l-coefficient influenced food intake. STATISTICA (StatSoft Inc, Tulsa, TX) was used for these analyses.

3. Results

3.1. Effect of fasting in women

The rate of deceleration [$F(2,40) = 13.77$, $p < 0.01$], and the initial speed of eating [$F(2,40) = 7.34$, $p < 0.01$] and food intake [$F(2,40) = 5.76$, $p < 0.01$], but not meal duration [$F(2,40) = 3.85$, *ns*], differed significantly in the three testing conditions (Fig. 1). Pair-wise comparisons showed that fasting with or without more available food caused a significant decrease in the rate of deceleration [$t(20) = -4.41$, $p < 0.01$ and $t(20) = -4.58$, $p < 0.01$] and a decrease in the initial speed of eating [$t(20) = 3.36$, $p < 0.01$ and $t(20) = 2.53$, $p < 0.05$] and food intake [$t(20) = 2.63$, $p < 0.05$ and $t(20) = 2.36$, $p < 0.05$]. There was no significant difference in these parameters between the two fasting conditions (t-values not shown).

Thus, fasting both increases the linearity of eating and decreases the initial speed of eating and food intake in women; serving more food had no effect on this outcome.

3.2. Rate of deceleration, initial speed of eating and the change in food intake after fasting in women

The rate of deceleration in the control condition correlated negatively with food intake after fasting [$r = -0.84$, $p < 0.01$] but the

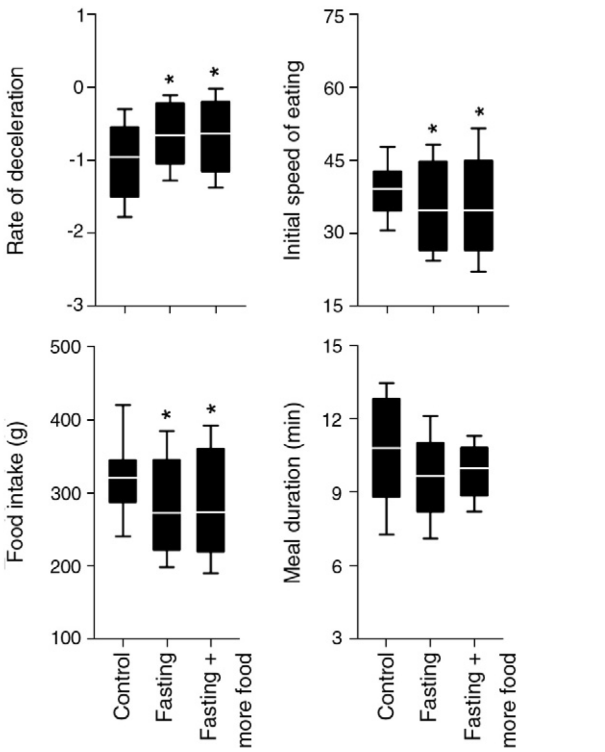

Fig. 1. Rate of deceleration, initial speed of eating, food intake and meal duration before (control) and after fasting without or with more food in 21 women. Values are box plots. *p at least <0.05, t-test after ANOVA.

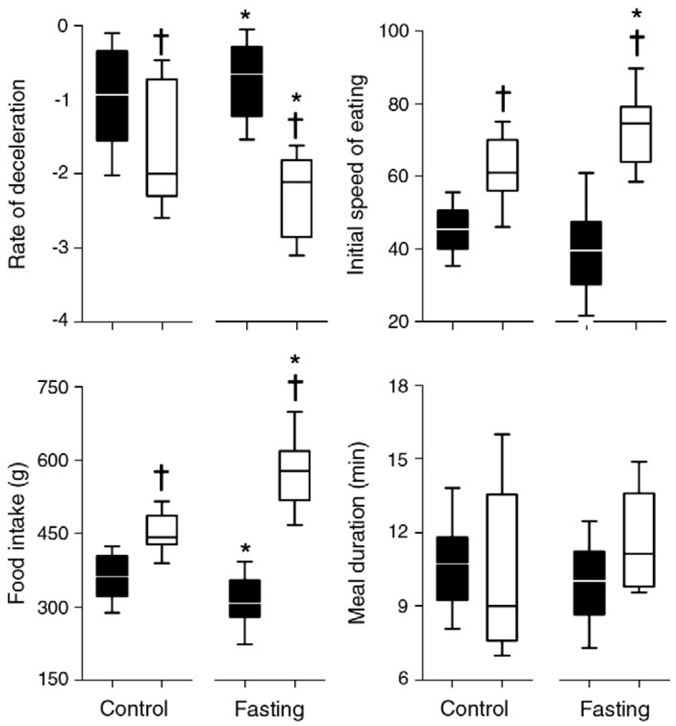

Fig. 3. Rate of deceleration, initial speed of eating, food intake and meal duration before (control) and after fasting in 13 women (black boxes) and 9 men (white boxes). Values are box plots. *p at least <0.05 compared to control; †p at least <0.05 compared to women, t-test after ANOVA.

correlation between the initial speed of eating did not [r = 0.45, *ns*] (Fig. 2). Thus, the more linear the eating in the non-deprived condition, the less food women ate after fasting.

