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Association of dopamine D2 receptor and leptin receptor genes with clinically severe obesity.

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Abstract

OBJECTIVE: The brain reward circuits that promote drug abuse may also be involved in pleasure seeking behavior and food cravings observed in severely obese subjects. Drug addiction polymorphisms such as the TaqI A1 allele of the dopamine D2 receptor (DRD2) are associated with cocaine, alcohol, and opioid use, but few studies have linked DRD2 to food craving. Other genes such as the leptin receptor gene (LEPR) and mu-opioid receptor gene (OPRM1) that affect appetite and pleasure centers in the brain may also influence food addiction and obesity. The three genes together may function synergistically.

DESIGN AND METHODS: To evaluate associations between candidate genes, food craving, overeating, and BMI, we administered questionnaires including Power of Food Scale and Food Craving Inventory, conducted anthropometric measures, and collected blood from patients undergoing weight-loss treatment. Questionnaires and DNA specimens were collected for 80 participants.

RESULTS: Participants were mostly female (74%) and Caucasian (79%), with an average age of 53 years old. Mean BMI for all participants was 43 kg/m2 and was significantly associated in a linear fashion with Food Craving Inventory scores (P=0.0001) and Power of Food (P=0.02). The DRD2 TaqI A1 allele was significantly associated with BMI (P=0.04), while LEPR Lys109Arg and OPRM1 A118G variants were not. We stratified DRD2 by LEPR and OPRM1, and observed a significant interaction (P = 0.04) between DRD2 and LEPR, and a marginally significant interaction (P=0.06) between DRD2 and OPRM1.

CONCLUSION: Genes associated with addictive behavior and appetite control may therefore, in combination, markedly influence development of clinically severe obesity.

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