Diet Quality and Genetic Association With Body Mass Index: Results From Three Observational Studies

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Background

In the most recent GWAS, of the 97 BMI-associated SNPs identified, more than half of the SNPs were highly enriched for expression in the central nervous system (CNS), which is the key site of central appetite regulation [1]. Significant interaction between consumption of sugar-sweetened beverages and genetic score in relation to BMI has been found [2]. However, it is not known whether diet quality could modify the genetic association with BMI. Moreover, identification of subgroup of established SNPs whose association with BMI could be most significantly modified by diet will provide evidence to individualized obesity prevention.

Hypotheses

- SNPs enriched in the CNS (CNS SNPs) were more likely to be associated with food and nutrient intakes featured in AHEI in comparison to SNPs enriched in other tissues (non-CNS SNPs).
- Higher diet quality was related with less pronounced association between genetic score and BMI, particularly the score of CNS SNPs.

Study Population

- 5,730 women in the NHS and 3,434 men in the HPFS who were sampled as controls
- 21,740 women in the WHGS

Exposure

- Dietary quality will be measured by AHEI-2010, AMED, and DASH diet scores. Diet was measured repeatedly in the NHS (1984, 1986, 1990, 1994) and the HPFS (1986, 1990, 1994), and was measured at baseline in the WGHS.
- Based on the most recent GWAS [1], we will classify the 97 BMI-associated SNPs into CNS SNP (54 SNPs) and non-CNS SNP (43 SNPs). Total, CNS, and non-CNS SNP scores will be calculated.

Outcome

BMI measured after diet assessment with 2-year lag in the NHS and the HPFS and 3-year lag in the WGHS

Statistical analysis

1. The associations of individual SNP with AHEI components at baseline will be examined using linear regression and the results will be presented in Heatmap.
2. The interactions between diet quality scores and genetic scores in relation to BMI will be examined using generalized linear model in the NHS and the HPFS and using linear regression in the WGHS. The genetic scores will include total SNP score, CNS SNP score, and non-CNS SNP score.
3. Two-way stratification analysis will be conducted: the association of diet quality score with BMI will be stratified by genetic score; the association of genetic score with BMI will be stratified by diet quality score.
4. The interactions between AHEI components and genetic scores in relation to BMI will be examined using generalized linear model in the NHS and the HPFS and using linear regression in the WGHS.

Reference

1. Locke AE, Kahali B, Berndt SI, et al. Genetic studies of body mass index yield new insights for obesity biology. Nature. Feb 12 2015;518(7538):197-206.
2. Qi Q, Chu AY, Kang JH, et al. Sugar-sweetened beverages and genetic risk of obesity. The New England journal of medicine. Oct 11 2012;367(15):1387-1396.