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Low ponderal index is associated with decreased muscle strength and fatigue resistance in college-aged women

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ABSTRACT

Poor fetal growth is associated with decrements in muscle strength likely due to changes during myogenesis. We investigated the association of poor fetal growth with muscle strength, fatigue resistance, and the response to training in the isolated quadriceps femoris. Females (20.6 years) born to term but below the 10th percentile of ponderal index (PI)-for-gestational-age (LOWPI, n = 14) were compared to controls (HIGHPI, n = 14), before and after an 8-week training. Muscle strength was assessed as grip-strength and as the maximal isometric voluntary contraction (MVC) of the quadriceps femoris. Muscle fatigue was assessed during knee extension exercise. Body composition and the maximal oxygen consumption (VO_2max) were also measured. Controlling for fat free mass (FFM), LOWPI versus HIGHPI women had ~11% lower grip-strength (P = 0.023), 9–24% lower MVC values (P = 0.042 pre-trained; P = 0.020 post-trained), a higher rate of fatigue (pre- and post-training), and a diminished training response (P = 0.016). Statistical control for FFM increased rather than decreased strength differences between PI groups. The PI was not associated with VO_2max or measures of body composition. Strength and fatigue decrements strongly suggest that poor fetal growth affects the pathway of muscle force generation. This could be due to neuromotor and/or muscle morphologic changes during development e.g., fiber number, fiber type, etc. Muscle from LOWPI women may also be less responsive to training. Indirectly, results also implicate muscle as a potential mediator between poor fetal growth and adult chronic disease, given muscle's direct role in determining insulin resistance, type II diabetes, physical activity, and so forth.

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1. Introduction

An association of early life conditions, specifically, low birth weight (BW), low ponderal index (PI, gm/cm^3), and infant catch-up growth, with obesity and increased chronic disease later in life is well documented at the population level [1–6]. The dominant explanation is the "fetal origins" hypothesis, which suggests that during critical periods of development, environmental stressors (especially under-nutrition) resulting in intrauterine growth retardation (IUGR), reprogram developmental pathways that permanently alter adult metabolism and subsequent chronic disease risk. These so-called fetal programming (FP) effects are well documented on body composition in a wide range of age groups. For example, studies of infants [7], children/adolescents [8,9], and adults [10–17], all show that FP results in a reduction in the relative amount of lean tissue compared to body fat. Skeletal muscle may be particularly susceptible to FP effects as restricted nutrients tend to be partitioned preferentially to the heart, brain, and other more vital organ systems. Further, myogenesis is sensitive to environmental perturbation, occurs very early during embryo formation, and ultimately determines a number of relatively fixed traits in adulthood including the muscle fiber number, the fiber size, and the fiber type distribution [18–20]. With respect to nutrient restriction, the animal data are consistent showing reductions in muscle fiber number as well as increases in type I versus type II fibers in adulthood [21–28]. Such developmental changes on muscle morphology could underlie the well-known association of fetal growth restriction with insulin resistance and type II diabetes, as insulin resistance is fundamentally a characteristic of skeletal muscle [29,30]. Morphological/metabolic changes could also have implications for exercise performance and physical activity levels in both children and adults.

Several studies have investigated the association of FP with muscle strength and/or muscle performance [29,31–35]. Of these, three large-

Abbreviations: FFM, fat free mass; MVC, maximum voluntary isometric contraction; FP, fetal programming; IUGR, intrauterine growth retardation; ^{31}PMRS, ^{31}P magnetic resonance spectroscopy; PCR, phosphocreatine; BW, birth weight; PI, ponderal index; Δ, change with training; VO_2max, maximal O_2 consumption; MET, metabolic equivalent.

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scale population studies showed positive associations of BW with grip strength, even after adjustment for various adult body size covariates [31–33]. For example, the study by Kuh et al. [33] showed a positive association of BW with grip-strength even after adjustment for age, sex, and adult height. The effect was present in both men and women, and a 1-kg difference in BW in the cohort meant going from the 10th to 80th percentile of the grip-strength distribution. These effects are likely qualitative and independent of muscle size, as is suggested by two direct studies of isolated muscle function. In a ^{31}P magnetic resonance spectroscopy [^{31}PMRS] study of the isolated working flexor digitorum superficialis, low PI at birth was associated with reduced exercise duration and a faster rate of phosphocreatine (PCR) depletion [34]. Another study by the same research group, using near-infrared spectroscopy, showed an increase in the rate of forearm muscle reoxygenation in low PI subjects after finger flexion exercise [29]. In both studies, the authors concluded that low PI is associated with a delay in the activation of glycolysis/glycogenolysis at the commencement of strenuous muscle contraction, thus resulting in a rapid depletion of PCR stores.