3.3. Sex difference in the response to fasting

The rate of deceleration was significantly affected by sex [$F(1,20) = 18.06$, $p < 0.01$], as well as testing condition [$F(1,20) = 4.60$, $p < 0.05$], and there was a significant interaction between these two factors [$F(1,20) = 17.17$, $p < 0.01$]. The rate of deceleration decreased significantly among women [$t(12) = -2.64$, $p < 0.05$], but increased among men [$t(8) = 2.91$, $p < 0.05$] in response to fasting (Fig. 3).

The initial speed of eating was significantly affected by sex [$F(1,20) = 46.93$, $p < 0.01$], but not testing condition [$F(1,20) = 0.82$, *ns*]. However, there was a significant interaction between these two factors [$F(1,20) = 11.61$, $p < 0.05$]; the initial speed of eating decreased among women, although not significantly [$t(12) = 2.12$, *ns*], and increased significantly among men [$t(8) = 12.11$, $p < 0.01$] in response to fasting (Fig. 3).

Food intake was significantly affected by sex [$F(1,20) = 78.73$, $p < 0.01$], as well as testing condition [$F(1,20) = 7.16$, $p < 0.05$], and there was a significant interaction between these two factors $F(1,20) = 45.67$, $p < 0.01$]. Women ate significantly less food [$t(12) = 3.58$, $p < 0.05$], and men ate more food [$t(8) = -6.89$, $p < 0.01$] after fasting (Fig. 3).

As in the first experiment, the rate of deceleration in the control condition correlated negatively with food intake after fasting in women [$r = -0.73$, $p < 0.01$]. However, there was no such correlation among men [$r = -0.12$, *ns*].

There was no effect of sex [$F(1,20) = 0.65$, *ns*] or testing condition [$F(1,20) = 0.43$, *ns*] on the duration of the meal (Fig. 3).

Thus, while women ate less food after fasting and their eating became more linear, men ate more food after fasting and their eating became more decelerated.

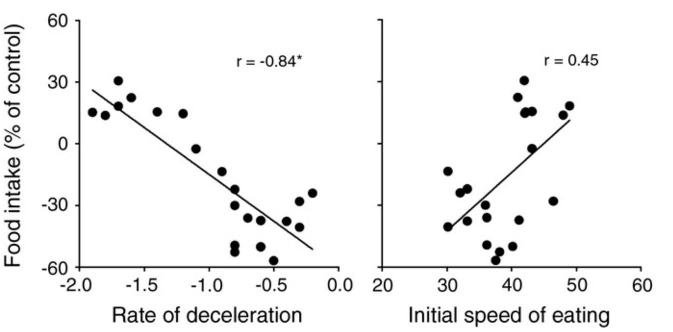

Fig. 2. Relationship between rate of deceleration or initial speed of eating and food intake after fasting in 21 women. Food intake is expressed as percent of the amount consumed in the non-deprived, control condition. *p<0.05, multiple regression.

3.4. Effect of feedback on food intake after fasting

Food intake was significantly affected by sex [$F(1,20) = 45.54$, $p < 0.01$] and testing condition [$F(2,40) = 5.89$, $p < 0.01$] and there was a significant interaction between these two factors [$F(2,40) = 5.89$, $p < 0.01$].

In comparison with the control condition, women ate significantly less food in response to fasting [$t(12) = 3.58$, $p < 0.05$], but more food in the fasting + feedback condition [$t(12) = 3.89$, $p < 0.05$] (Fig. 4).

By contrast, men ate significantly more food in response to fasting [$t(8) = -6.89$, $p < 0.01$], but not in the fasting + feedback condition [$t(8) = -1.47$, *ns*] (Fig. 4).

Men ate significantly more food than women in all conditions [control: $t(20) = -4.34$, $p < 0.01$, fasting: $t(20) = 9.67$, $p < 0.01$ and fasting + feedback: $t(20) = -2.56$, $p < 0.05$] (Fig. 4).

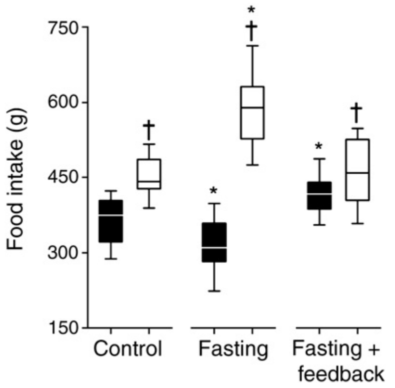

Fig. 4. Food intake before (control) and after fasting without or with feedback from a computer screen during eating in 13 women (black boxes) and 9 men (white boxes). Values are box plots, and the control and fasting values are double-plotted from Fig. 3. *p at least <0.05 compared to control; †p at least <0.05 compared to women, t-test after ANOVA.

