Author’s response to reviews

Title: The body politic: a reexamination of the cause of obesity-associated disease.

Authors:

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Author’s response to reviews: see over
Dear BMC Public Health,

This paper was forwarded to BMC Public Health at the request of Dr. Phillips, who felt that it was not appropriate for BMC Medicine. This decision may have been made in part because Dr. Chrousos (the second reviewer below) felt that the hypothesis I forward has previously been discussed in the medical literature. To my knowledge, this is the first appearance of this hypothesis. However, given the large body of literature on this topic, this is difficult to verify. I have attached the extensively revised manuscript as well as detailed responses to each reviewer comment. Comments appear in bolded text and responses in regular text. Thank you for considering this paper.

Best,

Peter Muennig

A. Dr. Tremblay

Overview

The paper presented by Dr. Muennig is mainly related to the preoccupation to demonstrate that the stress associated with social stigma and negative body image among obese persons explains some of the weight-associated morbidity that science has previously attributed to adiposity alone. This reviewer read with interest this paper that is innovative regarding the vision presented about co-morbidities of obesity. There are however several suggestions that are presented to improve some aspects of this manuscript.

Even if some references are made to the biological reality that may underly the effects of stress, this reviewer suggests to go a little bit further by trying to incorporate more objective mechanistic observations that could help the reader better understanding why stress could be at least partly responsible of the obesity-related morbidity. Specifically, the following examples refer to some issues that could be considered.

Comments and responses

1. First paragraph of the Results Section: The author refers to regulatory processes without describing which regulation is considered. In this regard, it is relevant to indicate that there is no regulation of triglycerides and cholesterol but there is maybe a regulation of their concentration.

Response: Very true. Please see changes to the second to last paragraph on p. 7, final sentence. Here, I draw upon work done by Dr. Tremblay’s team.

2. Last paragraph of page 12: When the author raises the possibility that the metabolic syndrome be caused by obesity or stress, it would be relevant to consider that variations in body fat might be part of the body strategies to help dealing with stress. In this regard, some comments pertaining to the role of the enzyme beta hydroxysteroid dehydrogenase 1 is certainly of interest regarding the potential role of fat cell metabolism in the management of stress.
Response: This is an important point. Please see changes to p. 18, second paragraph. I also speculate on the impact of fat distribution and type on cytokine secretion on p. 16, 3rd paragraph.

3. Second paragraph, page 19: When the author refers to the influence of genetic factors, it would be relevant to refer to the paper of Tremblay et al (J. Clin. Endocrinol. & Metab. 88: 3141-3145, 2003) demonstrating that the polymorphism of the glucocorticoid receptor influences to a significant extent long term changes in body fatness.

This is an interesting paper that I had overlooked. It raises the possibility of differences in the pathophysiology of folks who are “genetically overweight” versus those who are overweight secondary to environmental. It strikes me that obese people who have healthy metabolic profiles may also be overweight for reasons that greatly differ from overweight people who demonstrate metabolic disruptions. (See comments on p. 20, bottom.)

4. Last paragraph of page 19 continuing in page 20: The author appropriately refers to the case of heavy women in Mauritania who are very obese but non diabetic. Please present statistics about this case. In addition, a more detailed mechanistic description might lead the author to conclude that a certain time delay must elapse between the occurrence of obesity and the manifestation of diabetes.

I have elaborated on this case (please see changes to p. 15 final paragraph and p. 16). This country provides a great research opportunity. Obesity has been in vogue in Mauritania for many years. As a result, women of all ages strive to be heavier rather than thinner. Unfortunately, there is imperfect information on the overall distribution of BMI within the population and its relationship to diabetes.

Nonetheless, this is an important case study. Now with the advent of Western television, one might expect an increase in negative body image (a reversal of cultural norms) over time and the onset of diabetes. That would be fascinating to watch and study. At present, this analysis is highly confounded by the practice of administering prednisone to girls with the sole goal of increasing their body weight. Were one able to control for prednisone consumption, this analysis would add evidence supporting or refuting the psychological stress hypothesis.

6. The author might also be interested to include a brief perspective section in which he would present what could be expected in a foreseeable future about the obesity-related stress and its link with morbidity. Spontaneously, this reviewer would be tempted to believe that the situation might become even worst for obese individuals living in industrialized countries.

This is a great suggestion. I have done so. From body image surveys, it seems that industrializing countries are the last frontier in stigmatizing obesity. As nations industrialize, emphasis turns from being fed to having leisure time. Thus, the stigmatized overweight people of today may have been the stigmatized skinny people of earlier times. This way, we see a strong tie-in to the literature demonstrating that one’s place in a social hierarchy has profound effects on his or her metabolic profile. Please see changes to p. 21, final paragraph through p. 22.

B. Dr. Chrousos

1. The author has to refer to and recognize the scientists that have already proposed that obesity and stress are both increasing morbidity and mortality.

Response: I have not come across studies suggesting that psychological stress associated with stigma is a contributor. If you could provide a reference, I would be very grateful. In this draft, I have placed increased emphasis on the inflammatory hypothesis in the discussion of biological risk factors. Here, I propose that this inflammation arises from social stigma rather than from the endogenous production of
stress mediators from adipocytes.

There is one very interesting intersection between your research and the hypothesis I forward here. That is that there appears to be a strong linkage between cytokine production and stress-induced sleep deprivation/sleep quality in the SES literature. This is something I now mention, and would be interested in exploring further.

2. The article should be toned down and flow better.

Response: I have greatly revised the article, and have asked colleagues to provide additional input on the structure and flow of the article. I hope that it now reads with improved fluidity, clarity, and grace. I have also tempered the language I use throughout (e.g., see p. 18, second paragraph through the bottom of the page).

3. More biology is also necessary in the discussion.

The other reviewer also felt that this was needed. In addition to the points raised and responded to above, I have added more biological explanation throughout. (e.g., see p. 6, first paragraph through p. 8, final paragraph, where I outline the entire neurophysiological pathway involved in both the adiposity/inflammatory pathway as well as the stress response.)