Of the aforementioned studies, nearly all evaluated the performance of the finger flexors only as opposed to the performance of a larger isolated muscle group. Only one of these [35] evaluated a fitness outcome, including the performance on a static arm-pull test and a vertical jump test, but neither measure was associated with the BW and neither measure effectively isolated the performance of a single working muscle group. In the case of vertical jumping, other factors, including technique, are probably also important. To date, no human FP study has evaluated the fatigue characteristics of muscle, although hind-limb muscle fatigue has been evaluated *in vivo* in new-born piglets [21]. Also, no study has evaluated the responsiveness of skeletal muscle to resistance and/or endurance training. The latter issue is interesting with reference to the original thrifty-phenotype hypothesis [36], whereby FP is viewed as an adaptive response to fetal nutritional stress that results in a decreased investment in muscle given the high energy costs of muscle maintenance. It is not known whether the thrifty phenotype persists after muscle resistance training, or whether the phenotype resists the normal hypertrophy of skeletal muscle to an endurance or resistance training program.

The overall goal of this study was to determine whether birth-markers of FP were associated with the strength, fatigue resistance, and response to training of a large-muscle mass (the quadriceps femoris muscle complex). We focused on the PI as a marker of FP given the studies described above, which were successful at detecting FP effects in relatively modest samples of subjects. BW, as a marker of FP, may be more problematic in correctly identifying IUGR infants as not all IUGR babies are small-for-gestational-age, and not all small-for-gestational-age babies are small due to growth restriction. Also, the PI as a marker of thinness at birth appears to be better associated with catch-up growth in the first year of life and with obesity and insulin resistance later in adulthood [2,37], also hallmarks of the FP complex. To achieve these study goals, twenty-eight college-aged women were recruited to participate in an 8-week strength and resistance training program. Fourteen of these women were identified as falling below the 10th percentile of the ponderal index (PI)-for-gestational age [38], a cutoff which has relatively high sensitivity and specificity to predict IUGR [39,40]. Fourteen of the women served as age, sex, and physical activity matched controls. The strength and fatigue characteristics of the right quadriceps femoris were evaluated pre- and post-training using a modified static–dynamic knee extension protocol that was first described by Lewis and Fulco [41]. This protocol assesses both the maximal isometric strength of the quadriceps femoris, as well as progressive muscle fatigue following dynamic knee-extension exercise. In addition to this protocol, pre-training, post-training, and change (Δ) values with training for the aerobic capacity (VO_2max) and the body composition were evaluated for each participant.

2. Methods

2.1. Subjects and recruitment

Twenty-eight female undergraduates born to term (>37 weeks to 42 weeks gestation) were recruited into the study on the basis of birth measures. For the formation of study groups, participants were compared to sex specific reference curves of the ponderal index (PI)-for-gestational age [38]. Fourteen were at or below the 10th percentile of PI-for-gestational age (LOWPI, 2.2 ± 0.1 gm/cm^3) and fourteen were in the upper normal range (>10 percentile, HIGHPI, 2.7 ± 0.1 gm/cm^3). Participants were required to document birth measures via a hospital record and/or a birth certificate. Gestational-age was determined from the documented due date, if it was available in the medical record, or if not, from maternal recall. Maternal recall of birth measures have proven reliable for both clinical and epidemiological use [42], and our data showed the expected increase in both BW and PI with increasing gestational age from 37 to 42 weeks compared to standard reference populations [38,43]. All participants were interviewed to obtain a medical history. Exclusion criteria included current pregnancy or pregnancy within the previous year, asthma, cardiovascular disease, diabetes, musculoskeletal problems that would have contraindicated participation in the training program or study protocols, and anemia measured via a spot measure of hemoglobin concentration from finger-tip blood using a point-of-care hemoglobin analyzer (Hemocue, Angelholm, Sweden). This study was approved by the Institutional Review Board (IRB) of the University at Albany, SUNY. Participants gave written informed consent and were compensated for their time.

2.2. Study design

On entry into the study and before performance evaluation, diet and physical activity patterns were assessed. To evaluate activity patterns, participants wore GT1M Actigraph accelerometers (Pensacola, Fla.) during waking hours over 3 continuous days (2 weekdays and 1 weekend day). Accelerometer count data were processed according to the 2-stage regression model of Crouter et al. [44] to produce MET values of daily energy expenditure. Diet was assessed via the diary method and detailed instructions were given on how to record all caloric intake over 2 weekdays and 1 weekend day. The dietary data were analyzed by the same investigator using the N^2 Nutrition IV software package (N-Squared Computing, Salem, Oregon). After baseline evaluations, participants completed an 8-week training program with pre- and post-training evaluations of body composition, aerobic capacity, and muscle strength/fatigue characteristics.

2.3. Training

Training consisted of 1-hour sessions, three times a week, for eight weeks, with the goal of increasing VO_2max and the strength of the quadriceps femoris muscle complex. The first 40 min of each session consisted of interval training on a stationary spin-bicycle. Participants wore heart-rate monitors and were required to keep heart rate values within prescribed limits during structured intervals that included warm-up/warm-down periods, as well as intervals of varying intensity that lasted from 1 to 4 min. In total, training was structured so that 25% of time was spent in light cycling (heart rate range at 50–70% of VO_2max), 50% of time in moderate cycling (70–80% of VO_2max), and 25% in hard cycling (80–90% of VO_2max). Following cycling, participants performed knee extension resistance weight training on a standard knee-extension weight-bench (3 sets of 15 repetitions each, with approximately 5 min between sets). Participants were allowed to select the external weight settings for knee extension training and were instructed/encouraged that the final extensions of the final set should be a challenge to complete.

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