Are the causes of obesity primarily environmental?

John Wilding believes that changes in our environment are responsible for increasing obesity, but **Timothy Frayling** thinks that it is genetic factors that determine who gets fat

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"Are the causes of obesity mainly environmental?

Yes 604 (68%)
No 281 (32%)

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YES

The ongoing epidemic of obesity and its associated complications such as diabetes, increased cancer risk, and cardiovascular disease is creating an unprecedented challenge for healthcare systems around the world and threatens to slow or even reverse the gains in life expectancy that have been achieved over the past 50 years.[1] To tackle this growing problem it is essential to consider the fundamental causes of obesity and apply this knowledge to develop effective strategies to prevent and treat the condition and its consequences.

There is no question that regulation of body weight and fat content is under powerful biological control, and that much of this biology is rooted in genetics; identical twins are only rarely discordant for adiposity, and about 40-70% of body fatness is inherited.[2] Given the importance of this genetic component, it may seem counterintuitive to suggest that the main causes lie in our environment. However, known single gene defects, such as leptin deficiency, are rare causes of obesity,[3] and the only common gene polymorphism with well characterised effects on body weight, FTO, has a relatively small effect size (about 3 kg greater weight for those who are homozygous for the variant associated with obesity, and about 1.5 kg for heterozygotes).[4]

Such rapid change cannot be due to genetic (or even epigenetic) changes

For someone to become obese, overall energy balance (the difference between energy consumed in the form of food and that expended in normal biological processes and physical activity) must be positive over time. Of course, this is more likely to occur in those genetically predisposed to gaining weight, especially if the environment is more conducive to increased consumption and decreased activity. The increase in the prevalence of obesity has mainly occurred over the past 30 years and has been seen in most parts of the world. Such rapid change cannot be due to genetic (or even epigenetic) changes. In contrast, the evidence that the environment has changed is overwhelming. The environmental changes are complex

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NO

Genetic variation has not changed appreciably in the past 50 years and therefore cannot explain the secular increases in average body mass index observed over the past few decades. But changes in the environment (decreased need for physical activity and greater availability of cheap food) mean we are all at increased risk of obesity compared with our parents and grandparents. So why do many people remain slim, while others gain weight?

Genetic variation influences our appetites, metabolism, and tolerance of physical activity. This creates a strong genetic component to variation in body mass index in today's environment. An analogy can be made with smoking—if everyone inhaled the same amount of cigarette smoke every day, the strongest risk factor for lung cancer would be genetic susceptibility to the adverse effects of cigarette smoke (G Davey Smith, personal communication).

Size of genetic effect

Twin and adoption studies show consistently that variation in body mass index has a strong genetic component. One study assessed the heritability of body mass index in over 20 000 young adult twin pairs from eight European countries,[1] with data collected from 1963 to 2002 (although mostly from 1980 onwards). The correlation of body mass index between identical twins in the eight countries ranged from 0.65 to 0.83 and was consistently stronger than that between non-identical same sex twins (correlation 0.31 to 0.58). The estimated genetic effects, correcting for age and sex differences, were 60-70%. In a recent systematic review of five adoption studies with several hundred parent-biological child and parent-adoptee comparisons, children's body mass index was consistently more strongly correlated with that of their biological parents than of their adoptive parents.[2] Intrauterine "programming" did not account for the differences because the correlations were similar for father-biological child pairs and mother-biological child pairs.

Strong genetic effects remain even in contemporary environments. In a study of over 5000 twin pairs born in the UK during 1994-97, the correlation of body mass index at age 8-11 years between identical twins (0.86, 95% confidence interval 0.85 to 0.87) was stronger than that between non-identical same sex twins (0.51, 0.47 to 0.53).[3] Genetic effects were estimated as

and include substantial shifts in the production and availability of food, occurring simultaneously with alterations in the physical environment that encourage sedentary behaviour.

Environmental contributions

The relative cost of food has fallen in recent years, partly as a result of the industrialisation of food production. But the overall trend hides important differences—the cost of energy dense foods high in fat, sugar, and salt has fallen most, whereas that of healthier options has increased in relative terms. This may partly explain why obesity is more common in those on lower incomes.[5 6] The food industry, now an unhealthy alliance of producers and marketeers, has successfully promoted energy dense foods, many of which provide positive reinforcement that increases consumption,[7] effectively producing a "cafeteria diet" for the whole human population—a well proved way of causing obesity in experimental animals.[8]

At the same time as the food environment has provided fertile ground for the development of obesity, physical activity has declined and time spent being sedentary has increased. This can be attributed to changes in transport, especially increased use of the car, and in time spent being inactive during work and leisure time, partly as a result of developments in technology (television, computers, computer games, etc). The built environment does not always encourage outdoor activities, and safety fears may underlie the reductions in walking and cycling that have been seen in recent years.

