Review of: "Obesity and life events: the hypothesis of psychological phenotypes"

George Bray[1]

1 Pennington Biomedical Research Center

Potential competing interests: No potential competing interests to declare.

Prepared for Qeios January 30, 2023

Review: Obesity and life events: the hypothesis of psychological phenotypes

Reviewer: George A. Bray, MD

Professor of Medicine Emeritus

Pennington Biomedical Research Center

Louisiana State University

Baton Rouge, LA 70808

E-mail: george.bray@pbrc.edu

Funding: None

No Conflicts of Interest.

The commentary by Dr. Amelia Rizzo develops the concept of categorizing people with obesity into different phenotypes, be those psychological, metabolic, genetic or clinical. This is a worthy goal for her review. The title, however, did not describe the diversity of phenotypes which she discussed and a more appropriate title might be “The Hypothesis of Phenotypes for Obesity: Psychological, Metabolic and Clinical”.

In my review of her paper, I have used the headings which she provided. One of the earliest reports that “separated” causes of obesity was the recognition by Babinski in France and Frohlich in Germany at the turn of the 20th century that disease at the base of the brain – hypothalamic damage – could produce loss of appetite control and obesity [1]. This was followed 12 years later with the description by the American neurosurgeon, Harvey Cushing, that a tumor of the pituitary gland could also produce obesity [2]. Subsequently in 1953 Jean Mayer proposed use of genetic, traumatic and environmental factors as phenotypes for obesity [3], and in 1978 Bray and York proposed an anatomic and etiological classification with elements similar to those that Rizzo has developed in her paper [4].

Rizzo accepts the definition of obesity as excess adiposity and the concept that it must result from energy imbalance. The author’s point about the difficulty of maintaining weight loss is well taken. I would take exception with the use of “new normal weight” to define the weight after weight loss and prefer “new lower weight”. Weight regain after weight loss is the

usual outcome of treatment programs, and the lower weight is thus not a “new normal weight”, but rather a new, probably temporary, lower one.

There must be some “permanent” change in the regulatory systems for energy balance in the brain that prevents obesity from being easily reversed with a return to a lower weight. I am also not sure that “stigmatization” is involved in the failure of maintain weight loss as the author seems to imply.

Rizzo does a nice job when discussing “behavioral” phenotypes as an explanation for obesity. Like Dr. Rizzo, I view the studies of Hilde Bruch as seminal in understanding pediatric obesity. Rizzo concludes this section by saying that no personality, psychopathology or psychological profile could be identified to unify the causes of obesity. Since a unifying psychological cause couldn’t be identified behavioral scientists turned their attention to understanding the way in which people with obesity are psychologically impacted by their obese state.

Obesity Metabolic Phenotypes

The discussion of metabolic phenotypes by Rizzo focuses on 4 phenotypes that are very nicely described in the article by De Lorenzo et al [5]. These are (1) individuals with normal weight who are obese (NWO); (2) those that are metabolically obese but of normal weight (MONW); (3) individuals with metabolically healthy obesity (MHO); and (4) metabolically unhealthy obese (MUO) who have or are at risk for the metabolic syndrome.

There are 2 issues that confront this classification. First, the individual is identified at a single time point. As time passes the effects of obesity may change the individual and thus the category. Since in the words of the World Obesity Association, obesity is a “chronic relapsing disease process” identifying people at risk before other diseases develop is a desirable clinical goal [6]. It is now clear that many, if not most, individuals classified with “metabolically healthy obesity” will eventually convert to individuals with one or other disease associated with obesity. Thus, the time frame of reference becomes important since changes often happen slowly as we age.

The second issue confronting the use of Metabolic Phenotypes is related to the need for data bases of body fat and its distribution at different ages, taking gender into consideration. We know that women have more fat than men. We also know that as people grow older the proportion of fat in both males and females increases, with many older people developing “sarcopenic” obesity with loss muscle mass relative to fat mass. To define metabolic phenotypes we need to have tables showing appropriate levels of fat relative to age and sex – tables which do not currently exist. The challenge of getting detailed information about body fat and its distribution may be solved by use of optical scanning techniques now under development [7].

Individual Differences in Obesity History

Individual differences between people with obesity and their response to treatment were introduced by Rizzo in the section on Obesity and Metabolic phenotypes and are highlighted here. Variability between individuals during weight loss is evident with all techniques for weight loss including diet, exercise, lifestyle, medication and surgery [8] and in the studies

of identical twins in response to overfeeding by Bouchard and his colleagues [9].

This section also discusses the age of onset for obesity and factors that are associated with the beginning of weight gain. Rizzo identifies many triggers that occur at the onset of obesity. These triggers take on a different perspective when considering the obesity epidemic as a whole. An article by Rodgers et al in 2018 traces the change in BMI for many subgroups of the US population from 1962 to the year 2000[10]. They show that the US epidemic of obesity began about 1975 in all age, sex and ethnic groups and continued over the next 25 years. This fact limits the plausible explanations for the current epidemic of obesity. Rodgers and colleagues believe that it is implausible that each age, sex and ethnic group, with massive differences in life experience and attitudes, to have a simultaneous decline in willpower related to healthy nutrition or exercise, or that intrauterine exposures played a major causative role. Likewise changes in genetic make-up are unlikely to have occurred over this short period and to have affected all age groups simultaneously. Similarly, they note that it is unlikely that any factor with a long induction period had a major role in the US epidemic. Rather they believe that the epidemic must have been caused by factors that led to rapid population-wide changes such as changes in the food supply. I agree with their conclusion.

Obesity, Life Stressors and Emotional Abuse

The issue of sexual abuse as discussed in this section again runs into the dilemma noted above by Rodgers et al – that something happened to the population as a whole to produce the epidemic and sexual abuse would seem an unlikely candidate. This does not mean that individual experiences don't modify the outcome or course of obesity, but they are primarily of value for the individual practitioner treating an individual patient with obesity.

