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Insulin resistance as key factor for linking modulation of gut microbiome to health claims and dietary recommendations to tackle obesity

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ABSTRACT

Background: Current dietary and public health recommendations addressing obesity do not as yet include recommendations pertaining to the gut microbiome. As a corollary, no microbiome-related health claims made on foods have as yet been proposed.
Scope: The MyNewGut project aims, amongst others, to provide guidance for the establishment of dietary and public health recommendations related to the role microbiome in the onset and development of obesity. Moreover, the project's forthcomings should allow the compilation of a guidance document for microbiome-related health claims.
Key findings: Of all the physiological effects resulting from changes in the microbiome, insulin resistance is the most direct diet-modifiable parameter related to obesity. Improving insulin resistance is considered to be the key health benefit conferred by the targeted modulation of the gut microbiome, through the development and application of foods containing microbiome-targeted fibers and micro-organisms.
Conclusions: In order to facilitate guidance for the development of public health and dietary recommendations, as well as for health claim substantiation related to the gut microbiome, foods containing microbiome-targeting dietary fibers and microorganisms will be developed and studies with these foods should provide for the total body of clinical evidence specifically addressing the central theme of 'insulin resistance' in obesity, still leaving ample room for the inclusion of other parameters of interest. The latter is pivotal since an impact of other parameters on obesity should be addressed as well, particularly in view of the multifaceted modes of action of the microbiome.

1. Introduction

The project MyNewGut (FP7-KBBE-2013-7) is the EU-funded project devoted to unravel the influence of the gut microbiome on energy balance and brain development and function put into action to tackle diet-related diseases and behaviour. Primary objectives of the project are to fuel the development of microbiome-based dietary recommendations and interventions targeting the gut ecosystem, which can provide cost-effective measures to reduce the socioeconomic burden of diet-related diseases and, in particular, obesity and chronic-metabolic and behavioural disorders.

In addition, MyNewGut aims to provide proof-of-concept of reducing the risk and consequences of metabolic and brain-related disorders via intervention in the gut ecosystem with specific diets and innovative food ingredients and prototypes.

Worldwide, current dietary recommendations and their scientific background documents don't refer to the role of the gut microbiome. The Dietary Guidelines Advisory Committee for the 2015 guidelines for Americans conducted an exploratory search on the relationship between the role of the microbiome and various health outcomes but did not find sufficient evidence to address this question in the 2015 report. However, the Committee considered the microbiome to be an emerging topic of potential importance to future dietary guidelines (USDA Dietary Guidelines Advisory Committee, 2015).

In Europe, a large number of health claims referring to the importance of probiotics and prebiotics for specific health benefits

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have been proposed and evaluated by the European Food Safety Authority (EFSA). However, none of proposed claims pertaining to probiotics and their health benefits have been authorised, whereas the authorised health claims for dietary fibres don't pertain, as yet, to their prebiotic role in favourably modifying the composition of the human microbiome.

2. The issue

Obesity is one of the greatest public health challenges of the 21st century. In addition to causing various physical disabilities and psychological problems, excess weight drastically increases a person's risk of developing a number of non-communicable diseases, including cardiovascular disease, cancer and diabetes. Moreover, obesity not only impacts on individual health but has serious consequences for societies as a whole through an increased burden on health care systems. The prevalence of overweight and obese people in Europe is over 50%, of which 20% is in fact obese (Fig. 1). Of more recent date is the alarming significant development of overweight and obesity in children (Fig. 2).

A high-caloric diet and sedentary lifestyle seem to be among the primary driving forces of obesity though the pathological molecular processes that link a poor diet to obesity are still poorly defined. Furthermore, the key mediators that are essential checkpoints for the development of obesity and could potentially be targeted for prevention and therapy are also largely unknown. Nevertheless, insulin resistance appears to be the common denominator shared by many of the obesity-related physiological derailments including adiposity and appetite control (Kahn, 2000; Turnbaugh et al., 2006; Anthony et al., 2006; Zhao, 2013; Williams & Wu, 2016, Fig. 3).

