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Hypercaloric diets differing in fat composition have similar effects on serum leptin and weight gain in female subjects with anorexia nervosa☆,☆☆

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Abstract

Weight regain in subjects with anorexia nervosa is associated with an increase in serum leptin concentrations that is hypothesized to impair full weight restoration. As diets rich in n-3 polyunsaturated fatty acids (PUFA) have been described to lower serum leptin concentrations, we tested the hypothesis that consumption of a hypercaloric diet rich in n-3 PUFA is associated with an attenuated increase in serum leptin and a higher efficiency of body weight gain in subjects with anorexia nervosa. Twenty-five female subjects with anorexia nervosa were enrolled into this controlled dietary intervention study. Four subjects discontinued therapy or participation in the study prematurely, and six were excluded. 15 subjects completed the study. Subjects consumed hypercaloric diets rich in either saturated fatty acids (SFA, n = 8) or n-3 PUFA (n = 7) for 5 weeks. Primary endpoints were the change in serum leptin concentrations and body weight gain relative to energy consumed. Serum leptin concentrations increased distinctly throughout the study ($P < .001$), and to a similar extend in both groups [+2.9 (SD 2.4) vs. +2.8 (SD 3.4) ng/mL in the SFA- and n-3 PUFA group, respectively; $P = .487$]. The efficiency of body weight gain also did not differ significantly between groups, with a body weight gain of 63.1 (SD 12.4) vs. 79.2 (SD 26.0) g per 4.2 MJ (1000 kcal) consumed in the SFA- and n-3 PUFA group, respectively ($P = .132$). Hypercaloric diets rich in either SFA or n-3 PUFA do not differ in their effects on serum leptin concentrations and the efficiency of body weight gain in female subjects with anorexia nervosa.

Keywords: Anorexia nervosa; Body weight; Weight gain; Leptin; Dietary intervention study

Abbreviations: AN, Anorexia nervosa; BMI, Body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PUFA, Polyunsaturated fatty acids; RM-ANOVA, repeated-measures analysis of variance; SFA, Saturated fatty acids.

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☆☆ All authors contributed to writing the manuscript. BM was involved in study design and coordinated the patient-related activities within the Christoph-Dornier-Clinic; SD calculated the study diets, assessed actual food consumption, and performed laboratory analyses of serum leptin and plasma ghrelin; MP and DP were involved in the design and planning of the study and were the physicians of record for the study subjects; DSW provided expertise for laboratory analyses and contributed to the analysis and interpretation of the data; MK initiated and coordinated all aspects of the study and wrote the first draft of the manuscript.

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1. Introduction

Anorexia nervosa (AN) is a serious eating disorder characterized by fear of body weight gain and a distorted body image [1]. A pervasive fear of fatness leads to low energy intake, often in combination with increased physical activity, and a low body weight. An often extremely reduced body fat mass is associated with low concentrations of the hormone leptin in serum [2] and cerebrospinal fluid [3]. Leptin is an adipocyte-derived peptide that reduces appetite and increases energy expenditure by binding to the long form of the leptin receptor in specific hypothalamic neurons [4]. In AN, the low serum leptin concentrations are believed to mediate adaptive responses to reduce further weight loss by reducing body temperature and energy expenditure, as well as contributing to the amenorrhea that is seen in most female patients [5]. Under ordinary circumstances, the low leptin levels would also be expected to result in increased appetite and food consumption.

Treatment of AN typically includes a hypercaloric diet with the goal of a normalization of body weight [1]. The desired rapid increase in body weight and particularly body fat mass, however, leads to a disproportional increase in serum leptin concentrations [3,6], resulting in increases in satiety and energy expenditure [7] that oppose further weight gain or even could result in weight loss [8]. As a result, patients often need to consume large amounts of food, up to 16.7 MJ/d (4000 kcal/d) to achieve any weight gain [1].

We [9] and others [10] have shown that consumption of diets rich in n-3 polyunsaturated fatty acids (PUFA) is associated with reduced serum leptin concentrations in normal-weight subjects. The objective of the present study was to test the hypothesis that enrichment with n-3 PUFA of a hypercaloric diet given to AN patients attenuates the increase in serum leptin concentrations seen with weight gain, potentially resulting in greater weight gain per kcal consumed.