When considering "internal" signals, Rizzo could have discussed the functional phenotypes that Acosta and colleagues [11] used to classify obesity and predict response to treatment. Acosta et al identified 4 functional phenotypes one or more of which was present in 85% of their patients (383 of 450 participants). These included: (1) "the hungry brain" which they defined functionally as abnormal satiation); (2) emotional hunger or hedonic eating; (3) The "hungry gut" which was defined by abnormal satiety; (4) and finally "slow burn" which was identified as a decrease in metabolic rate. In 15% of participants, no phenotype was identified, and 27% of their patients had two or more phenotypes.

Surgical and Treatment Outcomes

The fact that some cases of bariatric surgery are labelled as "unsuccessful" is similar to the findings with all treatments for obesity [8]. As noted by Rizzo, bariatric surgery can improve behavioral outcomes and that some people no longer eat in response to emotional cues. One of the most intriguing features of bariatric surgery is that the offspring tend not to be fat and develop fewer metabolic abnormalities. The bariatric surgery or the changed metabolic milieu appears to change epigenetic signals which permit reversal of the higher set-point that seems to occur with slow weight gain making it difficult to maintain a lower weight after losing weight [12][13]

Conclusions and Psychotherapeutic Indications

In my review of the paper by Dr. Rizzo of phenotypes for obesity, I have noted the limitations in concept of metabolically healthy obesity since most of the individuals who are “healthy” at the initial measurement will develop the “unhealthy” phenotype over the course of time, since obesity is a chronic, relapsing disease process. I also needed that data on the age and sex distribution of body fat and lean body mass were needed. In the discussion of individual differences in onset of obesity I referenced the fact that the US epidemic seemed to begin in all segments of the population at the same time – around 1975 – which limits the number of potential explanations for its origin. Finally there are other phenotypes that could have been dealt with including treatment related phenotypes, and those that use distribution of body fat to develop predictions for future risk.

References

1. ^*Bray, G.A. Commentary on classics of obesity 4. Hypothalamic obesity. Obes Res 1(4):325-328, 1993.*
2. ^*Bray, G.A. Harvey Cushing and the neuroendocrinology of obesity. Obes Res 2:482-485, 1994.*
3. ^*Mayer J, Genetic, traumatic and environmental factors in the etiology of obesity. Physiol Rev. 1953 Oct;33(4):472-508. doi: 10.1152/physrev.1953.33.4.472. PMID: 13100066)*
4. ^*Bray G.A. and D.A. York. Hypothalamic and genetic obesity In experimental animals: An autonomic and endocrine hypothesis. Physiol Rev 59(3):719-809, 1979.*
5. ^*De Lorenzo A, Soldati L, Sarlo F, Calvani M, Di Lorenzo N, Di Renzo L. New obesity classification criteria as a tool for bariatric surgery indication. World J Gastroenterol. 2016 Jan 14;22(2):681-703. doi: 10.3748/wjg.v22.i2.681. PMID: 26811617*
6. ^*Bray GA, Kim KK, Wilding JPH. Obesity: A Chronic Relapsing Progressive Disease Process: A Position Paper of World Obesity. Obes Rev 2017 Jul;18(7):715-723.*
7. ^*Tinsley GM, Moore ML, Benavides ML, Dellinger JR, Adamson BT. 3-Dimensional optical scanning for body composition assessment: A 4-component model comparison of four commercially available scanners. Clin Nutr. 2020 Oct;39(10):3160-3167.*
8. [a, b]*Bray GA, Ryan DH. Evidence-Based Weight Loss Interventions: Individualized Treatment Options to Maximize Patient Outcomes. Diabetes Obes Metab. 2021 Feb;23 Suppl 1:50-62. doi: 10.1111/dom.14200. Epub 2020 Nov 24. PMID: 32969147*
9. ^*Bray GA, Bouchard C. The Biology of Human Overfeeding: A Systematic Analysis. Obes Rev. 2020 Sep;21(9):e13040. Jun 8. doi: 10.1111/obr.13040. Online ahead of print. PMID: 32515127*
10. ^*Rodgers A, Woodward A, Swinburn B, Dietz WH. Prevalence trends tell us what did not precipitate the US obesity epidemic. Lancet Public Health. 2018 Apr;3(4):e162-e163. doi: 10.1016/S2468-2667(18)30021-5. Epub 2018 Mar 1. PMID: 29501260*

11. ^*Acosta A, Camilleri M, Abu Dayyeh B, Calderon G, Gonzalez D, McRae A, Rossini W, Singh S, Burton D, Clark MM. Selection of Antiobesity Medications Based on Phenotypes Enhances Weight Loss: A Pragmatic Trial in an Obesity Clinic. Obesity (Silver Spring). 2021 Apr;29(4):662-671. doi: 10.1002/oby.23120. PMID: 33759389)*
12. ^*Kral JG, Biron S, Simard S, Hould FS, Lebel S, Marceau S, Marceau P. Large maternal weight loss from obesity surgery prevents transmission of obesity to children who were followed for 2 to 18 years. Pediatrics. 2006 Dec;118(6):e1644-9. doi: 10.1542/peds.2006-1379. PMID: 17142494*
13. ^*Guénard F, Deshaies Y, Cianflone K, Kral JG, Marceau P, Vohl MC. Differential methylation in glucoregulatory genes of offspring born before vs. after maternal gastrointestinal bypass surgery. Proc Natl Acad Sci U S A. 2013 Jul 9;110(28):11439-44. doi: 10.1073/pnas.1216959110. Epub 2013 May 28. PMID: 23716672*