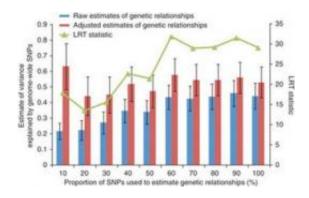


Genetic heritability may be hidden deeper than previously thought

June 21 2010, by Lin Edwards



Results are shown as estimates of variance explained by different proportions of SNPs randomly selected from all the SNPs in the combined set. Image: Nature Genetics (doi:10.1038/ng.608).

(PhysOrg.com) -- Geneticists trying to find a link between the genes and traits such as height have until recently found genetic variants that account for only around 5% of the heritability of these traits. The approximately 95% missing, which is seen in the heritability of most complex human traits and diseases, has been referred to as the "missing heritability" of the genome. This problem has led some geneticists to question the proposal that common genetic variants will explain complex traits and diseases, and to turn their efforts instead to searching for rare variants seen in individuals with the trait.

Now a new study on the genetics of height suggests the <u>heritability</u> is not



missing, but is actually buried in a large number of genetic variants that each have tiny effects.

The genetics of inherited traits and diseases is usually researched by genome-wide association studies (GWAS), in which the genomes of thousands of usually unrelated people are scanned to search for <u>single</u> <u>nucleotide polymorphisms</u> (<u>SNPs</u>), which are basically single-letter mutations believed to be associated with the trait or disease.

The new study by scientists in Australia and the US estimated the proportion of variance explained by over 290,000 genome-wide SNPs for the height of 3,925 unrelated individuals from Australia, UK, US, Europe, China, Japan, and Africa. The study used a linear model analysis and the researchers then validated the estimations with simulations based on the observed genotype data.

The statistical significance of individual variations is usually set around a million times higher than in other statistical studies (such as studies linking <u>environmental factors</u> and diseases), to ensure the associations are real, but the new study was a statistical analysis of the effects of all the SNPs combined rather than looking at each one individually.

The study was led by quantitative geneticist Peter Visscher, of the Queensland Institute of Medical Research in Brisbane, Australia, who said the research explained 45 percent of the genetic variation in height by considering all the SNPs simultaneously. Another analysis by the team suggests the remainder of the heritability might be explained by less common SNPs.

Visscher said their results suggest the effects of many common variants are likely to be small individually, and studies will need to look at many hundreds of thousands of genomes in order to identify them. He also said there is likely to be a "spectrum of variance," with many more



common variants to uncover.

The paper is published in the journal *Nature Genetics*.

More information: Common SNPs explain a large proportion of the heritability for human height, Jian Yang et al, *Nature Genetics* (2010), doi:10.1038/ng.608

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