Muscle energetics changes throughout maturation: a quantitative 31P-MRS analysis

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Introduction

Although it is well recognized that growth affects muscle function, the detailed effects of maturation on muscle metabolism have not been clearly determined.
The purpose of the present study was to investigate whether development quantitatively affected muscle energy production and proton handling during a standardized exercise in prepubescent boys and men.

Methods

- **The dominant forearm of 7 prepubescent boys** (11.7 ± 0.6 y.o., Tanner's stages ranging from 1 to 2) and **10 men** (35.4 ± 6.4 y.o.) was investigated. The stages of pubertal development were determined from pubic hair and genital development [1].
- **Maximal isometric digitorum flexor strenght (F_{max})** was measured using a home-built experimental setup including a force transducer (ZF, Scaime, France) connected to a handle bar. F_{max} was defined as the mean of three reproducible measurements. Each measurement was performed after a 1 min resting period.
- **Metabolic changes were recored using 31-Phosphorus Magnetic Resonance Spectroscopy (^{31}P-MRS)** at 4.7T (Biospec Avance 47/30, Bruker, Germany) with a 50 mm diameter surface coil. Spectra were continuously acquired during 5 min at rest, 3 min of exercise and 15 min of recovery. The exercise consisted in finger flexions repeated at 0.7 Hz against a weigh adjusted to 15 % of F_{max} for each subject.
- **^{31}P-MRS analysis:** During exercise, the rate of ATP synthesized from the net breakdown of PCr was determined from the rate of PCr decrease while glycolytic flux was calculated taking into account rates of proton consumption and production. Oxidative capacity was assessed using the PCr recovery kinetics parameters according to the method previously described by Kemp and Radda (1994) [2]. The total Energy Cost (EC) was calculated as the total ATP synthesis rate related to the ratio of power output to muscle volume**.**
  During recovery, PCr resynthesis was fitted using a monoexponential function from which the rate constant ($k_{PCr,}$) was determined and the maximal rate of oxidative ATP production (V_{max}) was calculated according to the model of Michaëlis Menten [2]. Additionally, the Proton efflux (V_{eff}) was calculated during the early recovery period considering together proton production from PCr resynthesis and pH changes [2].
- **Muscle volume (V_M) was quantified from T_1-weighted images** (9 to 13 slices depending on the forearm length) recorded at 1.5 T (Siemens –Vision Plus Imaging system) with the following parameters (TR=490ms, TE=12ms, field of view=200mm, matrix: 512*512, slice thickness= 5mm and inter-slice gap=10mm).

Results

Rest

We found no significant difference in pH, phosphocreatine ([PCr]), Inorganic phosphate ([Pi]) and adenosine diphosphate ([ADP]) concentrations. On the contrary, the resting PCr/Pi ratio measured in children (6.61 ± 1.4) was significantly lower as compared to men (8.76 ± 1.8).

Exercise

All the subjects performed the exercise at the same relative intensity (15 % of F_{max}). As a result, the absolute mechanical power output was significantly lower in boys (0.5 ± 0.2 W) than in men (1.5 ± 0.3 W, $p< 0.01$). However, it is noteworthy that this difference was abolished when muscle volume was taken into account (2.2 ± 0.6 and 2.8 ± 0.5 $W.dm^{-3}$ respectively in boys and men).

As illustrated in Figure 1A, the total energy cost (EC) of contraction was similar in both groups whereas the interplay of the different metabolic pathways changed with respect to age. At the onset of the exercise, oxidative ATP production was significantly larger in boys (Figure 1D) whereas the PCr contribution was significantly reduced i.e. the end-of-exercise PCr consumption was 46.9 ± 8.4 % of the resting value in boys and 62.2 ± 13.2 % in men. (Figure. 1C) No age-related difference was recorded for the glycolysis activity (Figure 1B). Likewise the pH measured at the end of exercise did not differ between children (6.6 ± 0.2) and adults (6.5 ± 0.2).

Recovery

The initial rate of pH_i recovery was significantly faster in children (0.03 ± 0.09 pH $units.min^{-1}$) as compared to adults (-0.04 ± 0.04 pH $units.min^{-1}$) for whom an initial acidosis was measured. The PCr recovery kinetics was also faster in boys (table 1) than in men indicating a larger proton load in children. The rate of proton efflux (V_{eff}) was logically faster in children than in men (Table 1)

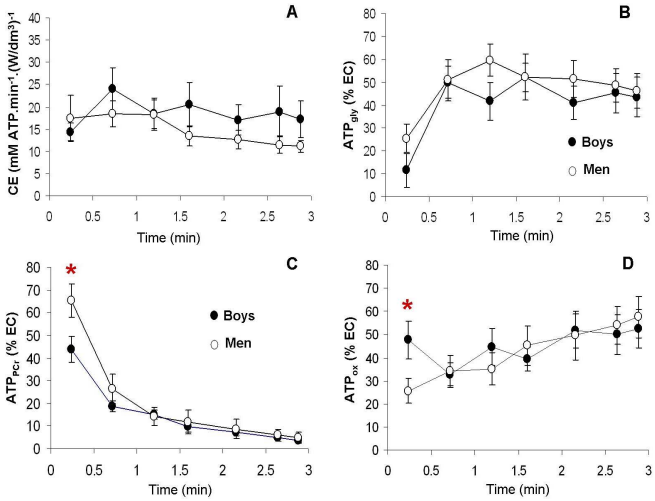

*Figure 1 : A Total energy cost (EC) at each time point; B C D: Relative contributions of PCr (ATP_{PCr}), anerobic glycolysis (ATP_{gly}) and oxydative phosphorylation (ATP_{ox}) to the total ATP turnover expressed as percentage of EC respectively. * means significant difference between children and men.*

Table 1: Metabolic variables measured during the recovery period

	Children	*Adults*
V_{eff} ($mM.min^{-1}$)	**6.15** ± 2.50 *	**3.80** ± 1.89
k_{PCr} (min^{-1})	**1.30** ± *0.52* *	**0.72** ± *0.39*
V_{max} ($mM.min^{-1}$)	**38.3** ± *15.5* *	**23.3** ± *12.4*

*Values are means ± SD, Veff, rate of proton efflux, kPCr rate constant of PCr recovery, Vmax theoretical maximum rate of oxidative phosphorylation. * means significant difference between children and adults*

Conclusion

To our knowledge, this study is the first ever quantitatively comparing changes in ATP production rates and proton handling during growth and maturation. **Our results clearly showed that maturation affect muscle energetics.** Although the total energy cost (EC) of contraction was unaffected throughout the maturation process, the relative contribution of each metabolic pathway to ATP production during a standardized exercise changed with respect to age. **Children rely more on oxidative metabolism and less on creatine kinase reaction to meet energy demand** during exercise whereas anaerobic glycolysis activity was unaffected by the maturational degree.
The greater aerobic contribution during exercise before puberty illustrates an increased oxidative capacity which might be linked to a larger relative content in slow twitch fibers.

Bibliography

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