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ARCHIVAL REPORT

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

Janice K. Kiecolt-Glaser, Diane L. Habash, Christopher P. Fagundes, Rebecca Andridge, Juan Peng, William B. Malarkey, and Martha A. Belury

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 and MDD history was assessed by the Structured Clinical Interview for DSM-IV.

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 ($p = .25$) and glucose ($p = .33$). Women with prior MDD had higher cortisol ($p = .008$) and higher fat oxidation ($p = .004$), without significant effects for REE ($p = .26$), insulin ($p = .25$), and glucose ($p = .38$). Women with a depression history who also had more prior day 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 104 kcal, 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.

Key Words: Cortisol, daily stressors, depression, insulin, resting energy expenditure, triglycerides

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).

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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.

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

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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 endocrinolog 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 kilocalorie 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.

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.

Research Meals

Both research meals included eggs, turkey sausage, biscuits, and gravy for a total of 930 kcals, with 60 grams fat, 59 grams carbohydrate, and 36 grams protein (percent of total kcals = 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 palmitic and 31.21 g oleic for the high oleic sunflower oil meal (ratio = .67). For the parent study, we wanted to contrast two different kinds of high-fat meals because some human studies have suggested that high saturated fat meals may fuel fatigue-inducing inflammatory responses, although others have not found these effects (21–23).

Metabolic Data

Metabolic data were obtained using indirect calorimeters (Ultima CPX and CCM Express, MedGraphics, St. Paul, Minnesota). Inspired and expired airflow of oxygen and carbon dioxide were measured after the participant had rested for 30 minutes in a thermoneutral room in a bed. During the 30-minute resting metabolic rate measurement process, women reclined at a 30-degree angle and remained still but awake. Resting metabolic rate was determined during the steady state, defined during the measurement as the consecutive 5-minute interval in which energy expenditure was the lowest, while oxygen consumption and carbon dioxide production changed by <10% (24,25). During the remainder of the admission, metabolic data were obtained 20 minutes out of every hour.

Macronutrient Oxidation Rates

Fat and carbohydrate oxidation (g/min) were calculated from oxygen consumption and carbon dioxide production using the Weir formulas (26). Adjustments for the protein respiratory quotient were based on estimations of urinary urea nitrogen using the protein consumption from the standardized meals consumed the day before the study (27).

Body Composition

Body composition was assessed by dual x-ray absorptiometry (28). Dual x-ray absorptiometry data provided a way to assess both lean body mass, which explains 70% to 80% of the variance in resting metabolic rate (29), and trunk fat, which contributes to adverse metabolic meal-related responses and obesity-related disease risk (28).

Interview Data

The mood disorder modules of the Structured Clinical Interview for DSM-IV, nonpatient version, provided data on lifetime prevalence of major depressive disorder (MDD) (30). Interviews were administered by well-trained clinical psychology graduate students or staff, and regular consensus meetings with recorded interviews were used to obtain diagnoses and maintain consistent, reliable, and valid interview data. Structured Clinical Interview for DSM-IV, nonpatient version, data showed that 29% ($n = 17$) had met MDD criteria. The average time since diagnosis was 8.32 years (SD = 10.94).

The Daily Inventory of Stressful Events provided data on the number of daily stressors within the last 24 hours (31). The Daily Inventory of Stressful Events interview utilizes investigator-rated measures of stressor severity, which provides a way to reduce the bias inherent in self-ratings of stressor severity and appraisal (31); an extensive electronic dictionary specifies codable events. In our sample, 31 women reported at least one recent stressor at one visit, 21 at both visits, and 6 women reported no stressors.

Questionnaires

Following CRC admission, participants completed several questionnaires. The Center for Epidemiological Studies Depression Scale (CES-D) assessed depressive symptomatology in the last week (32). The Community Healthy Activities Model Program for Seniors questionnaire assessed the weekly frequency and duration of various physical activities (33,34). These measures have well-established reliability and validity (32–34).

Dietary Assessment

Three 24-hour dietary recalls, administered via telephone interviews, used the validated US Department of Agriculture Multiple Pass Approach method (35,36). Data were averaged across the three interviews (including 1 weekend day).

