

Genetic Relationship Between Depression and Body Mass Index

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Introduction

Depression and obesity are highly prevalent major public health problems that frequently co-occur. Shared aetiological factors have been found between depression and obesity. The role of the fat mass and obesity associated (*FTO*) gene in body mass index (BMI) and obesity has been confirmed in many independent studies. Recently, we reported the first study implicating *FTO* in the association between depression and obesity.

Objectives

We aimed to confirm these findings by investigating the *FTO* rs9939609 polymorphism in a meta-analysis of 13,701 individuals.

Methods

The sample consists of 6,902 depressed cases and 6,799 controls from five studies (Radiant, PsyCoLaus, GSK, MARS and NESDA/NTR). Common inclusion criteria were information available on a lifetime DSM-IV diagnosis of major depressive disorder (MDD), BMI and genotype data. Linear regression models for quantitative traits assuming an additive genetic model were performed to test for association and interaction between rs9939609, BMI and depression. Fixed and random-effects meta-analyses were performed.

Results

Fixed-effects meta-analyses support a significant association between rs9939609 polymorphism and BMI (whole-sample: $\beta=0.07$, $p=1.29 \times 10^{-12}$, depressive-cases: $\beta=0.12$, $p=6.92 \times 10^{-12}$). No association was found in controls ($\beta=0.02$, $p=0.15$). Meta-analyses further support a significant interaction between *FTO*, BMI and depression (fixed-effects: $\beta=0.13$, $p=3.087 \times 10^{-7}$; random-effects: $\beta=0.12$, $p=0.027$), wherein depressed carriers of the risk allele have an additional increase of 2.2% in BMI.

Conclusions

This meta-analysis demonstrates a significant interaction between *FTO*, depression and BMI, indicating that depression increases the effect of *FTO* on BMI. Depression-related alterations in key biological processes may interact with the rs9939609 *FTO* risk allele to increase obesity risk.