We enrolled female patients with AN who were admitted to a psychotherapeutic clinic in Münster, Germany. Subjects were given hypercaloric diets rich in either saturated fatty acids (SFA) or n-3 PUFA for 5 weeks. Primary end points were changes in serum leptin concentrations and the efficiency of body weight gain, calculated as body weight gained in grams per 4.2 MJ (1000 kcal) consumed. Secondary end points were changes in serum lipid concentrations and 2 other hormones involved in the regulation of body weight, ghrelin and insulin.

Table 1
Baseline characteristics of subjects given a diet rich in n-3 polyunsaturated fatty acids (PUFA) or a control diet rich in saturated fatty acids (SFA) [a]

	n-3 PUFA diet (n = 7)	SFA diet (n = 8)	*P*
Age (years)	22.5 (8.0)	17.7 (2.1)	.203
Height (cm)	168 (6)	169 (7)	.727
Weight (kg)	37.7 (4.5)	39.6 (7.1)	.557
BMI (kg/m^2)	13.4 (1.1)	13.8 (1.5)	.565

[a] Data are means (SD); *P* values indicate results of Mann-Whitney *U* test (for age) and independent-samples *t* tests.

Table 2
Composition of the diet rich in n-3 polyunsaturated fatty acids (PUFA) and the control diet rich in saturated fatty acids (SFA) [a]

	n-3 PUFA diet (n = 7)	SFA diet (n = 8)
Energy (MJ/d) [b]	10.7 (0.9)	11.0 (1.1)
Protein (% of energy)	13.5 (0.5)	13.0 (0.6)
Carbohydrates (% of energy)	45.7 (0.5)	46.5 (0.7)
Fat (% of energy)	40.8 (0.7)	40.5 (1.1)
Saturated fatty acids (% of energy)	11.7 (0.6)	21.2 (0.5)
Monounsaturated fatty acids (% of energy)	16.8 (0.3)	11.8 (0.5)
n-6-PUFA (% of energy)	7.7 (0.1)	4.8 (0.2)
n-3 PUFA (% of energy)	2.4 (0.1)	0.6 (0.1)
Fiber (g/1000 kcal)	10.5 (1.3)	10.4 (1.0)

[a] Data are means (SD).
[b] To convert to kcal/d, multiply by 239.

2. Methods and materials

2.1. Subjects

This study was conducted in the Christoph-Dornier Clinic for Psychotherapy in Münster, Germany. The therapy employed by this clinic includes successive inpatient periods of several weeks duration, alternating with outpatient treatment phases during which patients learn to implement their new eating habits at home. During the first and longest clinical period, each subject is accompanied by a trained psychotherapist at all times of the day. All meals are consumed in a group of six patients with AN, in the presence of at least one psychotherapist. Patients are required to eat all food, and the energy content of their diet is adjusted to achieve a body weight gain of 1.2 kg/wk. Subjects enter the second clinical period when they reach a body mass index (BMI) of 18 kg/m^2. During subsequent clinical phases, subjects are allowed to choose part of their foods themselves.

Twenty-five female subjects, 12 to 45 years of age, who were about to start their first clinical phase, were enrolled into this study. Participation was voluntary, and the start of therapy was not linked in any way to participation in the study. During the five weeks of the study, 2 subjects discontinued therapy and left the clinic, and 2 further subjects quit participation in the study prematurely. Six subjects had to be excluded because they reached the second clinical phase during which they could choose part of their food freely during their first 5 weeks in the clinic (n = 2), because no blood draws were possible at one or more time points (n = 2) or because they admitted to having vomited regularly (n = 2). Other exclusion criteria were presence of any illness or infection, malabsorption syndromes, alcohol or drug abuse, or a BMI above 16.5 kg/m^2 at baseline. Fifteen subjects completed the whole study (age range, 15-36 years). Each subject or, in the case of minors, their legal