Statistical Methods

The primary analyses used linear mixed models, which allowed explicit modeling of the within-subject correlations both across visits and within a visit. Demographics and other premeal subject characteristics were compared across groups (cancer, control) using two-sample *t* tests and chi-square tests for data collected at only one time point (e.g., trunk fat, menopausal status) and linear mixed models with a random subject effect for data collected before each meal (e.g., fasting triglycerides). Triglyceride, insulin, and cortisol data were right-skewed; thus, all analyses for these outcomes used natural-log transformed values to better approximate normality of residuals. Initial exploratory data analysis revealed that the postmeal trajectories of postmeal energy expenditure, carbohydrate and fat oxidation, insulin, glucose, and cortisol were approximately linear; thus, models for these outcomes included a linear fixed effect of time (hours since the meal). The exception was the postmeal triglyceride data, which showed an initial rise for the first 3 to 4 hours postmeal followed by a decline until the end of the measurement period. Thus, in the triglyceride model, time was modeled as a quadratic effect.

Of primary interest for all models were the effects of number of prior day stressors and history of depression on the postmeal responses; thus, we included the interaction of each of these effects with time along with the respective main effects. Interactions of prior day stressors and depression were also investigated. Nonsignificant interactions ($p > .05$) were removed from the models. The number of prior day stressors was used as a continuous predictor in all models. All models controlled for the premeal outcome measurement by including it as a fixed effect. Additionally, to properly account for the design of the parent study, all models included the three-way interaction of group (cancer vs. control) by meal type (high saturated fat vs. high oleic sunflower oil) and by time, plus all lower order terms. To assess whether the effect of stressors might differ between groups (cancer vs. control), we added the interaction of stressors by group to each model; it was not significant for any outcome ($p > .3$ for all tests) and thus was not included in any final models. Additional covariates were controlled for in each model to guard against confounding; specific controlling variables for each model were selected a priori based on their relationships with target variables and are noted in the Results section. Random effects included subject-specific meal effects that were allowed to be correlated. This accounted for the different magnitude of within-subject correlations within the meal types and across the meal types. The Kenward-Roger adjustment to the degrees of freedom was used to control type I error (37), and no adjustments were made to *p* values to account for multiple testing.

Bang *et al.* (38) blinding indices were calculated using participant and experimenter guesses about the meal type, separately for the high oleic sunflower oil meal and the high saturated fat meal. All analyses were conducted in SAS version 9.3 (Cary, North Carolina).

Results

Primary Analyses

A larger number of stressors was associated with a steeper postprandial decline in postmeal energy expenditure (Figure 1), F1 controlling for premeal resting energy expenditure (REE), age, lean body mass, trunk fat, physical activity, and past depression, as evidenced by a significant stressors by time interaction ($p = .008$). For subjects with no prior day stressors, the estimated postmeal energy expenditure slope was −12.9 kcal per hour, and with each additional stressor, the slope decreased by an estimated 5.0 kcal. There was no effect of depression on postmeal energy expenditure ($p = .25$). Age ($p = .95$), lean body mass ($p = .67$), trunk fat ($p = .60$), and physical activity ($p = .18$) were not significant predictors of postmeal REE.

A larger number of stressors was also associated with decreased fat oxidation in the postmeal period, controlling for premeal fat oxidation, age, trunk fat, homeostatic model

Figure 1. Estimated postprandial decline in energy expenditure as a function of number of daily stressors on the previous day. Results are from a linear mixed model controlling for premeal resting metabolic rate, age, lean body mass, trunk fat, physical activity, history of depression, cancer/control status, and meal type. REE, resting energy expenditure.

assessment (HOMA) insulin resistance (13), physical activity, and depression (stressors by time interaction $p = .04$). Fat oxidation increased at an estimated rate of .011 g/min per hour for subjects with no prior day stressors (Figure 2), and with each additional stressor, this slope decreased an estimated .0033 g/min. The main effect of past depression was also significant in this model, after controlling for the effect of prior day stressors, with subjects who had a history of depression having higher fat oxidation than subjects without a history of depression (estimated mean difference = .069 g/min, $p = .004$). Age ($p = .15$), trunk fat ($p = .29$), HOMA insulin resistance ($p = .18$), and physical activity ($p = .67$) were not significant predictors of postmeal fat oxidation. There was not a significant effect of either prior day stressors or history of depression on change in carbohydrate oxidation postmeal ($p = .94$ and $p = .27$, respectively), controlling for premeal carbohydrate oxidation, age, trunk fat, HOMA insulin resistance, and physical activity. However, there was a marginal effect of depression on the average level of carbohydrate oxidation postmeal, with subjects who had a history of depression having lower carbohydrate oxidation (estimated difference = −.041 g/min, $p = .07$). The effect of HOMA insulin resistance was significant, with higher HOMA insulin resistance associated with lower postmeal carbohydrate oxidation ($p = .05$). Age ($p = .31$), trunk fat ($p = .30$), and physical activity ($p = .46$) were not significant in the model.

