Introduction

- The predominant positive and negative regulators of the mass of skeletal muscles are insulin-like growth factor one (IGF-1) and myostatin (Mstn), respectively.
- The regulation of the mass of skeletal muscles and activity of IGF-1 and Mstn by the gonadal steroids testosterone (T) and 17β-estradiol (E2) remains controversial.

Aims

- To determine the regulation of the mass of skeletal muscles by T and E2 in male and female mice.
- To determine the regulation of the activity of IGF-1 and Mstn by T and E2 in male and female mice.

Study design

- Male and female mice (C57BL/6 strain) underwent bilateral gonadectomy (Gdx) or sham surgery at 4 weeks of age with insertion of subcutaneous silastic implants containing T, E2 or cholesterol (placebo) (n = 8 per treatment and sex).
- Blood and hindlimb muscles were collected at 13 weeks of age.
- Muscle mass was normalised to acting bone length.
- Concentrations of IGF-1 in plasma and skeletal muscle were determined by ELISA.
- C2C12 myoblasts under differentiating conditions were treated for 24 hours with T (30 nM) or E2 (10 nM) and RNA and protein were harvested for quantitative PCR and Western blotting, respectively.
- Myoblasts were also treated for 96 hours and differentiation was assessed by immunocytochemistry.

Results

- Sexually dimorphic growth of hindlimb muscles was abolished post-gonadectomy (Figure 1).
- Replacement of T to male mice prevented the gonadectomy-induced reduction in normalised mass of hindlimb muscles and concentrations of IGF-1 protein and the gonadectomy-induced increase in the abundance of mature Mstn protein (Table 1).
- Administration of E2 to male mice attenuated the gonadectomy-induced reduction in the normalised mass of hindlimb muscles, but did not alter concentrations of Mstn or IGF-1 in skeletal muscle or plasma.
- Bilateral gonadectomy +/- replacement of E2 in female mice did not alter the abundance of mature Mstn protein or the normalised mass of hindlimb muscles, despite decreasing concentrations of IGF-1 in plasma and skeletal muscle.
- Administration of T to female mice increased the normalised mass of hindlimb muscles and concentrations of IGF-1, whilst decreasing the abundance of mature Mstn protein in skeletal muscle.
- Administration of T increased the hypertrophy of C2C12 myotubes (149%) to a greater extent than administration of E2 (61%; Fig. 2).
- Expression of IGF-1 mRNA in C2C12 myotubes was increased by administration of T, but not by administration of E2 (Figure 3).

Conclusions

- The anabolic action of T on skeletal muscles in mice is at least in part, due to modulation of activity of IGF-1 and Mstn.
- The E2-induced increase in mass of skeletal muscles occurred in male mice only and appeared to be independent of IGF-1 or Mstn.
- Gonadal steroids regulate the sexually dimorphic growth of skeletal muscles in mice.