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A Review on Obesity, Eating habits and genotype

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ABSTRACT

Obesity has been increasing at an alarming rate worldwide during past decades. Accordingly, the World Health Organization described obesity as a global epidemic. Obesity is usually associated with many metabolic abnormalities including dyslipidemia, insulin resistance and hyperglycemia, and increased risk of coronary heart disease, type 2 diabetes, asthma, sleep apnea, hypertension, certain cancers, and all-cause mortality. Obese and non-obese people vary in genes that could influence behaviors (such as a drive to over eat, or a tendency to be sedentary) or metabolism. Overweight and obesity tends to be higher in countries with high fat intakes. Obese people usually have mutations in the gene that codes for leptin. These mutations are often of the frame-shift type and lead to a complete loss of function in the resulting protein. Humans with such mutations overeat and become very obese. Weight gain essentially arises from an imbalance of energy supply and energy expenditure. Therefore it is not surprising that dieting (restriction of energy input) and exercise (increased energy output) are both recommended to reduce body weight and also for their additional health benefits.

Keywords: Obesity, Eating habit, genotype, gene and body weight.

INTRODUCTION

Childhood obesity has been defined as the XXI century epidemic by the World Health Organization (WHO) and it is presently one of the major public health challenges in developed countries [1]. In the United States, the prevalence of obesity in 2008 was 20% in boys and girls 6 to 11 years of age and 18% in youths 12 to 19 years of age, percentages three times as high as those observed in 1980 [2]. The prevalence of obesity has been increasing at an alarming rate worldwide during past decades [4]. Accordingly, the World Health Organization has described obesity as a “global epidemic [5]. In the United States, it is estimated that >60% of adults are either obese or overweight. The number of children and adolescents who are considered overweight (i.e., ≥95th percentile) or at risk for overweight (i.e., ≥85th percentile) has increased similarly. Obesity is usually associated with many metabolic abnormalities including dyslipidemia, insulin resistance and hyperglycemia, and increased risk of coronary heart disease, type 2 diabetes, asthma, sleep apnea, hypertension, certain cancers, and all-cause mortality [6]. On the other hand, an unhealthy diet, skipping breakfast or inadequate intake at breakfast and sedentarism have been identified as lifestyles associated with obesity in childhood and adolescence [7]. Classic genetic analyses performed in families, adoptees, and twins have clearly shown there is a genetic contribution to obesity [8]. The recent advances in genome-wide association (GWA) mapping holds tremendous potential for contributing to the

identification of human obesity genes and provides deeper insight into the genetic effects on obesity development [8]. Several genes such as *FTO* (fat mass and obesity associated) and *MC4R* (melanocortin-4 receptor) identified by GWA scans have been convincingly associated with obesity risk in various populations [9]. Obesity is a multifactorial abnormality that has a genetic basis but requires environmental influences to manifest [10]. Numerous epidemiological studies and clinical trials have examined the roles of lifestyle (physical inactivity) and dietary factors (fat, carbohydrates, protein, and minerals) in obesity prevention and weight control [11]. Several dietary guidelines have been implemented in the US for many years to improve the health of the general population and of those at high risk for specific diseases [cardiovascular disease (CVD), cancer, hypertension, and diabetes] [12]. However, past and current dietary guidelines have not been able to properly address and integrate the dramatic differences on the individual's physiological response to changes in nutrient intake [13]. These differences in response may greatly affect the efficacy of these recommendations at the individual level [14]. The mechanisms responsible for the inter individual differences in dietary response are very complex and poorly understood.