Prior day stressors were also a significant predictor of postprandial insulin, controlling for premeal insulin, age, trunk fat, physical activity, and depression, as evidenced by a significant stressors by time interaction ($p = .01$). However, the pattern was different than for postprandial energy expenditure and fat oxidation, where the effect of stressors increased over time. For insulin, the effect of stressors was strongest at the first postmeal measurement, where each additional stressor was associated with an estimated .061 ln-ulU/mL increase in ln-insulin ($p = .04$). By the next measurement (1.5 hours postmeal), there was not a significant effect of stressors on insulin levels. The effect of depression on insulin was not significant ($p = .25$). Trunk fat was significantly related to postprandial insulin with larger trunk fat associated with higher insulin levels ($p = .05$), while age ($p = .34$) and physical activity ($p = .68$) were not significant predictors. Neither stressors nor depression were significantly associated with postprandial glucose ($p = .33$ and $p = .38$, respectively).

Figure 2. Estimated postprandial increase in fat oxidation as a function of number of daily stressors on the previous day. Results are from a linear mixed model controlling for premeal fat oxidation, age, trunk fat, homeostatic model assessment insulin resistance, physical activity, history of depression, cancer/control status, and meal type.

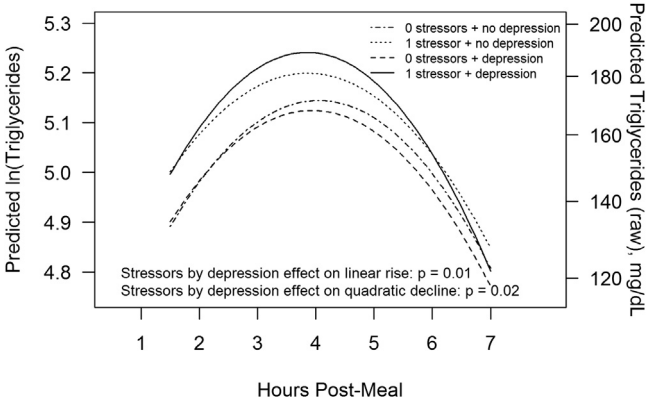

Figure 3. Estimated postprandial changes in triglycerides as a function of number of daily stressors on the previous day and history of depression. Results are from a mixed model controlling for premeal triglycerides, age, trunk fat, physical activity, menopausal status, cancer/control status, and meal type. ln, .

The effect of stressors and depression history on postprandial triglycerides was complex, as there were significant three-way interactions of stressors by depression by time ($p = .01$) and stressors by depression by time squared ($p = .02$), controlling for premeal triglycerides, age, trunk fat, physical activity, and menopausal status (39). As shown in Figure 3, subjects with both a larger number of stressors and a history of depression had a steeper immediate rise in triglycerides coupled with a subsequent steeper decline post peak compared with other subjects. The effects of age ($p = .95$), trunk fat ($p = .42$), physical activity ($p = .61$), and menopausal status ($p = .25$) were not significant.

Finally, there was a significant effect of history of depression on changes in cortisol postmeal (depression by time interaction, $p = .008$), controlling for premeal cortisol, age, trunk fat, physical activity, and number of stressors (Figure 4). For subjects with a history of depression, the estimated decrease in ln-cortisol levels postmeal was .047 ln-μg/dL per hour, compared with a decrease of .093 ln-μg/dL for subjects without a history of depression, a twofold difference in slopes. There was not a significant effect of stressors on postmeal cortisol levels ($p = .25$). The effects of age ($p = .16$), trunk fat ($p = .46$), and physical activity ($p = .27$) were not significant.

