Archival Report

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Daily Stressors, Past Depression, and Metabolic Responses to High-Fat Meals: A Novel Path to Obesity

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ABSTRACT

BACKGROUND: Depression and stress promote obesity. This study addressed the impact of daily stressors and a history of major depressive disorder (MDD) on obesity-related metabolic responses to high-fat meals.

METHODS: This double-blind, randomized, crossover study included serial assessments of resting energy expenditure (REE), fat and carbohydrate oxidation, triglycerides, cortisol, insulin, and glucose before and after two high-fat meals. During two separate 9.5-hour admissions, 58 healthy women (38 breast cancer survivors and 20 demographically similar control subjects), mean age 53.1 years, received either a high saturated fat meal or a high oleic sunflower oil meal. Prior day stressors were assessed by the Daily Inventory of Stressful Events.

RESULTS: Greater numbers of stressors were associated with lower postmeal REE ($p = .008$), lower fat oxidation ($p = .04$), and higher insulin ($p = .01$), with nonsignificant effects for cortisol and glucose. Women with prior MDD had higher cortisol ($p = .008$) and higher fat oxidation ($p = .004$), without significant effects for REE, insulin, and glucose. Women with a depression history who also had more stressors had a higher peak triglyceride response than other participants ($p = .01$). The only difference between meals was higher postprandial glucose following sunflower oil compared with saturated fat ($p = .03$).

CONCLUSIONS: The cumulative 6-hour difference between one prior day stressor and no stressors translates into 435 kJ, a difference that could add almost 11 pounds per year. These findings illustrate how stress and depression alter metabolic responses to high-fat meals in ways that promote obesity.

Keywords: Cortisol, Daily stressors, Depression, Insulin, Resting energy expenditure, Triglycerides

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Depression and stress promote obesity (1–3). Depressed people have a 58% increased risk of becoming obese (1). In addition, a large prospective study showed that older depressed adults gained visceral fat over 5 years, while nondepressed adults lost visceral fat (4). Stressful events have also been associated with weight gain and adiposity (5,6); longitudinal studies suggest that chronic stress and stressful life events enhance the development of the metabolic syndrome, which has central obesity as its cornerstone (2,7–9).

Depression and stressful events can alter neurochemistry, neurobiology, and behavior, providing multiple pathways for metabolic alterations. For example, both depression and stress elevate cortisol production; higher cortisol fosters increased intake of calorie-dense comfort foods, and insulin secretion rises as cortisol increases (10). Persistent hypercortisolemia and higher insulin enhance visceral fat accumulation (4,10).

Long-term weight maintenance or energy balance requires that caloric intake equals calories burned. Resting energy expenditure plays a key role in energy balance and weight control, accounting for 65% to 75% of the total daily energy expenditure (11). Lower daily energy expenditure increases risk for weight gain and obesity. In addition, metabolism of macronutrients, primarily fats and carbohydrates, also influences weight regulation (12), and lower fat oxidation rate clearly facilitates weight gain over time (13). Data from rodents have shown that psychological stressors provoke multiple metabolic changes, including alterations in energy expenditure as well as fat, carbohydrate, and protein metabolism (10,14,15), but parallel human studies are scarce.

Stressors and depression have important biological consequences, both separately and together. Depression confers vulnerability to stressors. People with a history of depression experience more major and minor stressors than those without a similar history, and past depression can also boost emotional reactivity to daily stressors (16–18).

We assessed the impact of daily stressors and past depression on metabolic responses to two different high-fat meals. Based on the research that has linked stressors and depression to visceral fat and obesity, we hypothesized that both stressors on the prior day and a history of depression would be associated with lower postmeal energy expenditure and fat oxidation, as well as heightened postprandial triglycerides, cortisol, and insulin.

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METHODS AND MATERIALS

Design and Overview

This double-blind, randomized, crossover study assessed metabolic responses following high-fat meals. Women received one high saturated fat meal and one high oleic sunflower oil meal during two separate full-day visits to the Clinical Research Center (CRC), a hospital research unit, with the meal order randomized. Visits were spaced 1 to 4 weeks apart. The institutional review board approved this study, and each participant provided informed consent.

After fasting for 12 hours, a catheter was inserted in the arm on admission. Women had 20 minutes to eat the meal. Metabolic data and blood samples were obtained before and at intervals for 6 to 7 hours after the meal.