Genotype and Obesity

Genotype-environment interactions arise when the response of a phenotype (eg, fat mass) to environmental changes (eg, dietary intervention) is modulated by the genotype of the individual [11]. There are 2 different levels on which genotype-environment interaction effects could be relevant for obesity. Firsty, they could be involved in determining the susceptibility to gain fat in response to environmental risk factors such as a high-fat diet or a low physical activity level [13]. Secondly, genotype-environment interaction effects could also be involved in the susceptibility of obese individuals to develop comorbidities associated with obesity (eg, diabetes, hyperlipidemia, hypertension, and coronary heart disease) or in response to treatment [16]. Genes give the body instructions for responding to changes in its environment [3]. Studies of resemblances and differences among family members, twins, and adoptees offer indirect scientific evidence that a sizable portion of the variation in weight among adults is due to genetic factors [6]. Other studies have compared obese and non-obese people for variation in genes that could influence behaviors (such as a drive to overeat, or a tendency to be sedentary) or metabolism (such as a diminished capacity to use dietary fats as fuel, or an increased tendency to store body fat) [7]. These studies have identified variants in several genes that may

contribute to obesity by increasing hunger and food intake. Rarely, a clear pattern of inherited obesity within a family is caused by a specific variant of a single gene (monogenic obesity) [8]. Most obesity, however, probably results from complex interactions among multiple genes and environmental factors that remain poorly understood (multifactorial obesity) [3]. Any explanation of the obesity epidemic has to consider both genetics and the environment. One explanation that is often cited is the mismatch between today's environment and "energy-thrifty genes" that multiplied in the distant past, when food sources were unpredictable. In other words, according to the "thrifty genotype" hypothesis, the same genes that helped our ancestors survive occasional famines are now being challenged by environments in which food is plentiful year round [4]. Other hypotheses have been proposed including a role for the gut microbiome as well as early life exposures associated with epigenetic changes [3]. With the exception of rare genetic conditions associated with extreme obesity, currently, genetic tests are not useful for guiding personal diet or physical activity plans [2]. Health care practitioners routinely collect family health history to help identify people at high risk of obesity-related diseases such as diabetes, cardiovascular diseases, and some forms of cancer [4]. Family health history reflects the effects of shared genetics and environment among close relatives. Families can't change their genes but they can change the family environment to encourage healthy eating habits and physical activity [8]. Those changes can improve the health of family members and improve the family health history of the next generation [7]. The phenotype commonly used in population-based studies of obesity is BMI. BMI does, however, not specify whether excess body mass is due to excess fat mass and how the body fat is distributed [8]. It is rather easy to assess BMI by self-report, since most people know their approximate height and weight. Using self reported information on height and weight does, however, intro-duce bias, since both men and women tend to over-report their height and especially women tend to underreport their weight with increasing level of overweight [9]. When calculating BMI this misreporting leads to an underestimation of BMI. Waist circumference is becoming more and more common in population-based studies because of the increasing evidence of the association between waist circumference and especially waist for given BMI and increased risk of co-morbidity and mortality [7]. Waist circumference can be assessed by self-report, but the best data are obtained by objective measurement. Other anthropometric phenotypes such as skin fold thicknesses, fat body mass and lean body mass are not assessable by self-report and the techniques (DXA, MRI) for assessing body fat mass are timely and

costly [4]. Large family-based studies in different populations have consistently demonstrated a familial correlation in adult body mass index BMI, at about 0.2 between parents and offspring and atabout 0.3 between siblings [13]. The development within the field of molecular genetics has made genotyping more accessible and affordable. It is now possible to perform genome-wide-scans of even more than 300,000 single nucleotide polymorphisms (SNPs) on large numbers of subjects [14]. This has lead to identification of ~20 common SNPs associated with BMI [15]. The SNP with the largest effect size is the rs99395609 in the fat mass and obesity associated (FTO) gene [11]. Also SNPs (rs17782313, rs17700633 and rs12970134) near the melanocortin-4 receptor (MC4R) gene have been found to be associated with increased BMI [12]. The function of the SNPs identified in the genome-wide-association studies (GWAS) is currently unknown and need to be further investigated.