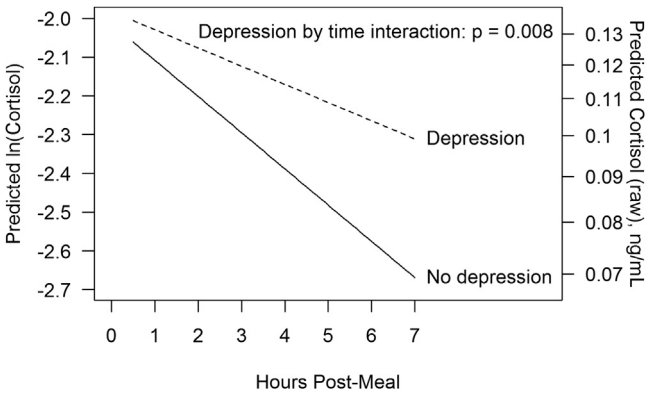

Figure 4. Estimated postprandial changes in cortisol as a function of history of depression. Results are from a mixed model controlling for premeal cortisol, age, trunk fat, physical activity, cancer/control status, and meal type. ln, .

There were no differences between cancer and control subjects in fasting levels of any outcome measure. The only group difference in postprandial measures was a difference in cortisol rate of decline after the meal, with cancer survivors experiencing a steeper decline. For cancer survivors, the estimated decrease in ln-cortisol levels postmeal was .10 ln-μg/dL per hour, compared with a decrease of .042 ln-μg/dL per hour for control subjects ($p = .01$).

The only significant difference between the high saturated fat meal and the high oleic sunflower oil meal was in postprandial glucose. Average glucose levels were higher immediately following the high oleic sunflower oil meal ($p = .03$ at 45 minutes postmeal) but this effect diminished over time (meal by time interaction, $p = .02$), and by 2 hours postmeal, there was not a significant difference.

Ancillary Analyses

The average hours of sleep the night before admission was 6.2 (SD = 1.3). Hours of sleep were not associated with either the number of stressors the day before ($p = .61$) or a history of depression ($p = .52$).

The most common medications taken regularly by participants were antidepressants ($n = 16$), aromatase inhibitors ($n = 14$), and selective estrogen receptor modulators ($n = 12$). Low dose antidepressants are commonly prescribed for breast cancer survivors as a treatment for menopausal symptoms. Inclusion of these medications in analyses did not alter the findings.

The CES-D was included in all models to assess the possibility that current mood was responsible for metabolic differences. Current depressive symptoms were not a significant predictor of any outcome except postmeal triglycerides, where more depressive symptoms were associated with a steeper rise in triglycerides immediately postmeal ($p = .05$). For all models reported in the primary analyses, the magnitude and significance of the effects were unchanged when the CES-D was included, except for the model for carbohydrate oxidation postmeal, where including CES-D actually increased the estimated effect of depression by 20%, causing the marginal effect ($p = .06$) to become significant ($p = .03$).

We evaluated each woman's typical diet and its relationship with premeal and postmeal REE, as well as recent stressors and history of depression. There were associations between reports of usual daily dietary calories from carbohydrates and fat with premeal REE levels, with a 1 gram increase in fat intake associated with a 3.4 kcal decrease in premeal REE ($p = .04$) and a 1 gram increase in carbohydrate intake associated with a 1.2 kcal increase in premeal REE ($p = .04$). There was no association between protein intake and premeal REE ($p = .55$), and there were no significant associations between dietary variables and postmeal REE levels or changes. Diet was also not associated with either prior day stressors or history of depression.

The Bang *et al.* (38) blinding index for the high oleic sunflower oil meal was .18 (95% confidence interval [CI]: −.02, .37; $n = 56$), and for the high saturated fat meal, it was −.28 (95% CI: −.48, −.08; $n = 57$). For the experimenter, these indices were .07 (95% CI: −.02, .16; $n = 57$) and .05 (95% CI: −.03, .14; $n = 58$) for the high oleic sunflower oil and high saturated fat meals, respectively. A blinding index of zero indicates perfect blinding, i.e., random guessing.

Discussion

This study provides novel evidence of metabolic pathways through which prior day stressors and past depression facilitate weight gain over time. Greater numbers of prior day stressors were associated with decreased postmeal energy expenditure. The cumulative difference between one recent stressor and no stressors over 6 hours translates into 104 kcal, averaged across meal type and group and all controlling variables. This difference would add up to almost 11 pounds across a year.

