EBioMedicine 2 (2015) 806–807

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

You Lose Some, You Win Some: Weight Loss Induces Microbiota and Metabolite Shifts

Elisabeth M. Bik

Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, CA 94305, USA

Obesity is an increasing problem worldwide. Nearly 30% of the world's population is overweight or obese, and this number is on the rise (Ng et al., 2014). Because high body-mass index is a strong risk factor for chronic conditions such as cardiovascular disease and diabetes, and is associated with increased mortality, the growing obesity rates are expected to have a significant impact on quality and expected length of life in the future (Prospective Studies Collaboration, 2009). Although obesity could simply be viewed as an imbalance between caloric intake and metabolism, work in the past decade has revealed an important role of the gut microbiota – the microbial communities present in our intestinal tract – in obesity as well (Turnbaugh et al., 2009). Gut microbes can extract calories from food that we humans cannot digest ourselves, and the composition of the gut microbiota from lean individuals has been shown to be distinct from that of obese persons (Ley, 2010). In addition, stool microbiota from human twin pairs discordant for obesity could transmit the obese phenotype to germ-free mice, suggesting that the gut microbiota plays an active role in obesity (Ridaura et al., 2013).

In this issue of EBioMedicine, Zhang et al. study the effect of weight loss on the gut microbiota and metabolism of severely obese children (Zhang et al., 2015). About half of these children had "simple obesity" (SO) without underlying pathology, while the other group had been diagnosed with Prader–Willi Syndrome (PWS). PWS is a rare genetic disorder caused by defects on chromosome 15, and is characterized by typical facial features, short stature, small hands, and motoric, behavioral, and learning problems (Cassidy et al., 2012). Furthermore, most PWS patients are always hungry and never feel full, often leading to morbid obesity in these subjects at a young age.

In the current study, SO and PWS children were hospitalized for a month and put on a strict diet rich in non-digestible carbohydrates. The intervention was very successful. Children in both groups lost 8–10% of their initial bodyweight and showed significant improvements in metabolic parameters and inflammation markers. Using bacterial profiling as well as metagenomic analysis, the authors found that the gut microbiotas of SO and PWS groups were very similar to each other, both before and after the intervention. This suggests that the underlying causes of obesity are less important determinants of microbiota composition than the differences between obese and lean persons. However, both cohorts showed significant microbiota shifts after the dietary intervention, with increased abundance of gene pathways for carbohydrate metabolism and decreased presence of fat and protein metabolism genes. The weight loss was associated with dramatic metabolite changes as well. In stool samples, non-digestible carbohydrates and certain short chain fatty acids increased, while particular toxic bacterial metabolites went down. Similar changes were seen in the urine samples, where human metabolites of bacterial synthesized compounds decreased significantly after the intervention. Finally, by transplanting before- and after-intervention stool samples from the same PWS patient into germ-free mice, the authors showed that the pre-diet stool samples had a higher capacity to induce gut inflammation and fat accumulation than the post-intervention gut microbiota from the same subject (Zhang et al., 2015).

Surprisingly, both the number of bacterial species as well as microbial gene richness decreased after dietary intervention. This is contrast to findings in another study where the gut microbiota of lean persons contained higher numbers of bacterial sequence types and phylogenetic diversity than that of obese persons (Turnbaugh et al., 2009). A recent paper, however, found a bimodal distribution of low and high microbial gene content among the stool microbiotas of both obese as well as lean persons (Le Chatelier et al., 2013). Together with the current findings, this suggests that it might be too simplistic to assume that the healthy gut from a lean person is characterized by high bacterial species counts and gene diversity.

The study by Zhang et al. further unravels the complex interactions between microbes and their hosts in health and disease. Strengths of this study are the use of human subjects instead of animal models, and the combination of complementary molecular approaches that allow finding correlations between bacterial genomes, metabolites, and clinical parameters during a strictly supervised dietary intervention. However, several questions remain. Although the diet intervention was successful in the short timespan of the study, it was not clear if the weight loss and microbiota changes were permanent. The probability that a person who loses weight can keep it off was recently estimated to be less than 50% (Fildes et al., 2015). The long-term weight and microbiota composition of these children will hopefully be addressed in a follow-up study. In addition, it is still unclear which specific bacteria are responsible for the inflammatory or toxin-synthesizing properties of stool samples from obese children. Learning more about the individual bacterial species involved in the dysbiosis found in obesity will provide us with better tools to fight this rising epidemic.

Disclosure

The author declared no conflicts of interest.

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2015.07.007.

http://dx.doi.org/10.1016/j.ebiom.2015.07.037

References

Cassidy, S.B., Schwartz, S., Miller, J.L., Driscoll, D.J., 2012. Prader–Willi syndrome. Genet. Med. 14 (1), 10–26. http://dx.doi.org/10.1038/gim.0b013e31822bead0 (Jan).

Fildes, A., Charlton, J., Rudisill, C., Littlejohns, P., Prevost, A.T., Gulliford, M.C., 2015. Probability of an obese person attaining normal body weight: cohort study using electronic health records. Am. J. Public Health 16, e1–e6 (Jul).

Le Chatelier, E., Nielsen, T., Qin, J., Prifti, E., Hildebrand, F., Falony, G., et al., 2013. Richness of human gut microbiome correlates with metabolic markers. Nature 500, 541–546. http://dx.doi.org/10.1038/nature12506 (29 August).

Ley, Ruth E., 2010. Obesity and the human microbiome. Curr. Opin. Gastroenterol. 26 (1), 5–11 (January).

Ng, M., Fleming, T., Robinson, M., Thomson, B., Graetz, N., Margono, C., et al., 2014. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 384 (9945), 766–781. http://dx.doi.org/10.1016/S0140-6736(14)60460-8 (Aug 30, The Lancet. DOI: http://dx.doi.org/10.1016/S0140-6736(14)60460-8).

Prospective Studies Collaboration, 2009. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet 373 (9669), 1083–1096. http://dx.doi.org/10.1016/S0140- 6736(09)60318-4 (28 March–3 April).

Ridaura, V.K., Faith, J.J., Rey, F.E., Cheng, J., Duncan, A.E., Kau, A.L., Griffin, N.W., Lombard, V., Henrissat, B., Bain, J.R., Muehlbauer, M.J., Ilkayeva, O., Semenkovich, C.F., Funai, K., Hayashi, D.K., Lyle, B.J., Martini, M.C., Ursell, L.K., Clemente, J.C., Van Treuren, W., Walters, W.A., Knight, R., Newgard, C.B., Heath, A.C., Gordon, J.I., 2013. Gut microbiota from twins discordant for obesity modulate metabolism in mice. Science 341 (6150), 1241214. http://dx.doi.org/10.1126/science.1241214 (Sep 6).

Turnbaugh, P.J., Hamady, M., Yatsunenko, T., Cantarel, B.L., Duncan, A., Ley, R.E., Sogin, M.L., Jones, W.J., Roe, B.A., Affourtit, J.P., Egholm, M., Henrissat, B., Heath, A.C., Knight, R., Gordon, J.I., 2009. A core gut microbiome in obese and lean twins. Nature 457 (7228), 480–484. http://dx.doi.org/10.1038/nature07540 (Jan 22, Epub 2008 Nov 30).

Zhang, C., Yin, A., Li, H., Wang, R., Wu, G., Shen, J., et al., 2015. Dietary Modulation of Gut Microbiota Contributes to Alleviation of Both Genetic and Simple Obesity in Children. EBio. Med. 2, 964–980.