Glucose and insulin were sampled before the meal and postmeal at 45 minutes, 1.5 hours, 2 hours, 2.5 hours, and then hourly (19). Triglycerides and salivary cortisol were assessed before the meal and then hourly afterward (19).

Participants

The parent study was designed to assess whether a high-fat diet fuels fatigue in cancer survivors; thus, the 58 healthy women included 38 breast cancer survivors and 20 benign control subjects (women who had an initial abnormal mammogram). Demographic data did not differ between survivors and control subjects (Table 1). Survivors averaged 27.03 months (SD = 17.45) since diagnosis and 19.87 months (SD = 16.47) since treatment completion. Exclusions included a history of any other prior cancer, chronic obstructive pulmonary disease, symptomatic ischemic heart disease, alcohol/drug abuse, and immune-related conditions such as diabetes, autoimmune disease, and major inflammatory diseases (e.g., rheumatoid arthritis and ulcerative colitis). Medication exclusions included blood lipid medications (fibrates, statins, Xenical, and niacin), angiotensin type I receptor blockers, and regular use of medications with major immunologic or endocrinological consequences, e.g., steroids.

Standardized Prestudy Meals

Participants were instructed to avoid alcohol use the day before the study and any strenuous physical activity 2 days previously (19). Participants were also asked not to take aspirin, vitamins, antioxidants, or other dietary supplements for the 7 days before each admission.

On the day before each of the two study visits, participants received three standardized meals from the CRC's metabolic kitchen to reduce the variability associated with recent intake. Equations from the dietary reference intakes were used to determine total energy requirements for each participant based on age, height, weight, and physical activity (20). Macronutrient targets (as percent of total energy) for these research meals were 54.9 ± 2.68% carbohydrate, 27.6 ± 2.13% fat, and 17.6 ± .95% protein. The fat content was 9.10 ± 1.20% saturated fats, 9.43 ± 1.55% monounsaturated fats, and 7.26 ± 1.25% polyunsaturated fats. Participants ate their last meal no later than 7:30 PM the night before admission; the dinner was light and low in fat (19). Compliance was good: women consumed 91.83 ± 8.41% of these meals.

Research Meals

Both research meals included eggs, turkey sausage, biscuits, and gravy for a total of 3894 kJ, with 60 grams fat, 59 grams carbohydrate, and 36 grams protein (percent of total energy = 60, 25, and 15, respectively). However, following Poppitt *et al.* (21), the saturated:unsaturated fatty acid ratio varied between the meals; the high saturated fat meal contained 16.84 g palmitic and 13.5 g oleic (ratio = 1.93), compared with 8.64 g

Table 1. Characteristics of Breast Cancer Survivors and Control Subjects

	Control Subjects (n = 20)	Breast Cancer Survivors (n = 38)	p Value
Age, Years	54.9 (10.2)	52.1 (7.3)	.22
Body Mass Index, kg/m^2	26.7 (4.1)	28.9 (5.3)	.12
Waist, cm	91.2 (10.3)	96.6 (12.8)	.11
Trunk Fat, g (DXA)	13994.1 (5218.7)	16983.8 (5758.6)	.06
Lean Body Mass, g (DXA)	40559.1 (3839.9)	42541.1 (5239.7)	.14
Activity, Hours per Week	12.5 (6.9)	11.1 (5.6)	.41
Systolic Blood Pressure, mmHg	127.3 (20.0)	126.6 (21.5)	.90
Diastolic Blood Pressure, mmHg	73.5 (8.0)	76.2 (9.0)	.27
Total Cholesterol, mg/dL	177.6 (40.3)	181.4 (24.9)	.66
High-Density Lipoprotein, mg/dL	53.3 (17.6)	52.0 (16.1)	.77
Low-Density Lipoprotein, mg/dL	101.8 (37.6)	102.6 (23.3)	.91
Fasting Triglycerides, mg/dL	112.6 (78.3)	133.1 (84.7)	.37
Fasting Glucose, mg/dL	95.1 (8.3)	96.8 (9.3)	.48
Menopausal Status			.09
Premenopausal	7 (35%)	6 (16%)	
Postmenopausal	13 (65%)	32 (84%)	
Number of Prior Day Stressors	1.2 (1.1)	1.1 (1.1)	.48
History of Major Depression	3 (15%)	14 (37%)	.08

Data shown are mean (SD) or n (%).
DXA, dual x-ray absorptiometry.