Greater numbers of prior day stressors were also associated with lower fat oxidation, as well as higher insulin production. People with lower fat oxidation are more likely to gain weight by storing fat than those with higher fat oxidation, and thus their risk for obesity is increased (40). Higher levels of insulin are lipogenic, further enhancing fat storage (10).

Women with a history of depression who had also experienced more stressors the prior day had a higher peak triglyceride response compared with other participants. Larger postprandial triglyceride responses are reliably associated with enhanced cardiovascular risk, with greater risks for women than men (41–47). The magnitude and duration of the postprandial triglyceride response are linked with the progression of atherosclerosis (41,48,49). Depression has well-established effects on cardiovascular morbidity and mortality, and these meal-related changes highlight a previously unrecognized depression-sensitive mechanistic pathway (50,51).

Women with a depression history also had higher postmeal cortisol values compared with women who did not have a similar history. Cortisol promotes triglyceride accumulations in visceral fat through two pathways (52). Cortisol binds to glucocorticoid receptors, which have a high density in visceral fat; cortisol increases lipoprotein lipase activity, stimulating triglyceride accumulation in visceral fat. Cortisol also restrains lipid mobilization in the presence of insulin, thereby fueling triglyceride accumulation and retention in visceral adipose tissue (4). Fat oxidation was significantly higher among women with an MDD history than those without, a surprising finding that was at odds with both the cortisol and triglyceride data.

Our study has several strengths. We controlled both the composition and energy content of each woman's diet on the day before admission, as well as during admission (53). Women were studied under sedentary conditions with uniform activity restrictions. We used the protein data from the prior day to calculate fat and carbohydrate oxidation; nitrogen excretion data (27) would have provided a more precise measure of substrate utilization, one limitation of our study.

The inclusion of breast cancer survivors, even though they were healthy, could have affected the results, another limitation. However, we found no reliable differences between cancer survivors and control subjects. Furthermore, other researchers have not observed metabolic differences between healthy cancer survivors and control subjects, in accord with our data (54–58).

Our sample's average body mass index was 28.1, in accord with the age-adjusted mean of 28.7 for US women (59). Similarly, in line with the 35.8% obesity prevalence among adult women (59), 36.2% of our women were obese (body mass index 30–38). Thus, the women in our sample were comparable with their agemates, a significant detail since obesity has multiple effects on metabolism (7).

Importantly, the metabolic differences associated with recent stressors and past depression did not appear in fasting metabolic data but were only observable in response to the high-fat meals. These data suggest that significant metabolic consequences of stress and depression may be missed in fasting assessments.

Both of our meals included 930 kcal and 60 g fat, values that are quite comparable with common fast food choices. For

example, a Burger King Double Whopper with cheese has 990 kcal and 64 g fat, while a McDonald's Big Mac cheeseburger and medium French fries contain 930 kcal and 58 g fat. Moreover, unlike our participants who were only given one meal, most people eat every 4 to 5 hours, in addition to having snacks that contain fat, and thus many of the adverse metabolic alterations, including triglyceride elevations, could persist throughout the day (19,41).

Our two study meals were both high in fat, so we do not know if recent stressors and past depression might have different metabolic consequences following low-fat meals. However, during stressful times, many people turn to calorie-dense high-fat comfort food (6,60). While the influence of stress and depression on food choice is well-established, our novel data suggest that stressors and depression also affect metabolic responses to these meals.

The only meal-related difference was the transiently higher postprandial glucose observed following the high oleic sunflower oil meal compared with the saturated fat meal. Some randomized controlled feeding trials have suggested that diets rich in monounsaturated fatty acids have a more favorable impact on lipid profiles than high saturated fat diets, consistent with the broader health benefits attributed to Mediterranean-style diets (61,62). The variability in customary background diets may make it difficult to demonstrate metabolic differences following a single high saturated fat meal compared with a high oleic sunflower oil meal, but this remains an important area for further studies.

Obesity increases the risk for many diseases, including coronary artery disease, stroke, type 2 diabetes, metabolic syndrome, and cancer. Our findings illustrate novel pathways through which stress and depression contribute to obesity and obesity-related diseases.

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The authors report no biomedical financial interests or potential conflicts of interest.

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