Social norms may also have changed over the last few decades, so that obesity is not as readily recognised as it would have been in the past. Eating and activity patterns have also changed in ways that may promote the development of obesity.

Solutions

It will be important to identify genetic causes for rare cases that may be treated, and both pharmacological and surgical options may be necessary for some people (and could be targeted on the basis of genetic or other biomarkers that predict response). However, changes to the food and physical environment are going to be essential if we are to have a meaningful impact on the obesity epidemic. Success will almost certainly require a comprehensive and radical approach across systems, backed by strong legislation influencing food production and marketing, and ensuring the built environment and transport systems are designed to encourage active living. Comprehensive community based public health interventions are beginning to show some encouraging results in reducing childhood obesity[9]; such an approach is being tested across Europe in the Ensemble Prévenons l'Obésité Des Enfants (EPODE) project, which engages whole communities, including local government and businesses, to try to reduce the prevalence of obesity in children.[10] It has been questioned whether initiatives such as the so called "responsibility deal" in England, in which companies pledge to reduce the energy content of their products and promote lower calorie options, are likely to be effective,[11 12] and if this approach fails, stronger legislative approaches may be required.

In summary, obesity is a complex disorder with both genetic and environmental causes. The predominant driver is environmental, and changes to the environment will be essential if we are to tackle the current epidemic.

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77%. Another study of over 2000 very young twin pairs found that appetite, estimated from parental questionnaires, had a genetic component.[4] Correlations between appetite measures in one twin and weight of the other twin were stronger in identical than non-identical twin pairs.

Twin studies may overestimate genetic effects because there is less variation in the environment between children raised in the same household and parents may treat identical twins differently to same sex non-identical twins. But these factors are unlikely to explain the large differences in correlations of body mass index between identical and non-identical twins. In theory, twin and adoption studies could be confounded by epigenetic effects. For example, differences in placentation and response to the maternal intrauterine environment could influence whether genes are permanently switched on or off by processes such as DNA methylation. However, there is little evidence for this causal pathway in humans.

Stronger effects in sedentary people

Genetic factors may have stronger effects in more sedentary individuals or those in more obesogenic environments. Genome-wide studies have identified DNA variation in 32 regions of the human genome associated with body mass index, with a DNA variant in the FTO gene having the strongest association.[5] People carrying two copies of the allele associated with obesity are, on average, 0.5 kg/m^2 heavier than those carrying two copies of the protective version. Recently, a study of over 200 000 people showed that the FTO variant had a stronger effect in people who were sedentary than in those who were physically active.[6] Studies in humans and mice suggest that the FTO gene affects appetite control,[7 8] and in inactive people there may be greater scope for genetic factors to influence body mass index through appetite control. Although the DNA variations explain only a small percentage of the variation in body mass index, they provide proof of principle that genetic factors influence it over environmental effects.

Education may not be as important as we think

There is a large amount of evidence that education or other measures of welfare are associated with body mass index, but studies of physical activity in schoolchildren suggest that education may not be as important as we hope. A recent report analysed data from 12 studies consisting of over 8000 children randomised to increased physical activity or normal activity at school. Children were followed up for a median of 18 months. The results showed no evidence that physical activity interventions influenced body mass index.[9] This result is consistent with one longitudinal study of 200 children that used actigraph accelerometers to objectively measure physical activity for seven consecutive days, once a year over three years. Inactivity in children preceded increases in percentage body fat, but increased body fat percentage did not precede reduced physical activity.[10] In the same study, children from wealthier households were no more active than those from poorer households, despite more out of school structured activity.[11]

Genetic factors influence substantially where you are on the body mass index scale in a given population at a given time

In conclusion, genetic factors influence substantially where you are on the body mass index scale in a given population at a given time. Evidence is accumulating that these genetic factors may operate largely through appetite control. If true, plans based on changing our environment, such as banning the sale of supersized sugary drinks,[12] will make genetic factors less important and be more successful than plans to increase awareness through education.

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