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Official Title of the Study:

Sex-specific Adaptation to Different Resistance Exercise Programs in Older Adults

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Objectives

The objectives of this study are to identify the sex-specific effects of low-velocity, high-load resistance training (RT) versus high-velocity, low-load power training (PT) on skeletal muscle function at the whole muscle, cellular and molecular levels in older adults.

Design

We will test our hypothesis by having healthy, sedentary older (65-75 years old) men and women exercise one leg using RT and the contralateral leg using PT, and examining muscle function from the molecular, cellular and whole muscle levels. This within subject, unilateral training design provides a powerful model to evaluate training differences by reducing between-subject variability. Unilateral exercise, with one leg exercised and the other as a control, has been commonly used in older populations to examine muscle gene expression to myofibrillar ultrastructure to whole muscle performance.

Methods

Recruitment. Healthy older (65-75 years) men and women will be recruited from Amherst, MA and surrounding areas. Using the 2010 census data, ~45,000 volunteers between the ages of 65-75 live within 25 miles of Amherst. The best evidence of our recruitment capacity in this area is the track record of members of the investigative team for conducting recent research studies in older adults and requiring multiple biopsies.

Pre-exercise testing (Baseline). Baseline testing will occur prior to exercise and include assessments of body composition, physical activity, and whole skeletal muscle to cellular and molecular function.

Body composition, physical activity and function: Body mass, total and regional body composition will be assessed by dual energy x-ray absorptiometry (DEXA) (2); knee extensor fat content (% total) and fat-free muscle mass by magnetic resonance imaging (MRI); and 7 days of free-living physical activity by Actigraph GT3X-BT monitor. Physical activity will be matched across sex groups to reduce this confounding factor, per our studies in diseased and healthy older adults. Participants will also complete the Advanced Short Performance Physical Battery (SPPB-A) to assess mobility function. The SPPB-A includes timed measures of walking, static and dynamic balance assessments (including single leg), and repeated chair stands. As one leg is undergoing RT and the other PT, single leg balance assessments will be performed for each leg to examine differences in RT and PT, as it has been shown to increase with RT. A single-step test (SST), which correlates well with other lower limb functional performance measures, will also be performed on each leg. To perform the SST, volunteers stand on one leg (test leg) on a 15 cm high, single step and must touch the ground with their contralateral leg by performing a squat with the test leg and return to the standing position. The time required to repeat this movement 20 times is recorded. The non-test leg is held straight by a knee immobilizer brace.

Whole skeletal muscle function: Knee extensor (KE) peak torques for each leg will be measured on an isokinetic dynamometer (Biodex System 4) during maximal voluntary contractions at 0, 60, 120, 180, 240, 300 and 500°s^{-1}. Range of motion will be 70°, beginning at 80° of flexion, with 2 repetitions per velocity. Maximal contractile velocity will be obtained from the 500°s^{-1} trial. Coin toss will determine which leg is tested first, and the order of contraction velocity will begin and end with 120°s^{-1}, to evaluate whether fatigue occurred, with the remainder of the contractions performed in random order. Motor point stimulation will be applied to the resting muscle to determine maximal rates of torque development (RFD_{stim}) and relaxation (RFR_{stim}) at 0°s^{-1}. In addition to quantifying intrinsic whole-muscle contractile properties, these values will be compared with the rates during ballistic, maximal voluntary contractions (RFD_{vol},

RFR_{vol}), to quantify differences in neural drive. An increase in the RFD_{vol}:RFD_{stim} ratio indicates increased contractile speed due to factors proximal to the point of stimulation. Electromyography (EMG) measures of muscle activation (amplitude, timing of burst) will be obtained during all voluntary contractions. All torque data will be expressed relative to KE fat-free muscle mass, quantified by MRI, and MRI measures will be used to evaluate fat content and distribution.

Skeletal muscle biopsy: A percutaneous biopsy of the vastus lateralis will be performed following an overnight fast. The majority of tissue will be immediately placed into cold (4°C) dissecting solution, dissected into bundles, tied to glass rods and processed for single fiber contractile and mechanical assessment with the remainder either prepared for immunohistochemistry or frozen in liquid nitrogen and stored at -80°C.

Muscle fiber contractile and mechanical function: Single chemically-skinned skeletal muscle fibers will be prepared for sinusoidal analysis or specific force-velocity-power experiments. Fiber mechanics and steps in the cross-bridge cycle will be obtained using sinusoidal analysis, a technique first applied to human skeletal muscle by our laboratories. Fiber mechanics results include myofilament stiffness (A-elastic), the number of myosin heads strongly-bound to actin, the cross-bridge stiffness and myosin-actin cross-bridge kinetics. Cross-bridge kinetics measurements include the rate of myosin force production, or the rate of myosin transition between the weakly- and strongly-bound states, and the average myosin attachment time (t_{on}) to actin. Specific force and velocity will be measured using a force clamp technique. These measurements will be performed primarily on MHC I and IIA fibers, as these are the most abundant fiber types. Hybrid fibers (ie, MHC I/IIA) will be analyzed if enough are available.

Resistance exercise training. Our overall approach to RT and PT training is based on studies, as well as our preliminary work, that have demonstrated improvements in whole muscle and single fiber function are apparent within 16 wks or less. After recovery from the baseline biopsy (~1 wk), volunteers will begin a 16 wk, facility-based, resistance exercise training program (3 times/wk). Volunteers will have their dominant or non-dominant leg randomly assigned to RT with the contralateral leg assigned to PT (1:1 allocation). The training program will include: 1) leg press; 2) knee extension; and 3) knee flexion. Each exercise will be performed for RT for one leg and then for PT in the other leg before moving on to the next exercise. Prior to and at the end of each exercise session, volunteers will warm-up/cool-down on an exercise bike (~30-50 W) for 5 min. Based upon the National Strength and Conditioning Association guidelines and our resistance training of older adults, we expect the exercise session during to be less than one hour. Patients will be required to complete at least 90% or greater of the prescribed sets and 80% of the training sessions over the 16 wk period to be included in the analyses.

Low-velocity, high-load resistance training (RT): The intensity of the RT program will be 80% of one repetition maximum (1RM) for 3 sets of 8 repetitions, as recommended for maximum strength gains and as previously performed by our laboratories. Concentric and eccentric contraction phases for RT will last 2-3 sec. Exercise intensity for RT will progress over the first 3 weeks, as we have previously done. The first week will be 50% 1RM for 1 set of 10 repetitions, second week will be 60% 1RM for 2 sets of 8 repetitions and the third week will be 70% 1RM for 3 sets of eight repetitions. 1RM will be updated bi-weekly.

High-velocity, low-load power training (PT): The intensity of the PT program will be 40% 1RM for 3 sets of 16 repetitions. The PT program will be performed at 40% 1RM, instead of the 80% 1RM in the RT program, in order to increase the contractile speed during training and maximize the potential to improve whole muscle performance. The ability of 40% 1RM to better ameliorate age-related decreases in whole muscle performance is based upon the findings that power output at 40% 1RM is a stronger predictor of ability to perform activities of daily living in both men and women than 1RM or 70% 1RM and contractile speed accounts for more of the decrease in functional performance than force decrements in older adults, especially in women. As PT improves the magnitude of muscle power output in older adults similarly from 20% to 80% 1RM, the main difference between a 40% and 80% 1RM should be the increased training contractile velocity that will occur with a reduced load. Notably, repetitions will be doubled with PT to equate to the total work performed with RT such that the two training programs will be equivalent. Concentric contraction phases for PT will be as quick as possible (~1 sec) with eccentric contractions lasting 2-3 sec. Exercise intensity for PT will progress over the first 3 weeks by increasing set and repetitions as the load will be set at 40% 1RM. The first week will be 1 set of 12 repetitions, second week will be 2 sets of 12 repetitions, and the third week will be 3 sets of 14 repetitions. 1RM will be updated bi-weekly.

Post-exercise testing. Post-exercise testing will include the same assessments of body composition, physical activity, whole skeletal muscle function as well as cellular and molecular structure and function as the pre-exercise testing listed above. Assessments will be made >5 days from the last whole muscle training session to eliminate residual exercise effects on fiber structure and function.