

The Androgen Receptor and Synthetic Hormones

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Numerous synthetic testosterone derivative hormones have been developed within recent decades. These anabolic androgenic steroids strongly resemble the testosterone molecule and bind with the androgen receptor within the cell's nucleolus in a similar but not identical manor. These differences between the synthetic hormone and testosterone yield similar but different effects on the cell, tissue, and central nervous system (thus behavior) of the organism in which the compound is interacting with[1][2][3].

Introduction

By binding to the androgen receptor (AR), synthetic derivatives of testosterone execute their mechanism of action, thus they are molecularly similar to the testosterone molecule in terms of structure and arrangement of functional groups. Though many also differ in these respects and thus exhibit different but similar properties to testosterone. These synthetic derivatives of testosterone, or anabolic androgenic steroids (AAS), provide enhanced anabolic and sometimes androgenic properties and activities within what is thought to be the more responsive androgenic tissues, such as the skeletal muscle. In addition to physical tissue enhancement synthetic testosterone derivatives can induce behavioral changes as well, in part because the use of such compounds bring about a rise in occupied androgen receptors in the central nervous system [1]. Synthetic testosterone derived hormones are sometimes subjected to interaction with the aromatizing enzyme aromatase, which converts testosterone and testosterone derived substances into estrogen in an attempt to maintain hormonal balance within the body, thus the introduction of synthetic testosterone based hormones into the body will directly interact with the androgen receptor, but may also have other hormonal implications and effects in the various systems of the body through estrogenic means. Though a complex phenomenon, substantial evidence suggest that masculine

sexual behavior and other like behaviors are associated not only with the occupation of the androgen receptor in a neuron, but also the relation with the conversion of testosterone to estrogen by aromatase in target neurons. Synthetic hormones also exhibit effects on this phenomenon [1]. Among any synthetic testosterone derived compound is that compound's Q-ratio, or anabolic to androgenic ratio, steroids with a high androgenic to anabolic rating are therapeutically used to rectify hypogonadism in males and other androgenic deficient disorders as well aid in hormone replacement therapy [2]. Compounds with strong Qratios are utilized for their anabolic properties, and are often applied to assist in situations such as protein loss after trauma, when the patient suffers from an inhibited immune system, or to aid in recovery. The hormonal androgen receptor is the site at which some potent biological changes can begin, thus the devices and its related mechanism can offer up some riveting implications.

Recent Progress

The Effect of Anabolic-androgenic Steroids on Aromatase Activity and Androgen Receptor Binding in the Rat Preoptic Area

An interesting study accepted to Science in 1998, in which castrated rates were administered a variety of AAS, including testosterone, dihydrotestosterone, stanozolol (winsterol or winny), nandrolone (deca), danazol

(danocrine), and methandrostenolone (dianabol). All of these compounds possess strong structural chemical similarities with the classic testosterone molecule but have modifications on the functional groups attached to the molecule. They act to enhance the secondary male sex characteristics within the specimen, however due to their similarities with testosterone they are also subject to interaction with the aromatase enzyme which then cleaves the molecule into a synthetic estrogen derivative. Both the testosterone and estrogen derived hormones have interaction with their respective binding sites including within neurons, which likely account for behavioral changes within the subject. These behaviors are thought to be equally dependent on both the synthetic testosterone and estrogen derivatives, and it is specifically this phenomenon which the study moves to investigate, quantifying the both of the derivatives' activity within the neural preoptic area of the central nervous system. Within the castrated male rat subjects it was found that the hormones possessed varying rates of aromatization; indeed some possessed substantially lower aromatization than the naturally occurring counterpart, which would ultimately have impacted within the neural binding sites. All of the hormones tested exhibited aromatase activity within the preoptic area though most were less than the naturally occurring hormones, with the exception of nandrolone. This imbalance between normal aromatizing levels likely leads to the behavioral changes associated with the abuse of AAS.

