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# Metabolism and Exercise During Youth

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**Abstract**
Three publications were selected based on the strength of the research questions, but also because they represent different research designs that are used with varying degrees of frequency in the paediatric literature. The first, a prospective, longitudinal cohort observation study from 7 to 16 years with girls and boys reports an intrinsic reduction in absolute resting energy expenditure after adjustment for lean mass, fat mass, and biological maturity. The authors suggest this could be related to evolutionary energy conservation, but may be problematic now that food energy availability is so abundant. The second focuses on the effect of acute exercise on neutrophil reactive oxygen species production and inflammatory markers in independent groups of healthy boys and men. The authors suggested the boys experienced a "sensitized" neutrophil response stimulated by the exercise bout compared with the men; moreover, the findings provided information necessary to design future trials in this important field. In the final study, a dose-response design was used to examine titrated doses of high intensity interval training on cardiometabolic outcomes in adolescent boys. Whilst the authors were unable to identify a recognisable dose-response relationship, there are several design strengths in this study, which was probably underpowered.

**Citation**
**Mostazir M, Jeffery A, Hosking J, Metcalf B, Voss L, Wilkin T. Evidence for energy conservation during pubertal growth. A 10-year longitudinal study (EarlyBird 71).** ***Int J Obes*****. 2016; 40(11):1619-1626. DOI: 10.1038/ijo.2016.158**

**Abstract**
**Background** Diabetes is closely linked to obesity, and obesity rates climb during adolescence for reasons that are not clear. Energy efficiency is important to obesity, and we describe a temporary but substantial fall in absolute energy expenditure, compatible with improved energy efficiency, during the rapid growth phase of puberty. **Methods** In a longitudinal cohort study lasting 10 years, we measured voluntary energy expenditure as physical activity (PA) by accelerometry, involuntary energy expenditure as resting energy expenditure (REE) by oxygen consumption, body mass index (BMI) and body composition by dual energy X-ray absorptiometry annually on 10 occasions from 7 to 16 years in the 347 children of the EarlyBird study. We used mixed effects modelling to analyse the trends in REE and their relationship to BMI, lean mass (LM), fat mass (FM), age, PA and pubertal stage. **Results** Relative REE and total PA fell during puberty, as previously described, but the longitudinal data and narrow age-range of the cohort (SD ± 4 months) revealed for the first time a substantial fall in absolute REE during the period of maximum growth. The fall became clearer still when adjusted for FM and LM. The fall could not be explained by fasting insulin, adiponectin, leptin, luteinising hormone or follicle stimulating hormone. **Conclusions** There appears to be a temporary but substantial reduction in energy expenditure during puberty, which is unrelated to changes in body composition. If it means higher energy efficiency, the fall in REE could be advantageous in an evolutionary context to delivering the

extra energy needed for pubertal growth, but unfavourable to weight gain in a contemporary environment.

Whilst exercise is not central to this study, the well-known decline in free-living physical activity during adolescence in girls and boys means that the findings are relevant for paediatric exercise scientists concerned with total energy balance and metabolism. Resting energy expenditure (REE), the largest component of total daily energy expenditure, is central to calculations of energy balance and has been linked to obesity. Yanovski (9) proclaimed that identification of sub-populations whose low REE predisposes them to weight gain is one of the "Holy Grails" of obesity research. To date, it is generally agreed that absolute REE rises throughout childhood and adolescence in line with growth in body mass, which is driven by the collective metabolic rates of increasing lean tissue mass (e.g., liver, kidneys, heart, brain and skeletal muscle). Relative REE, scaled to account for changing body size and composition, declines progressively with increasing age in young people, which has been attributed to changes in both cellular oxidative metabolism and a declining proportional contribution from highly metabolically active organs (6).

