Introduction:

Functional recovery (especially after prolonged denervation) of re-innervated muscle is often suboptimal. Well established contributing factors include loss of muscle mass, muscle fiber size, and contractile composition (so called “denervation atrophy”)(4). While prevention of denervation atrophy has received significant attention, strategies to reverse it are almost nonexistent. Anabolic steroids (including testosterone) have been shown to have modest effects in improving nerve regeneration (1-3) and even delaying atrophy (5) but their hypertrophic qualities have not been evaluated in re-innervated atrophic muscle. Our hypothesis is that the administration of anabolic steroids in the setting of re-inervation after denervation muscular atrophy has been established will lead to improved muscle functional recovery.

Materials/Methods:

Forty-five immature female Sprague-Dawley rats were included in this study. All experimental procedures and care of the animals was approved by our institution’s IACUC review board and was carried out according to approved national guidelines. The rats were divided into three groups (experimental, control, sham) with an N=15 per group. The animals in the experimental and control groups underwent exploration and transection of the left tibial nerve at the bifurcation from the peroneal nerve using a standard biceps femoris semi-tendinosus muscle splitting approach. The sham group underwent exposure of said nerves and then was closed without any nerve manipulation. At 3 months, the transected nerves were all repaired (using autograft from the contralateral tibial nerve approximately 1cm in length). The sham group had the contralateral autograft harvested only. After allowing one month of regeneration time, an alzet pump was inserted in a subcutaneous pocket in the back of all 45 rats. For the experimental group, the alzet pump contained nandrolone (0.11mg/kg/day x 28 days) mixed with a cottonseed oil carrier. For the control and sham groups, the pump contained carrier only. An additional 6 weeks of regeneration time was allowed before testing. Testing consisted of supramaximal stimulation of the proximal repaired tibial nerve and twitch contraction measurements of the medial gastrocnemius muscle using a force transducer. The muscle was then harvested, measured, weighed and stored in 10% formalin for histological analysis including muscle fiber measurements and counts. Means were calculated and reported with ±SEM and statistical significance was determined using unpaired Student’s t-test with p<0.05 considered to be significant.

Results:

The experimental limbs achieved contractions forces 73% of sham limbs while control limbs only achieved 56% contraction force of sham limbs (p<0.05)(Fig 1). There was no statistical difference in muscle belly diameter or gross muscle weights between the experimental and control groups although there was a trend for higher values for the experimental over the control group, but sham group muscle belly diameters and weights were statistically higher than both the experimental and control groups (p<0.05)(Fig 2a,b).

Conclusion:

The use of anabolic steroids does seem to improve muscle recovery strength in re-innervated rat hindlimb muscles following the establishment of denervation atrophy. The affect was not complete as there was still a significant difference between the experimental and sham groups in terms of contraction force, muscle belly weight, muscle belly diameter, and muscle fiber cross-sectional area. The experimental group did show a trend for larger cross-sectional muscle fiber areas as well as increased weights and diameters but these did not reach statistical significance. Although the use of rats as nerve models for experimentation is widely accepted this does introduce a degree of error when attempting to apply these findings to clinical scenarios. Further investigation into understanding the physiologic mechanism behind this observation as well as ways to augment this effect would be appropriate.

References: