Meta-analysis of genome-wide association scans reveals new loci for body mass index in early adulthood

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Obesity is an important risk factor for a multitude of diseases. Although obesity has high heritability, efforts to detect genetic loci associated with the trait have yielded a limited number of susceptibility genes. Considering the heterogeneity in obesity and that genetic determinants may be important particularly in early onset obesity, we conducted a meta-analysis of genome-wide association (GWA) scans from three studies (Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial, Nurses' Health Study, and Finland-United States Investigation of NIDDM Study) including ~ 5,400 individuals of European ancestry to identify genetic loci associated with body mass index (BMI) in early adulthood (ages 18-20 years). Based on scans of 300-500K SNPs, each study imputed genotypes for the ~2.5 million common SNPs in the CEU HapMap and tested the association under an additive genetic model (1 d.f.). SNPs with a minor allele frequency <1% or low imputation quality score ($r^2 < 0.3$) were excluded, and a meta-analysis of the associations using the square root of the sample size as weights was performed. The recently identified variants in *FTO* and near *MC4R* were associated with BMI in early adulthood ($p = 0.01$ and $p = 0.02$, respectively). We discovered one novel locus on chromosome 4 with a p-value $< 1 \times 10^{-6}$, and nine loci not previously implicated in obesity showed nominally significant associations with p-values $< 1 \times 10^{-5}$. Some of these loci are located near genes related to metabolism or growth factors, which are promising candidates for obesity. We are currently replicating the top findings in an additional 10,000 persons of European ancestry. In conclusion, our study identified several new promising genetic variants associated with BMI in early adulthood and will hopefully shed additional insight into the complex etiology of obesity.