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Stress, Depression, and Metabolism: Replies to Bohan Brown et al. and Barton and Yancey

Janice K. Kiecolt-Glaser, Rebecca Andridge, and Martha A. Belury

Institute for Behavioral Medicine Research (JK-G), Department of Psychiatry, College of Medicine (JK-G), Division of Biostatistics, College of Public Health (RA), Department of Human Sciences, College of Education and Human Ecology (MAB), The Ohio State University, Columbus, OH USA

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We recently reported adverse stress- and depression-related metabolic alterations following high-fat meals (1). In their commentary on our paper, Bohan Brown and colleagues (2) raise an interesting question related to our caloric calculations; they suggest that the differences we observed would translate to a gain of 6.4 pounds/year compared to the 10.8 that we had computed based on the 3500 kcal rule. Their argument is based on newer literature that has primarily addressed *decreased* caloric expenditure as weight loss occurs, but we acknowledge that the state of the field is such that we cannot calculate the total caloric impact over time with certainty.

We had conservatively based our calculations on the impact of only a single stressor on resting energy expenditure 6 hours after the meal (not 24 hours as they indicated in their note). Alternatively, if we calculate the impact of *two* stressors vs. none, the number that half our sample reported at one or both visits, the difference is 206 kcal for the 6 hours post-meal.

If we accept Bohan Brown et al.'s (2) argument that weight change over a year for a single stressor would be 6.4 pounds instead of the 10.8 that we projected, 6.4 pounds is far from trivial--particularly when considered in the context of the other stress- and depression-related postprandial metabolic data we reported: lower fat oxidation, higher insulin and cortisol production, and a heightened postprandial triglyceride response, all of which would promote central adiposity and simultaneously heighten the risk of cardiovascular disease. Moreover, as we noted in the paper, these data are quite consistent with literature linking stress and depression to central adiposity and obesity (3–6), as well as rodent and nonhuman primate studies (7–10).

Corresponding Author: Janice K. Kiecolt-Glaser, Institute for Behavioral Medicine Research, The Ohio State University College of Medicine, 460 Medical Center Drive, Columbus, OH 43210 (Janice.Kiecolt-Glaser@osumc.edu) 614-293-4418.

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Indeed, one noteworthy paper showed that higher levels of depressive symptoms predicted increased visceral obesity over a five-year period independent of changes in body mass index (6). Thus, even if our participants did not gain any weight at all, the fat oxidation, insulin, cortisol, and triglyceride differences we observed provide supportive mechanistic evidence for the depression-related changes in visceral obesity reported by Vogelzangs et al. (6).

The Kiecolt-Glaser et al. (1) paper in question reported the first of our studies addressing the impact of stress and depression on metabolism. In a second closely related study that used the same meal challenge paradigm, we recruited 43 healthy married couples who were asked to discuss a disagreement two hours post-meal when triglycerides would be starting to peak (11). In line with the results from our first study, participants who had a history of depression and whose marital discussions were more hostile had significantly lower postprandial energy expenditure, higher insulin, and a higher peak triglyceride response. Following the Bohan Brown method for calculating caloric differences, the cumulative 6.75-hour difference between high and low hostile behaviors among subjects with a mood disorder history translates into 128 kcal, so we would still see a difference of ~7.6 pounds/year. We also found other parallel data between the two studies: heightened insulin and triglyceride responses associated with past depression and hostile marital interactions. Thus, we have confidence that the stress- and depression-related effects we are seeing are reliable and represent an important area for further investigation.

A second commentary focused on the impact of carbohydrates and their relationship to metabolic rate and weight gain (12). Our paper (1) did not address the impact of carbohydrates and we did not discuss possible implications of a high carbohydrate diet, so their extensive high fat vs. high carbohydrate dietary discussion is outside the realm of our study. They also argue that insulin production is central to fat storage, a point on which we are in clear agreement; in both of our studies we found elevated post-meal insulin related to prior day stressors (1) as well as past depression and hostile marital interactions (11).

