Evidence from a mouse model that high levels of circulating dihydrotestosterone increases skeletal muscle mass and force production in isolated fast- and slow-twitch muscles in males and females but reduces recovery from fatigue in females

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It is well known that in humans men have more muscle mass and strength than women. There is strong, direct evidence that the effects of testosterone on muscle mass and strength are dose-dependent on circulating testosterone. However, these studies were largely performed in men and it is neither feasible nor ethical to subject women to high circulating testosterone levels for sufficiently long periods to test this dose-dependency in healthy women.

In this study, we use a mouse model to investigate the effects of high circulating concentrations of the potent pure androgen DHT directly on muscle mass and function in both mature male and female wildtype mice. Each mouse was treated with DHT by subdermally implanted silastic tube containing ~10mg crystalline DHT which provide prolonged, steady-state DHT delivery for months if required. DHT was implanted into sexually mature females and orchidectomized males to equalize endogenous androgen exposure. All operative procedures were performed under anesthesia administered by intraperitoneal injection of a 4 mg/ml solution of ketamine and xylazine 100microliter/10 g body wt. Fast-twitch EDL muscle and slow-twitch *soleus* muscle were dissected from the hind limb and tied to a dual force transducer/linear tissue puller. Each muscle was then placed in a bath containing Krebs solution and bubbled continuously with carbogen. The muscle was stimulated by delivering a current between two parallel platinum electrodes. Isolated muscle contractile properties were analysed using the 615A Dynamic Muscle Control and Analysis software (Aurora Sci, Ins.). Muscles were trimmed and weighed at the end of the protocol.

In DHT treated animals there was a significant increase in mass of EDL muscle from males and females. Male Blank 9.7mg ± 0.3 n=8 Male DHT 11.5mg ± 0.4 n=8 (P<.001); Female Blank 8.7mg ± 0.1 n=10, Female DHT 12.0mg ± 0.2 n=7 (P<0.0001). In *soleus* muscles, only treated females showed a significant increase in mass (Male Blank 10.0mg ± 0.5 n=10 Male DHT 11mg ± 0.3 n=8 (ns); Female Blank 9.0 mg ± 0.5 n=8 and Female DHT 11.5mg ± 0.4 n=8 (P<0.01). There was also a very significant increase in maximum force output from DHT EDL muscles in both males and females (Male blank 339mN ± 6 n=6 c.f. Male DHT 386mN ± 6 n=8 (P<0.0001); Female Blank 292mN ± 3 n=10 and Female DHT 377mN ± 7 n=7 (P<0.0001): t-test/SEM/n=muscles. Interestingly, in DHT-treated female mice both *soleus* and EDL muscles showed a significant (P<0.0001) 16% ±5 & 18% ± 4, slowing of recovery from fatigue, which was not present in DHT-treated male mice. Increasing circulating androgen levels in female mice and orchidectomized male mice appears beneficial for power activities but reduces endurance performance in females.