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Testosterone and body fat are controlled by the same genes

Genes that control percentage of body fat are also responsible for circulating levels of testosterone in men, research published in the latest edition of *Clinical Endocrinology* shows. The research shows a 23% overlap between the genes that control testosterone and those that regulate body fat composition, suggesting that these two variables are partly controlled by the same set of genes.

The study led by Dr Jean-Marc Kaufman at Ghent University Hospital, Belgium was carried out on healthy male sibling pairs and estimated the extent to which sex hormones and body fat are controlled by the same genes. The research involved a cohort of 674 men from 274 independent families, as part of a larger study investigating the origins of body composition, sex steroid status and peak bone mass in healthy men. Each participant had their weight, total body fat and BMI measured and a blood sample was taken to measure their levels of testosterone and SHBG (a protein that binds to sex hormones). The team then used two computer programs (SAGE and SOLAR 2.0) to carry out complex statistical modelling to calculate the 'heritability estimate' of each trait, that is, the extent to which each characteristic is influenced by genes (as opposed to environmental factors). The correlation between two different variables (e.g. testosterone and body fat) was then calculated, based on their individual heritability estimates.

A strong correlation was found between sex hormones and body fat, which was predominantly due to shared genes. Specifically, testosterone and SHBG both showed a 23% genetic correlation with body fat, and SHBG showed a 29% link with whole body fat. There was no link in terms of environmental factors between sex hormones and body composition.

When measured individually, testosterone had the highest heritability estimate of the sex hormones at 0.65 (heritability estimates are measured on a scale between 0 and 1, with 1 equalling 100% genetic influence). SHBG, weight and body fat also had high heritability estimates of 0.73, 0.83 and 0.65, respectively. Such high heritability values are similar to those previously published[1], and indicate that circulating testosterone levels are approximately 60% influenced by genes.

Previous studies have shown a well-established relationship between testosterone and body fat composition. For example, men with low testosterone levels are characterised by a high body fat percentage. However, despite this well documented link, the causal factors behind this relationship have remained unknown. In this study, the authors show the set of genes

that control testosterone levels also control body fat, providing for the first time an underlying causal link to explain this relationship.

Researcher Dr Jean-Marc Kaufman said:

"Body fat composition is influenced by environmental factors such as diet and exercise, but is also strongly controlled by genes. There is a well-established relationship between testosterone and body fat composition, which we have now shown is a result of shared genetic regulation. We know that testosterone and body fat show high degrees of heritability as individual traits, but in our cohort of young men we showed that they are partially controlled by the same set of genes. Our results help to explain the complex interplay between fat mass and sex hormones. Further research is now needed to investigate the individual genes that control sex hormone levels and body composition, which could provide further insight into the regulation of testosterone levels and testosterone sensitivity in men."

Background information

Testosterone is the principal male sex hormone, and is required for sperm production, development of male reproductive organs and appearance of secondary male sexual characteristics. SHBG is a transporter protein that binds to sex hormones such as testosterone in the bloodstream. Only a small fraction of circulating testosterone is free (and therefore biologically active), as the majority is bound to SHBG and therefore inactive. When measuring testosterone concentrations in the blood, 'free' testosterone is calculated from total testosterone and SHBG levels.

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Notes for editors

References

1. Ring, HZ *et al.,* (2005) Heritability of plasma sex hormones and hormone binding globulin in adult male twins. *Journal of Clinical Endocrinology and Metabolism,* 90: 3653-3658.

Contact information

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ABSTRACT

Heritability of blood concentrations of sex-steroids in relation to body composition in young adult male siblings

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Objective Sex steroid concentrations in men are related to body composition and both are determined by genetic and environmental factors. This study investigates heritability estimates of sex steroid serum concentrations and body composition as well as the genetic and environmental components of their interrelation.
Patients Six hundred and seventy-four men (25–45 years) were included in this study with 274 independent pairs of brothers.
Measurements Body composition and regional fat mass estimates were determined using dual-energy X-ray absorptiometry. Serum testosterone (T), SHBG, oestradiol (E2) and LH levels were determined by immunoassay; free T and E2 levels were calculated.
Results Both sex steroid hormone concentrations and indices of body composition exhibited significant heritability estimates. Among sex steroid hormones, T had the highest heritability (h2= 0·65), followed by free T (h2= 0·54). A heritability of 0·73 was observed for SHBG; a heritability estimate of 0·83 was obtained for body weight. Significant genetic correlations were found between whole body fat mass and serum T (ρG= –0·46), free T (ρG= –0·27) and SHBG (ρG= –0·48) concentrations. No genetic relationship was observed between total (F) E2 or LH concentrations, respectively, and body composition.
Conclusion Both sex steroid serum levels and body composition are under strong genetic control. Their interrelation is in part underlied by a genetic correlation, indicative of the action of shared genes.