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Gene-obesogenic environment interactions in the UK Biobank study

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Abstract:
Background and aims: Susceptibility to obesity and type 2 diabetes in today's environment has a strong genetic component. However, little is known about how genetic variation interacts with the modern environment to predispose some individuals to obesity and type 2 diabetes whilst others remain slim. Previous gene-obesogenic environment studies have been limited by the need to perform meta-analyses of many heterogeneous studies. We aimed to use 120,000 individuals from the UK Biobank to test the hypothesis that high risk obesogenic environments accentuate genetic susceptibility to obesity and therefore increase type 2 diabetes risk.
Materials and methods: We used 120,000 individuals from the UK Biobank study to test the hypothesis that high risk obesogenic environments and behaviours accentuate genetic susceptibility to obesity. We used BMI as the outcome and genetics and self-reported estimates of the obesogenic environment as exposures. We used a 69-variant genetic risk score (GRS) for obesity as the genetic exposure and 9 self-reported measures, including TV watching, westernised diet and physical activity and a composite of these factors, as obesogenic environment/behaviour exposures. We tested the association of the genetic risk score with BMI in high and low environment groups and tested for interactions.
Results: The self-reported measures of the obesogenic environment and behaviour were all associated with BMI in the expected directions (all $P<0.001$). We found evidence of gene-environment interactions with self-reported TV-watching ($P_{interaction}=7\times10^{-5}$), and self-reported physical activity ($P_{interaction}=5\times10^{-6}$). For example, within individuals reporting watching ≥4 hours TV per day, carrying 10 additional BMI-raising alleles was associated with approximately 4.0kg extra weight in someone 1.73m tall. In contrast, within individuals reporting watching <4 hours TV per day, carrying 10 additional BMI-raising alleles was associated with approximately 3.1kg extra weight. Evidence of interaction using a composite measure of the obesogenic environment ($P_{interaction}=2\times10^{-4}$) and permutations of the data based on randomly selecting groups of individuals of different BMIs, suggested that these differences were not specific to one

aspect of the environment. The main limitations of our findings are that the environmental measures are complex mixes of environment and behaviour and are based on self-report.

Conclusion: Our findings suggest that the there is no particular aspect of the environment or behaviour that if altered would have a preferential benefit over others. It is premature to suggest public health measures should be targeted specifically at fried food reduction, fizzy drink consumption and diet in those genetically predisposed to obesity. Instead, public health measures aiming to alter all aspects of the obesogenic environment in small ways may have more impact in lowering the prevalence of obesity and type 2 diabetes than targeting a single or few aspects.

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