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ANDROGENS AND THE BLOOD/BRAIN BARRIER
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The influence of sex steroids on the brain is often difficult to interpret, both because of uncertainty over which cross the blood-brain barrier, which are produced locally in different parts of the brain, and the interactions and conversions between them and other endocrine variables modifying behavior. The fact that there is a high concentration of aromatase in many regions of the brain, and that testosterone is the most abundant sex steroid in both men and women throughout life, especially after age 50, suggests that the many potentially beneficial actions of estrogens, might be extrapolated to testosterone. Transport of steroids into various tissues in the body is dependant on their binding to transport proteins, their rate of dissociation from these proteins, their membrane permeability, and their capillary transit time through an organ. Because steroids dissociate slowly from their specific binding proteins, and as transit time through the brain is rapid, being less than a second, apart from the free testosterone, virtually none of the albumin-bound fraction makes any significant additional contribution to exogenous brain levels. In practice therefore, the concentration of sex steroids in the cerebrospinal fluid is mainly limited to their free levels of 2% in the plasma as only this fraction can cross the blood-brain barrier. Calculations have been performed which show the amount of free testosterone and free estrogen available to the brain in both men and women with varying amounts of SHBG, and how this might be modified beneficially by danazol.

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TESTOSTERONE AND THE METABOLIC SYNDROME
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In the US 23% of men have the metabolic syndrome in which insulin resistance plays a key role. Epidemiologic studies indicate that insulin levels and testosterone (T) are inversely correlated. Aims 1) To define the dose response relationship between insulin sensitivity and T in men. 2) To elucidate the mechanism of the relative hypogonadism in men with insulin resistance. Methods 59 men (44 to 65 yr) were studied: 26 had normal glucose tolerance (NGT), 12 had impaired glucose tolerance (IGT), 21 had diabetes (DM). All had a euglycemic hyperinsulinemic clamp: 15 had testing with GnRH and hCG after endogenous LH and T were suppressed with a GnRH antagonist. Results T levels were lower in men with DM (390 ± 40 ng/dL) and IGT (380 ± 42 ng/dL) than those with NGT (518 ± 36 ng/dL), p<0.05 despite similar BMI. There was an inverse relationship between T and BMI (r=-0.44, p<0.05) and WHR (r=-0.35, p=0.008). Insulin sensitivity (M) correlated with T (r=0.35, p=0.007) particularly in men with IGT. Men with hypogonadal T levels (n=10) were more insulin resistant than those with normal T (n=49), M = 3.8 ± 2.2 vs. 6.1 ± 3.5, mg/kg/min, p<0.05. No correlation was seen between M and LH secretion. A strong correlation was observed between M and the T response to hCG (r=0.7, p<0.005). Conclusions Testosterone is an important modulator of insulin sensitivity in men. The relative hypogonadism in men with insulin resistance is due to impaired Leydig cell secretion of T.