WALKING-MEDIATED UPREGULATION OF FOLLISTATIN-LIKE 3 EXPRESSION IS INSUFFICIENT TO INCREASE MUSCLE CONTRACTILE FORCE

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INTRODUCTION

Molecular mechanisms coordinating muscle and bone strength and growth following exercise (EX) remain undefined. We have identified a TGF-β family protein, follistatin-like 3 (FSTL3), which is upregulated in mouse and human skeletal muscle, bone and serum in response to low intensity walking EX. We have previously determined by mineral apposition rate analysis of Fstl3-/- mouse bone that FSTL3 is required for EX-driven bone formation [1]. FSTL3 is known to bind and inhibit myostatin [2]; thus, this study was to determine if FSTL3 increases muscle hypertrophy and force generation through this mechanism to collectively regulate musculoskeletal function.

METHODS

C57/Bl6 mice (n=20, 10 male, 10-12 wks), wild-type (WT, n=5) or Fstl3-/- (FSTL3 knock-out, “FSTL3KO,” n=5), were treadmill walked for 45 min/day at 8 m/min for 6 weeks, a protocol that increases bone formation. Ten mice (male n=5) were used as NonEX controls. Intact extensor digitorum longus (EDL) and soleus (SOL) muscles were dissected and mounted vertically between two stimulating platinum electrodes and immersed in bathing chambers containing modified Ringer solution. A constant stimulatory voltage was applied to equilibrate muscles at maximum force, followed by stimulation at frequencies from 1-150 hz to generate force vs. frequency curves.

RESULTS AND DISCUSSION

No differences in stimulated force were observed in WT EX and WT NonEX mice, indicating that the walking EX protocol used was not sufficiently rigorous to produce a training effect on muscle force production (Fig.1). Interestingly, no force differences were observed in FSTL3KO EX and FSTL3KO NoEX groups (Fig. 2). These results indicate that endogenous FSTL3 may not be sufficient to alter muscle contractile force generation in response to walking EX training.

CONCLUSIONS

FSTL3 regulates bone health in response to low intensity, low impact walking EX; however, the walking protocol used here is insufficient for increasing muscle force and hypertrophy. This study provides information on the efficacy of walking to increase muscle strength that may be applied to designing EX programs in a clinical setting. While walking may be prescribed as a treatment regimen for increasing bone growth in humans, clinicians should be aware that walking may need to be supplemented with a resistance EX program to increase muscle strength/hypertrophy. In vitro and human studies to address FSTL3 mechanisms are ongoing.

REFERENCES

Figure 1: No differences in stimulated muscle force in walking WT EX and NonEX mice. Representative graph from male mouse EDL and SOL muscles. The walking exercise protocol used, although sufficient for producing bone growth in WT mice, was not sufficiently rigorous to produce a training effect on muscle force production.

Figure 2: No differences in stimulated muscle force in walking FSTL3KO EX and NonEX mice. Representative graph from male mouse EDL and SOL muscles.