The EarlyBird study, a longitudinal observation of over 300 girls and boys from 5 to 16 years in England has provided many important insights since its inception in 2000, some which have generated considerable debate (1,8). This paper was selected to highlight the author speculation about temporal energy conservation during puberty, which may have far-reaching ramifications on strategies to prevent and treat adolescent obesity. Mostazir and colleagues (3) present novel observations from their cohort study to promote an alternative paradigm that programmed reductions in physical activity (PA) and absolute REE during adolescence, conceived originally to save energy important for pubertal growth, may now predispose adolescents to obesity when exposed to the deleterious effects of an obesogenic environment. The methods used to provide the primary variables included in the linear mixed effects models (LMM) suggest that they are unlikely to be the cause of serious bias. Moreover, the data from which the patterns of change in PA, REE, growth velocities and body size/composition are derived use well-established, standardised protocols. The modelled (M1) accelerated decline in PA from 7 to 16 years in girls and boys, and the sex differences, generally mirror the literature. The first of two LMM used to characterise changes in absolute REE ($kcal \cdot day^{-1}$) from 7 to 16 years (M2) showed the anticipated rise,

but only up to 11 years of age; thereafter it declined unexpectedly until the participants were 15 years old before making a recovery in the final year of measurement – this model was not adjusted for lean or fat mass. In the second absolute REE model (M3), which was adjusted for metabolically active lean and fat mass, an expected plateau in absolute REE from 7 to 10 years was seen. However, the estimated absolute REE values spanning 11 to 15 years declined at a greater rate than seen in M2 and could not be ascribed to body composition during this period of rapid growth or any other variables entered into the model.

The measured mean increases in lean mass for girls (9.5 kg) and boys (18.6 kg) from 11 to 15 years resulted in estimated reductions in REE amounting to 284 and 114 kcal·day$^{-1}$, respectively. This is a meaningful reduction given it has been estimated that excessive weight gain might be prevented by reducing positive energy balance by 150 kcal·day$^{-1}$ in children and adolescents (7). The authors went on to suggest that when the fall in REE is considered independently of changes in both lean and fat mass, the real reduction in intrinsic REE is up to 450 kcal·day$^{-1}$ around 15 years of age. The magnitude of error in these estimations is not clear. Serial measurements of insulin, insulin-like growth factor-1, luteinising hormone, follicle stimulating hormone, leptin and adiponectin did not explain meaningful proportions of the decline in REE independent of body composition, age, sex or maturity.

Mostazir et al. (3) speculate that the changes in REE described above are energy efficiency savings that have evolved to “assure the extra energy needed for adolescent growth” and that “systematic change in biological systems implies control, and controlled change infers that there is a survival advantage to be gained” (p. 1623). They also state that using changes in body composition to explain changes in REE, which is commonplace, is incompatible with their longitudinal data. Whilst it appears they are the first to propose this novel paradigm, similar maturity-related reductions in REE were reported first by Sun et al. (5) in a shorter longitudinal study comparing African American and white young people from 7 to 12 years, spanning the full range of biological maturation. There was, however, a considerable imbalance in sample size from Tanner stage 1 to 5, which weaken the findings; hence, the current data provide welcome confirmation.

Available evidence increasingly supports population declines in physical activity and high levels of sedentary behaviour (4); add to this an intrinsic reduction in REE across adolescence and ineffective interventions to redress the energy balance through increased activity expenditure (2). Thus, an energy dense nutritional environment places adolescents at increased risk of unhealthy weight gain at a time when intuition might suggest additional energy intake is required to fuel puberty. Do we need to revisit nutritional reference intakes for adolescents?

