Direct effects of sex steroid hormones on adipose tissues and obesity.

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Abstract: Sex steroid hormones are involved in the metabolism, accumulation and distribution of adipose tissues. It is now known that oestrogen receptor, progesterone receptor and androgen receptor exist in adipose tissues, so their actions could be direct. Sex steroid hormones carry out their function in adipose tissues by both genomic and nongenomic

mechanisms. In the genomic mechanism, the sex steroid hormone binds to its receptor and the steroid-receptor complex regulates the transcription of given genes. Leptin and lipoprotein lipase are two key proteins in adipose tissues that are regulated by transcriptional control with sex steroid hormones. In the nongenomic mechanism, the sex steroid hormone binds to its receptor in the plasma membrane, and second messengers are formed. This involves both the cAMP cascade and the phosphoinositide cascade. Activation of the cAMP cascade by sex steroid hormones would activate hormone-sensitive lipase leading to lipolysis in adipose tissues. In the phosphoinositide cascade, diacylglycerol and inositol 1,4,5-trisphosphate are formed as second messengers ultimately causing the activation of protein kinase C. Their activation appears to be involved in the control of preadipocyte proliferation and differentiation. In the presence of sex steroid hormones, a normal distribution of body fat exists, but with a decrease in sex steroid hormones, as occurs with ageing or gonadectomy, there is a tendency to increase central obesity, a major risk for cardiovascular disease, type 2 diabetes and certain cancers. Because sex steroid hormones regulate the amount and distribution of adipose tissues, they or adipose tissue-specific selective receptor modulators might be used to ameliorate obesity. In fact, hormone replacement therapy in postmenopausal women and testosterone replacement therapy in older men appear to reduce the degree of central obesity. However, these therapies have numerous side effects limiting their use, and selective receptor modulators of sex steroid hormones are needed that are more specific for adipose tissues with fewer side effects.

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