Lifestyle and Dietary Effects

The role of dietary fat in the etiology of obesity was addressed in several studies but remains controversial [7]. It is generally accepted that high-fat diets induce an overconsumption of energy, which can lead to the development of obesity. One controversial question is whether or not a high-fat diet by itself, ie, independent of total energy intake, is a risk factor for obesity [9]. Overweight and obesity tends to be higher in countries with high fat intakes, an observation that supports the hypothesis of a role of dietary fat in the development of obesity [8]. Weight gain and obesity in free-living populations result from a long-term positive energy balance, the amount of energy consumed is greater than the amount of energy spent [3]. A wealth of evidence points to many dietary and lifestyle factors that can directly or indirectly tip the balance of energy input and output [7]. Increasing energy intake is a major contributor to the current obesity epidemic [2]. The past several decades have witnessed a marked increase in the total amount of energy intake, especially in populations with rising rates of obesity. For example, data from the National Health and Nutrition Examination Survey (NHANES) showed that energy intake increased from an average of 2450 kcal/day in 1971–1974 to 2618 kcal/day in 1999–2000, an increase of 168 kcal/day or 7%, among men in the United States [2]. The upward shift was greater among women, increasing by 335 kcal/day or 22% [5]. Because of the high energy density of fat and the enhanced palatability of high-fat foods, it was widely believed that high intakes of dietary fat contributed to the greater weight gain [5]. However, epidemiological studies and clinical trials have generated data that is quite mixed and there are diverse opinions about whether or not the

percentage of dietary fat plays an important role in the rising prevalence of obesity [4]. Dietary habits of young adults are affected by the fast-food market. As a consequence, overweight and obesity are increasingly observed among the young [5]. Obesity in combination with unhealthy life style, such as smoking and physical inactivity, may increase the risk of chronic diseases [15]. In this regards, nutritional knowledge may act as a deterrent against fast-food trend [16]. Thus, universities may contribute significantly in reducing the prevalence of obesity among the young population through the promotion of healthy eating habits [17]. Universities may provide an ideal forum for reaching out to a large number of young adults through nutrition education programs that may positively influence students' eating habits by advocating for the adoption of healthy food choices [18]. In the last half century, there has been a sudden upsurge in consumption of carbohydrates (CHOs) as the major component of the diet, and carbohydrates are now being eaten in a more refined form [19]. Few epidemiological studies have directly assessed the relationship between CHOs and obesity, while some evidence from short-term intervention trials indicate that CHO restriction may moderately promote weight loss [20]. The proportion of CHO in the diet tends to vary reciprocally with fat. Therefore, it is difficult to segregate the impact of the total amount of CHO in the diet from total fat. Many studies have shown that diets rich in whole grains and fiber were inversely related to BMI and weight gain which is likely due to the incomplete digestion and absorption and increased satiety caused by delayed gastric emptying and subsequent gastric distention [1]. In addition, other foods/nutrients such as nuts, fruits and vegetables, dairy products, coffee, and calcium were also associated with body fatness in some but not all studies [7]. The inconsistency in these observations is partly due to the complexity of confounding by other sociodemographic and lifestyle variables [20]. The abnormal eating habits are divided into two categories [14]. The first is related to eating disorders (EDs), which are included in the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5) and the International Classification of Diseases (ICD-10) [15]. The problematic eating behaviours (PEBs) consists of unhealthy and pathological eating patterns, including emotional eating, snacking between meals and food cravings [17] which are (in addition to the well-known role of eating disorders especially binge eating disorder [BED]) crucial elements in the development of excessive body weight [15]. The adverse effect of unhealthy dietary habit (e.g., more consumption of refined CHOs; reduced intake of fiber, vegetables, and fruit; and overeating) on obesity can be exacerbated by the lack of physical