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**Citation**


**Liu M, Timmons BW. The effect of acute exercise on neutrophil reactive oxygen species production and inflammatory markers in healthy prepubertal and adult males. *Pediatr Exerc Sci.* 2016;28(1):55-63. DOI: 10.1123/pes.2014-0221.**


**Abstract**


The adaptive effects of exercise-induced inflammation and reactive oxygen species (ROS) production has been well studied in adults, but not in children. Characterizing the exercise

responses in children compared with adults will start clarifying the transition from the child phenotype to that of an adult. Ten children aged 8–10 and 12 adults aged 19–21 performed 2 × 30-min bouts of continuous cycling, separated by a 6-min rest period, at a target work rate of 60% of their maximum aerobic capacity. Blood samples were collected pre- and immediately postexercise, and analyzed for neutrophil count, systemic oxidative and inflammatory markers, and intracellular neutrophil-derived reactive oxygen species. Although postexercise absolute neutrophils increased by approximately twofold in men ($2.72 \pm 0.49 \times 10^9$/L to $4.85 \pm 2.05 \times 10^9$/L; $p = .007$), boys showed no such change ($3.18 \pm 0.67 \times 10^9$/L to $3.57 \pm 0.73 \times 10^9$/L; $p = .52$). Contrary to these findings, boys did show an increase in overall intracellular neutrophil ROS production, whereas men did not. Boys also demonstrated higher overall protein carbonyl levels (0.07 nmol/mg vs 0.04 nmol/mg; boys vs men respectively), whereas men showed higher overall malondialdehyde (0.24 μM vs 0.67 μM; boys vs men respectively). The differences observed in the exercise-induced inflammatory and oxidative stress response may indicate growth-mediated adaptive responses to exercise during childhood development.

It is well established that research findings based on samples of adults cannot be translated directly to children due to a variety of child-adult metabolic and hormonal differences (1). However, exercise science studies rarely include samples of both children and adults to provide a direct comparison between these populations. Despite the potential for exercise to enhance growth and development in children, it also leads to the production of inflammatory cytokines that can counteract the anabolic response. Thus, it has recently been proposed that the reduced inflammatory response to exercise in children may be an inherent ‘protective’ mechanism to allow for the anabolic effects of exercise. Although the mechanisms underpinning the reduced inflammatory response to exercise in children are poorly understood, reactive oxygen species (ROS) production from activated neutrophils may be involved (5). However, very little is known about neutrophil-generated ROS production and the relation with inflammatory markers during acute exercise in either children or adults; this is partly because the invasive methods associated with studying such biological processes often preclude research with children. With this in mind, the publication by Liu and Timmons (3) is highlighted here due to the identification of novel child-adult differences in circulating inflammatory cytokines and both intracellular and systemic markers of ROS production in response to exercise. This topic is of further relevance because chronic low grade inflammation can contribute to the development of cardiovascular diseases, type 2 diabetes and cancer in adulthood (2,8). Thus, the research findings not only have implications for growth, but also for maintaining metabolic health in the transition from childhood to adulthood.

Using an acute exercise response study with two groups (i.e., children and adults), Liu and Timmons (3) assessed exercise-induced inflammation and ROS production in response to two, 30-min bouts of cycling separated by a 6 minute rest in 10 children aged 8 to 10 years and 12 adults aged 19 to 21 years. While the low sample size limits statistical power for some of the outcome variables (e.g., the reduction in elastase following exercise and the exercise-induced increase in ROS production), numerous significant age-related differences in exercise-induced oxidative stress were found. Firstly, the findings on inflammatory markers confirmed previous reports, with acute exercise resulting in no change in tumor necrosis factor alpha concentrations ([TNF-α]) in the boys and a small increase in the men, and the boys showing a smaller increase in interleukin-6 (IL-6) compared with the men (4,7). The authors also showed that the men experienced a 1.5-fold increase in post-exercise absolute neutrophils, but no change was found in the boys. This finding supports a small number of previous studies (6,7) and may relate to the smaller inflammatory cytokine response in the children. The main finding, however, pointed towards the potential for exercise to stimulate a "sensitized" neutrophil response in the boys, which has been shown for the first time in the study by Liu and Timmons (3). Indeed, the boys showed an increase in overall intracellular neutrophil-stimulated ROS production after exercise, whereas men did not. This finding is intriguing and opens up avenues for further research to ascertain the reasons for this "sensitized" neutrophil response. It is possible it may be related to the boys eliciting a relatively larger growth hormone response to exercise or recruiting neutrophils from the bone marrow rather than circulating pools in the blood, as suggested by the authors. With the link between ROS, inflammatory markers, growth and disease, these child-adult differences in responses to acute exercise may have meaningful implications for maintaining healthy growth in the exercising child.