In addition, Barton and Yancy (12) noted that the three meals that we gave our subjects on the day prior to the meal challenge were 55% carbohydrate; they suggested that the high carbohydrate content could have interacted with the prior day stressors we were assessing, such that the timing of the stressor would have had a greater impact because it coincided with the prior day's high carbohydrate intake. However, in our more recent study with couples (11) we evaluated responses to marital conflict discussions that *followed* the high-fat meals and obtained parallel results; accordingly, the pre-study day meals would not account for the effects. Finally, neither study found relationships between participants' typical diet (as measured by 24-hour recalls) and the metabolic postprandial changes we observed.

In summary, we have parallel data from two different studies suggesting that stress and depression have important metabolic consequences. Stressors--and the negative emotions they generate--are rarely addressed in metabolic studies despite considerable rodent and primate work that has highlighted their importance. A better understanding of how stressors, depression, and diet work together to alter metabolic processes will benefit behavioral and nutritional research, as well as the broader biomedical community (13).

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References

1. Kiecolt-Glaser JK, Habash D, Fagundes CP, Andridge R, Peng J, Malarkey WB, et al. Daily stressors, past depression, and metabolic responses to high-fat meals: A novel path to obesity. *Biol Psychiatry*. (in press).
2. Bohan Brown MM, Bown AW, Allison DB. Linear extrapolation results in erroneous overestimation of plausible stressor-related yearly weight changes. *Biol Psychiatry*. (in press).
3. Luppino FS, de Wit LM, Bouvy PF, Stijnen T, Cuijpers P, Penninx BW, et al. Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry*. 2010; 67:220–229. [PubMed: 20194822]
4. Raikonen K, Matthews KA, Kuller LH. Depressive symptoms and stressful life events predict metabolic syndrome among middle-aged women - a comparison of World Health Organization, Adult Treatment Panel III, and International Diabetes Foundation definitions. *Diabetes Care*. 2007; 30:872–877. [PubMed: 17392548]
5. Williams LJ, Pasco JA, Henry MJ, Jacka FN, Dodd S, Nicholson GC, et al. Lifetime psychiatric disorders and body composition: A population-based study. *J Affect Disord*. 2009; 118:173–179. [PubMed: 19249106]
6. Vogelzangs N, Kritchevsky SB, Beekman ATF, Newman AB, Satterfield S, Simonsick EM, et al. Depressive symptoms and change in abdominal obesity in older persons. *Arch Gen Psychiatry*. 2008; 65:1386–1393. [PubMed: 19047525]
7. Shively CA, Register TC, Clarkson TB. Social stress, visceral obesity, and coronary artery atherosclerosis in female primates. *Obesity*. 2009; 17:1513–1520. [PubMed: 19325545]
8. Laugero KD. Filling in the gaps of chronic psychological stress disease models: What's metabolic profiling have to do with it? *Endocrinology*. 2008; 149:2712–2713. [PubMed: 18493025]
9. Moles A, Bartolomucci A, Garbugino L, Conti R, Caprioli A, Coccorello R, et al. Psychosocial stress affects energy balance in mice: Modulation by social status. *Psychoneuroendocrinology*. 2006; 31:623–633. [PubMed: 16616814]
10. Dallman MF. Stress-induced obesity and the emotional nervous system. *Trends Endocrinol Metab*. 2010; 21:159–165. [PubMed: 19926299]
11. Kiecolt-Glaser JK, Jaremka LM, Andridge R, Peng J, Habash D, Fagundes CP, et al. Marital discord, past depression, and metabolic responses to high-fat meals: Interpersonal pathways to obesity. *Psychoneuroendocrinology*. (in press).
12. Barton AE, Yancy WS. Determining the culprit: Stress, fat, and/or carbohydrates. *Biol Psychiatry*. (in press).
13. Kiecolt-Glaser JK. Stress, food, and inflammation: Psychoneuroimmunology and nutrition at the cutting edge. *Psychosom Med*. 2010; 72:365–369. [PubMed: 20410248]