

Sex steroids and the growth hormone system in metabolic regulation

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GH regulates body composition by stimulating energy metabolism and protein anabolism. The liver is an important site of physiological interaction as it is a sex steroid responsive organ and a major target of GH action. Oestrogen, when administered orally impairs the GH-regulated endocrine and metabolic function of the liver via a first pass effect. It reduces circulating IGF-I, fat oxidation and protein synthesis, contributing to a loss of lean and a gain of fat mass. The effect of oestrogen is direct and involves inhibiting GH receptor signalling. We have also investigated the effects of SERMs (selective estrogen receptor modulator) in the light of their increasing use for osteoporosis which is prevalent in hypopituitarism. Raloxifene exert oestrogen-like effects on the liver, reducing hepatic fat oxidation and circulating IGF-I. In hypopituitary women, raloxifene in therapy doses exerts a greater attenuating effect than oestrogen on fat oxidation, protein anabolism and on body composition during GH therapy.

By contrast, testosterone enhances the metabolic and anabolic effects of GH. In hypopituitary men, testosterone amplifies GH stimulation of IGF-I, sodium retention, fat oxidation and protein anabolism. The major interaction between GH and testosterone on whole body protein anabolism occurs in the liver rather in extra hepatic tissues. The cellular mechanisms underlying the amplifying effects of testosterone on GH action are unknown. In summary, oestrogens and androgens exert opposite effects on the metabolic actions of GH. The liver plays a major role in mediating the regulatory effects of sex steroids on GH action. The strong modulatory effect of gonadal steroids on GH responsiveness provides insights into the biological basis of sexual dimorphism in growth, development and body composition and practical information for the endocrine physiologist.