Thus, while fasting decreases food intake in women and increases it in men, these effects can be prevented by feedback regarding the normal pattern of food intake during the meal.

3.5. Compliance with the feedback procedure

The message: “you are eating too slow” appeared significantly more often in women (8 (3–15) times) than in men (3 (1–6) times) [$t(45) = 12.57$, $p < 0.001$] when feedback was provided during the meal. The message: “you are eating too fast” did not appear for either group.

4. Discussion

Missing breakfast or dinner decreased daily energy intake in women [16,17], observations similar to our data [8] and serving more food had no effect on this outcome. More interestingly, we found that the more linear the eating in the non-deprived condition, the less food women eat after fasting. This effect was obtained in two independent experiments with a total of 34 women. We also confirmed our previous observation of a sex difference in the response to fasting; women eat less food and men eat more food [8]. The rate of eating was more decelerated among men than among women and as has been reported before, correlated with their higher initial speed of eating [18]. Both the rate of deceleration and the initial speed of eating increased after fasting in men.

There are only a few studies dealing with the effect of food deprivation on the pattern of food intake during meals; one study found no difference between 3 and 6 h of deprivation on either food intake, the rate of deceleration or on the initial speed of eating in men [12] and another reported a significant increase in intake among men deprived for 21 h compared to 1 h, but no clear change on either the rate of deceleration or on the initial speed of eating; there were no significant effects of food deprivation on women [18]. Yet another study showed no difference in food intake, meal duration, on the rate of deceleration and on the initial speed of eating for either 16 lean or obese women or two men who either had breakfast 3.5 h before the test, or who had fasted from midnight the previous day [19]. An enhanced rate of deceleration after deprivation was reported in newborn children but not in adults [20]. There are also a few studies using pharmacological intervention. Injection of cholecystokinin octapeptide induced satiety and reduced both food intake and the initial speed of eating in men [21]. Fenfluramine and amphetamine reduced food intake, meal duration and average speed of eating in men and women [22]. More recently, sibutramine was found to decrease food intake and the average speed of eating in obese women, but there was no significant effect on the rate of eating [23], partially confirming a study in which sibutramine decreased food intake but had no effect on the rate of eating [24]. In light of these relatively limited and discrepant findings further studies on the biological concomitants to the curve of cumulative food intake, including sex differences, seem warranted.

Thus, fasting may increase the risk of eating less and less food among women. This finding is interesting in the light of the fact that female college students, who are at risk for developing *anorexia nervosa*, are more likely to diet than men [9]. Prolonged food restriction in men, however, also increases the linearity of eating [25] and men who are being starved also develop the symptoms of anorexia [26]. Because we have previously found that experimental reduction of the speed of eating decreases food intake in linear eaters [3–5], these observations support our hypothesis that linear eating, particularly if combined with dieting, is a risk factor for the development of the pattern of eating typical of patients with anorexia.

Although there are sex differences in the response to fasting (e.g., free fatty acids, glucose, amino acids, gonadotrophins, corticotrophin and leptin [27–35]), none of these agents can be clearly related to the sex difference in eating behavior found in the present study. Other sex differences in metabolic parameters, such as lean body mass, metabolic rate, total energy expenditure, free fat mass and fat oxidation, are not pronounced in conditions of negative energy balance that are more severe than the level of fasting employed in the present study [36–40]. Although it is possible that sex differences in endocrine and/or metabolic parameters can explain the behavioral sex difference in food intake after fasting, it is premature to speculate on this topic.

The present finding that the sex difference in food intake after fasting was reversed if the subjects received feedback on how to eat, confirms that there are no physiological constraints over eating in fasted subjects [26]. This observation has considerable clinical importance, because feedback as used here may ensure a proper level of food intake after fasting, the main challenge that puts linear eaters at risk of developing the disordered eating behavior of anorexia [3–5]. We observed a sex difference in the difficulty of adhering to the method used to normalize food intake in the present study; fasted women were notified “you are eating too slow” more often than fasted men. However, eventual compliance has not been a problem in treating several hundred patients with eating disorders [13]. Further testing of the hypothesis that linear eating is a risk factor for loss of control over body weight [3–5] and that practicing eating at a decelerated rate can be used to treat those who have poor control over their food intake should determine whether women who are linear eaters can be prevented from developing anorexia.

Conflict of interest statement

C Bergh and P Södersten each have 28% and M Leon has 3% stock in Mando Group AB.

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