Ultimately, the reported findings contribute to an evolving understanding of the biological processes underpinning age and maturational differences in exercise-induced inflammatory and oxidative stress; highlighting that findings in adults often cannot be translated directly to children. In terms of exercise promotion, the use of a well-controlled acute exercise response design adds to the current evidence on the benefits of single exercise sessions, which complements the well-documented chronic adaptations. These 'immediate' benefits

could be used as an important motivator for individuals considering exercise. The acute design may also serve as an important start point to assess the effects of accumulating exercise in the transition from childhood to adulthood. In conjunction with the novel findings, the study design means that there is much scope to extend this research to females, children at different stages of maturation and to ascertain the responses to repeated, chronic exercise. Thus, this study stands to provide an important platform for further research in this field to help understand how exercise can maintain healthy growth and development of children.

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**Citation**


**Logan GRM, Harris N, Duncan S, Plank LD, Merien F, Schofield G. Low-active male adolescents: a dose response to high-intensity interval training. *Med Sci Sports Exerc*. 2016; 48(3):481–490. DOI: 10.1249/MSS.0000000000000799**


**Abstract**


**Purpose** High-intensity interval training (HIIT) is a potential alternative to traditionally recommended steady state exercise for providing health benefits in adolescents, yet its dose–response relationship in this cohort remains unclear, as does its translatability to real-world, nonclinical settings. The present study adopts a novel dose–response design to investigate the effects of undertaking 8 wk of HIIT on the cardiometabolic health of low-active male adolescents. **Methods** Twenty-six male adolescents (age 16 ± 1 yr), identified as low active by nonparticipation in structured sport and physical education classes, were randomly assigned to one of five treatment groups. Corresponding with their group

numbers (1–5), participants completed a number of HIIT ‘‘sets,’’ which consisted of 4 repeated bouts of 20-s near-maximal exertion interspersed with 10-s passive recovery. Participants performed two HIIT sessions and one resistance training session each week for 8 wk. Baseline and follow-up health measures consisted of peak oxygen uptake ($\dot{V}O_2$ peak) with an incremental ramp test to volitional exhaustion; body composition (including visceral fat mass, body fat, and lean tissue mass) with dual-energy x-ray absorptiometry; and lipid profile, glucose, insulin, and interleukin-6 from blood analysis. All health outcomes were analyzed as percentage changes, and data were modelled using a quadratic function to explore dose-response relationships. **Results** Significant improvements were observed for $\dot{V}O_2$ peak (~6%), body fat percentage (~4%), visceral fat mass (~10%), and waist circumference-to-height ratio (~3%), but there was no clear effect of dose across groups. **Conclusions** Low-active adolescent males performing a single HIIT set twice weekly, in addition to one resistance training session, gained meaningful improvements in fitness and body composition. Performing additional HIIT sets provided no additional improvements to those of the lowest dose in this study.

High-intensity interval training (HIIT) has been the focus of much attention in recent years with some evidence supporting the efficacy of HIIT to induce physiological adaptations comparable to those elicited by traditional higher-volume exercise training (4). Much of the allure surrounding HIIT stems from the priority afforded to exercise intensity over duration and, thus, its purported time efficiency (5). Logan and colleagues (7) highlight the relative dearth of research examining the efficacy of this form of exercise training on health-related risk factors in adolescents and the need for this research to be conducted in real-world settings. Both of these issues represent directives for future research that is required if experimental findings are to inform exercise recommendations for young people effectively. The rationale for the study by Logan and colleagues (7) centred on the uncertainty surrounding the issue of dose-response to HIIT; the importance of which is clear, and best illustrated when considering the ‘optimal dose’ of exercise. Although the relevance of these research questions has long been championed by eminent exercise scientists (6), there remains the need for experimental studies that are carefully designed to examine the dose-response to exercise in young people. Therefore, the main aim of this study was to examine the efficacy of incremental doses of HIIT performed over an eight-week period and establish the dose-response relationship in a low-active adolescent population for the first time.