3. What is overweight and obesity?

Overweight and obesity are defined as abnormal or excessive fat accumulation that may negatively impact on health (WHO, 2015). A measure of overweight and obesity is provided for by the Body Mass Index (BMI). BMI is a simple index of weight-for-height that is commonly used to classify overweight and obesity in adults. It is defined as a person's weight in kilograms divided by the square of his height in meters (kg/m^2). A BMI equal to or greater than 25 is termed "overweight" whereas a BMI equal to or greater than 30 indicates "obesity".

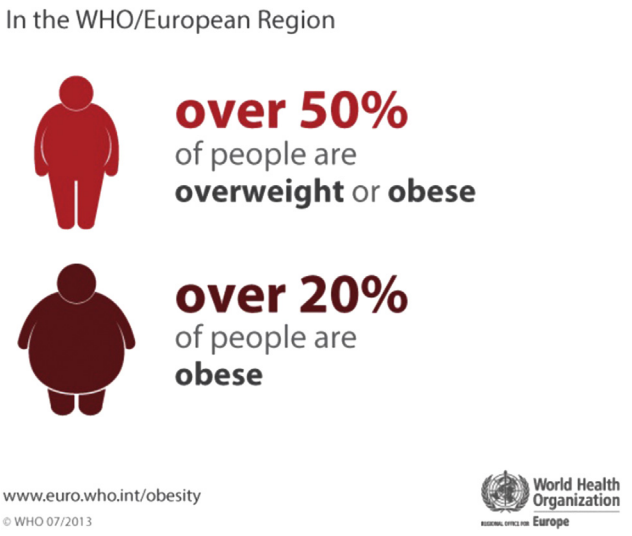

Fig. 1. Prevalence of overweight and obesity in Europe (WHO, 2015; http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/data-and-statistics/infographic-over-50-of-people-are-overweight-or-obese-download. Accessed 3 May 2016; reproduced with permission).

Fig. 2. Prevalence of overweight and obesity in 11-year-olds in Europe (WHO, 2015; http://www.euro.who.int/en/health-topics/noncommunicable-diseases/obesity/data-and-statistics. Accessed 3 May 2016; reproduced with permission).

BMI provides the most useful population-level measure of overweight and obesity as it is the same for both sexes and for all ages of adults. However, BMI should be considered a rough guide because it may not correspond to the same degree of fatness in different individuals (World Health Organization (WHO), 2015).

Indeed differences in whole-body obesity versus abdominal obesity may be obscured by just relying on BMI measurements. Després et al. (1990) showed that a subgroup of obese patients with metabolic abnormalities such as insulin resistance, low high-density lipoprotein and cholesterol atherogenic dyslipidemia were characterised by an excess of abdominal visceral adipose tissue, whereas those obese patients who had a normal metabolic risk profile were characterised by low levels of visceral adipose tissue and, instead, by subcutaneous obesity.

Of importance in this respect is that abdominal fat accumulation as assessed by waist circumference measurement is a more reliable and physiologically relevant indicator of obesity, with great implications to health. Moreover, features of fat accumulation differ between men and women and, hence, the risk of obesity related metabolic derailments, especially insulin resistance. Indeed, greater amounts of visceral and hepatic adipose tissue, in conjunction with the lack of a possible protective effect of oestrogen, may be related to a higher incidence of insulin resistance in men compared with women (Geer & shen, 2009).

4. The microbiome and obesity

The hallmarks of obesity are accumulation of excess abdominal body fat, chronic systemic low-grade inflammation and insulin resistance (Fig. 4). Excessive fat accumulation and impaired glucose homeostasis (insulin resistance) are strongly impacted by changes in the gut microbiota. Indeed, an increasing number of studies relate imbalances in the composition of the gut microbiota to obesity, insulin resistance and its associated diseases (reviewed in Zhao, 2013).

The host-microbiome interactions are multiple and complex. In relation to obesity numerous, yet partly understood mechanisms appear to be at work. Research focused on these mechanisms has shown unfavourable effects of shits[1] in:

- Insulin resistance
- Microbiota composition
- Sub-chronic inflammation

[1] List non-exhaustive.