Structural Characteristics of Anabolic Androgenic Steroids Contributing to Binding to the Androgen Receptor and to Their Anabolic and Androgenic Activities

Of the articles reviewed, this in particular contained the greatest span of information. The article goes into great depth highlighting a large variety of synthetic testosterone derived hormones and their typical intended activity within the receptor. Images of the structures and information upon their various modifications to the testosterone molecule have been exhibited for nearly fifty different compounds. The potential ligand activity is characterized and used to express each compound's specific anabolic and androgenic potency as well as the ratio between them. In addition, the binding site of the androgen receptor as well as an AAS' interaction with it is briefly described and depicted, which proved to be very useful. Several figures are expressed to depict the outcome of potential functional group addition and subtraction to the steroid molecule. The article summarized the activities of 46 compounds and provides depiction. This article then further goes on to briefly mention the side effects of AAS, particularly if the drug is abused as well as the research going into Selective Androgen Receptor Modulators (SARMs) which may produce similar benefits as AAS without the typical side

effects associated with them. The paper concludes with a brief summary of the data presented, overall the article is an exceptional reference and data guide to the structure and activity of numerous AASs.

Anabolic-androgenic steroid Interaction with Rat Androgen Receptor in Vivo and in Vitro: A Comparative Study

The article provides information in relation to a comparative study of in vivo and in vitro administration of several AAS as well as their effects upon the receptor. Rat subjects were used for the study. The compounds used in the study were testosterone, 17(alpha)-methyltestosterone (androide), methandienone (dianabol), methyltrienolone (methyl tren), stanozolol (winstrol or winny). It should also be noted that though extremely potent methyltrienolone also exhibits strong hepatotoxic activity and adversely affected many of the in vivo subjects. The relative competitive behavior for each drug's affinity to the androgen receptor was derived in both the in vitro and in vivo groups. Interestingly, many of the drugs expressed different levels of competition in either instance, suggesting that much of the molecular activity of AAS is still not fully understood as many of the rates expressed in the study were inconclusive. In addition many compounds did not exhibit constant predicted dose dependence within each experimental group. Anabolic and androgenic ratios were also very inconsistent with in the in vivo and in vitro groups. The article concludes that these ratios and variables of the AAS compound are very difficult to predict and understand.

Discussion

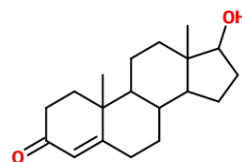


fig 1 Testosterone

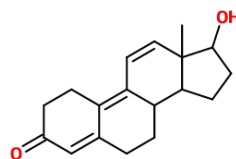


fig 2 Trenbolone

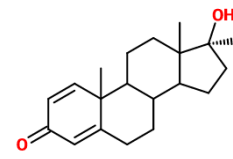


fig 3 Dianabol (Methandienone)

Several figures are displayed above in relation to the naturally occurring testosterone molecule; the different effects of these compounds in relation to testosterone will

be briefly described to summarize points found in the above articles.

Trenbolone is an extremely potent compound and is not orally available unless methylated, which greatly increases its toxicity [2]. Trenbolone was highlighted in this discussion as it is known for its intense androgenic activity and extreme mental stress that often occurs with its abusers [3][1]. Notice how the compound contains multiple double bonds when compared to the classic testosterone molecule. This results in a vastly different binding affinity and behavior to the receptor as described in the various above studies. It is this phenomena within the cells of the user that result in the harsh side effects both mental and physical associated with the drug, some described are night sweats, intense rise in body temperature, "tren cough", "tren somnia", "tren rage" and so on. Though it is thought that some of the highest potential strength gains and skeletal muscle hardening effects can result from abuse of this compound [3]. This is due to the compound's heavy affinity for androgenic activity over anabolic; why this is so though is still largely unknown.

Dianabol is a compound that is only orally available, and is known for its high anabolic potential and low androgenic affinity [3]. Dianabol has a relatively high conversion rate to estrogenic compounds when compared to other AAS, it is likely due to this behavior that many abusers report an elevated sense of wellbeing as well large gains in body mass and volume [1]. It is likely that dianabol was the second AAS to be synthesized after testosterone and has been widely abused since its creation, like the above mentioned trenbolone why this compound behaves in the way it does is not fully understood [1][2][3].

The effects produced from anabolic androgenic steroids can be quite riveting as the effects of these compounds produce substantial changes in the human body. Though they carry some medicinal use they are more widely used for their incredible performance enhancing ability[1][3]. Much of the specific mechanism of these compounds is still unknown, and there seems to be some inconstant patterns with in the structure and effects of AAS. Patterns and further understanding of their power within the human body are being discovered and developed [2]. Since the 1930's thousands of these compounds have been synthesized [3].

References

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