As acknowledged by the authors (7), dose-response research is inherently challenging. Repeated-measures study designs, in which each participant receives all exercise ‘treatments’ or doses, are optimal but often impractical due to the burden of undergoing

multiple training exposures and the extensive 'wash-out' period that must be observed between treatments. During childhood and adolescence, these issues are exacerbated by growth and maturation that will confound the interpretation of data collected over an inevitably extended period. In an attempt to circumvent these impracticalities, the authors employed a novel parallel-groups, dose-response study design (1,8) during which participants received one of five HIIT doses. Individual responses to training were plotted and the dose-response effect was represented as a quadratic function. Twenty-six, 16 year old low-active, asymptomatic adolescent boys completed the study and were allocated randomly to one of five exercise groups. Each exercise group performed two HIIT sessions per week for eight weeks with the exercise dose being titrated from 1 to 5 sets per session to correspond with the group allocation. The HIIT protocol duration per session, including recovery, ranged from 1 min 50 s to 9 min 10 s in the lowest and highest dose groups, respectively.

The prescribed dose of HIIT was achieved using a combination of common modes of exercise with those participants scheduled to perform more than one set of exercise allowed to change exercise modality upon completion of each HIIT set. The adoption of a mixed-exercise experimental design, performed in the school-setting, resulted in good exercise fidelity and compliance and facilitated a "translatable approach to HIIT" which should be commended. Unfortunately, however, this flexibility did cloud the issue of dose-response as the potential for disparate, exercise-specific training adaptations must not be underestimated. In future, a fixed exercise modality would be advantageous when examining the dose-response to HIIT more closely.

The tightly controlled laboratory-based assessments completed before and after eight weeks of HIIT represent a major strength of the study. When the data from all exercise groups were pooled, small (effect sizes 0.11 to 0.29) post-HIIT changes in a number of outcome variables were reported including improvements in cardiorespiratory fitness (+6%), body fat percentage (-4%) and visceral fat mass (-10%). Fasting plasma glucose, insulin and lipid concentrations did not change meaningfully. This is perhaps unsurprising given the tight glycaemic regulation exhibited in the absence of metabolic disorders in asymptomatic adolescents and the equivocal evidence surrounding blood lipid responses to exercise

intervention (2,3). The quadratic trend provided limited evidence of a dose response to exercise, with the authors (7) concluding that the performance of a single set of HIIT performed twice weekly resulted in meaningful improvements in fitness and body composition whist performing a greater volume of HIIT did not confer any additional benefit. Unfortunately, however, the heterogeneity of the cohort at baseline, coupled with the very small number of participants assigned to each exercise treatment sub-group (n = 5), greatly reduced the exploratory power of an otherwise well designed study and limits the conclusions that can be drawn from the data. Although Logan and colleagues (7) reported little evidence in support of a dose-response relationship, it would be difficult, at this stage, to conclude with much confidence that such a relationship does not exist. It remains to be seen whether similar quadratic modelling analyses performed on more extensive data sets would yield evidence of a dose-response to HIIT. Importantly, however, despite its limitations, this study provides a platform on which similar future studies, conducted on a larger scale, may look to build. Moving forward, the issue of dose-response must be addressed across the broad exercise spectrum as well as in younger age groups if we are to advance our understanding of how exercise might be optimally prescribed during childhood and adolescence.

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