perspectives

Do oxidative and anaerobic energy production in exercising muscle change throughout growth and maturation?

Sébastien Ratel,1 Anne Tonson,2 Patrick J. Cozzone,2 and David Bendahan2
1Clermont Université, Université Blaise Pascal, Laboratoire de Biologie des Activités Physiques et Sportives, Clermont-Ferrand; and 2Centre de Résonance Magnétique Biologique et Médicale (CRMBM), Faculté de Médecine de Marseille, Université de la Méditerranée, Marseille, France

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Although it has been stated that children experience a larger increase in peak anaerobic power than in peak oxygen uptake during growth (11, 12), experimental data derived from in vitro and in vivo muscle measurements, blood samplings, and oxygen uptake dynamics do not provide a consensus regarding the corresponding metabolic profile. Time-dependent changes in muscle oxidative capacity and anaerobic metabolism with respect to growth and maturation still remain a matter of debate. More specifically, it still remains unclear whether a metabolic specificity exists before puberty, i.e., whether a larger contribution of aerobic or anaerobic processes to energy production is present before puberty.

On the one hand, a reduced anaerobic glycolytic activity has been suggested in young children, considering lower muscle lactate accumulation resulting from maximal exercise and the lower activity of glycolytic enzymes, i.e., phosphofructokinase (PFK), lactate dehydrogenase, aldolase, pyruvate kinase (5, 9, 10, 20). Similar conclusions were also drawn on the basis of lower blood lactate and H+ ions accumulation resulting from supramaximal exercise in children compared with adults (8, 26). In addition, considering the significant positive relationships between testicular volume index and exercise-induced muscle lactate accumulation (9) and between salivary/serum testosterone concentration and peak blood lactate responses, some authors supported the contention that anaerobic glycolysis would be related to maturational status (14, 24).

On the other hand, no significant difference in glycolytic enzyme activity (i.e., PFK, aldolase, enolase, lactate dehydrogenase) has been reported in 13- to 15-yr-old adolescents compared with young adults (16). In addition, no significant relationship between salivary testosterone and blood lactate concentrations resulting from a 30-s supramaximal effort has been observed in children (11). Similar controversies have also been reported on the basis of pH changes recorded in exercising muscle. While some authors concluded a lower anaerobic glycolytic activity before puberty (22, 28, 30), others reported no apparent difference between children, adolescents, and adults (2, 25, 27).

These discrepancies might result, to some extent, to large experimental differences regarding exercise standardization and intensities, subjects’ maturity and size, subjects’ age independently of pubertal status, sample size, training status, etc. More specifically, several issues related to maturity status need careful consideration in metabolic studies of children and youth. Although valuable, stages of puberty are limited given that they only indicate the stage at the time of observation but do not provide information regarding how long the youngster has been in the stage (23). Also, prepubertal children with no overt manifestation of secondary sex characteristics do in fact differ in maturity status given that several hormones related to pubertal onset begin to increase before overt manifestation of pubertal status (23). In the case of girls, hormones of potential relevance become cyclical as menarcheal approaches and thereby thereafter. However, the intervals between early post-menarcheal cycles are quite variable. The specificity of salivary hormone assessments also need careful interpretation given that many hormones associated with pubertal maturation are released in a pulsatile manner (23). The same concerns also relate to the definition of “adult.” Age per se and post-pubertal status, although often used to indicate adult status, are not ideal indicators. The key issues are actually related to the time at which an individual reached “adulthood” and how long he/she has been an adult.

Another important issue is related to the standardization procedures linked to exercise intensity. Morphological differences between children and adults, especially muscle mass and the corresponding muscle force, might complicate the results analysis. It has been previously shown that the metabolic changes (i.e., phosphocreatine consumption) are strongly related to the power output normalized to muscle volume and that normalizing power to muscle volume results in a similar metabolic stress between individuals of different sizes (15). In that respect, metabolic changes occurring under those standardized exercise conditions could be reliably compared between children and adults and would not suffer from bias such as those related to different workloads, relative activated muscle mass, maximal capacity etc. Allometric modeling could also be used as standardization procedures to properly compare subjects with different sizes (29). However, because of a lack of consistency in body mass and height exponents in the literature, this approach warrants further comparative studies.
It is also of importance to keep in mind that pH or lactate changes recorded either in bloodstream or in exercising muscle cannot be considered as reliable indexes of anaerobic glycolytic activity per se. Regarding blood measurements, kinetics of lactate and proton transport into the bloodstream together with buffering capacity have to be taken into account (4, 8, 26). In particular, studies addressing the dynamic responses of blood pH or lactate using modeling approaches should take into account dimensionality differences between children and adults, namely, children’s smaller intramuscular perfusion distances and shorter circulation times. Furthermore, considering that anaerobic ATP production in exercising muscle, when coupled to ATP hydrolysis, is related to proton accumulation, whereas proton efflux, buffering capacity, and phosphocreatine (PCr) consumption have the opposite effects, i.e., muscle alkalinization (19), a reliable quantification of glycolytic ATP production cannot be dissociated from an appropriate analysis of proton handling (21).

Muscle oxidative capacity in children is also a matter of debate. Experimental data from biopsy measurements support a higher muscle oxidative activity in children compared with adults. With the exception of citrate synthase, enzymes of the tricarboxylic acid cycle (i.e., fumarase, NADP-isocitrate dehydrogenase or ICDH, malate dehydrogenase, succinate dehydrogenase) were found to show higher activities in children and adolescents compared with young adults (5, 10, 16). Furthermore, the larger PFK/ICDH activity ratio in adults as compared to 13- to 15-year-old (16) and the higher fumarase/PFK ratio activity (6) illustrate a larger relative oxidative activity compared with glycolysis in children than in adults. However, controversial results regarding muscle oxidative capacity have been reported from noninvasive measurements of postexercise PCr resynthesis rates in children compared with adults. While some studies have reported higher kinetic constants (kPCr) of postexercise PCr recovery and maximum rate of aerobic ATP production (Qmax) in prepubertal children compared with adults (27, 28), others reported no age-, sex-, or training-related differences (2, 22). These discrepancies might be related to different end-of-exercise pH and PCr concentration values that have not been systematically taken into account and are known to influence oxidative metabolism (3, 17). It is noteworthy that, on the basis of pulmonary oxygen uptake responses to heavy-intensity cycling exercise, longitudinal studies have demonstrated a decreased muscle potential for oxygen utilization throughout growth (7, 13), whereas cross-sectional studies indicated no significant difference between young children and adults (18).

Considering this whole set of confounding variables, comparative analyses between children and adults must be performed under carefully standardized conditions. Accurate quantitative investigations of rates of aerobic and anaerobic ATP production should eventually allow us to determine whether prepubertal children have fully efficient or immature glycolytic activity and whether any adaptive oxidative changes occur during maturation.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

REFERENCES


