Microbial Causes of Post-Dieting Weight Regain

A Critique

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December 05, 2016

Introduction

Post-dieting weight regain ("yo-yo effect") poses a substantial problem in weight management. Within the biopsychosocial model, not only social and habitual factors may contribute to post-dieting weight increase. Biological alterations may counteract habitual changes following prior psychotherapy. Subjective patient reports may point towards biological factors that psychologists need to include in their evaluation. There recently has been an increased study interest in the connection between alterations in the gut microbiome and its effect on metabolism as well as psychological conditions. Suez et al. (2014) established a link between the use of sweeteners and alterations in the gut microbiome with significant offset of metabolism. Thaiss et al. (2016b) report microbiota influence on circadian rhythms. Chorbak, Nowakowski, & Dudek (2016) summarized literature concluding "an association between large intestine microbiome and central nervous system functioning in humans." (p. 9). Particularly, Thaiss et al. (2016a)[1] explored weight regain after repeated bouts of high fat diet (HFD) with subsequent weight reduction

[1] Due to the preliminary nature of this accelerated article preview, page numbers may only be in reference to page numbering within the retrieved PDF file, cited with download link and DOI in the reference list.

phases in the mouse model, establishing a causal link between diet-induced changes in gut microbiome and post-diet fat metabolism.

Summary and Literature Research

The appropriate title establishes a clear link ("modulates") between microbiome alterations and post-dieting weight regain, although relevant variables are condensed. The statement is well-founded on the analysis of subsequently elaborated laboratory experiments. Thaiss et al.'s (2016a) study was conducted by 20 contributing researchers, 10 of whom were affiliated with the Elinav Lab of Weizmann Institute of Science at Rehovot, Israel, which advertises on personalized medicine, with the lab's principal investigator, Erin Elinav, mentioned last. An extensive list of supporting institutions and persons is given, and the contributing role of each researcher specified (p. 6). It is noteworthy that three studies on the effect of microbiota, quoted in the introduction to this critique, were incidentally conducted by members of the same institute, possibly owing to their citation in the news aggregator ScienceDaily.

Thaiss et al. include all relevant stages of the study (feeding and dieting experiments, microbiome alterations and analysis, predictive algorithms, flavonoid tracking and intervention stage) in their abstract, only briefly highlighting their results owing to the comprehensiveness of the study. References to probable treatments are backed up by experiment (antibiotic treatment and flavonoid substitution). Relevant flavonoids, although of therapeutic interest, were however only mentioned in the body of the study. This may be seen as a marketing approach to a journal article (ibid., pp. 2-6).

The literature review appears reasonably sized and well-founded in current research, citing 11 relevant titles, but no more than two sources to back up one singular argument, exploring social, physical, and biological axes. Purpose of the research is clearly stated in

exploring a gap in literature by determining biological causes of post-diet weight regain, defining major key-terms (metabolic homeostasis, non-genetic factors, weight cycling, and microbiome dysbiosis; ibid., p. 2).

Study Design and Results

Basing on a mouse model, the study does not rely on sampling or randomization, but introduces germ-free mice as relevant control group. Methods and sources for acquisition are specified as "littermates born and raised in the same vivarium and obtained through a single delivery" in all experiments (ibid., pp. 13-14). Detailed descriptions for mouse maintenance, glucose tolerance tests, imaging, metabolism evaluation, analysis of microbiota, classification and prediction of obesity, genomic analysis and expression, flavonoid measurements and blot analyses are given including used equipment, procedures and relevant units.

Independent variables are clearly defined as continuous "high-fat diet (HFD)", defining one cyclic consumption group ("cycHFD"), one single cycle HFD group ("primHFD"), and normal chow control group ("NC"), and subsequently antibiotics administration, microbiota transplantation or flavonoid substitution. Dependent measures include weight, weight gain, blood glucose, serum leptin and lipoprotein levels, energy expenditure, microbiota composition, bacterial operational taxonomic units (OTUs), Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways, and metabolite profile including apigenin and naringenin. Two-tailed Mann-Whitney U-tests were used on 2-group comparisons, with ANOVA analyses on multiple groups, with a significance threshold of $p < .05$, providing exact p-values for experiments in supplementary tables. Raw data are provided and sequencing data has been submitted to the European Nucleotide Archive. An abundance of relevant graphs is provided by experiment and relevant group, including scatter graphs, line graphs and error bar graphs, indicating significance

for each chart by star notation (* $p < .05$, ** $p < .01$, *** $p < .001$, **** $p < .0001$). Experiments are conducted including all four independent feeding and treatment groups respectively and number of cases given.

The article is clearly structured according to the progression of experiment: weight regain pattern, persistent changes of gut microbiome, factors for increased weight regain, predictive power of microbiota composition, role of metabolites, and isolation of relevant flavonoids along with their regulatory pathway on fat metabolism. The sequence of experiments is conclusive with cross-experiment methods detailed in separate sections. Treatment procedures are specified in detail and researcher roles clearly credited. In addition to specific information on the analytical methods and verbal discussion on the highlights of each experiment in the sequence, elaborate footnotes detail the graph sheet accompanying each experiment (ibid., pp. 7-12, 15-27).

Discussion

The brief discussion is classically framed by revisiting the initial hypotheses. As results, the obesogenic property of microbiota after transplant even in NC mice and persistence in changes of microbiota are emphasized. References in the discussion section partially refer back to reviewed literature, and additional references are given, attempting to frame observed behaviour. Phrasing of conclusions is careful and considerate ("findings described here suggest that," or, "metabolite therapy could serve as potential means") and points back to results whose significance has been established by the study ("obesity-induced loss of flavonoids", "replenishment" and subsequent "amelioration"). Suggestions for future studies specify clinical examination of metabolite substitution (ibid., p. 5).

In conclusion, the discussion is well-rounded and effective for the conducted experiments and obtained results. Obesity is one of the major contemporary health concerns, yet its underlying

biological complexities are still far from being thoroughly understood. In highlighting the role of microbiome alternations, and specifically depletion of certain flavonoids that play a substantial role in maintaining fat metabolism, the study makes a considerable contribution to the understanding of weight management and potential therapeutic interventions. The mouse model has been established for researching metabolic effects and their transfer to human physiology, however there is critique, for example, about the generalizability of neurodegenerative effects (Burns et al., 2015). The metabolic pathways investigated in Thaiss et al.'s study appear to be verified in both mouse model and human physiology. Internal medicine, as a discipline, trends from checking against standardized mean-values towards an individual approach within the biopsychosocial context. The reviewed study makes a substantial contribution paving the way toward that goal.

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