activity that results from the popularization of television and computers and the increasing use of labor-saving transportation devices [8]. Some large studies have shown that the risk of significant weight gain is greater in individuals who were sedentary than in those who were more active [10]. The role of sedentary behavior as a contributor to the obesity epidemic has also been evaluated in children and adolescents. Although television-watching and physical inactivity have been related to obesity, the increase in adiposity may be due to snacking that occurs during TV viewing [12]. In the context of mindful eating, individuals seeking to reduce their weight try to avoid chocolate (consider it as forbidden and a high-calorie product), and its consumption results in guilt and escalating dietary restrictions as well as a negative attitude toward one's own body [3]. From a clinical point of view, the more individuals, especially with problematic eating behaviours and disturbed body image-related behaviours (patients with excessive body weight) try to avoid thinking about food intake and their own body, the probability of eating a forbidden food (chocolate) and thinking about eating a forbidden food increase (which is based on the theory of paradoxical effects of thought suppression) [13]. Controlling thoughts are associated with stress and linked to increased tension, wherefore individuals try to reduce these negative states and may therefore be at risk of the over-consumption [15].

Obesity: balanced diets and treatment

An essential aspect of maintaining the body is the consumption of food [4]. The range of foods that we eat is known as our diet and the components of food that are digested, absorbed and used in bodily functions are known as nutrients [6]. Nutrients supply the body with both energy and with the components for growth and repair [8]. A balanced diet contains six key nutrient groups that are required in appropriate amounts for health. A deficiency of any one type of nutrient can lead to disease, starvation (or dehydration in the case of water) and subsequent death [4]. Fibre is a component of food that is not nutritious but is important to include in our diet. Fibre or roughage is non-digestible carbohydrate and it has an important role in aiding the movement of food through the gut [6]. There is also an absolute requirement for some specific molecules in the diet. This is because, although the body can manufacture most of the molecules it needs, some essential molecules cannot be made by the body [5]. These molecules are called essential nutrients, and must be supplied in the diet, for example lysine and methionine, which are essential amino acids [6]. Other components of the human diet are not nutrients at all, as they do not perform the functions of producing energy or promoting growth and repair, but are eaten for other purposes. For example, spices and other

flavourings help make food more palatable; tea and coffee drinks provide a good source of water and may also contain other valuable substances such as antioxidants [8]. Leptin is a hormone produced by adipose tissue that acts on specific nerve cells in the brain stem and hypothalamus to inhibit feeding behaviour [5]. It was first identified because a very obese strain of mice was discovered to have a mutation in the gene that codes for leptin [7]. Subsequently, a very small number of human families have been identified in which some individuals also have a mutation in the gene that codes for leptin [8]. These mutations are often of the 'frame-shift' type and lead to a complete loss of function in the resulting protein. Humans with such mutations overeat and become very obese [6]. If, as children, attempts are made to restrict their food intake, they may become aggressive and difficult to manage. Treatment with leptin leads to normalization of both appetite and body weight [7]. However, the administration of leptin turns out to be very much less effective in the great majority of morbidly obese individuals [8]. They typically already have very high leptin levels but have lost the normal physiological and behavioural responses to the hormone. Thus leptin has not, so far, proved to be the 'magic bullet' that will treat the human obesity epidemic [9]. In the hypothalamus, leptin acts on two groups of nerve cells, both of which influence feeding behaviour but with opposite actions [8]. Weight gain essentially arises from an imbalance of energy supply and energy expenditure. Therefore it is not surprising that dieting (restriction of energy input) and exercise (increased energy output) are recommended both to reduce body weight and also for their additional health benefits [9]. However, even a quick survey of the research literature makes it clear that dieting is not very effective in the medium or long term as a method of reducing body weight [10]. People find it hard to be compliant with a particular diet, and are also poor at simply recalling what they have eaten [11]. Thus, food diaries are a notoriously inaccurate way of estimating an individual's total food intake. In addition, reduction of food intake, especially with a low-fat diet, may be associated with a depression of metabolic rate that restricts the actual amount of weight that is lost [12].

CONCLUSION

Obese people usually have mutations in the gene that codes for leptin. These mutations are often of the frame-shift type and lead to a complete loss of function in the resulting protein. Humans with such mutations overeat and become very obese. Weight gain essentially arises from an imbalance of energy supply and energy expenditure. Therefore it is not surprising that dieting (restriction of energy input) and exercise (increased energy output) are

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